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fMRI study in posterior cingulate and adjacent precuneus cortex in healthy elderly adults using problem solving task

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ABSTRACT

Purpose: To explore the blood oxygen level dependent (BOLD) response in the posterior cingulate cortex (PCC) and the adjacent precuneus regions in healthy elderly adults during problem solving tasks.
Materials and Methods: Eighteen participants (7 women, mean age of 63.6 ± 6.0 years old) were analyzed. The functional magnetic resonance imaging (fMRI) tasks were simplified 4×4 Sudoku puzzles that were divided into simple tasks (using the row rule or the column rule to solve the puzzle) and complex tasks (using both the row and column rules to solve the puzzle).
Results: The mean accuracy on the simple task was higher than that on the complex task ($P = 0.04$); the reaction time on the simple task was shorter than that on the complex task ($P = 0.001$). On both tasks, the participants showed deactivation in the bilateral PCC/precuneus regions. The extent of deactivation on the complex task was greater than that on the simple task (left: $P = 0.04$; right: $P = 0.04$).
Conclusions: Healthy elderly adults showed deactivation in the bilateral PCC and precuneus regions during a problem solving task; in addition, the extent of deactivation was enhanced by increasing the difficulty of the problem solving task.

1. Introduction

From a cognitive neuroscience point of view, particular attention has been paid to one of the resting-state networks, the so called default mode network (DMN), which includes the medial prefrontal cortex, medial parietal cortex, and posterior cingulate cortex (PCC) [1–5]. The PCC/precuneus has been found to be a key part of the DMN, where normal subjects show deactivation during a task versus no task or during a high-level versus a low-level task [6–9]. Positron emission tomography (PET) investigations have revealed that the PCC shows an elevated metabolic activity levels [1]. In agreement with the studies reporting diminished posteromedial cortical deactivation during unsuccessful encoding in healthy subjects [10–12], some studies [13–19] have shown of evidence of an abnormal task-induced deactivation pattern in patients with Alzheimer's disease (AD) compared to elderly controls in the corresponding DMN posteromedial regions. Modulation of the PCC during working memory tasks [20] suggests that this region may be implicated in working memory dysfunction. Therefore, studies of the blood oxygen level dependent (BOLD) response, measured with functional magnetic resonance imaging (fMRI), in the PCC of healthy subjects during a cognitive task could help to determine whether the PCC could be a possible key marker of memory impairment.

Problem solving is a mental process and a very common routine in daily life. Considered the most complex of all intellectual functions, it has been defined as higher-order cognition [21,22]. From the perspective of information processing, it has the following general characteristics: (1) an initial state, or the state in which the problem solver sorts out the givens; (2) a goal state, the solution state that the problem solver tries to achieve; and (3) the steps that the problem solver takes to transform the initial state into the goal state that initially may not be obvious [23]. The core of problem solving is the representation of the problem, identification of the state of the problem, the selection of the operation and the application of the operation (involving the choice of reasoning strategies and knowledge). Since an individual usually chooses a

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heuristic rule (a heuristic rule here refers to an experience-based method in problem solving that can help the participants find an answer quickly without trying various possible choices) to reach the goal, problem solving implicates the retrieval of stored information. However, how the PCC is involved during problem solving remains unclear.

The purpose of this study was to explore the BOLD response in the PCC and the adjacent precuneus cortex (PCC/precuneus) in healthy elderly adults during a problem solving task. The Tower of Hanoi is a task used to observe individual behavior and investigate the problem solving process at the early stage of cognitive psychology. However, it is difficult to use such a traditional behavioral method as a paradigm of fMRI to study the problem solving process. In this study, simplified 4×4 sudoku puzzles with complexity were used as a new paradigm to show how the PCC/precuneus is involved during the problem solving process.

2. Materials and Methods

2.1. Participants

This prospective study was approved by the institutional review board. Each participant was given written informed consent. A total of 22 participants from November 2008 to March 2010 were included in the study.

2.1.1. Inclusion criteria

All participants were recruited from the local community through referrals. They were fluent in Chinese, had at least 6 years of formal education, and had normal vision or vision corrected to the normal standard by the use of MRI-compatible eyeglasses. All participants met the following criteria: (a) a Rosen-modified Hachinski vascular dementia rating score (RMHVDRS) [24] of 4 or lower; and (b) a Clinical Dementia Rating (CDR) [25] score of 0.

2.1.2. Exclusion criteria

Participants with any one of the following characteristics were excluded from the study: (a) uncontrolled depression or other psychiatric illness; (b) taking psychoactive medications known to substantially affect memory; (c) standard contraindications to MRI; (d) technical difficulties that prevented the completion of successful anatomic imaging or fMRI task runs; (e) excessive motion during the fMRI examination in excess of 5 mm in any of three orthogonal directions, as determined by center-of-mass plots; and (f) inability to have his or her behavioral responses adequately monitored while in the imaging unit, evidenced by > 50% non-responses.

