Acta neurol. belg., 2001, **101**, 96-109

Cerebellar neurocognition : a new avenue

Peter MARIEN, Sebastiaan ENGELBORGHS and Peter P. DE DEYN
Department of Neurology, General Hospital Middelheim, Antwerp, and Laboratory of Neurochemistry and Behavior, Born-Bunge Foundation, University of Antwerp, Belgium

Abstract

The functional role of the cerebellum is traditionally defined as a mere coordinator of automatic and somatic motor functions. This view determined most of the clinical and experimental investigations of the functions of the cerebellum and overshadowed many attempts to expand its role to non-motor functions. However, during the past decades the collaboration across contemporary neuroscience disciplines has brought about a substantial modification of traditional thinking about the cerebellum. Converging evidence from different neuroscientific angles established the view that the human cerebellum participates in a much wider range of functions than conventionally accepted. Studies have brought to the fore that the cerebellum also modulates neurocognitive functions of at least these parts of the brain to which it is reciprocally connected. In less than two decades, the concept of 'cerebellar neurocognition' evolved from a mere afterthought to an exciting new multifaced area of contemporary neuroscientific investigations. Within this area, one of the major avenues of current research is the role of the cerebellum in non-motor language processing. This paper reviews the recently acknowledged role of the cerebellum in neurocognition and linguistic processes.

Key words **:** cerebellum ; cognition ; aphasia ; mutism

General introduction

Bloedel and Bracha (1997) distinguished five periods in the conceptual growth and development of insights in cerebellar functioning during the 20th century : 1) coordination of goal-oriented voluntary movement and orientation of the body and the head in space, 2) regulation and integration of sensory information for cutanomuscular and proprioceptive reflex organization, 3) regulation of vestibulo-ocular movements and posture of the head, 4) learning of classically conditioned withdrawal responses, and 5) modification of linguistic, cognitive and affective behaviour. During the past decades the collaboration across contemporary neuroscience disciplines has brought about a substantial modification of the traditional view of the cerebellum as a mere coordinator of automatic and somatic motor functions. Increased insight in the functional role of the cerebellum has recently even brought to the fore that the cerebellum also modulates neurocognitive processes of at least these parts of the brain to which it is reciprocally connected.

That our understanding of the contribution of the cerebellum to neurocognition is currently still in a preliminary stage is essentially due to the historic neglect of the non-motor role of the cerebellum, but also follows the fact that the cerebellum primarily acts as a rather subtle modulator of neurocognitive processes. If this modulating function is impaired, deficits arise that are quantitatively and qualitatively different from the deficits produced by lesions of the supratentorial structures. Therefore standard psychometric test batteries which focus on the detection of well-delineated neurocognitive impairments are often not sensitive enough to reveal the 'subclinical' deficits that may follow cerebellar damage. Further refinement of neurocognitive test methodologies and development of specifically adapted clinical investigation tools are required to capture the rich spectrum of cerebellar-induced neurocognitive dysfunctions. In addition, the possibility of inadequate assessment even increases since neurocognitive impairment following cerebellar damage often evolves rapidly and is often transient.

This paper reviews the role of the cerebellum in neurocognition and addresses in more detail experimental and clinical data disclosing the modulating role of the cerebellum in linguistic processes. Table 1 and 2 display a summary of data indicating cerebellar involvement in neurocognitive and linguistic functions.

Cerebellar neurocognition

NEUROCOGNITIVE DYSFUNCTIONS FOLLOWING CEREBELLAR DAMAGE

Executive dysfunctions

Studies grounded the view that the cerebellum essentially contributes to so-called executive

Table 1

Cerebellar involvement in neurocognitive functions

Cognitive Domain	*Function*	*Studies*
Executive Planning :	frontal problem solving	e.g. Grafman *et al.*, 1992
	cognitive planning	e.g. Grafman *et al.*, 1992
	sequencing of plans	e.g. Hallett & Grafman, 1997
Temporal Sequencing :	judgment of time duration	e.g. Ivy & Keele, 1989
	timing of plans and actions	e.g. Hallett & Grafman, 1997
	judgment of velocity of movement	e.g. Ivry & Diener, 1991
	discrimination of vowel duration	e.g. Ackermann *et al.*, 1996
	discrimination of vot	e.g. Ackermann *et al.*, 1996
Attention :	enhancement neural responsiveness	e.g. Yeo *et al.*, 1985
	direction of selective attention	e.g. Akshoomoff *et al.*, 1997
Visuo-Perception :	visuo-spatial processing	e.g. Silveri *et al.*, 1997
	visuo-construction	e.g. Botez-Marquard *et al.*, 1994
Learning :	motor skill learning	e.g. Marr, 1969; Tack, 1997
	procedural & associative learning	e.g. Bracke-Tolkmitt *et al.* 1989
Memory :	long-term memory	e.g. Appolonio *et al.*, 1993
	phonological short-term memory	e.g. Paulesu *et al.*, 1993
Imagery :	visuo-motor imagery	e.g. Decety *et al.*, 1990

Abbreviations : VOT, voice onset time

Table 2

Cerebellar involvement in speech and language functions

Linguistic Levels	*Function*	*Disturbance*	*Studies*
Articulation	musular speech control	ataxic dysarthria	Holmes, 1917 ; Darley *et al.*, 1975 ; Ackermann *et al.*, 1992
	covert articulation		Fiez & Rachle, 1997
	articulatory planning	speech apraxia	Mariën *et al.*, 2001
Speech Perception	discrimination of VOT and vowel duration		Ackermann *et al.*, 1996
Spelling	visuo-spatial organisation	afferent dysgraphia	Silveri *et al.*, 1997 ; 1999
Linguistic Processing	verbal associations	lexical retrieval defects	Petersen *et al.*, 1988 ; 1989
	semantic associations	lexical retrieval defects	Fiez *et al.*, 1992
	phonological generation	verbal fluency defects	Leggio *et al.*, 1995
	expressive grammar	expressive agrammatism	Silveri *et al.*, 1994 ; Zettin *et al.*, 1997
	syntactic knowledge	agrammatism	Mariën *et al.*, 1996 ;2000 ; Riva 1998 ; Gasparini *et al.*, 1999 ; Fabbro *et al.*, 2000 ; Riva and Giorgi, 2000
	language dynamics	dynamic aphasia	Mariën *et al.*, 1996 ;2000 ; Riva 1998 ; Gasparini *et al.*, 1999 ; Fabbro *et al.*, 2000 ; Riva and Giorgi, 2000

Abbreviations : VOT, voice onset time

functions, such as planning, sequential reasoning, and mental operations closely associated with the functional role of the prefrontal cortex (Leiner *et al.*, 1986 ; Leiner *et al.*, 1989). Grafman *et al.*, (1992), for instance, showed that patients with cerebellar atrophy experience frontal problem solving and cognitive planning difficulties in much the same way as patients with frontal lobe dysfunction. Similar observations corroborated the view that the cerebellum helps to code timing and sequential relations between stimuli and actions**.** In this respect, Hallett and Grafman (1997) postulated that 'lesions of the prefrontal cortex would hypothetically affect the activation of plans and actions, subcortical structures might allow for their automatic execution, and the cerebellum would ensure their correct sequencing and timing'.

