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Memory: Reconsolidation Allows Modification of Motor Memories

A recent study using non-invasive transcranial magnetic stimulation has revealed how specific brain processing during memory reactivation makes possible the modification of existing memories that is required for motor learning.

Niels Birbaumer

Memory research represents one of the most challenging and exciting areas of basic and systems neuroscience. Our brain constantly encodes the features of the surrounding environment, a critical function for our everyday survival as well as for learning leading to successful interactions with the external world. Such interactions require constant updates and 'tune ups' of the brain's internal representations or memories.

In everyday life, memories can be automatically modified in healthy human beings. For example, we barely notice very slow changes in friends or family members whom we see everyday (as opposed to changes in people whom we haven't seen for longer periods of time). Our brain updates the internal representation of these memories probably every time we see that person again. Thus, changes are often unnoticeable to us.

When learning to perform a motor task in everyday life, the need to repeatedly update the memory trace becomes even more critical because most skills are acquired over time. Surprisingly, the mechanisms and the cerebral regions that mediate the human brain's ability to modify existing memories have still not been clearly identified. Animal researchers have used invasive approaches to inhibit specific brain areas, revealing the mechanisms underlying modification of existing memories following their reactivation during recall [1–4]. Such approaches are not possible in human research. In this issue of *Current Biology*, Censor *et al.* [5] report how they used non-invasive brain stimulation — specifically, repetitive transcranial magnetic stimulation (rTMS) — to virtually 'knock out' focal human brain areas during the susceptible time frame of memory reactivation, thereby unveiling human brain processes that allow modification of reactivated existing memories.

Transcranial magnetic stimulation operates by inducing a magnetic field, which results in flow of currents parallel to the stimulating coil and neural activation in the targeted brain area [6,7]. Generally, low-frequency rTMS (usually 1 Hz) induces inhibitory effects allowing a reversible 'virtual lesion' in focal brain areas [8]. This approach, somewhat resembling the 'gene knockout' technique of genetic research (though the direct effects induced by rTMS are temporal and reversible), makes it possible to study the functional role of the targeted brain area in spatial and temporal domains of learning and memory processes.

In this new study [5], subjects performed a sequential finger tapping motor memory task on three separate days. When receiving no stimulation, subjects improved from day 1 to day 2, and continued to improve when tested on day 3 [5,9]. Here, subjects showed off-line performance gains from day 1 to day 2, pointing to efficient consolidation of the motor memory as reported in previous studies [9,10]. Following testing on day 2, subjects received 15 minutes of 1 Hz rTMS to primary motor cortex (M1), while performing additional trials of the task during the stimulation period in order to reactivate the memory trace as required for reconsolidation [1–4]. This disruption of M1 activity during memory reactivation blocked further memory modification, with subjects showing no significant memory gains on day 3.

Censor *et al.* [5] used conventional physiological measurements in order to disturb M1 function in its appropriate location and intensity of stimulation and, furthermore, used a stereotactic brain navigation system and each subject's magnetic resonance image (MRI) to localize the stimulating coil online. In order to further control for the anatomical specificity of the rTMS effects, the authors conducted a similar experiment in which rTMS was applied to a control vertex position with the same stimulation parameters, with results showing that stimulation of a brain region different from M1 did not block memory modification. In an additional experiment, they showed that disruption of manual execution of the motor actions *per se* with peripheral nerve stimulation at the wrist also does not block memory modification. These experiments show that specific disruption of M1 processing during memory reactivation blocks memory modification.

Censor *et al.* [5] conclude by suggesting a model for human memory modification, susceptible to future further testing (Figure 1). The significance of this model lies in the fact that it differentiates between what the authors refer to as 'memory storage domains', allowing novel characterization of the actual human brain areas involved in modification of existing memories. According to the model, when the memory is

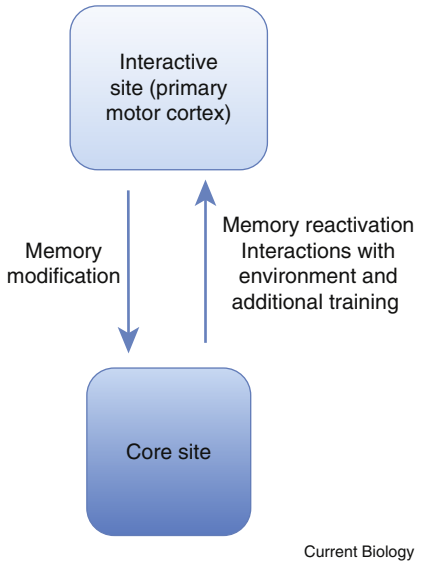

Figure 1. A model of human motor memory modification as proposed by Censor *et al.* [5].

reactivated, recurrent output from the core storage domain (stores the most updated representation of the memory) to the executing storage domain (which interacts with the environment) enables memory modification. Based on their results, the authors suggest that primary cortical brain areas such as M1 constitute the executing storage domain, whereas work is under way to identify in detail brain regions in the core storage domain. Secondary sensory and motor areas may constitute prime candidates for core storage of motor memory.

Different primary cortical areas in different sensory modalities were shown to have similar roles in memory processes such as memory consolidation. For example, both primary visual cortex (V1) and primary motor cortex (M1) were shown to play a crucial role in consolidation of visual and motor memories, respectively [11–14]. Therefore, it is possible that the model proposed by Censor *et al.* [5] may apply to reconsolidation in other sensory modalities as well. This intriguing proposal may suggest that primary cortical areas serve as executing storage domains for parallel additional sensory modalities, while core storage domains may receive integrated outputs from several executing storage domains. However, such accounts are somewhat speculative at this stage and should be further addressed experimentally.

In conclusion, the insights provided by this new study [5] into how the brain modifies existing motor memories could have an influential impact on memory research. Furthermore, such knowledge may be highly valuable for clinical purposes, helping improve memory processes and impaired skill performance by providing possible targets for interventions involving brain stimulation.

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Phenotypic Plasticity: Different Teeth for Different Feasts

A polyphenism in the nematode *Pristionchus pacificus* involves the development of different feeding structures in response to an environmental cue, providing a genetic model species for investigating ecologically relevant phenotypic plasticity.

Karin Kiontke and David H.A. Fitch

The genome is often compared to a blueprint, the ultimate plan for building the organism. Development is then the builder. Accordingly, a major goal of developmental genetics has been to determine the genetic architecture underlying a phenotype. This approach requires a careful study of model organisms under uniform laboratory conditions, avoiding the complications of environmental perturbation. In nature, however, organisms display 'phenotypic plasticity'; that is, a single genotype produces different phenotypes in response to different environmental conditions. Indeed, phenotypic plasticity has recently materialized as a key factor uniting evolutionary biology with the emergent field of ecological developmental biology, or 'eco-devo' [1–5]. In most cases, the spectrum of possible phenotypes expressed across a range of environmental conditions (the 'reaction norm') is continuous; however,