Motor engram as dynamic change of the cortical network during early sequence learning: an fMRI study

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Introduction

Practice is responsible for obtaining a motor skill which is characterized by speed and accuracy. The practice effect may differ depending on whether stressing on the speed or accuracy. Speed pressure is known to enhance the learning process. Motor learning is to establish an internal model which represents the exact matching between perceived sensory and motor information. Information is transmitted during learning by comparing the expected sensation by the internal model with the actual feedback sensation arising from the movement. So as to generate the information for the learning to occur, task difficulty should be kept challenging. Speed can adjust a specific difficulty level of the sequential finger tapping task. They usually requested the participants to practice the given sequence "as fast and as accurately as possible." However, even without speed pressure, sequence learning occurs by serial reaction time tasks which stress on accuracy. Little is known how these characteristics of the practice, the speed and accuracy, are integrated to form the neural substrates of the sequence learning, that is, engram.

An engram has four characteristics: persistence, ecphory, content, and dormancy. An engram is a persistent change in the brain by a specific experience or encoding. An engram is activated through interaction with retrieval cues, which activation is termed ecphory. The content of an engram reflects what transpired at encoding thus predicts what can be recovered during subsequent retrieval. An engram exists in a dormant state between the two active processes of encoding and retrieval. During dormant state, the strength of the synaptic connection is stabilized. At retrieval, the connections are destabilized so that the synaptic connections are modified. Thus the series of the active states of encoding and retrieval intervened by dormant state comprises the learning process, resulting in the serial change in the spatiotemporal pattern of the neural ensemble.

Previous neuroimaging approaches to find out the motor engram have mainly focused on the ecphory because they utilized task-related activation to evaluate the effect of learning. Regarding the dormant engram, recent resting-state fMRI studies before and after the visuomotor learning taskhave found learning-related change in frontoparietal and cerebellar networks. However, it is unknown how these two states of engram are dynamically represented in the neural network level.

To address this issue, I conducted functional MRI with sequential finger tapping execution epoch alternated with rest epoch. I hypothesized that the two learning modes, stressing on speed or accuracy, generate distinct engrams which in turn are integrated at the execution. I focused on the early phase of training of 30 min. Participants exercised a sequence as fast and as accurate as possible (maximum mode) or with constant speed by visual cues explicitly indicating the sequence (2 Hz, constant mode). Participants alternated constant mode with the maximum mode. I applied eigenvector centrality mapping (ECM) to the innovation. Eigenvector Centrality (EC) is a class of graph theory-based measures assessing the centrality or importance. Innovation is the residual time-courses of the neural activities obtained by modeling out the task-related effects and other confounding effects. The innovation of BOLD signals is thought to include task-non-specific neural fluctuations, corresponding to spontaneous brain activity. Regarding the innovation, I made a distinction between the task epoch in which encoding/retrieval occurred and the rest epoch which was in a dormant state. I expected that the M1 centered cortical network would represent the motor engram.

Methods

To discriminate the engrams formed by an emphasis on speed or accuracy targets, I conducted functional MRI with 58 normal volunteers (34 males and 24 females; mean age = 21.69 ± 3.88 years). We used a 3T whole-body scanner for this experiment. All participants performed a sequential finger tapping task with the non-dominant left hand inside of the scanner. Participants practiced a tapping sequence alternately as quickly as possible (maximum mode) and at a constant speed of 2 Hz, paced by a visual cue which specified the sequence (constant mode). There were three fMRI runs. The first and third run consisted of a block of constant-speed mode (C block) followed by a block of maximum mode (M block), however, third run started with C block finishing with M block. C block, 2.5 min in duration, started with a Rest epoch of 15 sec duration followed by a Constant mode epoch of 15 sec, alternatively repeated five times. The Rest epoch started with the appearance of the instruction “Rest” on the screen for 500 ms, followed by 500 ms of presentation of four blue circles aligned within an equally spaced horizontal array, corresponding to the left-hand fingers (from left to right, small, ring, middle, and index fingers). The instruction was to follow the blue circles (randomly moving at 2 Hz) with the eyes, without pressing the button. The Rest epoch lasted for 15 sec, at which time the target “CONSTANT” appeared to instruct the participant to respond by pressing the button indicated by the white circle. The visual cues were identical to those of the Rest epoch except for the color and sequence of lighting. One of the circles was filled in every 500 ms, indicating the tapping fingers and buttons on an MR-compatible button box. A sequence was composed of five-element sequences, either "index – little – middle – ring – index" (presented to 31 participants) or "ring – middle – little – ring – index" (presented to the other 27 participants). The frequency of the color and location change was kept at 2 Hz. The Constant epoch lasted 15 sec when alternated with Rest epoch. Rest and Constant epochs were conducted alternatively five times, constituting C block 1. M block 1, 3 min in duration, started with a Rest epoch that was identical to the C block except that its duration was 30 sec instead of 15 sec. The instruction "TEST" appeared for 500 ms to ask the participant to tap the memorized sequence as rapidly and accurately as possible, and then four closed white circles were presented for 500 ms, after which they changed to open circles. Visual feedback of correct tapping was provided by filling of the white circle corresponding to the tapped finger. If the participant made an incorrect response, the stimulus remained at the previous visual cue until the correct button was pressed. The Maximum epoch lasted 30 sec. Rest and Maximum epochs were conducted alternatively three times. The second run (Run 2) consisted of three C blocks separated by two M blocks. In total, the sequential finger tapping task for this study was composed with five C blcoks and Four M block.

To quantify brain changes at the network level that characterize the engram, even when dormant, I applied the EC to the residual time-series after modeling out the task-related activity, because the residual BOLD (Blood-Oxygen-Level-Dependent) signals were thought to include task-non-specific neural fluctuations, corresponding to spontaneous brain activity.

Result

In regard to task-related change, ECM provides patterns similar to SPM with a general linear model of task-related activation during both maximum and constant modes. During maximum mode, EC during rest significantly increased in the left anterior interior parietal sulcus (aIPS) as learning proceeded, and EC was enhanced by task execution. Seed-based analysis across the whole brain revealed that the functional connectivity with aIPS was enhanced only in the left IPL as learning proceeded. As sequential motor learning proceeded, the centrality during the rest state in constant mode significantly increased in bilateral dorsal premotor cortex and the right primary motor cortex (M1), and EC was enhanced by task execution.

Disucussion and conclusion

Learning-related enhancement of EC in the left aIPS during rest condition of the maximum mode probably represented the accumulation of information provided by the comparison between the action plan of the rapid transition of the one finger to the next in the sequence and the actual feedback. Thus, the left aIPS-IPL represented the sensorimotor integration of precisely tuned rapid finger movements the one finger to the next in the sequence.

The PMd is a probable substrate for the coordinate transformation from the visually presented spatial goals to joint movements in the response domain through associative learning, coding the accuracy with the M1. Therefore, within an M1-centered parietal-premotor network motor engram, the left aIPS-IPL appears to represent the sensorimotor integration of precisely timed rapid finger movements, and the PMd and M1 the accuracy of their assignment. In conclusion, present findings constitute the first demonstration of motor engrams formed by only 30 min of training.