Disturbed temporal sequencing and timing

Keele and Ivry (1989 ; 1991) demonstrated that patients with cerebellar atrophy not only show impaired motor programming but also defective perceptual timing. They hypothesized that the cerebellum acts as an 'internal clock' during any condition that requires temporal computations. Consonant with this view are the results of clinical studies which reveal that patients with cerebellar lesions are impaired at judging the relative duration of time intervals or the velocity of moving visual stimuli (Ivry and Keele, 1989 ; Ivry and Diener, 1991), and that they may display severe distortions in the discrimination of voice onset time and vowel durations (Ackermann *et al.*, 1997).

Attentional deficits

Cerebellar damage can cause deficits of selective attentional processes (orienting, distributing and shifting attention), probably due to dysfunction of cerebello-thalamo-cortical pathways.

In this respect, studies have shown that selective attention processes depend on coordinated interactions between the reticular activating system, and the frontal and parietal lobes (e.g., Mesulam, 1981 ; Posner and Petersen, 1990 ; Corbetta *et al.*, 1993). Within this integrated system, the cerebellum is considered to enhance neural responsiveness in advance to stimulation (e.g., Thompson, 1986 ; Yeo *et al*, 1985). In a large series of neurobehavioural, neurophysiological, and neuroimaging studies Courchesne and coworkers investigated the role of the cerebellum in selective attention (Courchesne, 1985 ; Courchesne *et al.*, 1988 ; Akshoomoff and Courchesne, 1994 ; Akshoomoff *et al.*, 1997). Their findings confirmed that the cerebellum coordinates the direction of selective attention and as a consequence subserves the execution of cortically generated commands for the enhancement and inhibition of different sources of sensory information.

Visuo-spatial processing disorders

Botez *et al.* (1985) encountered in a patient with chronic phenytoin intoxication reversible cerebellar ataxia and mild frontal- and parietal-like symptoms. They speculated that a dysfunction of cerebello-frontal and cerebello-parietal associative loops might act as the possible anatomophysiological substrate of these symptoms.

Many of the subsequent studies performed by this group (Botez *et al.*, 1991 ; Botez-Marquard and Botez, 1993 ; Botez-Marquard *et al.*, 1994 ; 1995 ; 1996) in patients with focal and neurodegenerative disorders of the cerebellum (especially olivopontocerebellar ataxia, Friedreich's ataxia, cerebellar cortical atrophy) further explored the role of the cerebellum in visuo-spatial and visuo-constructive procedures such as object assembly, digit symbol substitution, block design and visual problem solving tasks. Subserved by close anatomical pathways, the authors directly linked right hemisphere deficits of visuo-spatial organization to left cerebellar hemisphere damage.

A most illustrative case was reported by Botez-Marquard *et al.* in 1994. They described a 64-year-old right-handed woman with a well-delimited infarct in the territory of the left superior cerebellar artery. A hexamethyl-propileneamine oxime (HMPAO) SPECT of the brain disclosed a left cerebellar perfusion defect and a relative hypoperfusion of the basal ganglia and the frontoparietal areas of the right hemisphere. This phenomenon was coined 'crossed cerebello-cerebral diaschisis' by Broich and coworkers in 1987. Neuropsychological assessments revealed transient deficits indicating right hemisphere dysfunction. Botez-Marquard *et al.* (1994) concluded that unilateral cerebellar infarcts accompanied by crossed cerebello-cerebral diaschisis can cause neurocognitive defects indicative of contralateral cerebral hemisphere involvement.

Silveri *et al.* (1997 ;1999) reported a 67-year-old right-handed patient with cerebellar atrophy who in addition to ataxia also displayed typical features of spatial or afferent dysgraphia. This writing disorder usually occurs in patients with visuo-spatial disturbances following right cerebral hemisphere lesions**.** Silveri *et al.* (1997 ; 1999) explained their patient's writing disorder as an uncoupling of motor planning and proprioceptive feedback due to cerebellar damage and postulated that the functional substrate of afferent dysgraphia includes a defective interplay between the left hemisphere of the cerebellum and the contralateral supratentorial structures.

Disturbances of learning and memory

Experimental and clinical studies have demonstrated that the cerebellum is involved in many different aspects of memory such as procedural learning (eyeblink classical conditioning, motor adaptation learning and motor skill learning), paired-associative learning, short term-memory or working memory and long-term memory. In this section, the role of the cerebellum in memory processes, and especially those directly relevant to the processing of linguistic information, are concisely reviewed.

Procedural and associative learning

Classical conditioning of the eye blink response, (motor adaptation learning), sequencial learning (motor skill learning) and conceptual stimulus-response tasks (paired associate learning) have been used in many experimental studies to demonstrate the role of the cerebellum in associative learning and procedural learning tasks (McCormick *et al.*, 1981 ; Thompson *et al.*, 1997).

Apart from being involved in conditioned responses, it has been shown that the cerebellum plays an essential role in the acquisition of complex motor sequences. Marr (1969) first identified cerebellar involvement in motor learning. Brindley (1969) proposed that only in the initial learning phase the acquisition of skilled performance is guided by higher cerebral control. He speculated that when the movement is practiced it is given over to the cerebellum for the implementation of automatic motor control. Tach (1997) extended the idea of context-response linkage to the prefrontal brain functions and their role in the cognitive planning and execution of movement.

Bracke-Tolkmitt *et al.* (1989) demonstrated in heterogeneous groups of patients with cerebellar pathology selective impairment of paired-associative learning. In contrast to normal performance on

non-verbal associate learning tasks, defective results were obtained for verbally mediated tasks such as verbal paired-associate learning and stimulus-response tasks consisting of colour-word associations.

Clinical and neuroimaging studies on patients with cerebellar damage and on normal subjects (e.g. Jenkins *et al.*, 1994 ; Grafton *et al.*, 1995 ; Pascual-Leone *et al.*, 1993 ; Molinari *et al.*, 1997) have confirmed that the cerebellum (together with the prefrontal and subcortical structures) is involved in procedural and associative learning.

Long-term memory

The role of the cerebellum in long-term memory has been examined by means of various declarative memory tasks (e.g. story recall of the Wechsler Memory Scale). Non-demented patients with cerebellar neurodegenerative disorders were impaired in free delayed recall but not in recognition memory or in implicit learning (Appollonio *et al.*, 1993). This resembles the pattern found in amnesic patients with prefrontal lesions and contrasts with the pattern found in amnesic patients with temporal lobe lesions in whom both recall and recognition are deficient (Janowsky *et al.*, 1989).

Phonological short-term memory

Phonological short-term memory is a subcomponent of working memory that subserves the retention of verbal information for a brief period of time. It allows specific linguistic acts such as verbal repetition and sentence comprehension and is of crucial importance in language learning.

Salamé and Baddeley (1982) subdivided the verbal working memory system in two separate components : 1) the phonological short-term store which passively retains verbal information for a short period of time and 2) the rehearsal system which re-circulates stored verbal information to prevent rapid decay. In addition to a primary rehearsal function, the rehearsal system also acts 1) as a transcoder of non-verbal to verbal information to assure access to the phonological store and 2) as an operator between the phonological store and the phonological output buffer in which verbal information is temporarily stored to allow programming of various linguistic output processes. Vallar *et al.* (Vallar & Papagno, 1995 ; Vallar *et al.*, 1997) identified the neural representations of both components of phonological short-term memory. They showed that the phonological short-term memory store is located in the supramarginal gyrus and the inferior parietal lobe of the dominant hemisphere, the rehearsal system and phonological output buffer in Broca's area, the pre-motor cortex, the insula and supplementary motor area of the language dominant hemisphere. Within this framework, involvement of the right cerebellar hemisphere during performance of cognitive tasks relying on the rehearsal system was shown by Paulesu *et al.* (1993).

