The cerebellum’s involvement in the judgment of spatial orientation:
A functional magnetic resonance imaging study

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Abstract

A functional magnetic resonance imaging (fMRI) study was conducted to integrate the clinical observations of the impaired judgment of spatial orientation of cerebellar patients with recent theoretical discoveries about the role of the cerebellum in cognitive functions. Ten normal healthy male right-handed Chinese postgraduates consented to participate in this study. The experimental task employed was a modified version of Benton’s Judgment of Line Orientation Test, administered in a blocked fMRI study. The findings indicated activation of the cerebellar regions, the Hemisphere Lobules IV, VI and Crus I, while the subjects were performing the experimental task of the judgment of the orientation of lines. Furthermore, cortical regions were activated, including the bilateral precuneus (BA 7), the extrastriate regions (BA 19), and the bilateral prefrontal regions (BA 9, 10, 44, 46). The imaging data confirmed that the activity of the cerebellum is associated with judging spatial orientation. The theoretical and clinical implications of the findings are discussed.

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Keywords: Cerebellum; Spatial orientation; fMRI; Visuospatial function; Cognitive

Intact visual–perceptual function is the foundation of normal processing and organization of the enormous inputs from the visual world. It is one of the prerequisites for rapidly accessing semantic memory (Silverstein et al., 1996; Silverstein, Osborn, & West, 1998). Dysfunction of the ability to generate representations of segmented visual information could lead to reduced integration of visual stimuli with relevant stored memory. According to lesion studies, spatial perception is usually impaired by right parietal lesions (Lezak, 1995). This has been confirmed by functional magnetic resonance imaging (fMRI) studies (Ng et al., 2000, 2001). However, recently, there has been speculation that the judgment of spatial orientation could be subserved by a more widely distributed network than just the parietal regions.

Botez, Gravel, Attig, and Vezina (1985) found a number of cognitive deficits including visual–spatial impairments in a patient with chronic cerebellar ataxia after phenytoin intoxication. Difficulties with concept formation, learning of paired associates, visual–spatial abilities and general intellectual slowing were noted in patients studied by Kish et al. (1988). We speculated that the judgment of spatial orientation is subserved by regions beyond the parietals because we noticed that this judgment was impaired in two clinical cases of cerebellar stroke that spared the parietal regions. These cases were referred to our unit for neuropsychological assessment...
within 1 week after they were transferred to the rehabilitation hospital when their acute medical conditions had stabilized.

Case 1 was a 22-year-old right-handed Chinese man with 13 years of education who was suffering from a cerebellar AVM affecting the cerebellum bilaterally. Case 2 was a 38-year-old right-handed Chinese man with 11 years of education who was suffering from a cerebellar hemorrhage affecting the left cerebellum. The judgment of spatial orientation was measured by the Benton’s Judgment of Line Orientation Test (JLO), a visual measure of the judgment of spatial orientation (Montse, Pere, Carme, Francesc, & Eduardo, 2001). In this test, 30 test items, each containing two lines varying in their degrees of orientation (e.g., 80°), were presented to each participant. The participant was then asked to verbally indicate which numbers each pair of lines corresponded to in a radiating containing all possible line orientations with their corresponding degrees of orientation labeled. The results of the assessment indicated impairment in the judgment of spatial orientation by z scores of over 4 relative to their age peers (Lee, 2003). These clinical observations and the data of the published clinical studies contradicted the observation reported by Molinari, Leggio, and Silveri (2004) that there was no significant impairment in the performance on the JLO by their clinical subjects with cerebellar damage. The role of the cerebellum in the judgment of spatial orientation remains unclear.

Indeed, the notion that the cerebellum is exclusively involved in motor control has been challenged by studies of cerebellar damaged patients and by functional neuroimaging results (Desmond & Fiez, 1999). A number of functional imaging studies have reported changes in cerebellar activation during a variety of cognitive tasks, suggesting that this structure is involved in basic cognitive processes, such as working memory, implicit and explicit learning and memory, and language. New findings that have largely emerged from functional neuroimaging studies suggest that the cerebellum plays a role in multiple functional domains (e.g., Allen & Courchesne, 2003; Gos et al., 1996; Le, Pardo, & Hu, 1998; Paradiso, Andreason, O’Leary, Arndt, & Robinson, 1997; Townsend et al., 1999). Previous fMRI studies have reported activation of the posterior cerebellum in normal subjects during a visual selective attention task with no motor component (Allen, Buxton, Wong, & Courchesne, 1997), an attention-shifting task (Le et al., 1998), and spatial or temporal cuing tasks (Coull & Nobre, 1998).

