Involvement of the Cerebellum in Semantic Discrimination: An fMRI Study

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Abstract: We investigated, using functional magnetic resonance imaging (fMRI), whether semantic discrimination, an inner linguistic task without overt articulation, can elicit activation in the cerebellum. Six subjects performed three semantic tasks with different loads of discrimination while being scanned. All three semantic tasks activated distributed brain areas, including the right posterior inferior cerebellum. Much stronger activation was found in the cerebellum in more difficult tasks, in terms of the activation volume and signal intensity. These results suggest that the cerebellum activation is involved in semantic discrimination and is modulated by discrimination difficulty. *Hum. Brain Mapping 18:208–214, 2003.* © 2003 Wiley-Liss, Inc.

Key words: cerebellum; language; semantic discrimination; MRI; fMRI

INTRODUCTION

The cerebellum has long been viewed as a coordinator of autonomic and somatic motor functions [Holmes, 1939]. This traditional view is increasingly being challenged by both neuroimaging and psychophysical results demonstrating considerable cerebellar activity during non-motor tasks [Schmahmann, 1997]. For example, the cerebellum has been shown to be strongly active during tasks involving the perception of temporal order [Ivry and Keele, 1989], visual attention [Allen et al., 1997], executive planning, and spatial reasoning [Bracke-Tolkmitt et al., 1989; Grafman et al., 1992; Kim et al., 1994; Parsons et al., 1995], as well as semantic word generation [Petersen et al., 1989].

Over the last several years, we have been investigating the possibility that an overarching sensory data-related function might underlie the ever more diverse set of tasks reported to invoke cerebellar activity [Bower, 1997a,b]. Specifically, we have proposed that the function of the cerebellum may involve the coordination of the sensory data used by other regions of the nervous system. Originally emerging from anatomical, electrophysiological, and behavioral studies

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of tactile regions of the rat cerebellum [Bower and Kassel, 1990], support for the hypothesis was first generated in humans by showing that the lateral (dentate) nucleus is strongly activated when fine finger movements are used for tactile sensation and discrimination, but not with fine finger movements alone [Gao et al., 1996; Parsons et al., 1997]. Subsequent imaging studies have shown similar differential patterns of activity in the cerebellar associated inferior olive [Pu et al., 1998] and red nucleus [Liu et al., 2000].

One of the more important implications of the "sensory control hypothesis" is that the cerebellum provides a "metasystemic" [MacKay and Murphy, 1979] support function for the rest of the nervous system, and therefore that cerebellar activation should not be interpreted as implying direct involvement in the particular task under study. Thus, for example, while a tactile discrimination task might induce cerebellar activity [Gao et al., 1996], tactile discrimination itself is almost certainly a function of cerebral cortex and not the cerebellum. Accordingly, we have proposed that the cerebellum has no direct responsibility for any behavior, whether motor coordination, discrimination, or cognition, but instead facilitates the computational efficiency of those other neural systems that do actually perform these computations [Bower, 1997a,b].

We believe that the broad and growing set of tasks that induce cerebellar activity [Schmahmann, 1997] is strong evidence for a metasystemic cerebellar function. New interpretations of the nature of cerebellar cortical processing [Bower, 2002], are also consistent with such a function, as is the remarkable uniformity of cortical architecture in cerebellar regions receiving widely different types of input [Bower, 1997a]. However, the specific idea that the cerebellum performs a role in support of computation in other regions of the brain is also testable in its own right.

We have employed a semantic discrimination task to examine the effect of increased task difficulty on cerebellar activity. We have previously proposed [Bower, 1997b] that the amount of activity induced in the cerebellum should be directly related to the sensory requirements of a particular computation, and therefore that cerebellar activity should increase as a particular task becomes more difficult. We have tested that idea here by employing three linguistic semantic tasks with different loads of discrimination. Despite the fact that none of the tasks involved overt articulation, considerable activity is generated in the cerebellum. As predicted, the amount of cerebellar activity increases with task difficulty.

