Crossed Cerebro–Cerebellar Language Dominance

Andreas Jansen,¹ Agnes Flöel,^{1,2} Jutta Van Randenborgh,¹
Carsten Konrad,¹ Michael Rotte,³ Ann-Freya Förster,⁴
Michael Deppe,¹ and Stefan Knecht¹

¹Department of Neurology, University of Münster, Münster, Germany

²Human Cortical Physiology Section, National Institute of Neurological Disorders and Stroke,
National Institutes of Health, Bethesda, Maryland

³Department of Neurology II, University of Magdeburg, Magdeburg, Germany

⁴Department of Radiology, Ruhr-University Bochum, BG-Kliniken Bergmannsheil,
Bochum, Germany

Abstract: In addition to its traditional role in motor control, the cerebellum has been implicated in various cognitive and linguistic functions. Lesion, anatomic, and functional imaging studies indicate a link between left frontal language regions and the right cerebellum. To probe the specificity of this circuit, we examined the association between language-related lateralized activation of the frontal cortex with lateralized activation of the cerebellum. Functional magnetic resonance imaging (fMRI) was carried out during letter-cued word generation in 14 healthy subjects: 7 subjects displayed typical left-hemisphere and 7 subjects displayed atypical right-hemisphere language dominance. We found activation of the cerebellar hemisphere contralateral to the language-dominant cerebral hemisphere in each subject. The cerebellar activation was confined to the lateral posterior cerebellar hemisphere (lobule VI, VII B, Cr I, Cr II). This study demonstrates that crossed cerebral and cerebellar language dominance is a typical characteristic of brain organization. The functional significance of the reported activations can now be tested in patients with lesions of the lateral posterior cerebellum. *Hum Brain Mapp* 24:165–172, 2005. © 2004 Wiley-Liss, Inc.

Key words: cerebellum; language lateralization; motor theory of speech perception; fMRI

INTRODUCTION

Traditional neurologic teaching suggests that the cerebellum is involved mainly in motor control. This view has been challenged over the past two decades: Clinical and anatomic data as well as functional imaging studies have given rise to new ideas about cerebellar function, particularly stressing the importance of cerebrocerebellar interactions for a variety of cognitive functions, including language [Abe et al., 1997; Ackermann et al., 1999; Bohnen et al., 1998; Cotterill, 2001; Fiez and Raichle, 1997; Marien et al., 2001; Middleton and Strick, 2000; Molinari et al., 1997; Schmahmann, 1997]. Although some authors still hold that these “language” deficits in cerebellar patients are confined to the motor aspects of language, e.g., the lack of motor coordination of those muscles required for phonation, many linguistic deficits reported after cerebellar lesions, e.g., dysprosodia, agrammatism, anomia, or reduced verbal fluency, can scarcely be explained solely as a result of limited motor coordination

Contract grant sponsor: Stiftung Neuromedizin, Münster, Germany; Contract grant sponsor: Nachwuchsgruppen-Förderung, Ministry of Science, Nordrhein-Westfalen; Contract grant number: 516-400 01000; Contract grant sponsor: Bennisen-Förder-Preis of Nordrhein-Westfalen; Contract grant number: IVA 6-400 302 97; Contract grant sponsor: Innovative Medizinische Forschung of the Medical Faculty of Münster; Contract grant number: Kn-1-1-II/96-34, KN 3 2 98 01; Contract grant sponsor: Deutsche Forschungsgemeinschaft, Bonn; Contract grant number: Kn 285/4-1, Kn 285/6-1, Fl 379/1-1.

A. Jansen and A. Flöel contributed equally to this work.

*Correspondence to: Andreas Jansen, Department of Neurology, University of Münster, Albert-Schweitzer-Straße 33, D-48129 Münster, Germany. E-mail: anjan@uni-muenster.de

Received for publication 15 January 2004; Accepted 25 June 2004

DOI: 10.1002/hbm.20077

Published online in Wiley InterScience (www.interscience.wiley.com).

[Molinari et al., 1997; Schmahmann and Sherman, 1998]. This concept of a “linguistic cerebellum” has been reviewed by Marien et al. [2001].

Language processing is one of the most complex human capabilities. It involves an extended bilateral network of brain areas, the epicenters of which are lateralized to one hemisphere [Albert and Helm-Estabrooks, 1988a,b; Alexander et al., 1989; Binder et al., 1997; Dick et al., 2001; Fernandez et al., 2001; Frith et al., 1991; Knecht et al., 2003]. In most humans, the left hemisphere plays the predominant role in language processing. Only about 10% show atypical right-hemisphere language dominance [Knecht et al., 2000a,b; Rasmussen and Milner, 1977]. It is as yet unknown whether the cerebellar contribution to language processing is always right-lateralized, contralateral to the side of handedness, or contralateral to the side of cerebral language dominance. Anatomic data of crossed reciprocal connections between cerebellum and cerebral Brodmann areas (BA) 6, 44, and 45 [Leiner et al., 1986, 1989; Schmahmann and Pandya, 1997] would suggest contralateral cerebellar activation also in cases of right-hemispheric language dominance. A recent case study by Hubrich-Ungureanu et al. [2002] described left cerebellar activation in an individual with right-hemisphere language dominance during a silent word generation task; however, the hypothesis has not been tested systematically.

