Neuroscience 139 (2006) 299–309

SEQUENTIAL NEURAL PROCESSES OF TACTILE–VISUAL CROSSMODAL WORKING MEMORY

S. OHARA,[a] F. LENZ[a] AND Y.-D. ZHOU[a,b]*

[a]*Department of Neurosurgery, School of Medicine, Johns Hopkins University, 600 North Wolfe Street, Baltimore, MD 21287, USA*

[b]*Krieger Mind/Brain Institute, Johns Hopkins University, Baltimore, MD 21218, USA*

Abstract—Working memory is essential to learning and performing sensory-motor behaviors that in many situations require the integration of stimuli of one modality with stimuli of another. In the present study, we focused on the neural mechanisms underlying crossmodal working memory. We hypothesized that in performance of the tactile crossmodal working memory task, there would be sequentially discrete task-correlated neural activities representing the processes of crossmodal working memory.

Scalp-recorded event-related potentials were collected from 15 electrodes in humans performing each of four tasks: tactile–tactile unimodal delayed matching-to-sample task, tactile–visual crossmodal delayed matching-to-sample task, tactile unimodal control spatial task, and tactile crossmodal control spatial task. Two positive event-related potential peaks were observed during the delay of the task. One peak (late positive component-1) was at about 330 ms after the onset of the tactile stimulus, and the other (late positive component-2) was at about 600 ms. Late positive component-1 was observed in all four tasks. There was no significant difference in late positive component-1 either between the unimodal tasks, or between the crossmodal tasks, but late positive component-1 was significantly larger in the crossmodal tasks than that in the unimodal tasks, and showed a specific pattern of larger activity over parietal areas than activity over frontal areas. Late positive component-2 was not observed in the unimodal matching task but was observed in all other three tasks over parietal areas. During the late delay (1000 ms–1500 ms), significant differences in negative potentials (late negative component) were found between the tasks.

The present study shows sequential changes in event-related potentials during the retention period of working memory tasks. It indicates that in performance of a crossmodal working memory task, there are sequentially discrete neural processes that may represent neural activities related to different cognitive functions, such as crossmodal transfer of information, and the working memory of the stimulus.

Key words: ERP, EEG, working memory, human, crossmodal.

Working memory refers to an active short-term memory system capable of temporarily storing, manipulating, and maintaining sensory information for later action (Baddeley, 1992; Fuster, 1995). Working memory is essential to learning and performing sensory-motor behaviors (Baddeley, 1992, 1996; Fuster, 1997; Goldman-Rakic, 1992). Studies in the past three decades show that associative areas of primate cerebral cortex are involved in working memory, including prefrontal cortex (PFC), posterior parietal cortex (PPC) and inferotemporal cortex (Burton and Sinclair, 2000; Desimone, 1996; Funahashi et al., 1989; Fuster, 1995, 2003; Miyashita and Hayashi, 2000; Petrides, 2000; Tanji and Hoshi, 2001). Recent human working memory studies have also shown that associative areas of cerebral cortex play important roles in performance of various working memory tasks (Braver et al., 2001; Cornette et al., 2001; Curtis and D'Esposito, 2003; Honey et al., 2002; Mehta et al., 2000; Oliveri et al., 2001; Smith and Jonides, 1998). Activation of PPC or PFC in tactile–visual crossmodal discrimination tasks was reported in human imaging studies (Kawashima et al., 2002; Saito et al., 2003).

Recent studies have shown that in addition to association cortex, primary sensory cortex also participates in working memory (Romo and Salinas, 2003). Somatosensory cortex including primary somatosensory cortex (SI) and secondary somatosensory cortex (SII) has been shown to participate in tactile unimodal working memory in both monkeys (Salinas et al., 2000; Zhou and Fuster, 1996) and humans (Harris et al., 2001, 2002). Cells in monkey SI cortex have also been shown to be part of cortical neural networks that represent crossmodal association and crossmodal working memory (Zhou and Fuster, 1997, 2000). In a recent human scalp-recorded event-related potential (ERP) study (Taylor-Clarke et al., 2002), ERP components were elicited by tactile stimulation on the subjects' arm in a tactile discrimination task. Those ERP components related to activities of SI and SII were modulated by nontactile stimulation, i.e. visualization of the subject's own stimulated arm.