SUBJECTS AND METHODS

Subjects

Six healthy native Chinese speakers (five men and one woman, 21–36 years old) without any history of psychiatric and neurological problems participated in the study. All participants were right handed as determined by standardized inventory in the Chinese version [Li, 1983].

MRI equipment and imaging procedure

Experiments were performed on a 1.5 T Siemens SONATA MRI scanner at Anzhen Hospital of Capital Medical University (Beijing, China). Conventional anatomical images were collected with a multiple-slice T_1-weighted spin echo sequence (TR/TE = 442 msec/15 msec, field of view (FOV) = 19.2 × 19.2 cm, slice thickness = 5 mm, skip = 1 mm, imaging matrix = 256 = 256). Functional T_2*-weighted MR images, which covered the entire brain, were acquired using a gradient-echo echo planar imaging pulse sequence (TR/TE = 3,000 msec/60 msec, FOV = 19.2 × 19.2 cm, slice thickness = 5 mm, skip = 1 mm, matrix = 128 × 128, 20 slices). Finally, a FLASH 3D sequence (TR/TE = 30 msec/1.17 msec, FOV = 25.8 × 25.8 cm, thickness = 1.3 mm, skip = 0.26 mm, imaging matrix = 192 × 256) was used to collect a 3-D whole brain volume.

Semantic discrimination tasks

Chinese words were back projected onto a screen that could be visible from inside the scanner (via a mirror mounted on the head coil). In each trial, two target Chinese words were presented horizontally in the upper panel of the screen for 1.5 sec, followed by a third probe word that was presented in the lower panel of the screen for 3 sec. Subjects were asked to indicate which one of the target words was more semantically related to the probe word, by pressing the right button if the correct target was on the right or the left button if the correct target was on the left. There were three types of task. In task A, one of the target words belonged to the category, which the probe word referred to. For example, target words were 水仙(narcissus) and 排球(volleyball), and the probe word was 花卉 (flower). In task B, only one of the target words was semantically related to the probe word. For example, the target words were 商人(merchant) and 火车 (train), and the probe word was 地铁(subway). In task C, both target words were se-

mantically related to the probe words. For example, the target words were 椅子(chair) and 课桌(desk), and the probe word was 长凳(bench).

All subjects participated in two runs of the experiment. There were six task blocks in each run, two blocks for each type of tasks. Each block lasted 45 sec and consisted of 10 trials. Each task block was interleaved by a 27-sec fixation period, in which the subjects were asked to passively view the cross-hair fixation.

To control irrelevant factors, the Chinese words used for stimuli were matched on the dimensions of the number of strokes, familiarity, and frequency of usage. Subjects were instructed on the task prior to scanning and provided with a brief practice period.

The stimuli presentation and behavioral recording were controlled by an IBM personal computer using DMDX software [Forster and Forster, 1990], adapted for the purpose of fMRI experiments. The reaction times (RT) were collected for all subjects when they performed each task (A, B, and C). The difference in RT will be used as one of the important factors in judging the difficulty level of the tasks used in this fMRI study.

Data analysis

AFNI (analysis of functional neuro-images) [Cox, 1996] was used for image display and data analysis. The first four images from each slice were discarded to assure that the MRI signal had reached steady state. Functional MR images were co-registered to remove head-motion artifacts and normalized according to the standard coordination defined by the Talairach and Tournoux atlas [1988]. The images were then re-sampled and smoothed with an isotropic Gaussian kernel (FWHM = 8 mm) to enhance the signal-to-noise ratio. The voxel size for this procedure was $3 \times 3 \times 3$ mm^3.

Using the 3-D deconvolution program of AFNI, the impulse response functions were estimated and convolved with the stimulus functions to yield the estimated response. The F statistic was then calculated for each voxel to test the fitness between the observed time series and the estimated response. The single impulse at the beginning of each block was used to represent the whole block in the 1D files used in the Deconvolution program. Those voxels whose F values were equal to or greater than 1.833 ($P = 0.035$) were defined as task-relevant, and were superimposed on the anatomic images to produce activation maps. Finally, these data were averaged over voxels within ROI (region of interest) and then averaged over subjects. The difference in reaction time (RT), activation volume, and intensity for each type of the three tasks were analyzed by one-way ANOVA, respectively.