Acquired Speech and Language disorders

Articulation and Phonation

Ataxic Dysarthria

Holmes (1917) extensively documented disturbed muscular control of speech and phonation after cerebellar lesions and contributed to the view that the cerebellum plays a crucial role in motor speech production. He described the typical cerebellar speech characteristics as slow, monotonous, staccato, scanned, indistinct, remarkable irregular, jerky, explosive, slurred, and laboured. Darley *et al.* (1975) coined these alterations in phonation and articulation as 'ataxic dysarthria'. On the basis of a systematic auditory perceptual evaluation they identified imprecise production of consonants and vowels, irregular articulatory breakdown, excess and equal stress, and harsh voice quality as the cardinal symptoms of ataxic dysarthria.

Holmes (1922), and many investigators after him, maintained that the responsible lesion for ataxic dysarthria could be situated in either one or both cerebellar hemispheres. However, more recent studies adressing topographic aspects of cerebellar induced speech abnormalities have shown that dysarthria most frequently follows damage to the superior anterior vermal and paravermal regions within the vascular territory of the left superior cerebellar artery (Lechtenberg & Gilman, 1978 ; Amarenco *et al.*, 1991a,b ; Ackermann *et al.*, 1992 ; Barth *et al.*, 1993).

The majority of functional neuroimaging studies with PET and fMRI on overt (articulated speech) and covert articulation (inner speech) support the clinical results indicating superior paravermal representation of speech functions in the cerebellum (see Fiez & Raichle, 1997 for a review).

Apraxia of speech

Apraxia of speech (anarthria, verbal apraxia) is a selective impairment of speech movements following the inability to properly and smoothly traduce phonological knowledge into verbal-motor commands (Lebrun, 1990). It is typically characterized by inconsistent misarticulations, phonetic alterations of vowel and consonant production, articulatory groping inducing sequential errors, flattened voice volume, prosodic abnormalities, slow articulation, scanning speech and 'islands of fluent oral-verbal output'. The crucial anatomical seat of this articulatory planning and coordination disorder has been recently localized in the anterior part of the language dominant insula, directly anterior to the central insular sulcus (Dronkers, 1996).

Apraxia of speech shares striking semiological similarities with ataxic dysarthria. These

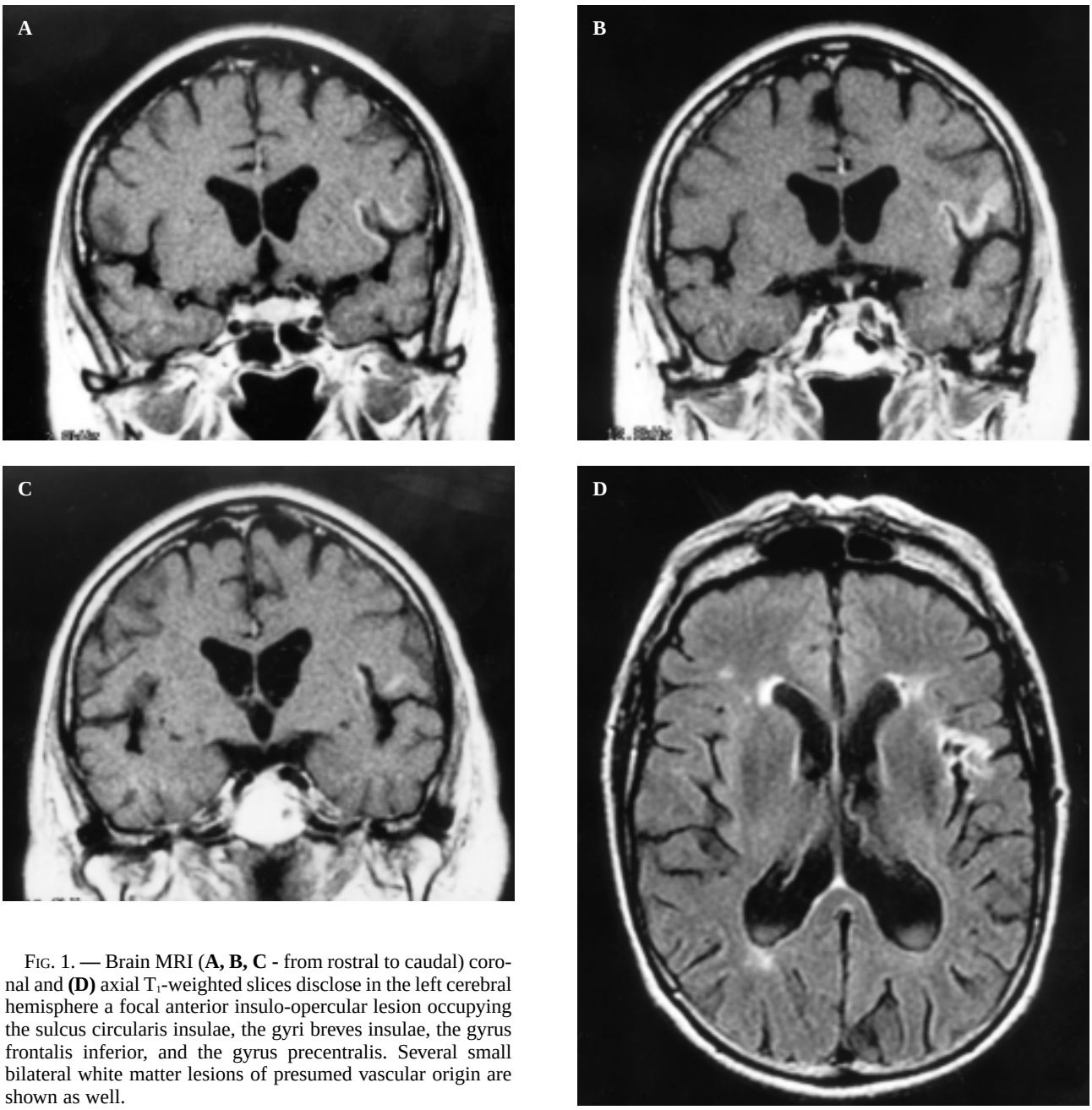

FIG. 1. — Brain MRI (**A, B, C -** from rostral to caudal) coronal and **(D)** axial T_1-weighted slices disclose in the left cerebral hemisphere a focal anterior insulo-opercular lesion occupying the sulcus circularis insulae, the gyri breves insulae, the gyrus frontalis inferior, and the gyrus precentralis. Several small bilateral white matter lesions of presumed vascular origin are shown as well.

similarities, already implicated in prior terms as 'ataxic aphasia' and 'cortical dysarthria', suggest a close functional cooperation between the anterior opercular speech area and the cerebellum. Support for a close functional interplay between the right hemisphere of the cerebellum and the anterior insulo-opercular region of the language dominant hemisphere is found in a patient recently described by Mariën *et al.* (2001). In this study, a 83-year-old right-handed patient is described with a unique infarction restricted to the left anterior insula and the adjacent part of the intrasylvian frontal opercular cortex (Figure 1). The patient acutely developed severe apraxia of speech that evolved into mere mutism within a few hours. After rapid recovery from mutism, oral language remained persistently characterized by apraxic speech symptoms. In addition, in-depth language investigations during the lesion phase disclosed an isolated, highly selective disturbance of the spelling system (phonological agraphia) which receded within a few weeks. A Tc-99m-ECD SPECT study of the brain disclosed hypoperfusions involving the gyrus frontalis inferior and gyrus precentralis of the left cerebral hemisphere and the contralateral right hemisphere of the cerebellum (Figure 2). This pattern of perfusional defects, representing crossed cerebellar diaschisis (Baron *et al.*, 1980 ; Pantano *et al.*, 1986 ; Engelborghs *et al.*, 2000), reflects the distant metabolic impact of the cerebral lesion on the contralateral cerebellar hemisphere and adds evidence to the view that these sites are anatomically and functionally closely interconnected.