In a previous publication [Knecht et al., 2003a], we demonstrated that the neural language organization of subjects with right-hemisphere language dominance is the mirror image of subjects with typical left-hemisphere language dominance; however, we did not assess the involvement of the cerebellum in the neural language network. In the present study, we therefore reanalyzed part of the data from the previous study to answer the following questions. First, to which side is cerebellar activation lateralized in subjects with atypical, i.e., right-hemispheric language dominance? Second, is it possible to infer cerebellar dominance in language tasks from handedness? Finally, what are the precise intrahemispheric localizations of cerebellar activation in subjects with typical and atypical cerebral language lateralization?

We investigated 14 healthy subjects, 7 with typical left-hemisphere and 7 with atypical right-hemisphere language dominance, during a language task using functional magnetic resonance imaging (fMRI). Participants were selected from a large cohort of individuals who had been evaluated for language lateralization by functional Doppler sonography (fTCD) [Knecht et al., 2000b].

SUBJECTS AND METHODS

Subjects

Based on the side of language lateralization, 14 native German-speaking subjects (7 with typical left-hemisphere and 7 with atypical right-hemisphere language dominance) were selected from a cohort of 326 healthy volunteers in whom language dominance had been assessed previously

TABLE I. Subject characteristics

Subject no.	Age (yr)	Gender	Handedness*	Language lateralization**
01	27	M	−17	1.7
02	25	F	40	1.5
03	28	M	100	2.5
04	24	M	88	2.0
05	24	F	70	3.2
06	27	M	100	5.0
07	25	F	45	3.2
08	27	M	−100	−3.3
09	30	F	−20	−3.4
10	35	M	100	−4.9
11	24	F	79	−4.1
12	25	F	−85	−5.0
13	25	M	40	−3.8
14	24	F	−100	−7.2

* Assessed by the Oldfield score, ranging from −100 (left-handedness) to +100 (right-handedness).

** As assessed by fTCD during a word generation task: Positive values indicate left hemispheric language lateralization, negative values lateralization to the right.

by fTCD (Münster Functional Imaging Study on the Variability of Hemispheric Specialization in Health and Disease) [Knecht et al., 1998a,b, 2000b]. From this cohort, we chose the subjects that had been investigated last and were accessible for reexamination. The subjects' characteristics are presented in Table I. Handedness was not a selection criterion. Because of the well established association of hemispheric language dominance and handedness [Knecht et al., 2000b], and because we had selected for comparable numbers of individuals with left and right hemispheric language dominance, left-handed subjects in our cohort were overrepresented.

The protocol was approved by the local ethics committee, and all subjects gave their written informed consent before participation, according to the declaration of Helsinki. None had a history of significant past or current medical, neurologic, or psychiatric illness, or any brain pathology or abnormal brain morphology on T₁-weighted MR images. All subjects had completed the equivalent of a high school degree (“Gymnasium”). Handedness was assessed by the Edinburgh handedness inventory [Oldfield, 1971].

The method used for previous determination of language lateralization by fTCD has been described elsewhere in detail [Deppe et al., 1997]. In short, fTCD determines language lateralization by measurement of relative hemispheric perfusion increases during word generation. This method has been validated by direct comparison with the intracarotid amobarbital injection and fMRI [Deppe et al., 2000; Knecht et al., 1998a].

Paradigm

For language activation, we used a word generation task (WGT) based on standard phonetic verbal fluency as as-

sessed in the Controlled Word Association Test [Lezak, 1995]. This task has been employed in numerous studies and produces marked lateralization of brain activation [Cuenod et al., 1995; Hertz-Pannier et al., 1997; Pujol et al., 1999]. Subjects were familiarized with the task in the prior fTCD examination. The paradigm consisted of an activation task and a control task lasting 20 s each. Tasks were carried out in an alternating sequence and repeated eight times. Before the first activation task, five dummy images were presented. During this period, MR signal equilibrium was reached.

Activation task

Five seconds after a color change on a computer screen, subjects saw a letter. They silently had to find as many words as possible starting with the displayed letter. Letters were presented in a random order. "Q," "X," and "Y" were excluded because very few German words begin with these letters. No letter was displayed more than once. After 15 s, a color change indicated the end of the task.

Control task

A cross was presented on the screen instead of a letter. Subjects had to silently repeat the phrase "bababa."

MRI Data Acquisition

MRI data were acquired on a neurooptimized GE 1.5 T whole-body scanner equipped with a standard circular polarized head coil. Functional images were obtained using a T_2^* weighted gradient echo echoplanar imaging (EPI) sequence (TE = 40 ms, TR = 2 s, flip angle 90 degrees, slice thickness 7 mm, 1-mm gap, matrix 64×64 , field of view [FOV] 200 mm, in-plane resolution 3.125×3.125 mm). Sixteen axial slices orientated parallel to the anterior commissure–posterior commissure (AC–PC) line covering the whole brain were taken. To investigate reproducibility, two functional runs were acquired from each subject. Only Subject 2 was not available for a second examination. Additional high resolution T_1 weighted anatomic images were acquired (TE = 8 ms, TR = 24 ms, flip angle 30 degrees, matrix 256×256 , FOV 250 mm, 124 sagittal slices, slice thickness 1.5 mm).