RESULTS

The mean reaction times (averaged over six subjects) in tasks A, B, and C were 885 ± 159 (msec), 1,035 ± 153 (msec) and 1,515 ± 270 (msec), respectively. There were significant differences across the three tasks (F (2, 15) = 16.007; $P = 0.0001$). Post-hoc analysis revealed a significant difference between task C and each of other two tasks (task C vs. task A: $P = 0.0001$; task C vs. task B: $P = 0.003$), but not between task A and task B ($P = 0.646$). These data show that the task difficulty is equivalent between tasks A and B; however, the level of difficulty in task C is significant higher than that in both tasks A and B.

Figure 1 shows mean group activation maps for each type of tasks. As can been seen in Figure 1, all three tasks (A, B, and C) activated a large set of brain areas. Table I provides Talairach coordinates, probabilities (number of subjects showing activation) and mean F values of activation for each type of tasks. While activation in task A and task B were similar, in task C probability of activation in most observed areas was greater than that in task A and task B. Moreover, significant activation was observed in all subjects in the right posterior inferior cerebellum in task C, but only few subjects showed activation in this area in task A and task B.

Figure 2 represents the mean activation volume (averaged over six subjects) of each type of tasks in the right posterior–interior cerebellum (Talairach coordinates: −10, 80, −26). Our data shows that the mean activation volume in tack C is approximately 10 times larger than that in both tasks in A and B. Overall difference across the three tasks was statistically significant (F (2, 15) = 46.386; $P = 0.0001$). Post-hoc test showed a significant difference between task C and each of the other two tasks (A and B, both $P = 0.0001$); the difference between task A and B was not significant ($P = 1.0$).

As demonstrated in Figure 3, the analysis of the mean activation intensity (percent signal changes between task with control, averaged over six subjects) also revealed a significant difference across three tasks (F (2, 15) = 27.17, $P = 0.0001$). Our data also show that the mean activation intensity in task C is approximately two times stronger than that in both tasks A and B. Post hoc analysis again indicated a significant difference between task C and each of the other two tasks (A and B, both $P = 0.0001$), but not between task A and task B.

