Specific Cerebellar Activation During Braille Reading in Blind Subjects

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Abstract: The traditional view that the cerebellum is involved only in the control of movements has been changed recently. It has been suggested that the human cerebellum is involved in cognition and language. Likewise, besides cortical activity in sensorimotor and visual areas, an increased global activation of the cerebellum has been revealed during Braille reading in blind subjects. Our purpose was to investigate whether there is cerebellar activation during Braille reading by blind subjects other than sensorimotor activation related to finger movements. Early blind and normal sighted subjects were studied with functional magnetic resonance imaging (fMRI) during Braille reading, tactile discrimination of nonsense dots, dots forming symbols, and finger tapping. The experiments were done in block design. Echo planar imaging sequences were carried out on a 1.5-T MR scanner. All blind individuals reading Braille showed robust activation of the posterior and lateral aspects of cerebellar hemispherical lobules Crus I bilaterally but more predominately on the right side. Additionally, activation was present in the medial cerebellum within lobules IV, V, and VIIIA, predominantly on the right. Discriminating nonsense dots did not reveal any activation of Crus I, but did reveal activation within the medial part of lobules IV, V, and VIIIA, predominately on the right. Analysis of sighted subjects during reading of printed text revealed activation of the posterolateral cerebellar hemisphere in Crus I bilaterally, predominantly on the right. Tactile analysis of dots representing symbols revealed an activation in lobules IV and VIII and in right Crus II but not in Crus I. In conclusion, parts of cerebellar activation during Braille reading in blind subjects (i.e., within lobules IV, V, and VIII) overlap with the known hand representation within the cerebellum and are likely related to the sensorimotor part of the task. Cerebellar activation during Braille reading within bilateral Crus I may be due to language processes or inner speech similar to those found during text reading in normal sighted subjects. Object recognition did not account for Crus I activation. *Hum. Brain Mapp.* 22:229–235, 2004. © 2004 Wiley-Liss, Inc.

Key words: fMRI; cerebellar function; Braille reading

INTRODUCTION

For many years, it was considered that the cerebellum was involved only in sensorimotor processes. Recent findings

suggest that the human cerebellum may be involved in various cognitive and language functions [Desmond et al., 1998; Gruber, 2001; Schmahmann and Sherman, 1997]. Both human lesion and functional brain imaging studies indicate possible involvement of the cerebellum in various higher and cognitive functions, including planning behaviour [Grafman et al., 1992; Neau et al., 2000], memory [Appollonio et al., 1993; Desmond et al., 1997; Mandolesi et al., 2001], visuospatial perception [Botez-Marquard et al., 1994; Neau et al., 2000], and attention [Allen et al., 1997; Le et al., 1998].

Other lesion studies in cerebellar patients revealed a significant role of the cerebellum in language processes [Fiez et al., 1992; Fiez and Raichle, 1997; Gebhart et al., 2002; Silveri

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et al., 1994]. Functional MRI (fMRI) studies in healthy volunteers suggest that the posterior cerebellar hemispheres are of particular importance.

Braille characters are used to form words and sentences in a manner similar to that with written letters. Braille texts therefore demonstrate a language system with a different way of perception. On this background, the question arose, whether part of the reported upregulation of cerebellar activity during Braille reading might be due to language performance. An increased global activation of the cerebellum has been revealed during Braille reading [Sadato et al., 1998]. This activation is related commonly to increased processing of somatosensory feedback during Braille reading compared to that in simple finger movement.

Increased cerebellar activation during Braille reading may also be related to language function of the cerebellum. To address this question in this fMRI study, we used Braille text, nonsense dots, and simple motor conditions as active conditions in early blind volunteers, as well as Braille dots formed to symbols, Braille text, and simple motor task in normal sighted volunteers. These results were compared to visual language perception in sighted volunteers.

SUBJECTS AND METHODS

Subjects

In total, 12 blind subjects (6 men, 6 women; mean age, 53 years; age range, 24–80 years) were studied. All subjects were right-handed, native German speakers, and had a history of peripheral blindness. Of 12 subjects, 9 were congenitally blind and 3 had minimal light perception before becoming blind early in life. All subjects had no residual light perception. They started to learn Braille at a mean age of 8 years, starting between 6 and 15 years of age. The Braille reading skills were judged by each subject on a scale from 0–10 (0, no Braille reading ability and 10, excellent reading ability). The range in blind subjects was 5–10. All blind subjects used the right hand to read Braille.

