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# Activation of the precuneus is related to reduced reaction time in serial reaction time tasks

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**Abstract**

Multiple brain areas are activated during serial reaction time (RT) tasks (SRTTs), but the part of the brain that facilitates reductions in RT remains unclear. The present study attempted to determine the brain region contributing most to improved RTs during explicit SRTTs. Subjects comprised 18 healthy volunteers who were instructed to press one of four buttons corresponding to visual stimuli as quickly as possible and with minimal errors during functional MRI. Stimuli were presented either in random order (control condition) or in a repeated six-item sequence (learning condition). Conventional analysis contrasting learning and control conditions revealed activation in the prefrontal–parietal area, which shifted to motor area. Subjects with high RT reduction showed more prominent activation in the precuneus than subjects with low RT reduction. Intra-subject correlation analysis revealed that time course of precuneus activation was unrelated to time-course of RT reduction. However, inter-subject correlation analysis revealed that RT changes correlate only with precuneus activation, meaning that subjects showing more prominent RT reduction revealed more prominent activation of the precuneus, which is known to play critical roles in controlling finger movements with reference to buffered memory.


*Keywords:* Motor sequence learning; Serial reaction time task; Functional MRI; Reaction time; Precuneus; Memory retrieval

## 1. Introduction

Reaction time (RT) is measured in various motor and cognitive tasks to evaluate subject performance, and is affected by factors such as attention and complexity of stimuli (Naito et al., 2000). Serial RT tasks (SRTT; Nissen and Bullemer, 1987) and variations thereof require the subject to react to items presented in a repeating sequence, and these tasks have seen extensive use in research investigating neural mechanisms for motor sequence learning. In explicit SRTTs, subjects are aware of repeating sequences during the task. Since the subject intentionally seeks to memorize the sequence and anticipate the next item in the explicit SRTT to react faster (Eliassen et al., 2001), learning function has been measured by reductions in RT. However, explicit motor sequence learning involves multiple steps, including acquisition, retention, retrieval, imagery and execution of the sequence and RT can be reduced by improvements in any of these steps, each of which may occur in different brain areas. Previous functional imaging studies using positron emission tomography (PET; Rauch et al., 1995; Hazeltine et al., 1997; Kawashima et al., 1998; Honda et al., 1998; Grafton et al., 1998) or functional magnetic resonance imaging (fMRI; Toni et al., 1998; Eliassen et al., 2001; Doyon et al., 2002; Muller et al., 2002; Schendan et al., 2003; Aizenstein et al., 2004) have revealed that several brain regions, including the pre-supplementary

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motor area (pre-SMA), premotor cortex, prefrontal cortex, superior and inferior parietal lobules and cerebellum exhibit activation during explicit SRTTs in normal subjects. These areas are also activated during various tasks for explicit motor sequence learning (for review, Hikosaka et al., 2002), and are thus regarded as common structures required for motor sequence learning. However, which of these regions contributes most to improvements in RT remains unclear.

Conventional designs used for fMRI studies that contrast task and control conditions do not necessarily isolate brain activity specifically related to task performance, and the regions associated with task performance are not always consistent with the most activated regions in these designs (Sidtis et al., 2003). We therefore sought to identify the area contributing most to reduced RT during an SRTT.

## 2. Materials and methods

### 2.1. Subjects

Subjects comprised 18 healthy, right-handed volunteers (11 women, 7 men; 21–39 years old). Handedness was assessed using the Edinburgh handedness inventory (Oldfield, 1971). Potential subjects with signs or history of medical or neurological disease were excluded by two neurologists. All subjects displayed normal results on brain MRI. Subjects were subdivided after the task according to degree of RT improvement during the task, into high performance (HP) and low performance (LP) groups. The criterion for determining performance status is mentioned in Section 2.4.1. Study protocols were approved by the institutional review board. All subjects provided informed consent conforming to the procedures set forth by the board.

### 2.2. Task procedures

The task used was a modified version of the SRTT described by Doyon et al. (2002) (Fig. 1), and comprised alternating 30 s control and learning blocks (10 each). Total task duration was 10 min, so improvements in RT during this period were predominantly assumed involve sequence-selective learning (Hikosaka et al., 1995). A video display in front of the subject showed four horizontally arranged squares, with a cross (target) appearing above one square. The target appeared for 800 ms, then shifted to the next position after a 200 ms interval. The right hand of the subject was fixed to a response collection device with four buttons corresponding to the four squares on the display. These buttons were positioned under the index, middle, ring and little fingers. Subjects were instructed to press the button corresponding to the target location as quickly as possible after target appearance, while attempting to minimize errors. The target was presented either in random order (control blocks) or in a repeated six-item sequence (learning blocks). Before fMRI, subjects were informed of the existence of a repeating six-item sequence in learning blocks (i.e., explicit motor sequence learning task), but the order was not revealed. Subjects were asked to report the sequence after the scan. Presentation of stimuli, sequence generation and response collection were controlled using an integrated functional imaging system (Psychology Software Tools, Pittsburgh, KS), which uses a liquid crystal display unit and a fiberoptic response collection device.

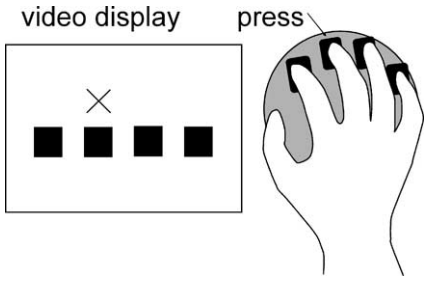


Fig. 1. Stimulus presented on the video display and the response collection device. The subject was instructed to press one of the four buttons corresponding to the stimulus (a cross). In the learning condition, stimuli were presented in a fixed six-item order. In the control condition, stimuli were presented in random order.

### 2.3. Image acquisition

All measurements were performed on a 3-T MR scanner (Signa VH/i 3.0T; General Electric Medical Systems, Milwaukee, WI). A forehead-holder and foam padding were used to minimize head motion during data acquisition. Functional images of the entire brain were obtained using a single-shot, gradient-echo echoplanar pulse sequence with the following parameters: repetition time (TR), 3000 ms; echo time (TE), 30 ms; flip angle (FA), 90°; axial slices; slice thickness, 3 mm; slice gap, 1 mm; number of slices, 30 slices; imaging matrix, 64 × 64; and field of view (FOV), 22 cm × 22 cm. The first four dummy scans of each session were discarded due to magnetic field instability. Before the acquisition of functional data, high-resolution, three-dimensional, anatomical T1-weighted axial images of the entire brain were obtained using a fast spoiled gradient echo sequence: inversion time, 400 ms; TR, 7.3 ms; TE, 2.4 ms; FA, 15°; slice thickness, 2 mm; number of slices, 60 slices; imaging matrix, 256 × 256 × 60; and FOV, 22 ×22 ×12 cm.

### 2.4. Data analysis

#### 2.4.1. Behavioral data

Total number of proper responses, rate of proper responses, and mean RT for each block of the task were calculated for each subject. Improper responses, such as pressing the wrong button or failure to respond within 1000 ms, were eliminated when calculating mean RT. Differences in rate of proper responses between learning and control blocks were analyzed using two-way repeated measures analysis of variance (ANOVA). After identifying