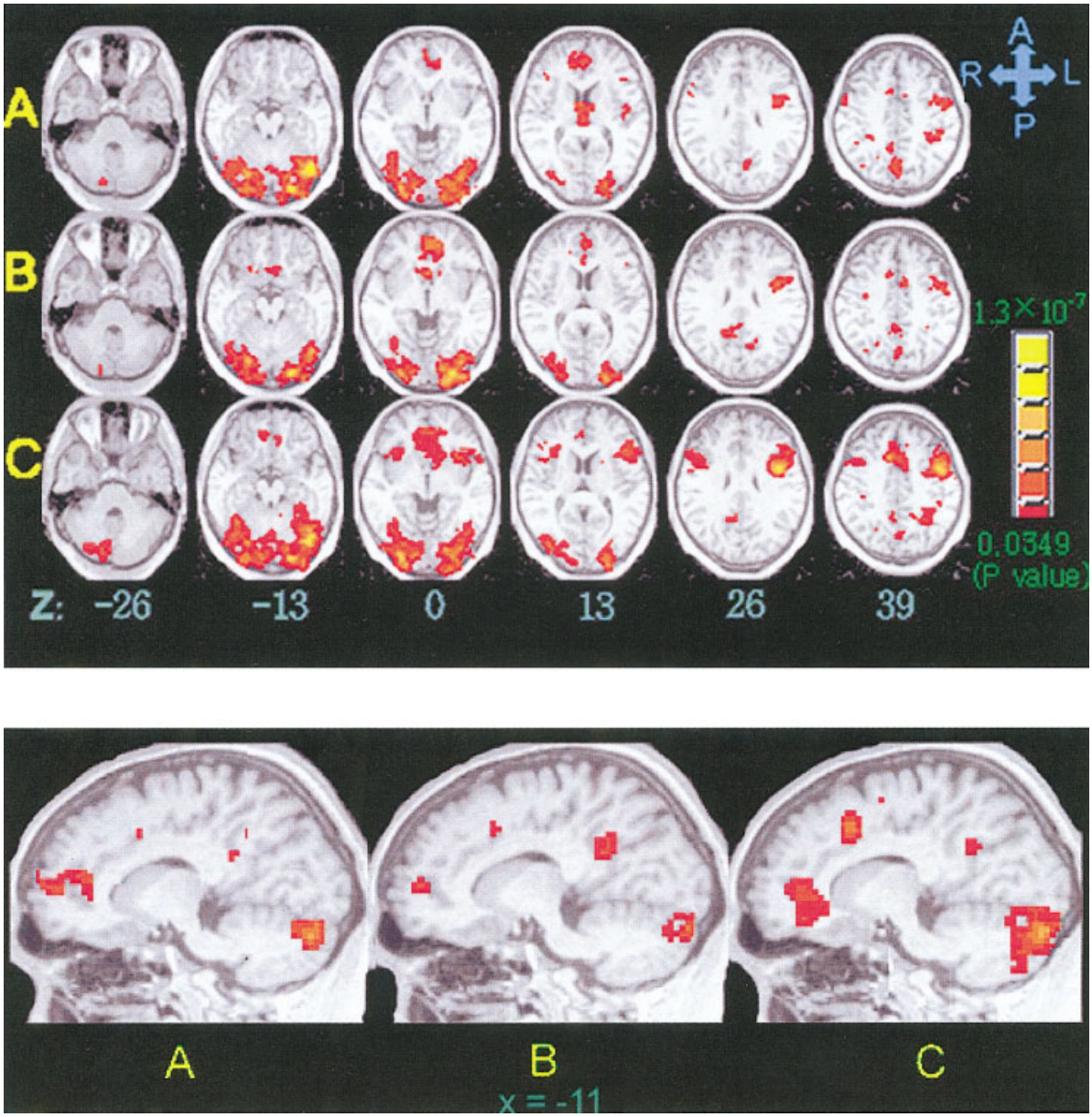

Figure 1.
Mean group activation maps for each type of tasks (**A–C**). **Top:** Whole-brain activation. **Bottom:** Activation in the right cerebellum. Color scale indicates significance of activation (*P* value).

DISCUSSION

The present study demonstrates that there are multiple sites of brain activation associated with semantic discrimination. This result is consistent with a number of neuroimaging studies using both logographic Chinese scripts as well as alphabetic scripts [Tan et al. 2000; Vandenberghe et al., 1996]. With respect to the cerebral cortex, a major focus of the activation seen is in frontal regions as also previously reported [Roskies et al., 2001]. In keeping with previous studies [Klein et al., 1999; Roskies et al., 2001], we also found considerable activation in the right cerebellar cortex.

The specific issue of interest to the present study was the extent to which brain activity scaled with semantic task difficulty. Such an effect has previously been shown for the frontal cortex [Roskies et al., 2001] and that effect is also seen in our data. However, the results presented here are the first direct demonstration of a similar scaling in cerebellar activity during a

TABLE I. Talairach coordinates for activated areas, probability, and mean value F of activation in each type of tasks (A–C)