That the role of the right hemisphere of the cerebellum in apraxic speech manifestations might have been underestimated is also suggested by

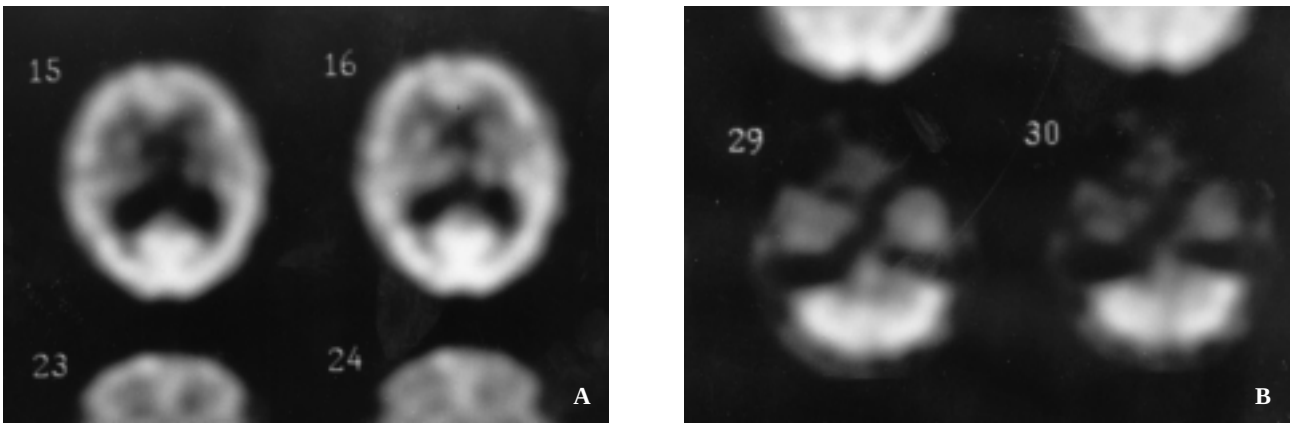

FIG. 2. — Tc-99m-ECD SPECT scan of the brain performed nine days after stroke demonstating **(A)** relative hypoperfusion in the left gyrus frontalis inferior and left gyrus precentralis and **(B)** crossed cerebellar diaschisis.

SPECT findings recently obtained in two personal observations of pure and persistent apraxia of speech (unpublished data). A SPECT scan of the brain in both these patients with fronto-opercular lesions of the language dominant hemisphere also disclosed crossed cerebellar diaschisis. This observation seems to indicate that diaschisis related phenomena affecting the right hemisphere of the cerebellum might constitute an important factor in apraxia of speech. To unravel the presumed role of the cerebellum in articulatory planning disorders, future studies are needed that focuss on a close semiological comparison between apraxia of speech and ataxic dysarthria following right cerebellar lesions.

Language Processing

Introduction

Leiner *et al.* (1986 ;1989) explained the functional expansion of the cerebellum as a consequence of structural changes that evolved during hominid evolution. Having traced newly evolved connections in the human brain, they postulated that the enlarged size of the dentate nucleus gave raise to new neural connections. These new connections end in some expanded prefrontal areas which evolved concomitantly with the human neodentate and which send back new connections. The composition of these loops consists of the phylogenetically new parts of the lateral cerebellum sending projections to Brodmann's areas 6, 44 and 45 via the nucleus ventralis intermedius and nucleus ventralis anterior of the thalamus (Engelborghs *et al.*, 1998) and backward projections from the prefrontal areas to the lateral cerebellum via the pons and the red nucleus. The discovery of major reciprocal neural pathways between the cerebellum and the frontal areas of the language dominant hemisphere (Broca's area and the supplementary motor area (SMA)) constitute a hallmark in the development of the concept of cerebellar contribution in non-motor linguistic processes. In the past ten years, close cooperation across disciplines has established the view that the right hemisphere of the cerebellum plays a crucial role within the language network.

Verbal Fluency and Word Retrieval

At the end of the 1980s, Petersen *et al.* (1988 ;1989) reported the results of innovative PET activation procedures that provided preliminary evidence in favour of the hypothesis of cerebellar involvement in non-motor language (Leiner *et al.*, 1986). Their paradigm required subjects : 1) to repeat a visually presented noun (motor task), and 2) to generate a semantically associated verb for a visually presented noun e.g., bike (to ride) and to say this verb aloud (cognitive and motor task). Subtracting the areas of motor activation of the first task (essentially motor) from the areas of motor activation of the second task (cognitive and motor) enabled identification of activated areas during cognitive word association. These tasks, which reflect the capacity to generate words according to a given rule, are generally considered to depend on a close cooperation between verbal and executive abilities and are clinically widely applied to explore frontal lobe functioning. During mere verbal-motor performance**,** an activated area in the superior anterior lobe of the cerebellum was found, just lateral to the loci involved in finger and eye movement. The verbal association task strikingly activated a totally different area : the inferior lateral part of the right hemisphere of the cerebellum which projects to the left prefrontal language areas. Despite variations on the original task design**,** several studies have consistently reproduced these findings (Raichle *et al.*, 1994 ; Martin *et al.*, 1995 ; Grabowski *et al.*, 1996). Leiner *et al.* (1989) interpreted the simultaneous activation of the right hemisphere of the cerebellum and Broca's language area during word generation as the reflection of accelerated transmission of signals between these two centers involved in word finding.

In addition to evidence derived from neuroimaging studies, clinical studies on patients with

cerebellar disease have confirmed the role of the right hemisphere of the cerebellum in word production. Motivated by the findings of Petersen *et al.* (1989), Fiez *et al.* (1992) conducted the first specially designed study on word generation in a 41-year-old right-handed lawyer who presented with semantic retrieval deficits after a vascular lesion of the right cerebellar hemisphere. Despite high-level conversational skills and normal performance on standard language tests, the patient failed in a number of semantic generation tasks.

Similar studies have been undertaken to identify the role of the cerebellum in word retrieval processes relying on sound relationships (phonological verbal fluency). Leggio *et al.* (1995) conducted both phonological and semantic verbal fluency studies in three etiologically distinct patient groups with cerebellar pathology. One group had atrophic lesions (mainly of the vermal and paravermal regions), the other two groups had restricted focal lesions (lateral part of the left or right cerebellar hemisphere). Their results showed that : 1) the cerebellar lesioned group performed at a lower level than the matched controls irrespective of the task involved (phonological or semantic), 2) atrophic patients obtained better results than patients with focal lesions, although they had more severe ataxia, 3) in comparison with the control group, the atrophic patients performed only significantly worse on the phonological task, and 4) patients with focal damage of the left hemisphere of the cerebellum performed better than patients with right hemispheric cerebellar damage. These findings, which extend the functional role of the cerebellum in linguistic processes, reveal a close association between 1) medial cerebellar lesions and the prevalence of motor deficits, and 2) lateral, especially right cerebellar damage and verbal fluency deficits.