As a control group, 12 normal sighted right-handed subjects (5 men, 7 women; mean age, 36 years; age range, 20–66 years) were imaged under the same experimental conditions and additionally during reading a written text and detecting dots presenting figures. No sighted volunteer was able to read Braille. No subject showed pathologic brain structure.

Informed written consent was obtained before scanning. The study was approved by the local ethics committee.

Experimental Design

All MR images were acquired using a 1.5-T MR (Sonata; Siemens, Erlangen, Germany) with a standard headcoil. A 3D FLASH sequence (TR = 10 msec, TE = 4.5 msec, flip angle = 30 degrees, field of view [FOV] 240 mm, matrix 512, slice thickness 1.5 mm) was acquired for individual coregistration of functional and structural images. Blood oxygenation level-dependent (BOLD) contrast images were acquired using a gradient-echo echo-planar technique (TR

= 3,300 msec, TE = 50 msec, flip angle = 90 degrees, FOV 240 mm, matrix 64) with 34 transversal slices with a thickness of 3 mm and 0.3-mm slice gap. Three dummy scans were eliminated before data analysis.

Each blind subject carried out three functional conditions. Standard Braille words (condition 1) and nonsense dots (condition 2) were presented on hard paper, which was placed on the subjects abdomen and could be reached easily by the reading hand. The subjects started reading after an acoustical cue and read the text in a speed according to their own reading ability. The factorial text consisted of common words. No response was requested during scanning but the subjects had to give a summary of the read text after the scan. Nonsense dots were in lines in a randomly ordered pattern according to real Braille word arrangement. In addition, a finger-tapping task (condition 3) was carried out with the right hand, opposing the thumb to every other finger after each acoustic cue.

Each sighted subject carried out four conditions. They had to discriminate dots presenting symbols like circles, arrows, crosses, and houses (condition 1) and Braille dots (condition 2). They had to carry out finger tapping with the right hand compared to rest (condition 3) and to read a written factorial text compared to senseless characters (condition 4), which was presented on a screen using a beamer standing outside the MR cage. The easy narrative text was the same used for the blind subjects in Braille characters; it was part of a children's book.

The conditions were run from 1 to 3 and 4. The stimuli were presented in a block design and alternated with resting periods every 34 sec. Each run was divided into 6 epochs. Before running the experiment, it was checked that subjects could hear the auditory commands for start and stop within the scanner. To avoid nonspecific activation, subjects were asked not to make any sort of response or reading aloud during the experiment. The eyes were closed during all conditions except the reading condition in sighted subjects.

Data Analysis

For data analysis, SPM 99 software (Wellcome Department of Cognitive Neurology, London, UK) was used. Before statistical analysis, images were realigned utilizing the sinc interpolation and normalized to the standard stereotactic space corresponding to the template from the Montreal Neurological Institute (available online at <http://www.mrc-cbu.cam.ac.uk/Imaging/Common/mnispace.shtml>; updated 14 February 2002). Bilinear interpolation was applied for normalization. The images were smoothed with an isotropic Gaussian kernel of 9 mm for group and 6 mm for single-subject analysis. A voxel-by-voxel comparison according to the general linear model was used to calculate differences of activation between active and resting condition. The model consisted of a boxcar function convolved with the hemodynamic response function (hrf) and the corresponding temporal derivative. High-pass filtering with a cut-off frequency of 120 sec and low-pass filtering with the hrf was applied.

For group analysis, single subject contrast images for every condition against resting condition were entered into a random effects model. Significant signal changes for each contrast were entered into a one sample *t*-test [Friston, 1995]. The resulting set of voxel values for each contrast constituted a SPM of the *t* statistic. The threshold was set to $P < 0.05$ (corrected for multiple comparisons).

For analysis of specific activation in blind subjects during Braille reading, a random effects analysis comparing conditions 1 and 3 (Braille reading and finger tapping, respectively) was carried out. The resulting contrast images were taken to the second level analysis and entered into a two-sample *t*-test. The threshold of the *t*-statistic was set to $P < 0.05$. For the sighted group, a random effects analysis comparing the conditions 2 and 3 (Braille reading and finger tapping, respectively) as well as condition 1 and 3 was carried out. The resulting contrast images were taken to the second-level analysis and entered into a two-sample *t*-test. The threshold of the *t*-statistic was set to $P < 0.05$. To evaluate differences in sighted and blind subjects the contrast images of Braille reading in both groups were taken into a two-sample *t*-test. The threshold of the *t*-statistic was set to $P < 0.05$. Concerning the Braille task, second-level analysis was performed on each group.

