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Learning and Memory: While You Rest, Your Brain Keeps Working

A recent study shows that brain activity recorded while the human subject is at ‘rest’ is significantly affected by a prior learning episode. These results suggest that understanding resting brain activity may be critical to understanding how humans learn from experience.

Justin L. Vincent^{1,2}

On average, the brain uses approximately a fifth of the energy consumed by the body, of which the vast majority is directly related to spontaneous neuronal signaling (for review see [1]). Most of this ongoing spontaneous brain activity is not random; it is correlated from the level of individual neurons [2] all the way up to widely distributed functional brain systems [3]. Functional magnetic resonance imaging (fMRI) studies in humans have shown that the blood-oxygen-level dependent (BOLD) signal — which is thought to reflect neural activity — is correlated within multiple distributed brain networks that closely correspond to the brain networks commonly activated during task performance. This correlated spontaneous brain activity is thought to reflect ‘functional connectivity’ within brain networks (for review see [4]). But despite the fact that most of the brain’s energy budget is devoted to maintaining highly organized patterns of coherent spontaneous activity, very little is known about the functional role of these spontaneous fluctuations. It has been previously

suggested that these spontaneous activity patterns may consolidate the past, stabilize brain ensembles, and prepare us for the future [5,6]. Until recently, however, there has been little evidence to support this view.

A study reported in this issue of *Current Biology* by Albert *et al.* [7] sheds new light on the role of spontaneous activity by demonstrating that a motor learning episode significantly modulated spontaneous BOLD fluctuations recorded during the *rest period* that followed the learning episode. The authors first recorded spontaneous signals in the brains of human participants while they rested, and found functional connectivity within two distinct brain networks that included regions in the cerebellum or in frontal and parietal cortex (Figure 1, left panel). These frontal, parietal, and cerebellar regions are typically engaged during motor learning (for example [8–10]). Then, the participants learned a complex task that involved hand–eye coordination and the learning of a novel motor skill (Figure 1, middle panel). Several minutes after the participants had learned the new task, the authors again recorded resting brain activity within the

cerebellar and frontal-parietal networks: they found that spontaneous BOLD fluctuations in these networks were more synchronized following learning (Figure 1, right panel). Further, these learning-related changes in brain functional connectivity were not limited to the time immediately following learning because the subjects performed a different, unrelated task between the learning episode and the final recorded rest period. Importantly, the authors showed that performance of a similar task that did not require learning a new skill did not result in any significant changes in the functional connectivity of the frontal-parietal network or cerebellar network. The implication is that motor learning, but not motor performance, increased the strength of subsequently recorded functional connectivity. These results suggest that newly formed memories leave a ‘trace’ that can be measured by examining spontaneous activity recorded during rest periods.

Learning to perform a complex motor task, such as playing a guitar, may be difficult initially. Once learned, however, the ability to perform that task becomes more automatic and can remain within one’s memory for years. This process of stabilizing a long-term memory is referred to as consolidation. It has long been thought that sleep plays a critical role in consolidation by reinforcing significant synaptic connections and eliminating accidental connections. The principle findings that linked sleep with learning were the correlation between the amount of time spent in rapid-eye-movement sleep

