Research report

Neural activities during Wisconsin Card Sorting Test — MEG observation

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Abstract

The present study recorded activities of magnetoencephalography (MEG) to the presentation of cards, and to the presentation of feedback signals in 12 normal subjects while they performed the Wisconsin Card Sorting Test (WCST), to observe temporal and spatial processing during the task. The MEG responses were compared between two different conditions in the presentation both of cards and of feedback signals: the cards proceeded by the first wrong [W1st(C)] and by the 4th correct feedback signals [C4th(C)]; and the feedback of the first wrong [W1st(FB)] and the 4th correct signals [C4th(FB)]. A multi-dipole model, brain electric source analysis (BESA), was used to explore the dipole sources responsible for the MEG activities. We found that MEG activity differences between the W1st(C) and the C4th(C) condition occurred in the period of 190–220 ms (M190 and M200), and 300–440 ms (M300 and M370) mainly at the supramarginal gyrus, the dorsolateral prefrontal, and the middle and inferior frontal gyrus. MEG differences between the W1st(FB) and the C4th(FB) condition occurred 460–640 ms (M460) after the presentation of the feedback signals, with the activation of the dorsolateral prefrontal cortex and the middle frontal cortex. No significant location differences were found between the frontal responses (M370) of the W1st(C) and M460 of the W1st(FB). Our results proved that the WCST task activates a broad frontal area and the parieto-frontal network across time streaming. Both shifting attention to the wrong feedback and enhanced visual working memory to the sorting shifting condition of the card presentation occur in the same areas at different time points. © 2001 Elsevier Science B.V. All rights reserved.

Theme: Neural basis of behavior

Topic: Cognition

Keywords: Wisconsin Card Sorting Test; Magnetoencephalography; Shifting attention; Working memory; Prefrontal cortex; Supramarginal gyrus

1. Introduction

The Wisconsin Card Sorting Test (WCST) is a task which requires subjects to match ‘target’ to ‘reference’ cards on the basis of one of three possible categories (color, number, or form). The correct sorting principle changes in a prescribed way (usually after 10 correct choices) which is known by the experimenter but not the subject. As patients with prefrontal lobe damage were found to have particular difficulty in shifting from one category sorting principle to another during performance of the task [17,27], the WCST has for many years been widely used as a neuropsychological index of prefrontal cortical function, especially shifting attention. However, its specificity has been questioned, since in some studies, the WCST was found incapable to discriminate patients with prefrontal lesions from those with lesions in other regions [1,20,29]. Multiple areas related to various functions are found to be activated during the task in addition to the prefrontal cortex. Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) showed that the bilateral inferior parietal lobe and inferior posterior temporal lobe [5], bilateral inferior parietal lobe and left superior occipital gyrus [30], and bilateral supramarginal gyrus and anterior cingulate cortex [22] were also activated during the WCST task. In other words, previous findings of fMRI and PET studies were not quite consistent and they...
Another problem is that the WCST is such a complicated task that it involves many cognitive operations besides shifting attention, such as working memory, inhibition, reasoning, and decision making. The working memory, inhibition and decision making processing may take place after the presentation of cards, whereas the attention shift processing might start immediately after the presentation of the feedback indicating change of the sorting principle [22]. Little is known, however, about the spatial changes with time during the WCST. Although an event-related fMRI study suggested that the peak of MRI signals was at 5–9 s after the neuronal activity during the WCST [22], it is impossible by PET and fMRI to observe neural activation in a sub-second scale.

Magnetoencephalography (MEG), which has a rather high temporal and estimated spatial resolution and allows one to record brain activities on a scale of ms and mm, might provide important information on how the cognitive processing occurs during the WCST. In the present study, we recorded MEG after the presentation of cards and after the presentation of the feedback signals, to understand the cognitive processing related to the WCST task temporally and spatially in detail.

2. Methods

2.1. Subjects

Eight male and four female healthy members of our staff (mean age 31.9±2.9 years, range 25–37 years) participated in the study. None of the subjects had any history of neurological, psychological or opthalmological disorders. All had normal or corrected to normal visual acuity. All subjects were right-handed. Informed consent to participate in this study, which was first approved by the Ethical Committee of the National Institute for Physiological Sciences, Okazaki, Japan, was obtained from all participants.

