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Research Report

Cerebral activation related to implicit sequence learning in a Double Serial Reaction Time task

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Using functional magnetic resonance imaging (fMRI), we examined the distribution of cerebral activations related to implicitly learning a series of fixed stimulus–response combinations. In a novel – bimanual – variant of the Serial Reaction Time task (SRT), simultaneous finger movements of the two hands were made in response to pairs of visual stimuli that were presented in a fixed order (Double SRT). Paired stimulus presentation prevented explicit sequence knowledge occurring during task practice, which implied that a dual task paradigm could be avoided. Extensive prescanning training on randomly ordered stimulus pairs allowed us to focus on the acquisition of implicit sequence knowledge. Activation specifically related to the acquisition of fixed sequence knowledge was highly significant in the right ventrolateral prefrontal cortex. The medial prefrontal and right ventral premotor cortex were more indirectly related with such procedural learning. We conclude that this set of activations reflects a stage of implicit sequence learning constituted by components of (i) spatial working memory (right ventral prefrontal cortex), (ii) response monitoring and selection (medial prefrontal cortex), and (iii) facilitated linkage of visuospatial cues to compatible responses (right ventral premotor). Comparing the random-order stimulus–response actions with fixed sequences showed activations in dorsal premotor and posterior parietal cortices, consistent with a dorsal pathway dominance in real-time visuomotor control. The relative long time during which performance improves in the DoSRT provides an opportunity for future study of various stages in both general skill and fixed sequence learning.

1. Introduction

Two main memory systems contribute to adaptive behavior, a declarative memory system and a procedural memory system (Cohen and Eichenbaum, 1993). Procedural memory mediates faster and more accurate task performance by repeated exposure to a specific task. As a consequence, less attention is required, and cognitive involvement is gradually reduced. An important characteristic of procedural memory is its task specificity (Karni et al., 1998; Stadler, 1989): the changes induced by procedural memory formation in the neural circuitry do not alter performance on other, non-related tasks. In contrast, declarative memory mediates learning that results in changes within neural circuitry that are accessible for use in other tasks too.

Performance of sequential finger movements has been widely examined as to elucidate mechanisms involved in procedural memory. The experimental designs applied in both

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behavioral and cerebral imaging studies on the formation of procedural memory concerning such sequential finger movements can roughly be divided into three groups: (1) explicitly learned sequences of finger movements are practiced (Doyon et al., 1996; Jenkins et al., 1994), (2) knowledge of the fixed sequence of finger movements is acquired by trial and error (Doyon et al., 1996; Jeuptner and Weiller, 1998), (3) knowledge of the fixed sequence of finger movements is acquired by stimulus guided movement without the subject being aware of the sequence content (Grafton et al., 1995, 1998; Hazeltine et al., 1997). The differences between these three experimental approaches point at the differences in the acquisition of knowledge on the fixed sequence. In all three, the result is improved performance based on optimization of both specific sequence execution and general skill. In practicing explicitly acquired sequences, subjects are aware of the particular response sequence, and the main improvement from practice will concern optimization of movement execution. The acquisition of knowledge on a specific serial order by trail and error implies processes of evaluation and decision making with reference to explicit memory. These processes occur in parallel to the reduction of response times due to optimized movement execution. When functional imaging techniques are applied for the identification of cerebral structures involved in procedural learning, tasks that allow explicit knowledge will thus confound the results aimed for. In contrast, when sequence knowledge is obtained by simply responding to a fixed stimulus order, subjects do not make use of explicit knowledge, i.e., they are not aware of the fixed order during this practice period, at least initially. In such studies, much effort is put in avoiding explicit knowledge while practicing a sequence. This can be achieved either by the introduction of secondary tasks to distract attention (Grafton et al., 1995, 1998; Hazeltine et al., 1997) or by using long and difficult sequences (Rauch et al., 1997; Stadler, 1992). Indeed, the main differences between the experimental approaches listed above concern the role of explicit learning on performance improvement and the use of either external or internalized sequence information. In the present functional imaging experiment, we minimized the contribution of explicit learning to sequence learning, without using a dual task paradigm. As a consequence, we were able to specifically focus on the implicit characteristics of procedural memory formation. Our strategy was based on the concept of a Double Serial Reaction Time task (DoSRT) (Fig. 1), a bimanual variant of the SRT, in which simultaneous finger movements of the two hands were made in response to pairs of visual stimuli, of which the positions were presented in either a fixed or a random order.