MRI Data Analysis

Imaging data were analyzed with SPM99 (Wellcome Department of Cognitive Neurology, online at <http://www.fil.ion.ucl.ac.uk/spm>). The first five scans of each time series were discarded to allow for magnetic saturation. Using each subject's coregistered structural T_1 -image, the data were realigned and spatially normalized to a template brain image created by the Montreal Neurological Institute (MNI) [Evans et al., 1994]. Finally, these images were resliced to $2 \times 2 \times 2$ -mm isotropic voxels [Friston et al., 1995]. The data were spatially smoothed with an isotropic Gaussian kernel (full-width half-maximum [FWHM] 6 mm). Subsequently, data were bandpass-filtered (HRF as low-pass filter, cut-off period of the high-pass filter was set to 82 s) and analyzed

statistically in the context of the general linear model, using boxcar regressors convolved with the canonical hemodynamic response to model responses during each experimental condition. Activation images were calculated by applying appropriate linear contrasts to the parameter estimates for the experimental conditions, resulting in a t -statistic for each voxel. These t -statistics constitute a statistical parametric map (SPM) and were interpreted by referring to the probabilistic behavior of Gaussian random fields.

To display group results, a conjunction analysis was carried out separately for subjects with left- and right-hemisphere language dominance. Only activations common to all subjects were reported with this approach. This type of analysis aimed to establish the observed effect as a "typical" characteristic of the population from which the group was sampled [Friston et al., 1999a,b]. A $P < 0.05$ activation threshold, corrected for multiple comparisons, was applied at voxel level. To eliminate the possibility that we missed additional activations that might be displayed by some but not all subjects, we took the single-subject activation maps into account. These activations would not appear in a conjunction analysis. Missing significant hemodynamic responses within a certain region might simply reflect threshold effects. Individual activation maps were thus calculated at a relatively liberal statistical threshold of $P < 0.001$ (uncorrected). Although the resulting activation patterns are more susceptible to artefacts, they might provide more detailed information about hemodynamic responses bounded to comparatively small areas of neural tissue.

After normalization to the MNI template, the anatomic localization of activated brain regions is often assessed by reference to the standard stereotactic atlas by Talairach and Tournoux [1988]. This approach is appropriate to answer the question of whether a subject displays activation in the cerebellum or not. However, it cannot be used for a precise anatomic localization of activated areas to specific cerebellar subregions. (The cerebellum had been removed from the brain used for the Talairach atlas, and it was sketched in by hand afterwards; therefore, in the Talairach atlas the cerebellum is merely a schematic drawing.)

There are a number of possible approaches to localize activated areas in the cerebellum. One approach is to use data normalized to the MNI space and look up the MNI coordinate in an atlas in which the cerebellum is in the same space as the MNI template, e.g., the cerebellar atlas of Schmahmann et al. [1999, 2000]. Another approach would be the introduction of a specific cerebellar transformation procedure [Grodde et al., 2001]. We did not introduce a normalization procedure, but instead coregistered the functional data of each subject to its individual structural image and assessed the anatomic localization in a suited brain atlas [Schmahmann et al., 1999, 2000]. This method takes the anatomic variability between subjects into account. The anatomic nomenclature of the cerebellum used in the present study refers to the classification of Schmahmann et al. [1999, 2000].

TABLE II. Anatomic localization of activated cerebellar regions

Subject no.	Session 1	Session 2
01	VII B	VII B, Cr II
02	VII B	— ^a
03	VII B	VII B
04	Cr I, Cr II, VII B	Cr I, Cr II, VII B
05	VII B	VII B, VIII A
06	VII B	VIII B, IX
07	VII B	VII B
08	VII B, VIII A	Cr I, Cr II, VII B
09	VII B, Cr II	Cr I
10	Cr I, Cr II, VII B	Cr I, VI
11	Cr I, VI	Cr I, Cr I/VI
12	Cr I, VI	Cr I, VI
13	Cr I, VI	Cr I, VI
14	Cr I, VI	Cr I, VI

^a Subject 02 was not available for a second measurement.

Nomenclature refers to the classification of Schmahmann et al. [1999, 2000].

For an anatomic localization of cerebellar activation, the preprocessing was carried out in a slightly different way. After realignment, the functional images were coregistered to the individual anatomic image, but not normalized. Subsequently, the functional images were smoothed using a Gaussian kernel of $3 \times 3 \times 6$ mm. Statistical analysis was carried out as described above. The cerebellar activation was localized anatomically at its point of maximal activation.