2.2. Stimulation (Fig. 1)

This modified WCST task was based on the modified version of Nelson [33]. The subjects were asked to match the target card to the reference cards on the basis of one of three categories: number, color or shape. Four reference cards in the upper part of the screen and a target below the reference cards were presented. The shapes and colors of the four reference cards were exactly the same as the Nelson’s version. The subject was required to decide which reference card matched the target card and press one of the four buttons held in his/her hands. The four buttons (two in each hand) were arranged in an array corresponding to the layout of the four reference cards. The cards disappeared when the subject responded, and 100 ms later, a feedback signal (□) or (●) which indicated whether the subject’s decision fit the examiner’s (computer’s) category or not was presented. The feedback signal lasted for 200 ms, and there was an interval of 700–900 ms from the disappearance of the signal to the next trial (Fig. 1). In the beginning, the correct category was told to be color. When the subject maintained a correct progression through six to nine (random) trials during one run, the principle was changed without warning. The subject had to search for the new correct category when the wrong feedback signal (●) was shown, indicating the subject’s choice was different from the principle (Fig. 1). One recording for a subject included approximately 120 runs, and took in total about 40 min with a brief break after every five to seven runs. Before recording, all subjects were given a training period until they could press appropriate buttons without difficulty.

The stimuli were presented by a video projector (XV-TZZ, Sharp) outside of the magnetically shielded room (Vacuumschmelze GmbH). The stimulus presentation was controlled by a personal computer (PC-9801B52, NEC). A crystal liquid shutter (LUMP6, Nippon Sheet Grass) was set in front of the video projector and adjusted the stimulus onset time. It took about 20 ms for the projector to present the stimuli. The luminance of the stimuli was about 79.6 cd/m², with a background of about 2.2 cd/m² from the viewpoint. The fixation point was in the center of the target card, which enabled the subjects to look straight ahead. The subjects were asked to gaze at the fixation point during the experiment.

2.3. Data acquisition

MEG recordings were carried out with dual 37-channel biomagnetometers (Magnes, Biomagnetic Technologies Inc. San Diego, CA). The device was 144 mm in diameter and its radius was 122 mm. The outer coils were 72.5° apart. Each coil was 22 mm. Each coil was connected to a superconducting quantum interference device (SQUID). In order to exclude the artifacts caused by eye movement, we simultaneously recorded a vertical-horizontal electrooculogram (EOG) from the left eye. The epochs of EOG with signals larger than 80 μV were excluded from averaging. MEG recordings in which more than 20% of the epochs were rejected were excluded from analysis. Responses were filtered with a 0.1–100 Hz bandpass filter, and digitized at a sampling rate of 297.6 Hz. About 120 trials were averaged for each recording condition in both the card presentation and the feedback signal presentation experiment.

2.3.1. The card presentation experiment

Stimuli (0.13×0.13 m²) were projected on the ceiling in front of the subjects. The distance of the stimuli from the eyes was about 1.5 m. Since our device was not a whole-
Fig. 1. The scheme of the stimuli during the modified WCST task. One run comprised six to nine correct response trials. C4th (FB)=the recording to the fourth correct feedback signal; C4th (C)=the recording to the card presentation preceded by the fourth correct feedback signal; W1st (FB)=the recording to the first wrong feedback signal; W1st (C)=the recording to the card presentation preceded by the first wrong feedback signal.
head type, we had to select particular areas of interest. Although there is some controversy over the laterality of prefrontal activation during the WCST task [27], the left predominant findings [5,14,18,25,30] are somewhat more consistent than the right [23,26]. Therefore, in this study, we focused on the MEG responses in the left hemisphere. The measurement device was centered at three different positions, around F3 and Oz (the left frontal and occipital recording) and C3 (the left temporo-parietal recording) of the International 10-20 System in each subject. The F3 and Oz conditions were recorded simultaneously. The C3 position was recorded independently (Fig. 2). The left hemisphere was almost entirely covered by these placements. A previous event-related potential (ERP) study showed that the reaction time was usually at least 600 ms after the presentation of cards [4]. Therefore, in order to avoid artifacts due to movement, we collected epochs from 100 ms before and 500 ms after the presentation of cards in two trials during each session: one proceeded by the first ‘wrong’ feedback signal [W1st(C)], and the other proceeded by the 4th correct feedback signal [C4th(C)] (Fig. 1). These two trials were interesting, because the W1st(C) was considered to be a sorting shift condition, the period of searching for a new category and making a decision; whereas the C4th(C) was thought to be a continuously performing condition, the period of recalling and maintaining the previous sorting rule. We recorded responses to the C4th trails instead of the later correct trials to reduce the habituation effect.