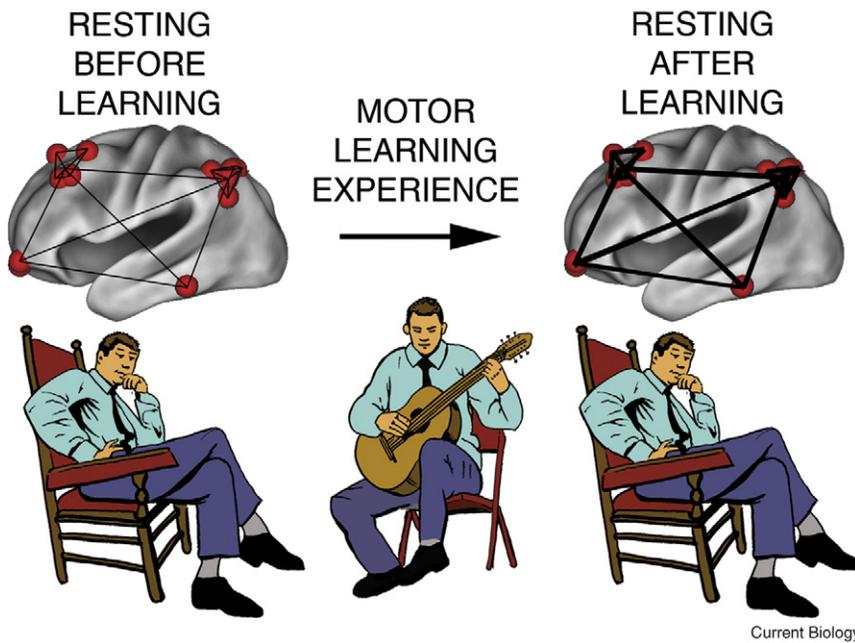


Figure 1. A learning episode enhances the synchrony within large-scale functional brain networks.

During rest periods preceding the learning episode (left), functional activity is correlated between functionally related brain regions. During rest periods following a learning episode (right), functional activity within the large-scale functional brain network is more tightly synchronized. The red spheres projected onto the surface of the inflated left cerebral hemisphere correspond to peak regions within the fronto-parietal network identified by Albert *et al.* [7]. The black lines represent functional connectivity between regions. The increased thickness of the lines after learning represents an increase in synchrony between the regions. Illustrations by John W. Campbell.

and the subsequent performance on the recently learned behavioral task (for review see [11]). Even if processes occurring during sleep are required for consolidation, however, it remains unclear how recently acquired memories are maintained throughout the wake cycle before participants have the opportunity to sleep. The data reported by Albert *et al.* [7] suggest that associations made during learning episodes may leave behind a ‘memory trace’ that is measurable as a functional connectivity change during rest periods following the learning episode. These learning-related functional connectivity changes suggest that some form of consolidation may take place during the resting periods that follow learning.

Two recent studies [12,13] provide clues about how resting state activity may relate to learning episodes. In these studies, rats were trained to run back and forth within a simple maze. As the rats traversed the maze, neurons that are sensitive to the rats’ spatial location fired sequentially in a manner that corresponded to their

current location within the maze. Interestingly, when the rats stopped running, these same cells spontaneously fired with the same sequential patterns observed when the rats were actively moving throughout the maze, but much faster and in reverse order. In other words, the neurons were ‘replaying’ the maze learning experience in reverse order while the rats rested. Interestingly, similar ‘replay’ events have been documented during sleep [14,15]. While it is difficult to extrapolate these results to the findings of Albert *et al.* [7], the similarities are intriguing.

As mentioned above, spontaneous activity recorded while subjects rest constitutes a significant proportion of the brain’s energy budget. But the amount of energy devoted to spontaneous activity may not be constant throughout the day. Braun *et al.* [16] recorded cerebral blood flow (CBF), which is linked to brain energy consumption, in subjects as they quietly rested before and after sleep. They found that sleep resulted in a decrease of waking CBF by about

20% (Figure 2). One possibility is that the learning episodes that occur throughout the day significantly modify patterns of spontaneous activity [7,12,13,17] and result in an increase in the brain’s metabolic load [16]. Consolidation processes that occur during sleep may reduce this metabolic load by storing newly acquired information in a more stable and energy efficient manner.