For analysis of specific activation in sighted subjects during Braille reading and tactile discrimination of dots forming symbols, a random effects analysis of the two tasks was carried out. Additionally, we created individual contrasts for every blind subject (Braille reading > nonsense dots).

Cerebellar lobules were defined according to the 3D MR atlas of the human cerebellum developed by Schmahmann and colleagues [2000] and the cerebellar nuclei according to the 3D MR atlas of the human cerebellar nuclei developed by Dimitrova and colleagues [2002]. The lateral extent of the vermis is difficult to define, particularly within the anterior lobe [Schmahmann et al., 2000]. As an approximation, vermal activation was defined as activation within an x-range of -10 mm and 10 mm. Activation more laterally than 10 mm from the AC-PC line were defined as activation within the cerebellar hemispheres.

RESULTS

During Braille reading, group analysis of all blind individuals revealed robust activation of cerebellar hemispherical lobule Crus I bilaterally with a right pronouncement (Fig. 1a). Additionally, activation was present in the medial cerebellum within both the anterior and posterior lobes, the medial parts of hemispherical lobule V extending into cerebellar hemispherical lobule VI, and in lobule VIIIA. Activation was present bilaterally, predominantly on the right. Within cerebellar nuclei, activity in the right and less strong in the left dentate nucleus was revealed (coordinates were $x, y, z = 20, -56, -27$ mm and $-19, 56, -27$ mm). The activity in the vermis clustered in parts of lobules V, VI, and VIII.

Discriminating nonsense dots did not lead to any activation of Crus I. Activation was found within the medial part of anterior lobule V with extension into cerebellar hemi-

spherical lobule VI and lobule VIIIA. Activation was bilaterally, predominantly on the right. In the left hemisphere, the activity was clustered in lobules IV and VIII. Activity in the vermis was present in parts of V, VI, and VIII in both tasks. Within the cerebellar nuclei, activity in the right and less strong in the left dentate nucleus was found ($x, y, z = 20, -56, -27$ mm and $-19, 56, -27$ mm).

Sensorimotor activation during finger tapping with the reading hand showed activation of the vermis (VI and VIII) as well as right hemispherical lobules IV and VIIA. Hemispherical activation was less prominent on the left. The activity during this task was smaller compared to discrimination of nonsense dots, i.e., it did not extend into lobule V. Again, no activation of Crus I was present. Within the cerebellar nuclei, activity in the right dentate nucleus was revealed (coordinates were $x, y, z = -23, -56, -32$ mm).

Analysis of sighted subjects during reading of printed text revealed bilateral activation of Crus I (Fig. 1b). Feeling Braille characters led to an activation of the medial part of hemispherical lobules V and VIIIA similar to discriminating nonsense dots in the blind subjects. Tactile analysis of dots demonstrating symbols revealed activation in hemispherical lobules IV and VIII, more pronounced on the right side, but no further activity in Crus I (Fig. 1c). In both tasks, activity in the vermis was present in parts of lobules V, VI, and VIII and in dentate nucleus bilaterally. Data of the group analyses are summarized in Table I.

Analyses of the sighted group revealed activation of the vermis (V and VIII) as well as right hemispherical lobules IV and VIIA during finger tapping. Activation in the left hemisphere was less prominent. The activity during this task was smaller compared to that with Braille and symbols, i.e., it did not extend into hemispherical lobule V or VI. Again, no activation of Crus I was present. There was no significant difference between the activation during Braille and symbol tasks for activation in hemispherical lobules IV and VIII.

Random effects analysis of differences in blind subjects during Braille reading and discriminating nonsense dots (Braille > nonsense dots) revealed bilateral activation of Crus I (Fig. 2a,b). Additionally, activation of the vermal lobule V was present (Fig. 2c).

Statistical parametric maps of the activated areas of sighted subjects during discriminating symbols against discriminating Braille dots in random effects analysis revealed an activation of the right Crus II (Fig. 3).

Blind volunteers did not show any more extended activity of the cerebellar hemispheres in lobules IV and VIII than normal sighted volunteers during the motor task of finger tapping with equivalent activation cluster; the activated clusters were equal in sighted and blind subjects. Second-level analysis of the blind group reading Braille and the sighted group in the same task revealed activation of Crus I predominantly on the right (Fig. 2d).