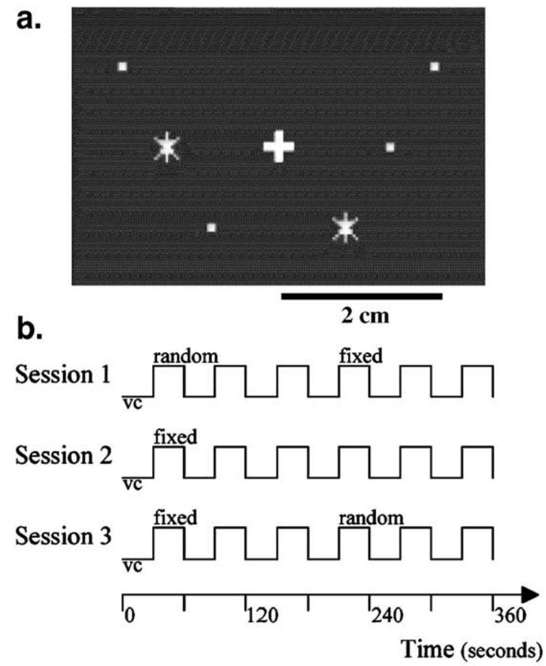

Fig. 1 – (a) Stimulus display of the Double Serial Reaction Time task (DoSRT). In both the task and visual control condition of the Double Serial Reaction Time task (DoSRT), the stimulus background consisted of a continuously presented fixation marker and six dots marking the position at which a stimulus could appear. Stimuli appeared as a pair of asterisks at either side of the fixation marker. Inside the MR scanner, subjects made use of a mirror in order to watch the screen on which the stimuli were presented. Two response boxes were used for responding. On each response box, three buttons corresponded with digits 2, 3 and 4 of each hand. When a response was made, i.e., two keys were pressed, the stimulus pair disappeared, whereas the next stimulus pair appeared after a 100-ms delay (see methods). The display covered 4° of the visual field, which was similar in both the circumstance of scanning and practice. (b) Task design for fMRI. During scanning, the visual control condition (VC) was alternated with the stimulus–response task condition. In the first set of 3 task blocks of session 1, as well as the 3 final blocks of session 3, the stimulus order was random. During the other task blocks, the stimulus order was following a fixed 6-item sequence. In each block, 10 measurements of a complete brain volume were obtained. A 10-min rest period was present between each session.

Originally, the SRT requires subjects to respond with the fingers of one hand to coded stimuli, displayed in either a random or fixed sequence order (Nissen and Bullemer, 1987). The stimulus order switches between random and fixed sequences, which remains unknown to the subject. Response times decrease during fixed sequence practice and subsequently increase on reintroduction of the randoms. In the absence of explicit sequence knowledge, the differences in response times to a fixed sequence and a subsequent random-order test block reveals the behavioral improvement due to implicit sequence knowledge. The presently applied DoSRT task enabled us to use relatively short repeating sequences, whereas none of the subjects developed explicit sequence knowledge during practice. Indeed, without using a dual task design. This did not only exclude a confounding variable, it has been suggested that the supposedly secondary task is not really secondary but rather an expansion of the primary task into a more complex composite task (Hsiao and Reber, 2001). By introducing the DoSRT and an extended prescanning period of random-order training in this fMRI study, we aimed to identify brain structures specifically involved in implicit sequence learning with reduction of the abovementioned non-specific variables.

Previous imaging studies have generally employed SRT designs with fixed stimulus–stimulus intervals, often as a