The results of Albert *et al.* [7] raise several other fascinating issues for future research. Are increases in functional connectivity following learning related to individual differences in subsequent performance on the newly learned behavioral task? How long do these functional connectivity changes persist (minutes or hours) and do they persist during performance of unrelated tasks (for

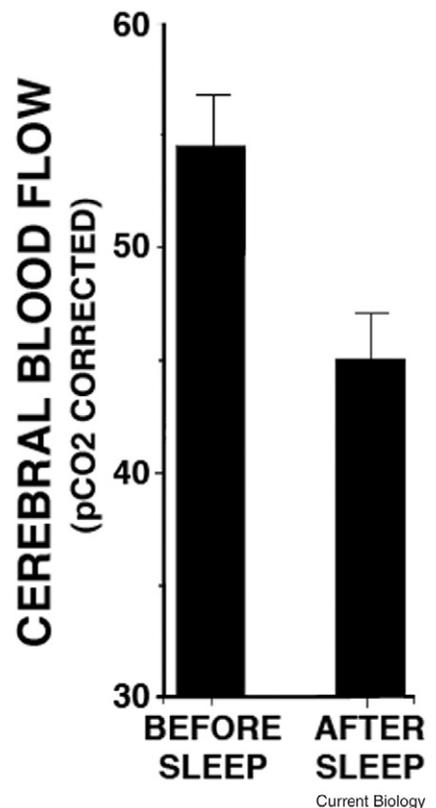


Figure 2. The effect of sleep on resting brain metabolism during quiet wakefulness.

Bar graphs represent global cerebral blood flow (CBF) during resting wakefulness preceding and following a period of sleep. Global CBF is approximately 20% lower during rest periods that followed sleep vs. rest periods that preceded sleep. Data represent absolute end-tidal CO₂ (pCO₂)-corrected CBF rates (ml/100 g/min, mean ± SEM). Bar graphs adapted from [16].

example [17,18]? What information is being represented in the strengthened functional connectivity patterns that follow learning episodes? Does the enhanced functional connectivity represent off-line 'replaying' of the learning experience as shown in the rat studies [12,13]? Does off-line processing of recently acquired memories represent an early process of consolidation (see also [19])? How do learning related resting state functional connectivity changes relate to activity patterns recorded during subsequent periods of sleep (for example [20])? The authors' approach may prove promising in revealing novel connections between off-line processing of recently acquired memories and subsequent resting state activity.

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Cognitive Ecology: Environmental Dependence of the Fitness Costs of Learning

A recent study has found that butterflies maintain behavioural plasticity useful to them in rare environments by reducing associated costs in common environments. Butterflies use innate sensory biases to locate common green hosts, but learn to modify these preferences to find rare, red host-plants.

Nigel E. Raine

Learning allows animals to modify their behaviour in response to changes in their environment. If the environment remains relatively constant, however, it could be adaptive to rely on inflexible innate behavioural patterns to reduce (or eliminate) costs associated with learning [1]. Yet species living in relatively consistent environments can often adjust their phenotype successfully in alternative environments, suggesting that the costs of maintaining phenotypic

plasticity could be low [2,3]. In a recent study Snell-Rood and Papaj [4] experimentally tested these theoretical predictions for the maintenance of phenotypic plasticity under consistent environmental conditions.

In theory, phenotypic plasticity should be adaptive if an organism regularly encounters at least two different environmental conditions with similar frequencies. As the chances of an organism encountering an alternative environment decrease, so too do the benefits of retaining plasticity. But plasticity could be

maintained if the operating costs in the common environment are reduced, such that costs are only paid when the organism encounters alternative (rare) conditions. Operating costs in the common environment could be reduced by using a fixed, innate, behavioural pattern adapted to these specific conditions. If the organism encounters the rare environment, the default, innate, behavioural phenotype can be modified by learning. Hence, the organism only pays the operating costs of plasticity when (or if) it encounters the rare environment (Figure 1).

Snell-Rood and Papaj [4] addressed these predictions empirically using the flexibility in host-plant choice of cabbage white butterflies (*Pieris rapae*) as their behavioural phenotype. They assessed the costs of maintaining phenotypic plasticity in this behavioural trait by controlled manipulation of the environment in