Agrammatism

Recently, the role of the right hemisphere of the cerebellum in non-motor language functions has been expanded by evidence derived from agrammatic patients. Silveri *et al.* (1994) and Zettin *et al.* (1997) reported two patients in whom a right cerebellar lesion caused expressive agrammatism. In two other patients with vascular lesions (Mariën *et al.*, 1996 ;2000 ; Gasparini *et al.* 1999), the linguistic deficits following right cerebellar damage extended beyond the restricted boundaries of distorted expressive grammar. Similar observations were made by Riva (1998) in a child with cerebellitis and Riva and Giorgi (2000) in two children after posterior fossa surgery.

Agrammatism has long been considered a pure syntactic impairment of both language production and comprehension, closely associated with Broca's aphasia. According to classical definitions (Benson and Ardila, 1996), it is typically characterized by maximum difficulty in using and understanding grammatical morphemes such as functors and affixes. Disrupted grammatical competence is further reflected by telegrammatic style resulting from omission of functional-grammatical markers and preserved use of content words, incorrectly used verbs, deletion of tense, person, and number designation. More recently, however, psycholinguistic research has broadened this concept of a pure syntax disorder. The observation of various combinations of differential syntax impairments (Tissot *et al.*, 1973 ; Miceli *et al.*, 1983 ; Kolk *et al.*, 1985 ; Jerema *et al.*, 1987 ; Caramazza and Hillis, 1989) led to the hypothesis that a distinct neuroanatomic organization subserves these dissociations : a primarily syntactic component being localized in the dominant frontal lobe and a primarily morphological component being located in the dominant postcentral perisylvian cortex (Nadeau, 1988 ; Nadeau and Gonzalez Rothi, 1992).

For the first time, Silveri *et al.* (1994) reported a consistent correlation between focal damage of the right hemisphere of the cerebellum and agrammatic symptoms. They described a 67-year-old right-handed patient who after a right cerebellar stroke presented with a right-sided cerebellar syndrome, ataxic dysarthria and transient expressive agrammatism. Linguistic analysis of the agrammatic manifestations showed the deficit to be of the morphological type (relevant omissions of auxiliaries and clitic pronouns and many substitutions of bound grammatical morphemes). Repeated structural neuroimaging studies did not reveal any supratentorial abnormality to account for the observed language deficits. SPECT, however, evidenced a relative hypoperfusion in the entire left cerebral hemisphere, more stable and consistent in the posterior regions. During follow-up, the perfusion defects paralleled the clinical course of motor and linguistic symptoms. Four months after onset of neurological symptoms, amelioration of the motor deficits and agrammatic symptoms was reflected by a marked improvement of left hemispheric perfusion. Silveri *et al.* (1994) interpreted this selective speech production impairment as a 'peripheral disorder' reflecting a linguistic behavioural adaptation to a deficit outside the mental linguistic system**.** The deficit was not considered to affect syntactic competence but the on-line application of syntactic rules that put grammatical morphemes in accordance. Zettin *et al.* (1997) accounted in a similar sense for the sentence production impairment of their patient with a hemorrhagic stroke in the right cerebellar hemisphere. They described the disturbance as a compensatory mechanism to circumvent a disorder that goes beyond the strictly articulatory level.

In the patients reported by Mariën *et al.* (1996 ; 2000) and Gasparini *et al.* (1999), a vascular lesion

of the right hemisphere of the cerebellum induced a structural impairment at the syntactic selection level producing agrammatic manifestations in different language modalities (expressive and receptive language). Given the evidence of impaired syntactic knowledge, agrammatism in these patients could not be sufficiently explained as a compensatory result of a timing disorder lying outside the linguistic system. Following the observation that even genuine aphasic deficits might accompany expressive and receptive agrammatism we maintained that right cerebellar lesions may provoke a genuine aphasic syndrome (Mariën *et al.*, 1996). This view is corroborated by the observations of Riva (1998), Fabbro *et al.* (2000) and Riva and Giorgi (2000).

Cerebellar induced aphasia

Hassid (1995) documented a 17-year-old left-handed man with a right cerebellar infarction who in addition to classical cerebellar motor symptoms displayed a moderate anomia, mild difficulties in auditory reception and reading, and severe difficulties in writing and mathematics. CT and MRI of the brain only disclosed a right-sided wedge-shaped cerebellar infarction. SPECT scan images of the brain showed a relative hypoperfusion in the right cerebellar hemisphere and the frontal, temporal and parietal region of the left hemisphere, consistent with a right cerebellar infarction and crossed cerebral diaschisis. In support of the notion of the role of the cerebellum in neurocognition, Hassid (1995) concluded from these observations that cognitive abnormalities after cerebellar infarction can be easily overlooked and that standardized neurocognitive assessments in patients with focal cerebellar lesions may be more reliable in accurately delineating subtle, but significant cognitive abnormalities. The finding of aphasic disturbances in association with a right cerebellar lesion was not discussed.

Mariën *et al.* (1996 ; 2000) reported a 73-year-old right-handed patient who acutely developed cerebellar and brainstem symptoms. Involvement of the right cerebellum was reflected by slight dysarthric speech problems and right-sided dysdiadochokinesia, dysmetria, and rebound phenomena. The left hemiparesis and hemisensory deficit indicated pontine involvement. During the subsequent course of the acute phase the patient progressively developed an aphasic syndrome and more severe dysarthria. The unexpected finding of non-fluent aphasia with marked adynamic speech characteristics, prompted us to suspect a focal dysfunction of presumed vascular origin of the prefrontal areas of the language dominant hemisphere. However, repeated structural brain imaging studies with CT and MRI did not disclose any supratentorial abnormality. During a five year follow-up period both ataxia and aphasia improved. Repeated SPECT studies of the brain yielded positive findings to account for the language symptoms. Perfusion deficits were encountered in the anatomoclinically suspected brain areas that paralleled the alterations in the language profile during longitudinal follow-up. In addition to a marked hypoperfusion in the right cerebellar hemisphere, a SPECT scan performed 30 days post-onset neurological symptoms revealed left frontoparietal perfusion deficits which involved the gyrus frontalis medius and inferior, as well as the gyrus precentralis and postcentralis. Along the lines of an improvement of the adynamic language symptoms, a less pronounced hypoperfusion was found in the frontal areas six months after onset. In association with near remission of the aphasia, near normalisation of the perfusion pattern in the left frontoparietal area was found five years post-onset.