2.3.2. The feedback presentation experiment

Stimuli (0.1×0.1 m²) were projected on the wall in front of the subjects. The distance of the stimuli from the eyes was about 1.5 m. One of our aims in this study was to compare location differences within the frontal cortex between the MEG responses to the presentation of feedback signals and the presentation of cards. Therefore, we collected MEG responses to the feedback signals only from the left frontal area. The measurement device was placed at the left frontal position centered at F3. As there was no motor task after the presentation of the feedback signals, the responses were recorded for as long as possible. The analysis time was from 100 ms before and 700 ms after the presentation of the feedback signal. For the reason mentioned above, we focused on two conditions during each run: one after the presentation of the first wrong feedback signal [W1st(FB)], the other after the presentation of the 4th correct feedback signal [C4th(FB)] (Fig. 1). Brain responses to the W1st(FB) were considered to reflect the attention shifting to a new category dimension and inhibition processing, and responses to the C4th(FB) to represent the reinforcement of a positive link to a series of successful decisions [37].

2.4. Data analysis

The root mean square (RMS) was calculated as the strength of activities (amplitude) at each sampling point in each subject. Then, the group-mean RMS of all subjects at each sampling point was calculated and its curve was drawn in each condition to compare amplitude change between the W1st(C) and C4th(C), or the W1st(FB) and C4th(FB). In order to compare the averaged MEG waveforms between the W1st and C4th in both the card presentation and the feedback presentation study statistically, we used the paired t-test at each time point (every 3.36 ms) based on the previous studies [21]. P<0.05 was considered to be significant. When the significance continued at least three sequential time points (over 10 ms in duration), we recognized the waveforms within this time.

Fig. 2. The placement of the MEG device. The left hemisphere was almost entirely covered by these three placements.
period as meaningful components. The peak latency of each recognizable component was measured.

2.5. Source analysis

The source analysis was done for each component determined as mentioned above. At first, we estimated the position of an assumed single source for each component using the single equivalent current dipole (ECD) model in a spherical volume conduction [39]. Two criteria were used in the application of the ECD model to calculate the single source for a magnetic response. One is that the dipole location determined by the ECD model must remain stationary (lasting at least 10 ms) during the period of the response; the other is that the correlation between the recording field and the estimated field is >0.95. As the components recorded in the present study did not meet the criteria in the application of a single ECD model, probably due to overlapping activities in multiple areas, we used a brain electric source analysis (BESA) software package (NeuronScan, McLean, VA) for the computation of theoretical source generators of the MEG activities in a 3-layer spherical head model. This method allows the spatio-temporal modeling of multiple sources over defined intervals. The location (x, y, and z positions) and orientation of the dipoles were calculated by an iterative least-squares fit. The origin of the head-based coordinate system was the point exactly halfway between the preauricular points. The x-axis indicated the coronal plane with positive values to the nasion; the y-axis, the sagittal plane with positive values to the left; and the z-axis, the transaxial plane with positive values up [32]. A four-step strategy was applied independently to the waveforms recorded from different areas. We basically adopted a robust repeatable procedure to refine limited dipole sources, since fewer valid sources should be more reliable than many potentially questionable sources. Only if a good model was not obtained using the two-dipole analysis, did we try to add another dipole. Therefore, at first, we analyzed the two-dipole localization in each time period.

In step 1, one dipole source for the activity was calculated in the frontal and the parietal area when the device was placed at the F3 and C3 position, respectively. Its orientation was calculated with the first location constraint in the prefrontal or parietal area. Then, the location constraint was released and re-fitted, retaining the orientation obtained. In step 2, after determining the temporary location and orientation of the first source, the second dipole was added with no constraint. In step 3, retaining the orientation and location of the second source, the location and orientation of the first source were released and re-calculated. Then in step 4, the orientations for both sources were fitted with the new location constraint. Finally, in order to compare the sources among individuals, we named the major source as S1, and the other as S2. The same procedures with a two-dipole model were followed both for the card presentation study and for the feedback presentation study.