Brain region	Talairach coordinates (center of mass) (x, y, z)	Number of subjects activated in each task (C/B/A)	F
Right post inferior cerebellum	−10, 80, −26	6/3/2	3.008
Left middle gyrus of frontal lobe (BA 9)	41, −7, 32	6/6/6	5.889
Broca's area (BA 45)	37, −14, 0	6/4/4	2.810
SMA (BA 6)	−5, −16, 44	6/6/6	4.426
Left extrastriate area (BA 18, 19, 37)	32, 81, −7	6/6/6	5.378
Right extrastriate area (BA 18, 19, 37)	−31, 87, −7	6/6/6	4.875
Precentral gyrus (BA 6)	42, 6, 53	6/6/5	4.011
Superior parietal lobue (BA 7)	29, 58, 47	6/6/6	4.280
Left insula (BA 13)	30, −16, 2	6/6/5	3.135
Anterior cingulate/medial frontal gyrus (BA 11, 24, 32)	−3, 39, 0	6/4/6	3.111
Precuneus (BA 7)	0, 70, 43	6/5/6	2.218
Wernicke's area (BA 22)	57, 32, 17	3/2/3	1.891

language task although evidence for such an effect was published in a study by Roskies et al. [2001] focused on the involvement of the left inferior frontal cortex in an English semantic discrimination task.

As is generally the case with many modern cerebellar imaging studies, the significance of cerebellar activation during language processing remains controversial. Viewed in the more traditional motor context [Holmes, 1939], some investigators have proposed that cerebellar activation is related to movement associated with voice production [Petersen et al., 1989; Petrides et al., 1993, 1995]. A direct relationship to voice production is not likely in the current studies, as no overt articulation was involved in any of the three tasks. While some have suggested that cerebellar activity in overtly non-motor tasks could be related to phantom movement effects [Decety et al., 1990; Parsons et al., 1995], it is not clear why phantom cerebellar activity would scale with task difficulty. Required

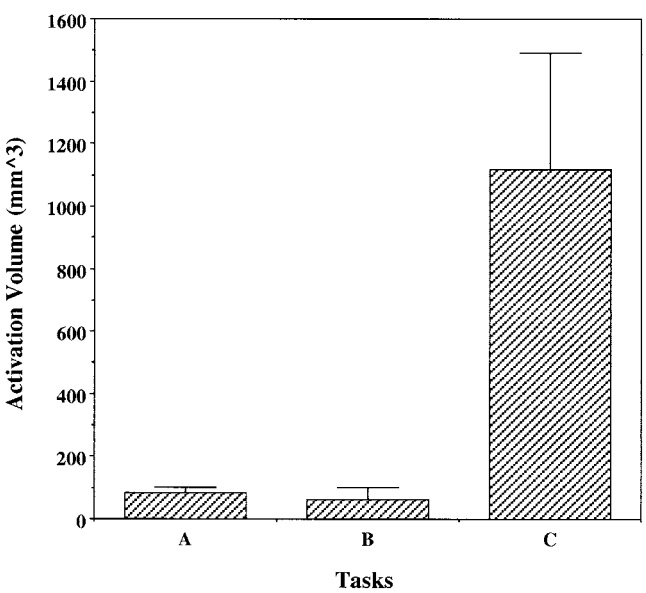

Figure 2.
Mean activation volume in the right posterior–inferior cerebellum (Talairach coordinates: −10, 80, −26) for each type of task.

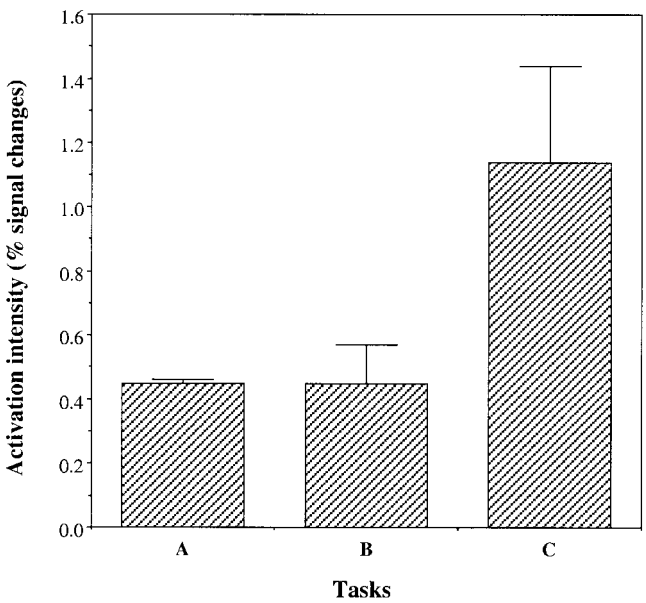

Figure 3.
Mean activation intensity in the right posterior-inferior cerebellum (Talairach coordinates: −10, 80, −26) for each type of task.

