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fMRI investigation of cortical and subcortical networks in the learning of abstract and effector-specific representations of motor sequences

Raju S. Bapi,[a,*] K.P. Miyapuram,[a] F.X. Graydon,[b] and K. Doya[c,d]

[a] Department of Computer and Information Sciences, University of Hyderabad, Gachibowli, Hyderabad 500 046, India
[b] Brain Imaging Research Division, Dept of Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine, Detroit, MI 48201, USA
[c] Department of Computational Neurobiology, Computational Neuroscience Laboratories, Advanced Telecommunications Research International, Kyoto, Japan
[d] Initial Research Project, Okinawa Institute of Science and Technology, Okinawa, Japan

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A visuo-motor sequence can be learned as a series of visuo-spatial cues or as a sequence of effector movements. Earlier imaging studies have revealed that a network of brain areas is activated in the course of motor sequence learning. However, these studies do not address the question of the type of representation being established at various stages of visuo-motor sequence learning. In an earlier behavioral study, we demonstrated that acquisition of visuo-spatial sequence representation enables rapid learning in the early stage and progressive establishment of somato-motor representation helps speedier execution by the late stage. We conducted functional magnetic resonance imaging (fMRI) experiments wherein subjects learned and practiced the same sequence alternately in normal and rotated settings. In one rotated setting (visual), subjects learned a new motor sequence in response to an identical sequence of visual cues as in normal. In another rotated setting (motor), the display sequence was altered as compared to normal, but the same sequence of effector movements was used to perform the sequence. Comparison of different rotated settings revealed analogous transitions both in the cortical and subcortical sites during visuo-motor sequence learning—a transition of activity from parietal to parietal–premotor and then to premotor cortex and a concomitant shift was observed from anterior putamen to a combined activity in both anterior and posterior putamen and finally to posterior putamen. These results suggest a putative role for engagement of different cortical and subcortical networks at various stages of learning in supporting distinct sequence representations.

Keywords: Sequence representation; Anterior striatum; Posterior striatum; DLPFC; Pre-SMA; SMA

Introduction

It is commonly observed that when a skill is being acquired subjects are circumspect and deliberate in the initial attentive phase but later on as the skill is acquired they move into an automatic phase when attention can be engaged in other tasks simultaneously (Fitts, 1964). When performing well-mastered skills, it appears as if the body parts know what to do and no overt attention is necessary. Furthermore, the memory of over-learned skills seems robust and lasts for a long time. In this scenario, it is interesting to find out if the representation of skill memory and the associated neural bases are different at various stages of learning. Previous studies on sequence learning addressed where and when activity is found in various cortical and subcortical areas using implicit learning (Grafton et al., 1995) and explicit learning by trial and error (Sakai et al., 1998; Toni et al., 1998). This paper addresses the question of what is actually learned in different areas at different stages of explicit sequence learning.

Earlier studies that investigated representational changes during motor sequence learning emphasized either implicit sequence learning in the serial reaction time (SRT) paradigm (Grafton et al., 1998), explicit sequencing but without learning (Harrington et al., 2000), or the recall of motor sequences at various stages of learning (Karni et al., 1995; Penhune and Doyon, 2002). Grafton et al. (1998) found learning-related increases in regional cerebral blood flow (rCBF) in the sensorimotor cortex reflecting effector-specific representation and in the inferior parietal cortex reflecting abstract representation of motor sequences. Sakai et al. (1998) and Toni et al. (1998) used trial and error learning paradigm to study the time course of changes during explicit visuo-motor sequence learning.

Hikosaka et al. (2002) proposed that a sequence of movements is represented in two ways—spatial sequence and motor sequence. In their hypothetical scheme, spatial sequence learning and representation are supported by parietal–prefrontal cortical loops with the

* Corresponding author. Fax: +91 40 23010780.
E-mail addresses: bapics@uohyd.ernet.in, bapiks@yahoo.co.in (R.S. Bapi).
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associative region of the basal ganglia (anterior striatum) and cerebellum (posterior cerebellum). Motor sequence learning and representation are mediated by the motor cortical loops with the motor region of the basal ganglia (posterior striatum) and cerebellum (anterior cerebellum). Furthermore, in their scheme, premotor area mediates the transformation of spatial to motor coordinates and presupplementary motor area (pre-SMA) participates in coordination or switching between the two representations. In this connection, it is interesting to note that this scheme is partly based on an earlier proposal of Alexander et al. (1986) of distinct cortico-basal ganglia-thalamus loops serving different functions. In this scheme that stresses parallel information processing, the dorsolateral prefrontal cortex (DLPFC)–caudate nucleus loop takes part in spatial sequencing whereas the supplementary motor area (SMA)–putamen loop mediates motor sequencing.

Our hypothesis was that motor sequence learning involves two representations—an early acquisition of effector-independent (abstract) representation and a late consolidation of effector-dependent representation (Hikosaka et al., 1999, 2002; Bapi et al., 2000; Nakahara et al., 2001). In an earlier behavioral study (Bapi et al., 2000), we used a sequential button-pressing task in which subjects performed either the same visuo-spatial sequence with altered finger movements or a different visuo-spatial sequence with the same finger movements. We found that the response time was significantly shorter when the finger movements remained the same compared to when the visuo-spatial sequence was the same. These results suggest that an effector-independent representation develops early in the learning process and subsequently an effector-dependent sequence representation is formed.

