How the brain consolidates memory during deep sleep

We spend a third of our lives sleeping. During sleep, our brains are decoupled from sensory input. Nevertheless, brain activity remains high and varies by sleep stages. Sleep is broadly classified into non-rapid eye movement (NREM) sleep (consists of stage 1, 2 and 3), and rapid eye movement (REM) sleep. Our study mainly focused on NREM stage 3 sleep, also referred as “deep sleep” or “slow-wave sleep (SWS)”. Many studies suggested that deep sleep is crucial for learning and formation of new memories. Current experiments suggest that memories are consolidated by the interaction between high-frequency oscillatory events (known as sharp-wave ripple, SPW-R) of the hippocampus and low-frequency oscillations (known as slow oscillations) of the neocortex. But exactly how the memory is consolidated in cortex during sleep is not well understood and remains a central question of sleep research.

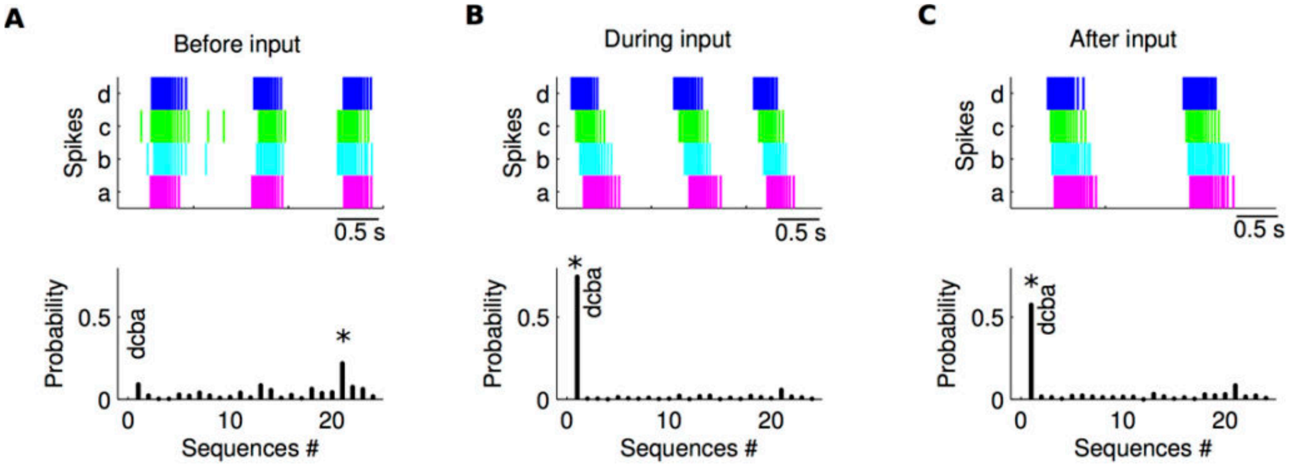

Fig. 1. The firing order of four selected neurons before (A), during (B) and after (C) hippocampal input reaches cortex during deep sleep. Representative examples of four neurons (neuron #: a= 20, b=35, c=50, d=65) spike activity (top), and probability of each sequence (bottom) before (A), during (B), and after (C) hippocampal input during deep sleep.

Using a biologically realistic computational models, we explained how the hippocampal SPW-R input influences slow oscillations in the cortex and how the pattern of slow oscillations affect synaptic connections between neurons during deep sleep. The model included thalamus and cortex that can spontaneously generate sleep slow oscillations like activity, manifested by periodic alternating activity of the cortical neurons between silent (Down) and active (Up) states. The model implemented spike time dependent synaptic plasticity (STDP) between excitatory neurons that adjusted the synaptic connections based on the relative timing of the presynaptic and postsynaptic spikes. The change in synaptic strength between neurons -- synaptic plasticity-- is widely thought to underlie learning and memory storage in the brain.

Before memory was imprinted to the cortex, a set of four randomly selected cortical neurons (a, b, c, d; see Figure 1) could fire in any order during the Up states of slow oscillation (Fig. 1A, top); probability of Up state initiation was equal across all cortical sites (Fig. 1A, bottom). We next mimicked hippocampal SPW-R input to the cortex as an external stimulation applied to a small selected group of pyramidal cells in the cortex. In the presence of stimulation, most of the Up states were initiated at specific location defined by the stimulation site and the same four cortical neurons fired is particular order (d->c->b->a) most of the time (Fig. 1B, top). The probability of the sequence “dcba” became high (Fig. 1B, bottom). As a result of repetitive firing, the synaptic connections between cortical neurons in the direction of “dcba” became strengthened by synaptic plasticity. The probability of cortical cell firing in sequence “dcba” remained high even after hippocampal input was removed, (Fig. 1C).

Our study showed that the input from the hippocampus to the cortex during deep sleep could influence the firing order of neurons, leading to persistent change of synaptic connections between neurons. These synaptic changes promoted replay of specific firing sequences of the cortical neurons -- representing a replay of specific memory. Our study provides for the first time a mechanistic explanation for how deep sleep may be promoting the consolidation of recent declarative memories that initially depends on the hippocampus. These predictions can be tested experimentally, including specific interventions to suppress or augment memory consolidation processes.

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