movements of the left and right hands were also counterbalanced across all three tasks. It is also unlikely that the very large differences in cerebellar activation between the easy and more difficult tasks can be accounted for by differences in the response reaction times.

In the absence of evidence for a direct association of cerebellar activity with overt movement production, it seems more likely that the cerebellum is contributing to some computation more directly involved in the language task itself. Other researchers, noting cerebellar activation in non-motor tasks, have suggested that the cerebellum may provide a pure language function [Fiez et al, 1992; Gasparini et al., 1999]. However, as discussed in the introduction, it is our view that the cerebellum is more likely to be involved in a support function. This argument is based, in part, on the lack of evidence that cerebellar patients have difficulties with language interpretation, but also on our analysis of cerebellar involvement in other systems [Bower, 1997a,b]. We believe that the data presented here provide further support for this idea demonstrating a correlation between task difficulty and the amplitude of cerebellar activation. In fact, we have previously predicted [Bower, 1997b] that the amount of activity induced in the cerebellum should be directly related to the sensory requirements of a particular computation, and therefore that cerebellar activity should increase as a particular task becomes more difficult.

The suggestion that the cerebellum may be involved in the coordination of the sensory data used by other regions of the nervous system as they compute was actually first developed in the context of the rat somatosensory system [Bower and Kassel, 1990; Gao et al., 1996; Parsons et al., 1997]. In this case, we suggested that the control of somatosensory data is accomplished through direct modulation of the positioning of tactile receptors in the sensory periphery during task performance [Bower, 1997a,b], a proposal consistent with patterns of cerebellar activity recorded in rats during tactile sensory exploration [Hartmann and Bower, 2001]. In the case of the semantic tasks studied here, it is possible that the cerebellum is involved in monitoring the visual signals through which the subject is informed of the semantic task, but it is also possible, as suggested by the connectivity data of Middleton and Strick [2001], that the lateral hemispheres of the human cerebellum has a direct modulatory effect on processing in frontal cortex. This interpretation is consistent with the largely lateral location of cerebellar activity in this task.

While the short format of this report does not allow a complete discussion of these issues, viewing the cerebellum as a structure in support of computation in other regions of the brain has important implications for the interpretation of imaging data. Over the last few years, individual reports of cerebellar activation in an ever wider range of tasks has largely been interpreted as evidence that the cerebellum plays a specific role in whatever particular behavior is being studied [Schmahmann, 1997]. For example, if a lesion causes motor discoordination, the cerebellum is a motor control device [Bastian and Thach, 1995]. If the cerebellum is activated during a task involving timing, it is involved in the control of timing [Jueptner et al., 1995]. If imaging and cerebellar damage is correlated with attention deficits, then the cerebellum is involved in coordinating shifts in attention [Courchesne et al., 1994]. If cerebellar lesions produce deficits in classical conditioning, then the cerebellum is responsible for classical conditioning [Thompson, 1988]. Cerebellar activation during language tasks suggests a direct role for the cerebellum in language processing [Fiez et al., 1992; Gasparini et al., 1999]. If, instead, the cerebellum provides a "metasystemic" [MacKay and Murphy, 1979] support function for the rest of the nervous system, then cerebellar activation does not imply direct involvement in the particular task under study. The current study extends this concern about the interpretation of cerebellar imaging data to include the importance of determining the relative difficulty of the different tasks being performed. The degree of difficulty, and thus the data requirements for a task may be as important as the task itself in determining the degree of cerebellar involvement.

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