RESULTS

The word generation task led to unilateral activation of the posterior middle and inferior frontal gyrus, including the classic area of Broca and the premotor cortex. Additionally, BA 22 and 38 in the superior temporal gyrus and BA 40 in the supramarginal gyrus were found activated. Bilateral activation was seen in BA 32, 38, and 47. This pattern corresponds to that described by others using similar activation tasks [Pujol et al., 1999]. The activation pattern in standard MNI space as obtained by a conjunction analysis are displayed in Figure 1 for subjects with left- and right-hemisphere language dominance, respectively ($P < 0.05$, corrected for multiple comparisons).

The main focus of the present study was the cerebellar activation. In all subjects, we found strongly lateralized activation of the cerebellar hemisphere contralateral to the dominant cerebral hemisphere for both sessions (marked in red in Fig. 1). This does not exclude the possibility that both cerebellar hemispheres play a role in the neural language network. However, the cerebellar contribution to language is strongly lateralized.

Using individual anatomic data, cerebellar activation was confined to the respective lateral posterior cerebellar hemisphere (lobule VI, VII B, Cr I, and Cr II; see Table II for individual anatomic localization of activated cerebellar re-

gions). The cerebellar activation of two subjects with left- and right-hemisphere language dominance, respectively, is displayed in Figure 2.

The dissociation of cerebral and cerebellar activation cannot be attributed to handedness. Ten subjects showed cerebellar activation ipsilateral to the dominant hand and four subjects ipsilateral to the nondominant hand (see Table I).

DISCUSSION

The main finding of the present study is a crossed laterality of cerebral and cerebellar language dominance in subjects with left- and right-hemispheric language dominance during word generation. The cerebellar activation was found in the lateral posterior cerebellar hemisphere (lobule VI, VII B, Cr I, and Cr II).

Lateralized Cerebellar Activation for Language Processing

Lateralized cerebral dominance for language with a pre-dominant role of the left hemisphere in most humans is well established from both lesion [Albert and Helm-Estabrooks, 1988a,b; Alexander et al., 1989] and imaging studies [Binder, 1997; Fernandez et al., 2001; Frith et al., 1991; Knecht et al., 2003]. The involvement of the right cerebellum in language tasks has been well described in subjects with left-hemispheric language dominance. Several functional imaging studies have demonstrated activation of the right lateral cerebellum during language tasks, including verbal fluency [Martin et al., 1995; Petersen et al., 1988; Raichle et al., 1994] semantic word retrieval [Binder et al., 1997; Frost et al., 1999; Xiang et al., 2003], and verbal working memory tasks [Desmond et al., 1997]. In contrast, simple repetition of syllables, as compared to baseline, activates the cerebellum bilaterally [Riecker et al., 2002; Wildgruber et al., 2001]. Clinical studies on patients with cerebellar disease likewise support a role for the right lateral cerebellum for language processing. Although lesions of both cerebellar hemispheres can influence linguistic abilities, right cerebellar lesions are more likely to do so [Fiez et al., 1992; Gasparini et al., 1999; Leggio et al., 2000; Marien et al., 1996; Riva and Giorgi, 2000; Silveri et al., 1994]. This hypothesis gained further support from observations in dyslexics [Nicolson et al., 1999]. Compared to a control population, the dyslexics exhibited significantly smaller right anterior lobes of the cerebellum. The right cerebellum is considered one of the most consistent locations for structural differences between dyslexic and control participants in imaging studies [Eckert et al., 2003]. Combined lesion and functional imaging studies show crossed diaschisis between the left hemisphere and the right cerebellum [Abe et al., 1997; Bohnen et al., 1998; Metter et al., 1987].

There is no consensus yet on the precise role of the cerebellum in language processing. Although some researchers [Fiez et al., 1992; Gasparini et al., 1999; Marien et al., 2001; Schmahmann and Sherman, 1998] argue for genuine linguistic function of the cerebellum, others [Bower, 1997a,b; Xiang et al., 2003] attribute only a support function to the cerebel-

(a) Subjects with left-hemisphere language dominance **Figure 1.**

Activated brain regions associated with word generation relative to rest obtained by a conjunction analysis ($P < 0.05$, corrected for multiple comparisons) for subjects with left- and right-hemisphere language dominance (results of Session 1 are displayed, respectively). Cerebellar activation is marked in red. Activated areas are shown as through-projections onto representations of standard stereotactic space. P, posterior; A, anterior; R, right; L, left.

(b) Subjects with right-hemisphere language dominance **Figure 2.**

Cerebellar activation for two subjects with left- and right-hemisphere language dominance, respectively, superimposed on individual anatomic images (top, coronal; bottom, axial). Results of Session 1 are marked in red; results of Session 2 are marked in yellow. The anatomically high reproducibility of the cerebellar activation can be seen clearly.

lum, e.g., computations involved in language. Their reluctance to assign a more linguistic function is because the cerebellum is involved in many other systems [Bower, 1997a,b], and because of the lack of evidence that cerebellar patients have difficulties with language interpretation [Ackermann et al., 1997; Ivry and Baldo, 1992].