To integrate the clinical observations of the impaired judgment of spatial orientation of our cerebellar patients with the recent theoretical discoveries about the role of the cerebellum in cognitive functions, we employed fMRI technology and examined if the cerebellum was involved in the judgment of spatial orientation in our study. Ng et al. (2000, 2001) studied neural activations associated with performing the JLO. Using 14 near-axial non-contiguous 7-mm thick slices, with a 0.7-mm interslice gap, covering the cortical regions, they observed a bilateral parietal lobe participation in visual–spatial processing in terms of making judgments of line orientation. In this study, we did full brain coverage, from the cortex to the cerebellum. The functional data obtained from the cortical regions would serve to validate our work if the observations of activations in the cortical regions were consistent and comparable with those in the published reports of Ng et al. (2000, 2001). We then inspected if the cerebellum played a role in judging spatial orientation.

1. Methods

1.1. Participants

We recruited 10 normal healthy male right-handed Chinese postgraduates (their ages ranged from 22 to 25 years) for this study. They had a normal visual field and attention, and were strongly right-handed, as judged by the handedness inventory devised by Snyder and Harris (1993). They did not have any history of neurological or psychiatric illness. Informed consent was obtained from all the subjects after the nature of the study was explained to them.

1.2. Experimental task

The experimental task (Ng et al., 2000) contained both control and experimental conditions. Under the control conditions, the subject was asked to judge whether two stimulus lines were on the same level. Since the lines were always horizontal, the decision did not involve angle judgment. Under the experimental conditions, the subject was asked to judge whether the two stimulus lines displaced with varying degrees of orientation matched the angles of the two highlighted lines in the exemplar. By contrasting the cerebral activity measured during the experimental conditions with that observed during the control conditions, a clear picture of the pattern of brain activation underlying the judgment of spatial orientation could be derived.

Matching responses were made with the right index finger and non-matching responses were made with the middle finger on a computer response pad. Motor and visual aspects of the task were controlled by a matched number of correct responses in the control and experimental conditions. The experimental task was administered in a blocked fMRI study to investigate if the cerebellum is involved during the judgment of spatial orientation measured by judgment of the orientation of lines. Each epoch represented one condition containing 15 trials and a 3-s instruction. To further dissociate neuroanatomical from cerebellar involvement in visual movement (Petit et al., 1996) in performing this experimental task, we used a stimulus exposure time short enough to control for eye movement (Fischer, 1987). Each stimulus was exposed for 0.25 s, with an interstimulus interval of 1.75 s when the subject could make the response. Each condition was repeated four times, giving a total of eight blocks in each run, the duration of which were 264 s. The stimuli were delivered through a goggles display system (Resonance...
The experiment was performed on a 1.5 T Magnetom Vision MRI scanner (Siemens, Erlangen, Germany) at the Chang Gung Memorial Hospital. Prior to the fMRI, the subject was visually familiarized with the procedures and the experimental conditions to minimize anxiety and enhance task performance. Following this familiarization, the subject lay supine on the scanning table and was fitted with plastic ear-canal molds. The subject’s head was immobilized by a tightly fitting, thermally molded, plastic facial mask that extended from the hairline to the chin. A single-shot T2*-weighted gradient echo planar imaging (EPI) sequence was used for the fMRI scans (slice thickness = 5 mm, in-plane resolution = 3.3 mm × 3.3 mm, and TR/TE/θ = 3000 ms/60 ms/90°). The field of view was 211 mm × 211 mm and the acquisition matrix was 64 mm × 64 mm. Twenty-four contiguous axial slices were acquired to cover the whole cerebellum and most of the cerebrum. The anatomical MRI was acquired using a T1-weighted, three-dimensional, gradient-echo pulse sequence. This sequence provided high-resolution images of the entire brain.