Using a whole-brain fMRI study, we set out to investigate the question of the brain areas subserving such representations acquired at various stages of explicit learning of motor sequences. In the current study, subjects learned a sequence of 12 finger movements, using a 2 × 6 task (Fig. 1a) modified from Hikosaka et al. (1995), in two settings—normal setting where the visual display and keypad are arranged in the usual position and a rotated setting. In the rotated (motor and visual) conditions, subjects were required to rotate the visual cues by 180° and press the

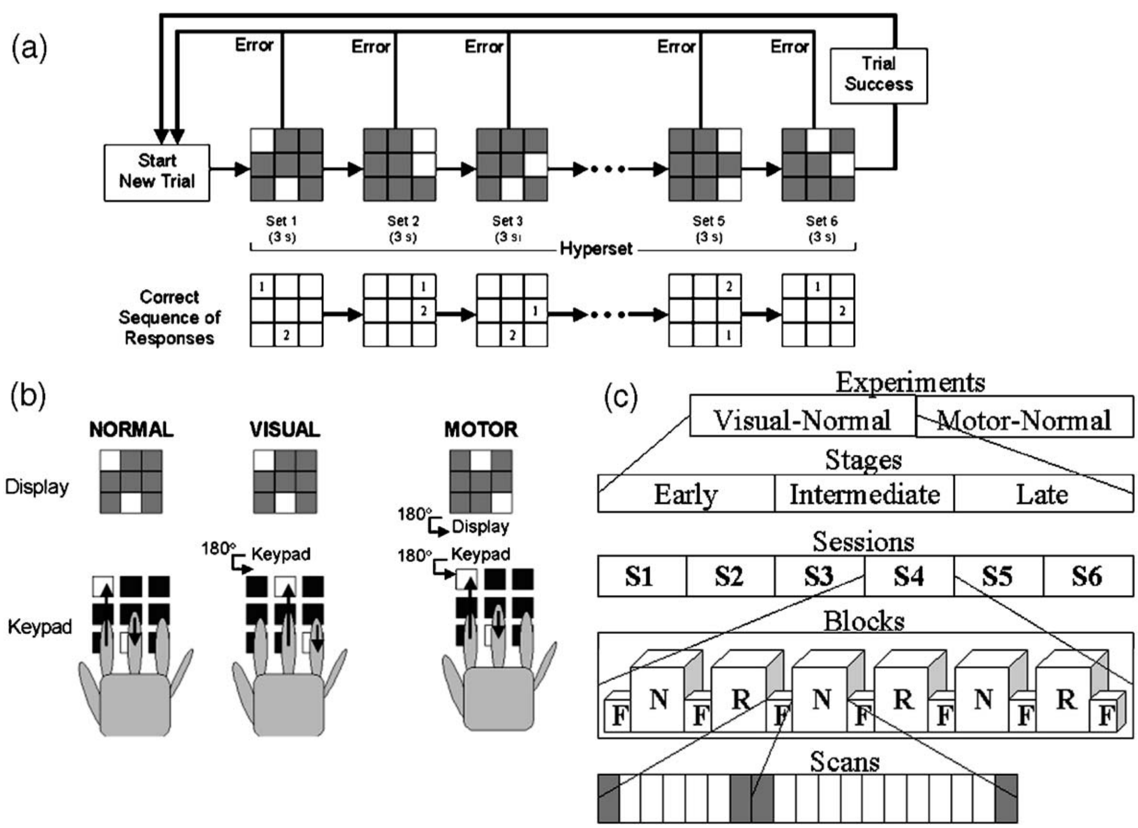

Fig. 1. Sequence task setup. (a) In 2 × 6 sequence task, a sequence of 12 key presses is learned by trial and error, two at a time (called a 'set') in a series of six sets (called a 'hyperset'). The two key presses belonging to a set need to be executed within 3 s and after an appropriate delay the subsequent set is displayed. A new trial is started by resetting the presentation of the hyperset to the beginning either upon an error in any set or on successful completion of the entire hyperset. The bottom panel indicates the correct order of key presses for the example shown in the top panel. (b) Normal and Rotated settings for set 1 of the example are shown. In the normal setting, the visual display and keypad are arranged in the usual upright position and in the rotated settings the display-to-keypad relationship was altered. In the visual setting, the keypad was rotated by 180°, while the display remained unaltered. In the motor setting, both the keypad and the display on the screen were rotated by 180°. Consequently, in the visual setting, the sequence of visuo-spatial cues (visuo-spatial sequence) remained identical, while in the motor setting, the sequence of finger movements (somato-motor sequence) remained the same as that of the normal setting. Finger movements to be executed for an example are indicated by arrows in all the settings in the lower panel. Six such sets constituted a hyperset as shown in panel a. (c) Subjects performed two experiments—visual-normal and motor-normal. Each experiment consisted of six sessions of which the first two and the last two represented 'early' and 'late' stages of learning, respectively. We utilized an on–off (box-car) design for the experiments. In every session, subjects alternated between sequence learning tasks in the test blocks (N: normal and R: rotated) and followed random visual cues in the control blocks (F: follow). The duration of the test block was 36 s and that of control block was 21 s. 12 and 7 scans were acquired during the test and control blocks, respectively. Scans identified in gray shade represent instruction scans at the beginning and end of a block.