ERPs recorded from the scalp in humans have been used effectively to study human cognitive functions since they provide high temporal resolution. In the present study, we investigated changes in ERPs during the delay period when normal subjects performed tactile unimodal, or tac-

---

*Correspondence to: Y.-D. Zhou, Meyer 8-181D, Department of Neurosurgery, School of Medicine, Johns Hopkins University, 600 North Wolfe Street, Baltimore, MD 21287, USA. Tel: +1-410-955-5774; fax: +1-443-287-8044.
E-mail address: yzhou12@jhmi.edu (Y.-D. Zhou).

Abbreviations: ANOVA, analysis of variance; CR, correct rate; EEG, electroencephalogram; EOG, electrooculogram; ERP, event-related potential; HEOG, horizontal electrooculogram; LED, light-emitting diode; LNC, late negative component; LPC-1, late positive component-1; LPC-2, late positive component-2; MANOVA, multivariate analysis of variance; PFC, prefrontal cortex; PPC, posterior parietal cortex; RT, reaction time; SI, primary somatosensory cortex; SII, secondary somatosensory cortex; S-1, stimulus-1; S-2, stimulus-2; TMS, transcranial magnetic stimulation; VEOG, vertical electrooculogram.

0306-4522/06$30.00+0.00 © 2005 IBRO. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.neuroscience.2005.05.058

tile–visual crossmodal delayed matching-to-sample tasks. We compared ERPs recorded during delays between unimodal and crossmodal tasks to examine the significance of any differences. We hypothesized that in performance of the tactile crossmodal working memory task, sequentially discrete neural activities would be observed, and that they would be different from neural activities when the tactile unimodal working memory task was performed. Those sequentially discrete activities may represent neural activities at different cortical levels correlated with performance of the task.

EXPERIMENTAL PROCEDURES

Subjects and stimuli

Nine normal adult human volunteer subjects were recruited for the study (seven males, two females, aged 19–47 years). All participants signed informed consent. The protocols of the experiments were approved by the IRB of the Johns Hopkins School of Medicine.

Experiments were carried out in a quiet, dimly lit room. Participants sitting in a comfortable chair faced at eye level a light-emitting diode (LED) 5 mm in diameter in the center of the visual field. A white circle 10 mm in diameter surrounded the LED on a black background. The visual stimuli (LED) comprised green or red light 100 ms in duration. The distance between the stimuli and the participants' eyes was about 1.5 m. A plastic probe attached to a mechanical vibrator was used to deliver tactile stimuli on the subject's left index finger-tip (Chubbuck, 1966). This mechanical vibrator was successfully used to evoke responses recorded directly over SI and the parasylvian cortex (electrocorticogram, ECoG) in our study (Ohara et al., 2004). The frequency range of the tactile stimuli, 0–150 Hz, was controlled by a frequency generator. The resolution of displacement of vibration was 1 μm over a range of 0.1 inch. Participants were requested to maintain a comfortable posture and place their left hand on a supporter in their usual position during performance of tasks. Their right hand was also placed on a supporter and positioned to press two buttons, left and right, with their fingers (the index finger for left button; the middle finger for right button) required by tasks.

ERP recording

Electroencephalograms (EEG) were recorded by using an EEG recording system (Neuroscan SynAmp) made by Neuroscan, Ltd. Corp., El Paso, TX, USA. This system has been approved for clinical use by the Food and Drug Administration and the Department of Clinical Engineering, Johns Hopkins Hospital. Ag–AgCl scalp electrodes (Quick-Caps, Neuroscan) were used in a standard arrangement for locations (Fisch, 1999). Activities measured from all these electrodes were in reference to linked earlobes. The impedance of each electrode was kept below 5 kΩ. Electrooculograms (EOG) were recorded for both horizontal eye movements (HEOG) and vertical eye movements (VEOG). HEOG was recorded from two electrodes located at the outer canthi of the eyes. VEOG was recorded from a pair of electrodes, one about 1 cm below and the other about 1 cm above the left eye. EEG and EOG were amplified by an amplifier with a 0.1–100 Hz band-pass filter (-6 db), digitized at 500 Hz sample rate, and saved for off-line analysis.