1.3. Scanning procedure

The experiment was performed on a 1.5 T Magnetom Vision MRI scanner (Siemens, Erlangen, Germany) at the Chang Gung Memorial Hospital. Prior to the fMRI, the subject was visually familiarized with the procedures and the experimental conditions to minimize anxiety and enhance task performance. Following this familiarization, the subject lay supine on the scanning table and was fitted with plastic ear-canal molds. The subject’s head was immobilized by a tightly fitting, thermally molded, plastic facial mask that extended from the hairline to the chin. A single-shot T2*-weighted gradient echo planar imaging (EPI) sequence was used for the fMRI scans (slice thickness = 5 mm, in-plane resolution = 3.3 mm × 3.3 mm, and TR/TE/θ = 3000 ms/60 ms/90°). The field of view was 211 mm × 211 mm and the acquisition matrix was 64 mm × 64 mm. Twenty-four contiguous axial slices were acquired to cover the whole cerebellum and most of the cerebrum. The anatomical MRI was acquired using a T1-weighted, three-dimensional, gradient-echo pulse sequence. This sequence provided high-resolution (1 mm × 1 mm × 1 mm) images of the entire brain.

1.4. Data analysis

The analysis of the imaging data was conducted using the SPM99 procedure (Wellcome Department of Cognitive Neurology, London, UK). Each participant’s T2*-weighted images were realigned to the first image of the series using a rigid-body transformation procedure and resliced using sinc interpolation adjusting for residual motion-related signal changes. A mean image was created from the realigned and unwarped time series data. The mean T2*-weighted images were spatially normalized via non-linear basis functions to the EPI template image, the stereotaxic space of which was based upon the Talairach and Tournoux system. The non-linear transformations for the mean T2*-weighted images were subsequently applied to the realigned MRI time series data. The data sets were then spatially smoothed by convolution with a three-dimensional Gaussian kernel (FWHM = 8 mm). Data were analyzed by modeling the experimental conditions using boxcar functions convolved with a hemodynamic response function in the context of the general linear model employed by SPM99. The resulting time series data across sessions were high-pass filtered with a cutoff of two block cycles to remove low frequency drift. The effect of global differences in scan intensity was removed by scaling each scan in proportion to its global intensity.

The contrast between conditions was examined by voxel-specific t-tests (SPM(t)) across all participants. The t-statistics were subsequently transformed to Z statistics to create a statistical parametric map (SPM(z)) of the contrast. The SPM(z) map was then interpreted by referring to the probabilistic behavior of Gaussian random fields. The regionally specific differences with an uncorrected threshold of p < 0.001 (with cluster size > 50 voxels) were considered statistically significant.

Maxima were localized on the normalized T1 structural template image and labeled using the nomenclature of Talairach and Tournoux by means of the TD database (Research Imaging Center, The University of Texas, Austin, TX). Anatomical labels (lobes, gyri) and Brodmann area (BA) designations were applied automatically using a three-dimensional electronic brain atlas (Lancaster et al., 1997).

2. Results

The performances of the 10 male subjects were 100% accurate under the control conditions. The accuracy of their performance under the experimental conditions was about 97%.

Cortical regions activated included the bilateral precuneus and the extrastriate regions. Activation of the bilateral prefrontal regions was also observed (Table 1 and Fig. 1). The pattern of activation observed in the cortical regions was largely consistent with the results reported by Ng et al. (2000). We then examined the activity recorded in the cerebellum and observed activation of the cerebellar regions while the subjects were performing the experimental task of judging line orientation (Fig. 1). The imaging data suggested bilateral activation of the cerebellum during task performance.

3. Discussion

Prompted by the impaired judgment of line orientation of our patients suffering lesions in the cerebellum that had spared the parietal regions, we conducted this fMRI study to examine the neural activity associated with this judgment. Neural activation were observed in regions including the extrastriate cortex (BA 19; for processing visual information), the precuneus (BA 7; for higher sensory integration and form perception), and the prefrontal regions (BA 9, 10, 44, 46; for making judgments). The pattern of neural activation at the cortical regions observed in our subjects was largely consistent with the results reported by Ng et al. (2001) study examining the role of the parietal lobe in spatial function. This consistency increased our confidence in the validity of our imaging data. The activation that we observed was bilateral, which indicated that not only the right hemisphere but also the left hemisphere were involved in the judgment of spatial orientation. This observation is consistent with the updated theory on spatial perception that both hemispheres participate in the process (e.g., Cook, Fruth, Meht, Regard, & Landis, 1994; Kosslyn et al., 1989), with the right parietal region playing an initial and dominant role and the left parietal region possibly being involved in other perspectives.
of spatial perception such as abstract geometrical pictures, image generation imaging and distracting visual information (Ng et al., 2000). We then examined the imaging results in the cerebellum and observed bilateral activation of the cerebellum, including the Hemisphere Lobules IV, VI and Crus I (Schmahmann, Doyon, Toga, Petrides, & Evans, 2000), when our subjects were engaged in the judgment of line orientation. These findings provide evidence of the role of the cerebellum in the judgment of spatial orientation.