The residual variance (%RV) indicated the percentage of data which could not be explained by the model. The goodness-of-fit (GOF) was expressed in percentage as (100−%RV). Since the signal-to-noise ratio of the MEG recording was much smaller than that of the EEG recording, GOF values larger than 90% are considered to indicate a good multiple dipole model.

Magnetic resonance imaging (MRI) was performed with a Magnex 150XT 1.5 T system (Shimadzu, Kyoto, Japan). T1-weighted coronal, axial and sagittal images with a continuous 1.5 mm slice thickness were used for overlays with the theoretical sources calculated by BESA. The common MEG and MRI landmarks (the nasion and bilateral preauricular points) allowed easy transformation of the head-based 3D coordinate system used by MEG source analysis for the MRI. The MEG source locations were converted into pixels and slice values using the MRI transformation matrix and inserted onto the corresponding MR image.

3. Results

3.1. Behavior and reaction time

All the subjects understood and performed the task well with perseverative errors (failed to shift from one category to another) and mistake errors of less than 1%. Mean reaction time to the W1st(C) condition (914.6±306.0 ms) after the card presentation was not significantly different from that to the C4th(C) condition (920.4±287.0 ms)(paired t-test).

3.2. MEG to the card presentation

Four subjects were excluded from the study due to large eye movement artifacts. Therefore, we analyzed the results of eight subjects. At first, we describe results recorded from the frontal and temporo-parietal recordings, since they were relatively similar. Although there were MEG waveform variations among individuals, the activities started approximately from 100 ms after the stimuli and continued until the end of the analysis (500 ms) in the recordings of both regions. From 100 to 500 ms, four major peaks could be recognized (Fig. 3): 1M (mean peak at 150 ms), 2M (220 ms), 3M (320 ms), and 4M (400 ms). From the occipital recording, there were two or three components peaking at about 150, 300 and 400 ms.

We compared the group-mean RMS at each time point between the two conditions (Fig. 4). In the frontal recording, the RMS at 200–220 ms (M200) and 370–440 ms (M370) to the sorting shift condition [the W1st(C)] was significantly larger than that to the continuously performing condition [the C4th(C)] (paired t-test, P<0.05). In the
temporo-parietal recording, the RMS at 190–210 ms (M190) to the W1st(C) was significantly smaller than that to the C4th(C) (paired t-test, P < 0.05). The RMS at 300–440 ms (M300) to the W1st(C) was significantly larger than that to the C4th(C) (paired t-test, P < 0.05). No significant difference in RMS at any time point was found between the two conditions in the occipital recording.

A two-dipole model for analyzing the M190, M200, M300, and M370 components in the W1st(C) condition was successfully made for each subject. The dipole locations varied among individuals. Table 1 summarizes the locations of the two sources responsible for these components in all eight subjects. The source 1 (S1) of the M190 component from the temporo-parietal recording [TP(C)] was mainly located at the supramarginal gyrus (SMG, Brodmann’s area 40), and source 2 (S2) was located in the hand region of the primary sensorimotor cortex. Both the S1 and S2 for M200 from the frontal recording [F(C)] were found to be located at the dorsolateral, middle, and inferior frontal cortex. For M300 from the Tp(C) recording, S1 was at the SMG and S2 was at the middle and inferior frontal gyrus. For the M370 component from the F(C) recording, S1 was found at the dorsolateral prefrontal and middle frontal gyrus. S2 was located at the dorsolateral prefrontal, middle frontal, and inferior frontal gyrus. Fig. 5 shows the BESA results at the
above times in one subject. We overlaid the sources calculated by BESA onto MRI. Fig. 6 shows the dipole sources on MRI in six subjects. There were no significant location differences between the S1 or the S2 of M200 and M370 (paired t-test) (Table 2).

The two-dipole model for analyzing the M200, M300, and M370 components in the C4th(C) condition at the same locations as the W1st(C) condition showed a low value of GOF (approximately 70%) which did not reach the criteria of significance. However, only M190 in the TP(C) recording showed a significant two-dipole model at the same locations as the W1st(C) condition (Fig. 5).