Our study demonstrates that in atypical right-hemispheric language dominance, language tasks lead to atypical left cerebellar activation. The asymmetric functional organization of the cerebrum is well known, with left-hemispheric language dominance in most right-handed individuals, and right hemispheric language dominance in up to 27% of strong left-handed persons [Knecht et al., 2000b]. It has not been known whether such atypical lateralization for linguistic functions could also be found at the cerebellar level. Based on anatomic data of crossed reciprocal connections between cerebellum and cerebral BA 6, 44, and 45 [Leiner et al., 1986, 1989; Schmahmann and Pandya, 1997], we hypothesized contralateral cerebellar activation also in cases of right-hemispheric language dominance. Our data confirm this hypothesis, and suggest that the crossed laterality of cerebral and cerebellar language dominance constitutes a typical characteristic of brain organization.

Role of the Cerebellum in Speech and Language

The data of the present study do not allow conclusions about the precise role of the cerebellum in linguistic functions. Its lateralized nature, in accordance with hemispheric language dominance, points to the interpretation that the cerebrocerebellar interaction in language tasks is driven more specifically by linguistic components of the task. This view receives support from different areas. Ontogenetic evidence suggests that the cerebellum may help establish phonologic representations during development [Nicolson et al., 2001]. Articulation and phonology may then remain closely coupled [Ivry and Justus, 2001]. In fact, data on patients with cerebellar lesions suggests that regular speech requires sequencing of articulatory gestures, mediated by the anterior intrasylvian cortex and the cerebellum [Ackermann et al., 1997]. Psycholinguistic studies suggest that syllables may constitute the basic elements of both articulatory movements and phonology [Levelt, 1999]. When seen from this perspective, the cerebellar activation during speech/language may stem from the close link of the language and the motor system (motor theory of speech perception) [Arbib, 2000; Liberman and Mattingly, 1985; Rizzolatti et al., 1996]. Cerebellar involvement during speech would then move beyond purely motor function (e.g., articulation) in speech because according to the theory, articulatory gestures directly transmit the linguistic meaning from the speaker to the listener [Arbib, 2000; Corballis, 1992; Liberman and Mattingly, 1985; Rizzolatti et al., 1996].

Cerebellar Lateralization and Handedness

Based on theories that postulate a strong link between the manual motor system and speech [Arbib, 2000; Corballis, 1992; Rizzolatti et al., 1996], an alternative possibility must

be considered. Because the modern system of language may have developed from a manual gesture system [Corballis, 1992; Hewes, 1973; Rizzolatti and Arbib, 1999], the cerebellar activation during speech might represent this earlier stage of manual communication. The side of cerebral language dominance (the neural language system) may co-vary with the neural systems for manual dexterity, and activation of the cerebellum may thus reflect primarily the processing of efferent copies [Thier et al., 2000] for covert manual “gesturing” with the dominant hand during speech. This interpretation, however, is unlikely given the findings of the present study: the side of cerebellar activation could be predicted by cerebral hemispheric lateralization but not handedness. Rare lesion studies concur with this notion; Hassid [1995] reported a left-hander with right cerebellar infarction and subsequent moderate anomia, whose single photon-emission computed tomography (SPECT) revealed relative hypoperfusion of left hemispheric language areas [Hassid, 1995]. In summary, the present study suggests that language-related cerebellar activation is coupled tightly to the lateralized cerebral network processing language but not to hand dominance.

Localization of Cerebellar Language Activation

Studies of cerebellar activations during language processing [for review, see Fiez and Raichle, 1997], as well as lesion studies in patients [Molinari et al., 1997], have pointed to the lateral hemispheres of the cerebellum for language processing, whereas the vermis and the paravermal regions were more likely to be involved in motor aspects of speech [Ackermann and Ziegler, 1992; Amarenco, 1991; Arbib, 2000; Barth et al., 1993; Rizzolatti et al., 1996]. The topography within the cerebellar hemispheres reported across studies, however, has been variable [Fiez and Raichle, 1997; Molinari et al., 1997]. Some functional studies have reported the inferior part of the lateral posterior cerebellum [Petersen et al., 1988]; others have reported the anterior lobe [Raichle et al., 1994]. Studies of patients with verbal fluency deficits have likewise indicated different sites of cerebellar lesions [Leggio et al., 2000; Levisohn et al., 2000; Schmahmann and Sherman, 1998]. These inconsistencies across studies may be attributable to differences in task design, patient population, or the anatomic extent of the lesion [Daum and Ackermann, 1995]. Additionally, precise localization of language-related activity was difficult to assess in the earlier positron emission tomography (PET) studies due to low spatial resolution. Our study, demonstrating the same cerebellar intrahemispheric activation pattern regardless of side of dominance, provides strong evidence that *posterior* lateral cerebral hemispheres (lobule VI, VII B, Cr I, and Cr II) are the sites specifically involved in linguistic processing.

Outlook

Functional imaging studies alone are not able to provide answers about the functional significance of the cerebellum for language tasks. Although they show involvement of specific brain areas in language tasks, they cannot determine

their relevance; however, they may serve to generate hypotheses regarding the type and location of computations in the cerebellum. With the information on topography and relation of cerebral–cerebellar language dominance acquired in the present study, it is now possible to examine patients with lesions in this region for subtle deficits in language processing.