The scalp-ERPs were recorded from the subjects when they performed a tactile–tactile unimodal working memory task or a tactile–visual crossmodal working memory task. At the beginning of a recording session, the subjects were instructed to focus on the LED throughout the session to avoid any voluntary eye movement, and also to avoid blinking during any trial of the task. Trials with eye-blinks, excessive eye movements, or excessive muscle artifacts were excluded from the analysis.

Behavioral tasks

Matching tasks. Several working memory tasks (unimodal and crossmodal) were used in this study. In the tactile–tactile delayed matching-to-sample task (the unimodal matching task) (Fig. 1), a trial started with stimulus-1 (S-1) applied to the subject's left index finger-pad. S-1 was a 100-ms tactile vibration of either high (150 Hz) or low (80 Hz) frequency. It was followed by a delay of 1500 ms. At the end of the delay, stimulus-2 (S-2) was presented. S-2 was a 100-ms tactile vibration again (either high or low frequency). The subject was instructed to memorize the frequency of S-1 during the delay, to expect S-2 at the end of the delay, and to indicate at the end of each trial whether S-2 matched S-1 by pressing one of two buttons (e.g. left for match, right for nonmatch assigned for the subject before performance of the task). The assignment of the buttons (match or nonmatch) was random among subjects and counterbalanced across subjects. Presentation of S-1 or S-2 was in random order from trial to trial to prevent the subject from getting any clue for the choice. The intertrial interval between trials was chosen randomly in a range of 4–5 s. The subject's response time to S-2 was recorded.

The crossmodal task (the tactile–visual crossmodal matching task) (Fig. 1) was identical to the unimodal task except that in this task S-2 was a visual cue (LED, 100 ms) presented in front of the subject at eye level (FRONT condition). At the end of each trial, the subject indicated whether the visual S-2 was associated with the tactile S-1 (e.g. green associated with high frequency; red with low frequency). Associations between the tactile stimuli and the visual stimuli were assigned before the subject started performing the task, and counterbalanced across subjects.

Control tasks. Fig. 1 also shows two control tasks. The sequence of the control task, unimodal or crossmodal, was identical to its corresponding matching task except that the subject was instructed to take the S-2 as a go-signal, irrespective of the features of the S-2 (frequency of the vibration in unimodal task; color in crossmodal task). Immediately after the onset of S-2 at the end of the delay, the subject pressed one of two buttons to indicate whether S-1 was of high or low frequency (e.g. left button for high, right button for low). The button-assignment was also counterbalanced across subjects in the control tasks. Therefore, tactile vibrations in those two tasks were associated with positions of motor responses.

SIDE condition. In performance of tasks in FRONT condition, there was a spatial shift in attention when the subject shifted his/her attention from S-1 to S-2. In order to test whether there was any significant effect of this spatial shift on tactile working memory, the LED was moved from the center of the frontal visual field to the side of the subject (SIDE condition), and was attached to the vibrator. The subject's fixation moved to the side accordingly, but the subject would not see either the vibrator or his/her own hand. The LED (S-2 generator) was thus nearly at the same spatial position as the vibrator (S-1 generator). Control tasks were not performed in the SIDE condition.

Strategies for task performance. Each subject had a full training session to learn all the tasks a day before ERP recording. To ensure that all subjects used the same strategies to perform the tasks, they were instructed to learn and practice how to control their eye movements and eye-blinking, and how to perform the tasks with strategies required by the study.

In the crossmodal matching task, during the delay period the subjects were instructed to retain the visual stimulus (S-2) that was associated with the tactile frequency (S-1). That is, if, in the trial, the S-1 was a vibration of high frequency, a subject would