3.3. MEG to the feedback signals

MEG activities started from 180 ms and continued until the end of the recording (700 ms) with three major peaks: 180–250 ms (mean peak at 220 ms), 280–400 (350 ms) and 400–650 ms (540 ms) (Fig. 3). The RMS at 460–640 ms (M460) after the presentation of the 1st wrong feedback [W1st(FB)] was significantly larger than that after the 4th correct feedback [C4th(FB)] (paired t-test, P<0.05) (Fig. 4).

Analyzing the sources for M460 from the frontal recording in the W1st(FB) condition [F(FB)], we found that the S1 located at the dorsolateral prefrontal and middle frontal gyrus. S2 was at the dorsolateral prefrontal, middle, and inferior frontal gyrus (Table 1, Fig. 6). There were no significant differences in location of either the S1 or the S2 between the M460 component to the presentation of the feedback signals and the M370 component to the card presentation experiment (paired t-test) (Table 2).
Table 1
A summary of the two dipole locations responsible for the components of M190, M200, M300, M370 and M460 in the eight subjects

<table>
<thead>
<tr>
<th>n</th>
<th>Source 1</th>
<th>n</th>
<th>Source 2</th>
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<tbody>
<tr>
<td></td>
<td>Source 1</td>
<td></td>
<td>Source 2</td>
</tr>
<tr>
<td></td>
<td>supramarginal gyrus (BA40)</td>
<td></td>
<td>primary sensori-motor cortex (BA1, 4)</td>
</tr>
<tr>
<td>7</td>
<td>posterior parietal lobe (BA7)</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>3</td>
<td>dorsolateral prefrontal cortex (BA9, 46)</td>
</tr>
<tr>
<td>3</td>
<td>dorsolateral prefrontal cortex (BA9, 46)</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>middle frontal gyrus (BA8, 9)</td>
<td>2</td>
<td>middle frontal gyrus (BA8)</td>
</tr>
<tr>
<td>1</td>
<td>inferior frontal gyrus (BA44)</td>
<td>3</td>
<td>inferior frontal gyrus (BA44,45)</td>
</tr>
<tr>
<td>8</td>
<td>supramarginal gyrus (BA40)</td>
<td>6</td>
<td>middle frontal gyrus (BA46)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>inferior frontal gyrus (BA45)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>supramarginal gyrus (BA40)</td>
</tr>
<tr>
<td>4</td>
<td>dorsolateral prefrontal cortex (BA9)</td>
<td>3</td>
<td>dorsolateral prefrontal cortex (BA9)</td>
</tr>
<tr>
<td>4</td>
<td>middle frontal gyrus (BA8,9)</td>
<td>2</td>
<td>middle frontal gyrus (BA9,46)</td>
</tr>
<tr>
<td>3</td>
<td>inferior frontal gyrus (BA44,45)</td>
<td>3</td>
<td>inferior frontal gyrus (BA44, 45)</td>
</tr>
<tr>
<td>3</td>
<td>dorsolateral prefrontal cortex (BA9, 10)</td>
<td>3</td>
<td>dorsolateral prefrontal cortex (BA10,47)</td>
</tr>
<tr>
<td>5</td>
<td>middle frontal gyrus (BA9,46)</td>
<td>1</td>
<td>middle frontal gyrus (BA46)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4</td>
<td>inferior frontal gyrus (BA44, 45,47)</td>
</tr>
</tbody>
</table>

*a*, the numbers of the subjects; BA, Brodmann’s area; F(C), frontal recording, card presentation experiment; TP(C), temporo-parietal recording, card presentation experiment; and F(FB), frontal recording, feedback presentation experiment.

4. Discussion

4.1. The card presentation experiment

Normal subjects could continuously sort the cards in a certain category while the feedback showed ‘correct’, and shift sorting to a new category while the feedback showed ‘wrong’. The patients with the ‘perseverative errors’, however, could persist in sorting to a particular category when the feedback showed ‘correct’, but were unable to shift from one sorting principle to another while the feedback showed ‘wrong’ [14,27,33]. Therefore, the information processing between performing the sorting shift (the W1st) and the continuously performing trials (the C4th) must be different. In this study, no MEG activity differences were found between the two conditions from the occipital recording around the visual cortex. The result suggested that different neuronal activities during the two different events [the W1st(C) and the C4th(C)] occurred after the primary visual processing.