4 participants were eliminated because of technical factors or insufficient quality of functional MRI data (see exclusion criteria). Finally, a total of 18 participants (7 women) were analyzed, the mean age for the participants was 63.6 year (standard deviation 6.0 year), the mean education was 12.4 year (standard deviation = 2.5 year).

2.2. fMRI paradigm

Event-related fMRI data were recorded while participants were solving simplified 4×4 sudoku puzzles (Sudoku; Nikoli Publishing, Tokyo, Japan). Sudoku is a combinatorial number placement puzzle, the goal of which is to fill a 4×4 grid so that each column, each row, and each of the four 2×2 boxes contains the digits from 1 to 4 only one time each (Fig. 1a,b). As shown in this study, we simplified the puzzle and asked participants to give the answer for the cell marked with "?" in the grid using digits from 1 to 4 (Fig. 1c,d). The heuristic rules to solve the puzzle were as follows:

- If there were any three arbitrary digits from 1 to 4 in the grids of the row in which the "?" was located, the participants were asked to give the answer for "?"' using the remaining digits (this was the "row rule") (Fig. 2a);

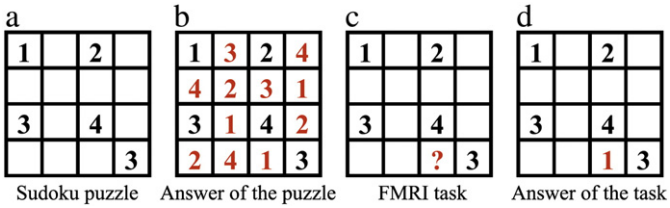

Fig. 1. Experimental design of the functional MR imaging *(fMRI)* study with a 4×4-grid number placement puzzle (Sudoku; Nikoli Publishing). (a) Puzzle. (b) Answer to the puzzle. (c) Simplifi ed puzzle (task). (d) Answer to the simplifi ed puzzle (task).

- If there were any three arbitrary digits from 1 to 4 in the grids of the column in which the "?" was located, the participants were asked to give the answer for "?" using the remaining digits (this was the "column rule") (Fig. 2b);
- If there were any three arbitrary digits from 1 to 4 in the grids of both row and column in which the "?" was located, the participants were asked to give the answer for "?" using the remaining digits (this was the "both row and column rule") (Fig. 2c).

The fMRI tasks were divided into two types according to heuristic rule: using the row rule or the column rule to solve the puzzle was the simple task (Fig. 2a,b), whereas using the both row and column rule was the complex task (Fig. 2c). As shown in Fig. 3, a trial of the experiment started with a red star shown for 2 seconds as a warning (the stimulus was visually shown on a black screen), then the participants solved the puzzle in a maximum period of 20 seconds. When participants found the answer for "?", they were asked to press a button immediately and to speak the answer during a 2 second period. One study assistant recorded the participant's answer in the imaging room. Participants were encouraged to finish the problem as correctly and quickly as possible. Next, the correct answer was provided on the screen for 2 seconds as feedback. There was an inter-trial interval (a white cross shown on the screen) that lasted for ~10 seconds during which the participants were asked to rest. For each participant, there were two sessions each that contained ≥ 360 images and each session involved the two types of tasks randomly selected with equal probability. Before the participants underwent fMRI examination, they were trained to accord to the experimental requirements: if they had solved the puzzles and had answers for them, they should press the button immediately and then spoke the answers. After they were familiar with and mastered the experimental requirements, they underwent functional experiments.

2.3. Image acquisition

The fMRI images were obtained using an eight-channel phased-array head coil at 3.0 T MR system (Siemens Magnetom Trio, Tim, Iselin, NJ, USA). A computer with a software package (E-Prime; Psychology Software Tools, Inc., Sharpsburg, Pennsylvania, USA; http://www.pstnet.com/eprime.cfm) was used to deliver visual stimuli and to record responses.

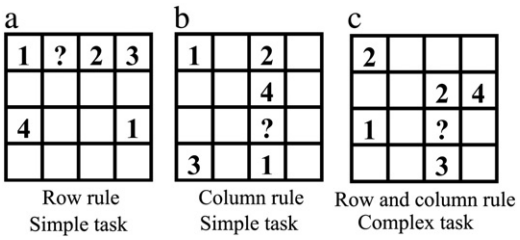

Fig. 2. Examples of the functional MR imaging task. (a) Simple task, with use of the row rule to solve the puzzle. (b) Simple task, with use of the column rule to solve the puzzle. (c) Complex task, with use of both row and column rules to solve the puzzle.