ACKNOWLEDGMENTS

We thank V. Besmens and J. Sommer for technical support and J. Hempleman for linguistic support on an earlier version of the article.

REFERENCES

- Abe K, Ukita H, Yorifuji S, Yanagihara T (1997): Crossed cerebellar diaschisis in chronic Broca's aphasia. *Neuroradiology* 39:624–626.
- Ackermann H, Graber S, Hertrich I, Daum I (1997): Categorical speech perception in cerebellar disorders. *Brain Lang* 60:323–331.
- Ackermann H, Graber S, Hertrich I, Daum I (1999): Cerebellar contributions to the perception of temporal cues within the speech and nonspeech domain. *Brain Lang* 67:228–241.
- Ackermann H, Ziegler W (1992): [Cerebellar dysarthria—a review of the literature.] *Fortschr Neurol Psychiatr* 60:28–40.
- Albert ML, Helm-Estabrooks N (1988a): Diagnosis and treatment of aphasia. Part I. *JAMA* 259:1043–1047.
- Albert ML, Helm-Estabrooks N (1988b): Diagnosis and treatment of aphasia. Part II. *JAMA* 259:1205–1210.
- Alexander MP, Benson DF, Stuss DT (1989): Frontal lobes and language. *Brain Lang* 37:656–691.
- Amarenco P (1991): The spectrum of cerebellar infarctions. *Neurology* 41:973–979.
- Arbib MA (2000): The mirror system, imitation, and the evolution of language. In: Nehanio C, Dautenhahn K, editors. *Imitation in animals and artifacts*. Cambridge, MA: MIT Press. p 229–280.
- Barth A, Bogousslavsky J, Regli F (1993): The clinical and topographic spectrum of cerebellar infarcts—a clinical magnetic-resonance-imaging correlation study. *Ann Neurol* 33:451–456.
- Binder JR (1997): Neuroanatomy of language processing studied with functional MRI. *Clin Neurosci* 4:87–94.
- Binder JR, Frost JA, Hammeke TA, Cox RW, Rao SM, Prieto T (1997): Human brain language areas identified by functional magnetic resonance imaging. *J Neurosci* 17:353–362.
- Bohnen NILJ, Beran-Koehn M, Mullan B, Fulgham JR (1998): Crossed cerebro-cerebellar diaschisis in a patient with melas with aphasia but without hemiparesis. *Int J Neurosci* 93:181–184.
- Bower JM (1997a): Control of sensory data acquisition. *Int Rev Neurobiol* 41:489–513.
- Bower JM (1997b): Is the cerebellum sensory for motor's sake, or motor for sensory's sake: the view from the whiskers of a rat? *Prog Brain Res* 114:463–496.
- Corballis MC (1992): On the evolution of language and generativity. *Cognition* 44:197–226.
- Cotterill RMJ (2001): Cooperation of the basal ganglia, cerebellum, sensory cerebrum and hippocampus: possible implications for cognition, consciousness, intelligence and creativity. *Prog Neurobiol* 64:1–33.
- Cuenod CA, Bookheimer SY, Hertz Pannier L, Zeffiro TA, Theodore WH, Le Bihan D (1995): Functional MRI during word generation, using conventional equipment: a potential tool for language localization in the clinical environment. *Neurology* 45:1821–1827.
- Daum I, Ackermann H (1995): Cerebellar contributions to cognition. *Behav Brain Res* 67:201–210.
- Deppe M, Knecht S, Henningsen H, Ringelstein EB (1997): AVER-AGE: a Windows program for automated analysis of event related cerebral blood flow. *J Neurosci Methods* 75:147–154.
- Deppe M, Knecht S, Papke K, Lohmann H, Fleischer H, Heindel W, Ringelstein EB, Henningsen H (2000): Assessment of hemispheric language lateralization: a comparison between fMRI and fTCD. *J Cereb Blood Flow Metab* 20:263–268.
- Desmond JE, Gabrieli JDE, Wagner AD, Ginier BL, Glover GH (1997): Lobular patterns of cerebellar activation in verbal working-memory and finger-tapping tasks as revealed by functional MRI. *J Neurosci* 17:9675–9685.
- Dick F, Bates E, Wulfeck B, Utman JA, Dronkers N, Gernsbacher MA (2001): Language deficits, localization, and grammar: evidence for a distributive model of language breakdown in aphasic patients and neurologically intact individuals. *Psychol Rev* 108:759–788.
- Eckert MA, Leonard CM, Richards TL, Aylward EH, Thomson J, Berninger VW (2003): Anatomical correlates of dyslexia: frontal and cerebellar findings. *Brain* 126:482–494.
- Evans AC, Kamber M, Collins DL, MacDonald D (1994): An MRI-based probabilistic atlas of neuroanatomy. New York: Plenum. p 263–274.
- Fernandez G, de Greiff A, von Oertzen J, Reuber M, Lun S, Klaver P, Ruhlmann J, Reul J, Elger CE (2001): Language mapping in less than 15 minutes: real-time functional MRI during routine clinical investigation. *Neuroimage* 14:585–594.
- Fiez JA, Petersen SE, Cheney MK, Raichle ME (1992): Impaired non-motor learning and error detection associated with cerebellar damage. A single case study. *Brain* 115:155–178.
- Fiez JA, Raichle ME (1997): Linguistic processing. *Int Rev Neurobiol* 41:233–254.
- Friston KJ, Holmes A, Worsley KJ, Poline JB, Frith CD, Frackowiak RSJ (1995): Statistical parametric maps in functional imaging: a general linear approach. *Hum Brain Mapp* 2:189–210.
- Friston KJ, Holmes AP, Price CJ, Buchel C, Worsley KJ (1999a): Multisubject fMRI studies and conjunction analyses. *Neuroimage* 10:385–396.
- Friston KJ, Holmes AP, Worsley KJ (1999b): How many subjects constitute a study? *Neuroimage* 10:1–5.
- Frith CD, Friston KJ, Liddle PF, Frackowiak RS (1991): A PET study of word finding. *Neuropsychologia* 29:1137–1148.
- Frost JA, Binder JR, Springer JA, Hammeke TA, Bellgowan PS, Rao SM, Cox RW (1999): Language processing is strongly left lateralized in both sexes. Evidence from functional MRI. *Brain* 122: 199–208.
- Gasparini M, Di Piero V, Ciccarelli O, Cacioppo MM, Pantano P, Lenzi GL (1999): Linguistic impairment after right cerebellar stroke: a case report. *Eur J Neurol* 6:353–356.
- Grodd W, Hulsman E, Lotze M, Wildgruber D, Erb M (2001): Sensorimotor mapping of the human cerebellum: fMRI evidence of somatotopic organization. *Hum Brain Mapp* 13:55–73.
- Hassid EI (1995): A case of language dysfunction associated with cerebellar infarction. *J Neurol Rehabil* 9:157–160.
- Hertz-Pannier L, Gaillard WD, Mott SH, Cuenod CA, Bookheimer SY, Weinstein S, Conry J, Papero PH, Schiff SJ, Le Behin D, Theodore WH (1997): Noninvasive assessment of language dominance in children and adolescents with functional MRI: a preliminary study. *Neurology* 48:1003–1012.