A possible explanation for aphasia following right cerebellar damage might be found in a loss of excitatory impulses through cerebello-ponto-thalamo-cortical pathways (Sönmezoglu *et al.*, 1993). To substantiate this pathophysiological mechanism underlying so-called cerebellar induced aphasia, we relied on the extensive cerebellar output connections projecting to the frontal lobe (Mariën *et al.*, 1996 ; Engelborghs *et al.*, 1998). In 1987, Broich and coworkers described the first case of so-called ‘crossed cerebello-cerebral diaschisis’ (cCCD). In this patient, a right cerebellar ischemic lesion produced a remote contralateral left hemisphere hypoperfusion with the most marked metabolic reduction in the premotor areas. Since then, the phenomenon of cCCD has been documented in several cases of unilateral cerebellar stroke and neurodegenerative pathologies of the cerebellum (e.g., Kimura *et al.*, 1989 ; Yokoji *et al.*, 1989 ; Rousseau and Steinling, 1992 ; Botez *et al.*, 1993 ; Sönmezoglu *et al.*, 1993 ; Deguchi *et al.*, 1994) and in an increasing number of patients with focal neurocognitive (Attig *et al.*, 1991 ; Boni *et al.*, 1992 ; Botez *et al.*, 1994) and neurolinguistic deficits (Silveri *et al.* 1994 ; Mariën *et al.*, 1996 ; 2000 ; Zettin *et al.*, 1997).

Fabbro *et al.* (2000) thoroughly investigated four right-handed patients with tumoural cerebellar lesions before and after surgery. Irrespective of the lesion type and lesion localization (vermis, left and right cerebellum), all four patients displayed linguistic dysfunctions, mainly affecting morphosyntactic knowledge and lexical retrieval. After surgery, only two patients partially recovered. Fabbro *et al.* (2000) related the linguistic deficits to an alteration of language control processes rather than to a structural impairment of specific components of the language system. In their view, the vermis and portions of the cerebellar hemispheres operate within a large neurofunctional language network as an organizational control mechanism via the frontal lobe system. Rapid recovery of lin-

guistic disturbances following acute cerebellar damage was attributed to partial functional reactivation of linguistic centers after regression of diaschisis phenomena.

Transient cerebellar mutism syndrome

So-called 'fossa posterior syndrome' or 'transient cerebellar mutism syndrome with subsequent dysarthria' (Van Dongen *et al.*, 1994) following fossa posterior tumour resection in children constitutes a well-recognized neurobehavioural disorder. Though it has sporadically been described in adults (e.g., Salvati *et al.*, 1991 ; D'Avanzo *et al.*, 1993 ; Çakir *et al.*, 1994) and in association with brain stem tumour surgery (e.g., D'Avanzo *et al.*, 1993 ; Frim and Ogilvy, 1995), the syndrome occurs most frequently in children who underwent vermian tumour surgery (estimated incidence up to 15%) (Pollack, 1997). Other etiologies such as traumatic cerebellar injury (e.g., Yokota *et al.*, 1990 ; Ersahin *et al.*, 1997), and viral infections of the cerebellum (Riva, 1998) have exceptionally been reported. The condition of speechlessness, frequently associated with a spectrum of abundant neurobehavioural changes, typically develops with a latency of one to four days after surgery and recedes after a period of weeks to four months. Aside from residual dysarthria, recovery on the linguistic level has long been conceived to be complete. However, Levisohn *et al.* (2000) and Riva and Giorgi (2000) recently identified long-term clinically relevant neuropsychological and affective changes.

Several risk factors for the development of the fossa posterior syndrome have been proposed : preoperative hydrocephalus, tumour location (Pollack, 1995), tumour type and size (Catsman-Berrevoets *et al.*, 1999), rostrocaudal length of the vermian incision (Dailey, 1995 ; Pollack, 1995), acute bilateral cerebellar injury (Rekate *et al.*, 1985), dentate nucleus injury (Ammirati *et al.*, 1989 ; Çakir *et al.*, 1994), postoperative oedema within the brachium pontis and/or brachium conjunctivum, post-operative hydrocephalus and meningeal reactions (Humphreys, 1989 ; Ferrante *et al.*, 1990), transient dysfunction of the A9 and A10 mesencephalic dopaminergic cell-groups and ascending activating reticular system (Catsman-Berrevoets *et al.*, 1992), postoperative arterial spasms causing ischemia, and disturbed cerebellar perfusion (Nagatani *et al.*, 1991).

Aside from long-lasting neurocognitive deficits, Riva and Giorgi (2000) also reported for the first time in a paediatric population linguistic dysfunctions after vermal medulloblastoma resection. In the early phase of recovery from mutism, two of six children presented with a predominantly expressive language syndrome, essentially consisting of prosodic abnormalities (bradylalia, flattened intonation) and expressive syntax disturbances 'reminescent of the agrammatical language frequently encountered in aphasic patients (including children) with acquired left frontal lesions'. Formal language assessments later revealed excellent auditory-verbal comprehension, normal repetition, 'severe lack of spontaneity in terms of active language, and a tendency to speak very little even after being encouraged to do so'. Three years after the operation, the syntax disturbances had resolved but language quality was considered poor. In contrast to the four children with a classical presentation of the syndrome, the linguistically impaired children had (aside from a partial excision of the vermis) an additional lesion of the right cerebellar hemisphere. The authors consequently related the linguistic manifestations to focal damage of the right hemisphere of the cerebellum and concluded in the absence of functional imaging data that 'it is impossible to determine whether the deficits (…) are directly due to the cerebellar lesion or to diaschisis arising from the sudden interruption of the reciprocal connections between the different cerebral regions and the cerebellum'.

Our findings corroborate the observations of Riva and Giorgi (2000) and might further contribute to the understanding of the pathophysiological substrate of the intriguing spectrum of neurobehavioural disturbances that may follow ischemia or tumour resection in the fossa posterior. Firstly, our adult case with cerebellar induced aphasia sheds some light on the above raised issue (Mariën *et al.*, 1996 ;2000). In agreement with Riva and Giorgi's observations (2000), an aphasic syndrome was found that typologically resembled Luria's frontal dynamic aphasia (Luria and Tsvetkova, 1967 ; Luria, 1977) with agrammatism. In our patient, the possibility of a distant functional impact of the right cerebellar lesion on the contralateral prefrontal language areas was confirmed by positive SPECT findings, revealing hypoperfusion in the anatomoclinically suspected brain regions. During longitudinal follow-up, a significant regression of crossed cortical and subcortical left hemisphere diaschisis, as demonstrated by SPECT, parallelled the improvement of self-generated speech and syntactic abilities. In addition, longitudinal neurocognitive and SPECT findings evidenced that the aphasic symptoms resulted from diaschisis affecting the contralateral prefrontal cortical areas probably through cerebello-ponto-thalamo-cortical pathways. Secondly, we also encountered in several children almost identical aphasic disturbances after fossa posterior tumour resection. Given the overt clinical resemblances and the frontal-like nature of the neurobehavioural alterations observed in these children we started to investigate this group of patients with SPECT and an extensive neuropsychological test protocol. The preliminary results of this study (unpublished data) reveal a correlation between type and extent of the neurobehavioural dysfunctions and the area and