Focusing on the locations of the major source, S1, of each component, as shown in Fig. 6, we found that the MEG activity differences between the two conditions occurred at the parietal and frontal cortex along with the visual information stream flowing from the posterior to the anterior of the brain across time: 190–210 ms (M190), mainly at the SMG (Brodmann’s area 40); 200–220 ms (M200), at the dorsolateral prefrontal, middle and inferior frontal gyrus; 300–440 ms (M300), mainly at the SMG; 370–440 ms (M370), at the dorsolateral prefrontal and middle frontal gyrus. As source locations of both the early components (M190 and M200) and the late components (M300 and M370) were found at the SMG and frontal areas, we speculate that the information might be processed in a way of input and feedback along the parieto-frontal network. The anatomical [7,15] and functional cortico-cortical connections between the frontal and the parietal lobes had been reported in many early studies, especially its important role in the operation of working memory [8,10,28,38]. Our results supported the notion that working memory is important in the performance of the WCST task after the presentation of cards [3,5,16,37].

There are reports of PET, fMRI, and event-related potentials (ERP) stressing the activation in the SMG and the posterior parietal cortex during the WCST task [4,5,22,37]. The activation of the left SMG was assumed to reflect the short-term storage of phonological information [9,19,34,38] or the nonphonological codes in working memory [2]. In this task, it is possibly related to the storage of the subvocal rehearsal of the recently processed sorting rule, as all of the subjects admitted that they did subvocally repeat the recently processed sorting category in order to keep it in mind. For M190 at both of the W1st(C) and C4th(C) conditions, the SMG were activated with larger activities to the C4th(C) condition. It is reasonable for the SMG activities to be stronger during the C4th(C) condition, considering that temporal storage of the present correct sorting category was the key process for performing the C4th(C) trials. At the period of 300–440 ms (M300), the SMG again were activated, but with larger
responses to the W1st(C) condition. In order to find out the new sorting category, subjects must subvocally rehearse the recently presented wrong sorting category (such as color) and consider the other two possibilities (shape and number). Therefore, the continuous or reactivated response at the SMG during the period of 300–440 ms confined to the W1st(C) condition might reflect the feedback processing of these subvocal rehearsals. We did not find these areas to be activated in response to the C4th(C) condition, possibly because no feedback occurred, as there was no
Fig. 6. The estimated sources using BESA overlaid on MRI for six subjects. The sources in each time period and each task condition shown in this figure were the sources being projected to the brain surface. Source 1, closed symbols; Source 2, open symbols. The activity of source 1 was much larger than that of source 2 in each condition. Although there appeared a relatively large inter-individual difference, two major findings were identical; (1) multiple areas were activated during the WCST task, but the supramarginal gyrus (Brodmann’s area 40) and the dorsolateral prefrontal cortex (Brodmann’s area 9 and 46) were mainly activated; (2) from the view of the activity flow across time, there appears to be an afferent and feedback information circuitry between the supramarginal gyrus (Brodmann’s area 40) and the frontal cortex activities.

Table 2
The mean (±S.D.) values (cm) of co-ordinates (x, y, z) for the source locations calculated by BESA.

<table>
<thead>
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<th>Source 1</th>
<th>Source 2</th>
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<tbody>
<tr>
<td></td>
<td>x</td>
</tr>
<tr>
<td>TP(C) M190</td>
<td>-0.55±1.42</td>
</tr>
<tr>
<td>F(C) M200</td>
<td>4.43±2.14</td>
</tr>
<tr>
<td>TP(C) M300</td>
<td>-0.21±1.02</td>
</tr>
<tr>
<td>F(C) M370</td>
<td>5.14±0.87</td>
</tr>
<tr>
<td>F(FB) M460</td>
<td>5.75±1.34</td>
</tr>
</tbody>
</table>

Note that x, y, and z positions are different in our system [32] from the MRI system.
necessity to search for a new sorting category in the C4th(C) condition.