Cortical activation in blind individuals reading Braille have been reported previously [Gizewski et al., 2003]. In brief, significant activation of the primary, secondary, and higher visual cortex was shown, compared to that in sighted

Figure 1.

a: Statistical parametric maps of activation within the group of blind subjects reading Braille with their right hand compared to that in the rest period. Task-related increase in MR signal is superimposed on three orthogonal sections of 3D T1-weighted standard brain. Statistical corrected threshold is $P < 0.05$. Results reveal bilateral activation of Crus I accompanied by activation of sensorimotor areas in lobule IV and VIII. **b:** Statistical parametric maps of activation within the group of normal sighted subjects reading a printed text compared to that during rest. Statistical corrected threshold is $P < 0.05$. Results show bilateral activation of Crus I. **c:** Statistical parametric maps of activation within the group of normal sighted subjects during tactile discrimination of symbols compared to that in the rest period did not reveal activity in Crus I but did show activation of sensorimotor areas in lobule IV and VIII bilaterally. Statistical corrected threshold is $P < 0.05$.

subjects. In all subjects, expected activation of sensorimotor brain areas was revealed. Additionally, blind subjects revealed activation in posterior-superior temporal cortex predominantly on the left side.

Results in single-subject analysis, especially of all blind subjects reading Braille and sighted subjects reading written text, were consistent in revealing bilateral activity in Crus I.

DISCUSSION

Extended cerebellar activation was revealed during Braille reading in blind subjects compared to that in sighted subjects who were not able to understand Braille letters. According to our results, this pronounced activation was not due to an extended somatosensory area as former studies have suggested [Sadato et al., 1998]. Our results indicate, that the extended cerebellar activation may be due to the fact that Braille reading is not only a sensorimotor finger movement task.

The accompanying cortical activation patterns were similar to those found in former studies with activation of striate cortex during Braille reading in blind subjects. No activation of this area was revealed during simple somatosensory tasks [Gizewski et al., 2003]. Cortical activation patterns therefore represent plasticity for higher and complex brain functions in blind subjects.

All sensorimotor tasks in the group of blind subjects (discriminating nonsense dots, finger tapping) and in the group of sighted subjects (Braille, discriminating symbols, finger tapping) revealed activation in the medial part of hemispherical lobules V and VIIIA bilaterally, but none of these conditions activated Crus I.

Somatotopic representation in the cerebellum with two homunculi, one located upside down in the anterior lobe and a second one in the posterior lobe, was described by Adrian [1943] and Snider and Stowell [1944]. A similar somatotopic representation has been found in humans using fMRI [Grodd et al., 2001; Rijntjes et al., 1999]. The main activated clusters in lobules IV/V and VIII correspond to the hand areas of the two homunculi in the anterior and posterior cerebellar lobes. Furthermore, it is known that activity during sensorimotor tasks is more pronounced ipsilaterally, which corresponds to our results. Vermal activity in lobules V and VII during the sensorimotor tasks, as shown in our study, has been described previously [Nitschke et al., 1998]. Additionally, we could show activity in the dentate nucleus during all sensorimotor tasks, indicating control of voluntary movements.

During tactile discrimination tasks in the group of blind subjects, extended activity from lobule V to VI was revealed. This activity could not be found during the finger-tapping

TABLE I. Summary of the activated areas during different active tasks

Subjects	Hemispherical lobules	Side	x, y, z	Max. Z
Blind				
Braille	Crus I	R, L	48, -70, -26	8
	IV	R, L	21, -48, -21	15
	VIII A	R, L	24, -62, -46	13
Nonsense dots	IV	R, L	21, -48, -21	13
	VIII A	R, L	24, -63, -48	12
Finger-tapping	IV	R, L	21, -58, -27	14
	VIII B	R, L	23, -65, -45	15
Sighted				
Braille	IV	R, L	21, -58, -21	14
	VIII A	R, L	24, -63, -48	16
Symbols	IV	R, L	21, -48, -23	15
	VIII A	R, L	24, -63, -48	13
Reading text	Crus I	R, L	48, -64, -31	6
Finger-tapping	IV	R, L	21, -58, -27	14
	VIII B	R, L	23, -65, -45	15
Comparisons				
Blind > sighted; Braille reading	Crus I	R, L	47, -65, -30	6
Blind: Braille > nonsense dots	Crus I	R, L	47, -65, -30	7
	Vermis V	—	-4, -81, -24	4
Sighted: symbols > Braille dots	Crus II	R, L	43, -74, -45	5

Summary of the activated areas during different active tasks: Braille reading, finger tapping, tactile discrimination of nonsense dots in blind subjects, and reading a printed text, tactile discrimination of symbols in normal sighted subjects. Comparisons using a two-sample *t*-test are given for blind versus sighted subjects and comparisons between Braille and nonsense dots in blind and symbols and Braille in sighted subjects. Statistical corrected threshold is $P < 0.05$. R, right; L, left.

task in the second-level analysis. This finding could be due to the more extended finger movement during discrimination tasks than during finger tapping. The finger movements during discrimination tasks are likely more specialized and the sensory impressions more extended than during simple finger tapping.