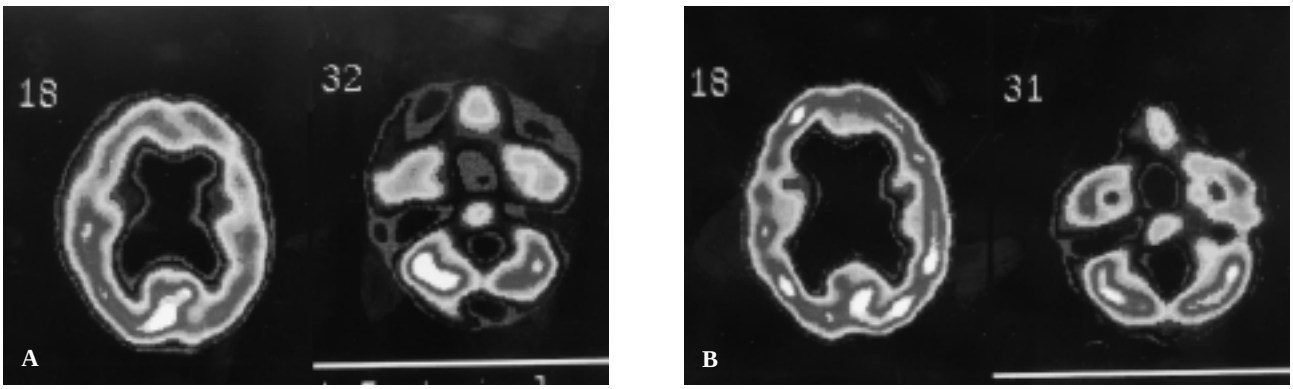

FIG. 3. — **(A)** ^{99m}Tc-HMPAO SPECT of the brain performed during a three week period of akinetic mutism following posterior fossa surgery. In addition to a pronounced relative (antero-posterior) bifrontal hypoperfusion, a marked relative hypoperfusion in the left hemisphere of the cerebellum is shown. **(B)** Repeated SPECT performed during the early phase of recovery from akinetic mutism reveals clearly improved perfusion of the frontal lobes with minimal perfusion decrease in the parietal lobe of the left cerebral hemisphere. A slight asymmetry of the cerebellar hemisphere persists (relative hypoperfusion of the left cerebellar hemisphere).

degree of crossed cerebral diaschisis and further support the pathophysiological view on cerebellar induced language disturbances as a diaschisis phenomenon. For instance, in a 10-year-old right-handed boy surgically treated for a pilocytic astrocytoma, ^{99m}Tc-HMPAO SPECT disclosed severe bifrontal perfusion defects during a three week period of akinetic mutism (Figure 3A). When the boy gradually recovered, he presented with dynamic aphasia, agrammatism and slight behavioural alterations. Repeated SPECT showed a reduction of the frontal perfusion deficits which were, however, still significantly more pronounced in the left frontal region (Figure 3B). In several other children with fossa posterior tumours, a similar parallelism was found between the regional distribution and extent of perfusion deficits and the type and course of neurocognitive symptoms.

In some of the patients under consideration, this correlation was even found in the preoperative phase of investigation. Preoperative neurocognitive assessments in a five-year-old right-handed child with a cerebellar medulloblastoma demonstrated an isolated deficit consisting of a significant diminuition of self-generated speech. This finding was reflected by a left frontal hypoperfusion on SPECT (Figure 4A). After tumour resection, adynamia of spontaneous speech worsened and correlated with an aggravation of hypoperfusion in the left frontal areas (Figure 4B).

Though carefully controlled studies with larger groups of patients are needed to draw sound conclusions, these findings support the view that aphasic dysfunctions observed after right cerebellar lesions can be interpreted as a direct effect of diaschisis via the cerebello-ponto-thalamo-cortical pathways.

Conclusion

The development of insights in the causal relationship between cerebellar pathology and a variety of neurocognitive deficits has been overshadowed by the cerebellar role in motor functioning. In the late 1970s and early 1980s, new neuroimaging techniques created increased interest in the non-motor functions of the cerebellum. As a result, case reports began to appear in the literature alluding to the possible pathogenic role of the cerebellum in various neurocognitive dysfunctions. In addition, funtional neuroimaging studies demonstrated that the cerebellum is activated during the performance of various cognitive and linguistic tasks even in the complete absence of any motor activity. Following the notion that the cerebellum may be crucially involved in non-motor functions, an impressive number of experimental and clinical studies has explored the concept of cerebellar cognition. These studies evidenced the modulatory role of the cerebellum through reciprocal cerebello-cerebral pathways in executive processes, temporal ordening and timing, attentional mechanisms, visuo-spatial processing, memory and learning. In a similar way, the long-standing conviction that the cerebellum solely participates in motor speech started to change at the end of the 1980s. Newly-traced neuro-anatomical connections between the lateral part of the right cerebellum and the frontal areas of the language dominant hemsiphere (Brodmann areas 6, 44, and 45) suggested the possibility that cerebellar signals to these areas can contribute to linguistic skills beyond the pure motor processes of articulation and phonation. Soon thereafter, neuroimaging and clinical studies provided evidence in support of the modulatory role of the cerebellum in lexical retrieval, syntax and the dynamics of language and even led to the concept of cerebellar induced aphasia.

As demonstrated in this review, neurocognitive dysfunctions in cerebellar pathology likely represent diaschisis-related phenomena. Consequently, cerebellar induced neurocognitive disturbances

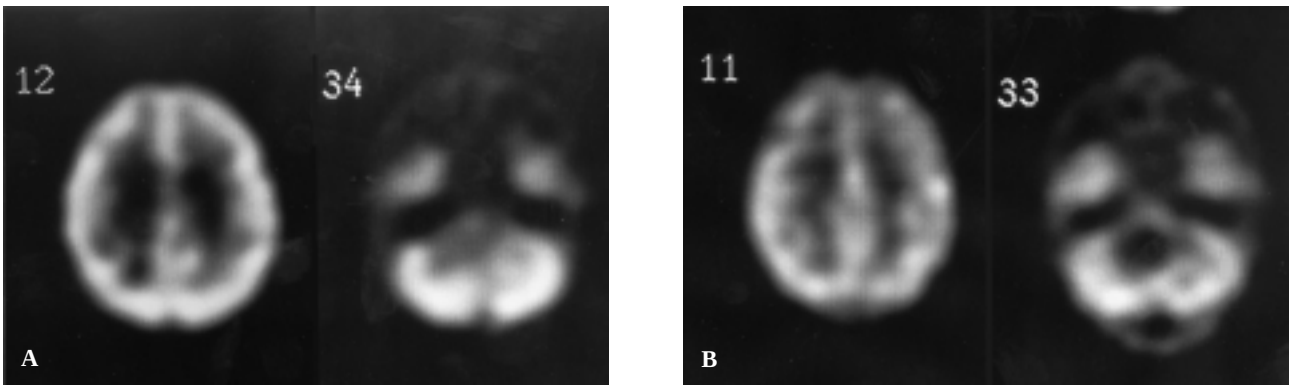

FIG. 4. — **(A)** Preoperative ^{99m}Tc-HMPAO SPECT of the brain performed in a 5-year-old right-handed child with a cerebellar medulloblastoma and linguistic deficits. A relative hypoperfusion of the right cerebellar hemisphere is shown. Although there is no breach of the cerebral cortex, there is less physiological activation of the left frontal lobe. **(B)** Postoperative SPECT demonstrates a large scintigraphic defect in the cerebellum slightly off-centre to the right. A strikingly increased hypoperfusion deficit in the left frontal lobe is shown.

do not imply representation of neurocognitive functions at the level of the cerebellum but reflect diminished or abolished dysfunction of the remote supratentorial areas in which these functions are localized due to reduced input via cerebello-cortical pathways.

As the result of combined neuroscientific efforts, the concept of cerebellar neurocognition evolved within the last two decades from a mere afterthought to an exciting new multifaced area of contemporary neuroscientific investigations in which many avenues are still to be explored.

Acknowledgements

OCMW Medical Research Foundation and Born-Bunge Foundation, University of Antwerp. S.E. is a Research Assistant of the Fund for Scientific Research - Flanders (F.W.O. - Vlaanderen).