Although the M200 component from the frontal recording had some time overlap with the M190 (10 ms earlier than M200) from the temporo-parietal recording, we considered the two components to reflect different neuronal activities, as their source locations were very different. Moreover, the M200 to the W1st(C) condition was larger than that to the C4th(C) condition (Fig. 4). The activities to the W1st(C) condition varied among subjects widely at the dorsolateral prefrontal cortex, and the middle and inferior frontal gyrus (Brodmann’s area 44 and 45). Activities in the same area in response to the C4th(C) condition were not found. As it took about 20 ms for our projector to present the stimuli, the M200 component was thought to start actually at 180–200 ms after the presentation of the cards. This is consistent with a previous ERP study [3], which showed a negative field potential in the left frontal area (F7 of the international 10-20 system) at 170 ms after the onset of the card presentation. The reason for the difference in MEG amplitude between the W1st(C) and C4th(C) in this time period might be: selective attentional shift to a new category and inhibition of an ongoing reaction to the previous category similar to a ‘no-go’ reaction. Evidence has proved that the dorsolateral prefrontal cortex (Brodmann’s area 9) operates attentional shift processing [13,37]. A frontal negativity specific to the ‘no-go’ trial was found to occur as early as 150 ms after the stimulus onset [40,41]. Therefore, M200 activity in a relatively wide area of the frontal cortex could reflect the selective attention or inhibition processing.

The S1 for the M370 component was found mainly at the Brodmann’s area 9 during the W1st(C) condition. The same location was not activated during the C4th(C) condition. The M370 activity to the W1st(C) condition at the dorsolateral frontal areas (Brodmann’s area 9) could reflect the increased workload of visual working memory for making a decision for a new sorting principle during the W1st(C) condition, an interpretation supported by a number of earlier studies that reported dorsolateral prefrontal activities specific to working memory [6,11,12,24]. That the WCST task engages the working memory systems has already been proposed by many authors as we mentioned above.

As a minor source, S2 of M190, the primary sensorimotor area was activated. The activation in the primary sensorimotor area for hand might be related to some processing for the motor preparation. The S2 of M200, M300 and M370 were also found to be widely distributed in the frontal area, which might imply a complicated cognitive processing during this task, although their activities were not so large (Fig. 5).

In general, we found the specific activities of the frontoparietal network during the W1st(C) condition started from 200 ms after the presentation of cards. The activation of the frontoparietal network might be related to the operation of working memory system which is a critical processing in sorting cards. Insofar as we know, this is the first MEG study on the WCST to investigate the spatial and temporal course during the performance of the task.

4.2. The feedback presentation experiment

In the analysis of the feedback series, MEG differences between the responses to the wrong feedback and those to the correct feedback were found at 460–640 ms after the presentation of feedback signals, located in the dorsolateral prefrontal and the middle frontal gyrus (mainly Brodmann’s area 9, source 1). The inferior frontal gyrus was also activated in some subjects (source 2). As the processing of shifting attention to other categories and inhibition of the previous category might occur shortly after the presentation of the wrong feedback [22], the activity at 460–640 ms after the feedback signals in the dorsolateral prefrontal and middle frontal gyrus could reflect the processing of shifting attention. There is also the possibility that this was only a response to the ‘wrong’ signal itself, or only a response to surprise and an odd event, like the P300 component. A recent fMRI study found some transient increase of neural activities in the medial superior frontal gyrus and precuneus gyrus with the attention shift task, but no activities to the feedback itself without the attention shift requirement [31]. Moreover, a visual P300 component usually starts from 350 ms and ends at 500 ms with a peak at about 400 ms. The MEG response at 460–640 ms was a little delayed as a P300 potential. Therefore, the activities in the dorsolateral prefrontal and the middle frontal areas at 460–640 ms to the wrong feedback could reflect the shifting attention processing instead of a P300 component. We did not find the source location differences between the M460 to the feedback experiment and the M370 to the card presentation experiment. Both of the components were found to be widely distributed in the frontal area. This is not surprising, given that a widely spread area including the dorsolateral frontal, middle frontal, and inferior frontal areas was reported to be involved in working memory processing [8,35,36].

In summary, the present study proved the activation of the frontoparietal network, mainly at the supramarginal gyrus and the dorsolateral frontal region, during the performance of WCST across time streaming. The specific activities to the wrong feedback happened at 200 ms after the presentation of cards, and at 460 ms after the presentation of the feedback. There were no significant differences in location between the MEG activities to the card presentation and that to the feedback presentation. Our results suggested that both shifting attention to the wrong feedback signal and enhanced visual working memory to sorting shift condition of the card presentation occur in a broad frontal area at different time points.
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