- Hewes GW (1973): Primate communication and the gestural origin of language. *Curr Anthropol* 14:5–32.
- Hubrich-Ungureanu P, Kaemmerer N, Henn FA, Braus DF (2002): Lateralized organization of the cerebellum in a silent verbal fluency task: a functional magnetic resonance imaging study in healthy volunteers. *Neurosci Lett* 319:91–94.
- Ivry RB, Baldo JV (1992): Is the cerebellum involved in learning and cognition? *Curr Opin Neurobiol* 2:212–216.
- Ivry RB, Justus TC (2001): A neural instantiation of the motor theory of speech perception. *Trends Neurosci* 24:513–515.
- Knecht S, Deppe M, Dräger B, Bobe L, Lohmann H, Ringelstein EB, Henningsen H (2000a): Language lateralization in healthy right-handers. *Brain* 123:74–81.
- Knecht S, Deppe M, Ebner A, Henningsen H, Huber T, Jokeit H, Ringelstein EB (1998a): Non-invasive determination of hemispheric language dominance using functional transcranial Doppler sonography: a comparison with the Wada test. *Stroke* 29:82–86.
- Knecht S, Deppe M, Ringelstein EB, Wirtz M, Lohmann H, Dräger B, Huber T, Henningsen H (1998b): Reproducibility of functional transcranial Doppler sonography in determining hemispheric language lateralization. *Stroke* 29:1155–1159.
- Knecht S, Dräger B, Deppe M, Bobe L, Lohmann H, Floel A, Ringelstein EB, Henningsen H (2000b): Handedness and hemispheric language dominance in healthy humans. *Brain* 123:2512–2518.
- Knecht S, Jansen A, Frank A, Van Randenborgh J, Sommer J, Kanowski M, Heinze HJ (2003): How atypical is atypical language dominance? *Neuroimage* 18:917–927.
- Leggio MG, Silveri MC, Petrosini L, Molinari M (2000): Phonological grouping is specifically affected in cerebellar patients: a verbal fluency study. *J Neurol Neurosurg Psychiatry* 69:102–106.
- Leiner HC, Leiner AL, Dow RS (1986): Does the cerebellum contribute to mental skills? *Behav Neurosci* 100:443–454.
- Leiner HC, Leiner AL, Dow RS (1989): Reappraising the cerebellum: what does the hindbrain contribute to the forebrain? *Behav Neurosci* 103:998–1008.
- Levelt WJM (1999): Models of word production. *Trends Cogn Sci* 3:223–232.
- Levisohn L, Cronin-Golomb A, Schmahmann JD (2000): Neuropsychological consequences of cerebellar tumour resection in children: cerebellar cognitive affective syndrome in a paediatric population. *Brain* 123:1041–1050.
- Lezak MD (1995): *Neuropsychological assessment*. New York: Oxford University Press.
- Liberman AM, Mattingly IG (1985): The motor theory of speech perception revised. *Cognition* 21:1–36.
- Marien P, Engelborghs S, Fabbro F, De Deyn PP (2001): The lateralized linguistic cerebellum: a review and a new hypothesis. *Brain Lang* 79:580–600.
- Marien P, Scaerens J, Nanhoe R, Moens E, Nagels G, Pickut BA, Dierckx RA, De Deyn PP (1996): Cerebellar induced aphasia: case report of cerebellar induced prefrontal aphasic language phenomena supported by SPECT findings. *J Neurol Sci* 144:34–43.
- Martin A, Haxby JV, Lalonde FM, Wiggs CL, Ungerleider LG (1995): Discrete cortical regions associated with knowledge of color and knowledge of action. *Science* 270:102–105.
- Metter EJ, Kempler D, Jackson CA, Hanson WR, Riege WH, Camras LR, Mazziotta JC, Phelps ME (1987): Cerebellar glucose metabolism in chronic aphasia. *Neurology* 37:1599–1606.
- Middleton FA, Strick PL (2000): Basal ganglia and cerebellar loops: motor and cognitive circuits. *Brain Res Brain Res Rev* 31:236–250.