Beside these sensorimotor hand areas, we found an activity in Crus I that has been described by Fulbright and coworkers [1999] for reading tasks. The same area was activated in our group of sighted volunteers reading the narrative text. Activation in Crus I may be related to language or reading-specific processes of Braille reading rather than to sensorimotor functions. The present results are in line with previous fMRI studies of different language tasks in healthy subjects. Desmond and colleagues [1998] found that word stem completion tasks activate hemispherical lobules VII and VI including Crus I. During verbal working memory tasks, activity in right lateral cerebellum has been described [Gruber, 2001]. We used simple narrative texts written in Braille for the blind subjects and printed text for the sighted volunteers to test cerebellar activation during different text perception forms. We did not differentiate in either group between different parts of lexical analysis and language perception; we focused on global text perception and understanding.

Braille characters have, besides the language component, an object character and geometrical structure. As a control for object recognition, we therefore analyzed sighted subjects during tactile detection of symbols. This task did not

reveal any activity similar to that observed during Braille reading in blind volunteers and reading printed text in sighted volunteers. The activity that was specific for the symbol task was in the right Crus II, similar to those found by Allen and coworkers [1997] during visual geometric focused attention. The coordinates of the activated areas given by Allen and colleagues [1997] were correlated to the cerebellar nomenclature of the Schmahmann atlas [Schmahmann et al., 2000].

The results of our study suggest that large cerebellar activation during Braille reading is not due simply to increased areas involved in sensorimotor processing of finger movement. In our group of blind subjects, there was no general increased cerebellar activity during the finger-tapping task with respect to cerebellar areas involved in sensorimotor conditions in lobules V and VIII compared to that in sighted subjects. Crus I activation during Braille reading in blind subjects therefore is difficult to explain with pure sensorimotor activation. There are three possibilities besides involvement in higher speech functions.

First, it may reflect increased attentional demands during the Braille reading task. Previous studies have implicated involvement of Crus II in focusing [Allen et al., 1997, Le et al., 1998] and Crus I activation, especially of the left side, in shifting attention [Le et al., 1998]. During Braille reading in blind subjects, we found cerebellar areas in Crus I that did not correlate with areas detected by Allen and coworkers [1997] for attention activation. Directed attention to lexical tasks can not be excluded for this area due to our results,

Figure 2.

Statistical parametric maps of the activated areas of blind subjects during Braille reading compared to discriminating nonsense dots in random effects analysis (Braille > nonsense dots). Statistical corrected threshold is $P < 0.05$. Activation of right Crus I and activation of the left Crus I seems to be specific for Braille reading (a and b). Additional activation was found in the vermis part V (c). Blind group reading Braille compared to the sighted group in the same task revealed activation in Crus I, predominantly on the right (d).

even if our activated clusters are more caudolateral than were the activations described by Le and associates [1998]. The view of cerebellar involvement in attention tasks has been changed recently. Bischoff-Grethe and colleagues [2002] have found cerebellar involvement in response reassignment rather than attention. Second, and more importantly, activation in Crus I may reflect sensorimotor activation, based not on the finger movements, but on inner

speech. Blind subjects reading Braille and sighted subjects reading written text may use inner speech during these tasks that may involve the same cerebellar areas during Braille reading and reading printed text. It is known that inner speech activates areas in right cerebellar hemisphere, concomitant with an asymmetric activation pattern toward the left side at the level of the motor strip. Ackermann and coworkers [1998] could show that highly overlearned word

Figure 3.

Statistical parametric maps of the activated areas of sighted subjects during discriminating symbols compared to discriminating Braille dots in random effects analysis (symbols > Braille). Bilateral activation of Crus II seems to be specific for symbol discrimination in sighted subjects. Statistical corrected threshold is $P < 0.05$.

strings, presumably, pose few demands on controlled response selection and that the observed cerebellar activation seems to be related to the articulatory level of speech production rather than to cognitive operations, as suggested by previous positron emission tomography (PET) studies. Further studies therefore have to discriminate between these modalities.

Finally, it should be noted that performance parameters were not measured during scanning. It cannot be excluded that part of the differences between tasks and groups are due to differences in motor performance.

In conclusion, bilateral cerebellar activation in Crus I in blind subjects during Braille reading may be due to processes similar to those found in normal sighted volunteers during text reading and not due to extended somatosensory activation during complex finger discriminating tasks, as previous studies have suggested.

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