The human cerebellum is characterized by a remarkable divergence and convergence of signals, and has physiological connections with all major divisions of the central nervous system (Brodal, 1978; Courchesne & Allen, 1997; Middleton & Strick, 1994; Schmahmann, 1996; Schmahmann & Pandya, 1997), receiving inputs and directing outputs to multiple cortical areas (Middleton & Strick, 1998). There are multiple closed-loop circuits between the cerebellum and the cerebral cortex, the main one being the cortico-ponto-cerebellar pathway. Through this pathway, the cerebral cortex inputs information to the contralateral cerebellum, which processes the information and returns it to the cerebra through cerebello-thalamo-cortical projections so that it can be processed mutually and nearly synchronously, making it possible for the cerebellum to process the mo-

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Note: BA, approximate Brodmann area; n, number of subjects; L, left cerebral hemisphere; R, right cerebral hemisphere.
Fig. 1. Functional maps. Normalized activation brain maps averaged across 10 male subjects demonstrating the statistically significant activations (uncorrected \( p < 0.001 \), cluster > 50) in making the judgment of line orientation. Planes are axial sections, labeled with the height (mm) relative to the bicommissural line. L, the left hemisphere; R, the right hemisphere.

tor function as well as participate in higher-order cognitive processing (Voogd, 2003). Indeed, neuropsychological abnormalities in patients with cerebellar cortical atrophy have included impaired cognition (e.g., Appoloni, Grafman, Schwartz, Massaquoi, & Hallett, 1993; Courchesne et al., 1994; Grafman et al., 1992; Landis, Rosenberg, Landis, Schut, & Nyhan, 1974; Molinari, Leggio, & Silveri, 1997; Pascual-Leone et al., 1993; Silveri, Leggio, & Molinari, 1994). These neuropsychological findings are consistent with the suggestion that the cerebellum is important for a range of behaviours beyond just motor function. The evidence provided by Yamamoto, Wagner, Hasler, and Sasaki (1983) and Yamamoto, Ypshida, Roshikawa, Kishimoto, and Oka (1992) that the cerebellum projects to the parietal cortex, together with the findings of Clower, West, Lynch, and Strick (2001) that the cerebellum provides second-order input to the inferior parietal lobe, make it anatomically possible for the parietal and cerebellar regions to work together in the judgment of spatial orientation.

The findings of this study are consistent with those of previous clinical studies by Bracke-Tolkmitt et al. (1989) and Akshoomoff, Courchesne, and Townsend (1997) that suggested the cerebellum was involved in visual–spatial function. Botez-Marquard and Botez (1993) reported a mild parietal-like syndrome with visual–spatial disturbances in OPCA patients. Wallesch and Horn (1990) reported visual–spatial disturbances in cognitive operations in three-dimensional space in patients who had tumors excised from the left cerebellar hemisphere. Visual–spatial dysfunction was also reported by Botez-Marquard, Leveille, and Botez (1994) following infarction in the territory of the left superior cerebellar artery. We observed impaired judgment of
line orientation in two patients suffering from cerebellar stroke. Botez et al. (1985) found visual–spatial impairments in a patient with chronic cerebellar ataxia after phenytoin intoxication. Difficulties with visual–spatial abilities were noted in patients studied by Kish et al. (1988, 1994). Our work thus compliments previous functional imaging and clinical studies, and adds to the literature showing that the cerebellum together with the parietal regions are involved in the judgment of line orientation as measured by the JLO.

The data reported above, however, are inconsistent with a study by Molinari et al. (2004) that found no significant impairment in the performance on the JLO by clinical subjects with cerebellar damage. An examination of their data indicated that the subjects who were suffering from focal left cerebellar lesions or idiopathic cerebellar ataxia did indeed commit more errors when performing the JLO, though the difference did not reach a significant level, which could relate to the power of their study. Further examination of Molinari’s data suggested that the patients with focal right cerebellar lesions performed as well as the control subjects on the JLO, which seems to contradict our finding that the right cerebellum is involved in the judgment of spatial orientation. Since the right parietal cortex is dominant in spatial perception, and given the contralateral connection between the cerebral and cerebellar cortices, we speculated that the left cerebellum–right parietal projection might play a critical role in the judgment of spatial orientation. Therefore, lesions in the left or bilateral cerebellum would produce impaired performance on the JLO, as observed in our study, as well as in some previous studies examining the impact of left or bilateral cerebellar lesions on the judgment of spatial orientation. The right cerebellum–left parietal connection, on the other hand, may play a more supplementary role when a subject performs the JLO, and therefore, a lesion to the right cerebellum, which would leave the left cerebellum–right parietal connection intact, may preserve the function of the judgment of line orientation. Verification of this speculation requires further research. In this connection, it would be interesting to study if there were a threshold of lesions at or above which behavioral changes in the judgment of spatial orientation would be observed. Indeed the clinical phenomenon of crossed cerebral–cerebellar diaschisis has implied the speculated dose–response effect (Komaba, Osono, Kitamura, & Katayama, 2000; Miyazawa et al., 2001).