- Molinari M, Leggio MG, Silveri MC (1997): Verbal fluency and agrammatism. *Int Rev Neurobiol* 41:325–339.
- Nicolson RI, Fawcett AJ, Berry EL, Jenkins IH, Dean P, Brooks DJ (1999): Association of abnormal cerebellar activation with motor learning difficulties in dyslexic adults. *Lancet* 353:1662–1667.
- Nicolson RI, Fawcett AJ, Dean P (2001): Developmental dyslexia: the cerebellar deficit hypothesis. *Trends Neurosci* 24:508–511.
- Oldfield RC (1971): The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9:97–113.
- Petersen SE, Fox P, Posner M, Mintum M, Raichle M (1988): Positron emission tomographic studies of the cortical anatomy of single-word processing. *Nature* 331:585–589.
- Pujol J, Deus J, Losilla JM, Capdevila A (1999): Cerebral lateralization of language in normal left-handed people studied by functional MRI. *Neurology* 52:1038–1043.
- Raichle ME, Fiez JA, Videen TO, MacLeod AM, Pardo JV, Fox PT, Petersen SE (1994): Practice-related changes in human brain functional anatomy during nonmotor learning. *Cereb Cortex* 4:8–26.
- Rasmussen T, Milner B (1977): The role of early left-brain injury in determining lateralization of cerebral speech functions. *Ann N Y Acad Sci* 299:355–369.
- Riecker A, Wildgruber D, Dogil G, Grodd W, Ackermann H (2002): Hemispheric lateralization effects of rhythm implementation during syllable repetitions: an fMRI study. *Neuroimage* 16:169–176.
- Riva D, Giorgi C (2000): The cerebellum contributes to higher functions during development: evidence from a series of children surgically treated for posterior fossa tumours. *Brain* 123:1051–1061.
- Rizzolatti G, Arbib MA (1999): From grasping to speech: imitation might provide a missing link: reply. *Trends Neurosci* 22:152.
- Rizzolatti G, Fadiga L, Gallese V, Fogassi L (1996): Premotor cortex and the recognition of motor actions. *Brain Res Cogn Brain Res* 3:131–141.
- Schmahmann JD (1997): The cerebellum and cognition. In: Bradley RJ, editor. *International Review of Neurobiology*, Vol. 41. New York: Academic Press.
- Schmahmann JD, Doyon J, McDonald D, Holmes C, Lavoie K, Hurwitz AS, Kabani N, Toga A, Evans A, Petrides M (1999): Three-dimensional MRI atlas of the human cerebellum in proportional stereotaxic space. *Neuroimage* 10:233–260.
- Schmahmann JD, Doyon J, Petrides M, Evans A, Toga A (2000): *MRI atlas of the human cerebellum*. San Diego: Academic Press.
- Schmahmann JD, Pandya DN (1997): The cerebrocerebellar system. *Int Rev Neurobiol* 41:31–60.
- Schmahmann JD, Sherman JC (1998): The cerebellar cognitive affective syndrome. *Brain* 121:561–579.
- Silveri MC, Leggio MG, Molinari M (1994): The cerebellum contributes to linguistic production: a case of agrammatic speech following a right cerebellar lesion. *Neurology* 44:2047–2050.
- Talairach J, Tournoux P (1988): *Co-planar stereotaxic atlas of the human brain*. New York: Thieme.
- Thier P, Dicke PW, Haas R, Barash S (2000): Encoding of movement time by populations of cerebellar Purkinje cells. *Nature* 405:72–76.
- Wildgruber D, Ackermann H, Grodd W (2001): Differential contributions of motor cortex, basal ganglia, and cerebellum to speech motor control: effects of syllable repetition rate evaluated by fMRI. *Neuroimage* 13:101–109.
- Xiang H, Lin C, Ma X, Zhang Z, Bower JM, Weng X, Gao JH (2003): Involvement of the cerebellum in semantic discrimination: an fMRI study. *Hum Brain Mapp* 18:208–214.