The inconsistent findings concerning the role of the cerebellum in the judgment of spatial orientation could be related to the incomplete reporting of the precise location and severity of the cerebellar lesions, compounded by the small sample sizes employed in these reported clinical studies. A more stringent control and reporting of the lateralization and localization of the lesions is essential to ensure the repeatability of the data in this area and hence help develop a much clearer picture of the role of the cerebellum in judging spatial orientation. Indeed, specific areas of the cerebellum critical for the judgment of line orientation might not be affected in all studies, and the level of severity of the lesion might not have yet reached the critical level necessary for impaired performance.

In addition to accurate reporting of the site and size of lesions, a larger-scale clinical study would be required to confirm the critical role of the cerebellum in visual–spatial processing. Though we observed impaired judgment of spatial orientation measured by the JLO in our two cerebellar patients, the size of the sample is considered to be very small for confirmatory findings. Other clinical studies, limited by practical constraints, also employed a small sample size and yielded inconsistent findings on the role of the cerebellum in the judgment of spatial orientation.

The experimental conditions are more difficult relative to the control conditions. This gives rise to the possibility that the cerebellar activation observed in our study could be related to the increased demand of the experimental task. This alternative explanation of the findings requires verification in future research. Nonetheless, Prabhakaran, Narayanan, Zhao, and Gabrieli (2000) suggested that the pattern of activation reflects the unique cognitive nature of the task rather than simply the cognitive load. Furthermore, our two clinical cases obtained normal scores on the Hooper Visual Organisation Test, a test of visual–spatial processing, which suggests that the cerebellum should play a unique role in the judgment of spatial orientation.

While we attempted to control for the potential confounds from eye movements in our study by using a very brief stimulus presentation time, eye movements could have been initiated, though not completed, during the stimulus presentation. This could have added unknown error variance to our findings, compounded by the unknown error contributed by the timing precision of the software program we used. Nonetheless, Petit et al. (1996) suggest that eye movements are associated with the activation of the cerebellar vermis. In our study, no significant activation of the vermis was observed. Gender differences on spatial orientation were not investigated in our study. Since gender differences for spatial capabilities have been widely reported, and the effect of gender differences on the judgment of spatial orientation may contribute to the inconsistent findings reported, it is a topic worth further investigation. Moreover, other studies, such as a real-time fMRI study to unveil the temporal sequence of neural activity during the judgment of spatial orientation, would provide a better understanding of the different roles played by each of the neural correlates in the circuits recruited for the judgment of spatial orientation. Could the role of the cerebellum in visual–spatial processing be one of monitoring and adjusting the acquisition of the sensory data for precise operation by the parietal circuits and the rest of the cortical circuits subserving the judgment of spatial orientation (Bower, 1997)? Could the cerebellum serve as a regulatory organ for the adaptive control mechanism of visual–spatial processing (Bö, 1993)? Clower et al. (2001) suggest that the cerebellar projection to the posterior parietal cortex may provide signals that contribute to the sensory recalibration that occurs dur-
ing the adaptive process. Clinically, since spatial perceptual difficulty could be an early sign of cerebellar dysfunction, the association between damage to the cerebellum and impaired judgment of spatial orientation requires further investigation. The early diagnosis of cerebellar dysfunction may be enabled by the evaluation of spatial perception.

Our studies illustrate how IMRI and clinical data can be integrated to further knowledge of the realm of neuropsychology, so that the behavioral impact of neurological diseases can be better understood. Clinical studies have been a powerful method for studying brain and behavior relations. However, the specific area of the cerebellum involved in the judgment of spatial orientation might not be affected in some cases, and patient studies are not without complications and controversy, likely related to the heterogeneity of the clinical subjects interacting with other medical and psychosocial factors. Correlating structure and function through imaging and clinical studies could enhance our understanding of brain-behavior relationships.

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