REFERENCES

ACKERMANN H., GRÄBER S., HERTRICH I., DAUM I. Categorical speech perception in cerebellar disorders. *Brain and Language*, 1997, **60** : 323-331.

ACKERMANN H., VOGEL M., PETERSEN D., POREMBA M. Speech deficits in ischaemic cerebellar lesions. *Journal of Neurology*, 1992, **239** : 223-227.

AKSHOOMOFF N. A., COURCHESNE E. ERP evidence for a shifting attention deficit in patients with damage to the cerebellum. *Journal of Cognitive Neuroscience*, 1994, **6** : 388-399.

AKSHOOMOFF N. A., COURCHESNE E., TOWNSEND J. Attention coordination and anticipatory control. In : *The cerebellum and cognition* (International Review of Neurobiology, Vol 41). SCHMAHMANN J. D. (ed.). San Diego CA, Academic Press, 1997, 575-598.

AMARENCO P., CHEVRIE-MULLER C., ROULLET E., BOUSSER M. G. Paravermal infarct and isolated cerebellar dysarthria. *Ann. Neurol.*, 1991a, **30** : 211-213.

AMARENCO P., ROULLET E., GOUJON C., CHERON F, HAUW J.-J. *et al.* Infarction in the anterior rostral cerebellum (the territory of the lateral branch of the superior cerebellar artery). *Neurology*, 1991b, **41** : 253-258.

AMMIRATI M., MIRZAI S., SAMII M. Transient mutism following removal of a cerebellar tumour : a case report and review of the literature. *Child. Nerv. Syst.*, 1989, **5** : 12-14.

APPOLLONIO I. M., GRAFMAN J., SCHWARTZ V., MASSAQUOI S., HALLETT M. Memory in patients with cerebellar degeneration. *Neurology*, 1993, **43** : 1536-1544.

ATTIG E., BOTEZ M. I., HUBLET C. I., VERDONCK C., JACQUY J., CAPON A. Cerebral diaschisis following cerebellar lesion : contribution of the cerebellum to cognitive functions. *Rev. Neurol.*, 1991, **147** : 200-201.

BARON J. C., BOUSSER M. G., COMAR D., CASTAINGNE P. Crossed cerebellar diaschisis in human supratentorial brain infarction. *Trans. Am. Neurol. Ass.*, 1980, **105** : 459-461.

BARTH A., BOGOUSSLAVSKY J., REGLI F. The clinical and topographic spectrum of cerebellar infarcts : a clinical-magnetic resonance imaging correlation study. *Ann. Neurol.*, 1993, **33** : 451-456.

BENSON D. F., ARDILA A. Aphasia : a clinical perspective. New York, Oxford University Press, 1996.

BLOEDEL J. R., BRACHA V. Duality of cerebellar motor and cognitive functions. In : *The cerebellum and cognition* (International Review of Neurobiology, Vol 41). SCHMAHMANN J. D. (ed.). San Diego CA, Academic Press, 1997, 613-634.

BONI S., VALLE G., GIOFFI R. P., BONETTI M. G., PERRONE E. *et al.* Crossed cerebello-cerebral diaschisis : a SPECT study. *Nucl. Med. Commun.*, 1992, **13** : 824-831.

BOTEZ M. I., GRAVEL J., ATTIG E., VÉZINA J.-L. Reversible chronic ataxia after phenytoin intoxication : possible role of the cerebellum in congnitive thought. *Neurology*, 1985, **35** : 1152-1157.

BOTEZ M. I., LÉVEILLÉ J., LAMBERT R., BOTEZ T. Single photon emission tomography (SPECT) in cerebellar disease : cerebello-cerebral diaschisis. *Eur. Neurol.*, 1991, **31** : 405-412.

BOTEZ-MARQUARD T., BOTEZ M. I. Cognitive behavior in heredodegenerative ataxias. *Eur. Neurol.*, 1993, **33** : 351-357.

BOTEZ-MARQUARD T., LÉVEILLÉ J., BOTEZ M. I. Neuropsychological functioning in unilateral cerebellar damage. *Can. J. Neurol. Sci.*, 1994, **21** : 353-357.

BOTEZ-MARQUARD T., PEDRAZA O. L., BOTEZ M. I. Neuroradiological correlates of neuropsychological disorders in olivopontocerebellar atrophy (OPCA). *Eur. J. Neurol.*, 1996, **3** : 89-97.

BOTEZ-MARQUARD T., ROUTHIER I. Reaction time and intelligence in patients with olivopontocerebellar atrophy. *Neuropsychiat. Neuropsychol. Behav. Neurol.*, 1995, **8** : 169-175.

BRACKE-TOLKMITT R., LINDEN A., CANAVAN A. G. M., ROCKSTROH B., SCHOLZ E. *et al.* The cerebellum contributes to mental skills. *Behav. Neurosci.*, 1989, **103** : 442-446.

BRINDLEY G. S. The use made by the cerebellum of the information that it receives from the sense organs. *Int. Brain. Res. Org. Bull*., 1969, **5** : 299-322.

BROICH K., HARTMANN A., BIERSCK H. J., HORN R. Crossed cerebello-cerebral diaschisis in a patient with cerebellar infarction. *Neurosci. Lett.*, 1987, **83** : 7-12.

BUCKNER R. L., PETERSEN S. E., OJEMANN J. G., MIEZIN F. M., SQUIRE L. R., RAICHLE M. E. Functional anatomical studies of explicit and implicit memory retrieval tasks. *J. Neurosci.*, 1995, **15** : 12-29.

ÇAKIR Y., KARAKISI D., KOÇANAOGULLARI O. Cerebellar mutism in an adult : case report. *Surg. Neurol.*, 1994, **41** : 342-344.

CARAMAZZA A., HILLIS A. E. The disruption of sentence production : some dissociations. *Brain and Language*, 1989, **36** : 625-650.

CATSMAN-BERREVOETS C. E., VAN DONGEN H. R., MULDER P. G. H., PAZ Y GEUZE D., PAQUIER P. F., LEQUIN M. H. Tumour type and size are high risk factors for the syndrome of "cerebellar" mutism and subsequent dysarthria. *Journal of Neurology, Neurosurgery, and Psychiatry*, 1999, **67** : 755-757.

CATSMAN-BERREVOETS C. E., VAN DONGEN H. R., ZWETSLOOT C. P. Transient loss of speech followed by dysarthria after removal of posterior fossa tumour. *Dev. Med. Child Neurol.*, 1992, **34** : 19-29.

CORBETTA M., MIEZIN F. M., DOBMEYER S., SHULMAN G. L., PETERSEN S.E. A PET study of viuso-spatial attention. *J. Neurosci.*, 1993, **13** : 1202-1226.

COURCHESNE E. The missing ingredients in autism. Paper presented at the conference on brain and behavioral development. Elridge MD, Biosocial Dimension, 1985.

COURCHESNE E., YEUNG-COURCHESNE R., PRESS G., HESSELINK J., JERNIGAN T. Hypoplasia of cerebellar vermal lobules VI and VII in autism. *N. Engl. J. Med.*, 1988, **318** : 1349-1354.

DARLEY F. L., ARONSON A. E., BROWN J. R. Motor speech disorders. Philadelphia, WB Saunders, 1975.

D'AVANZO R., SCUOTTO A., NATALE M., SCOTTO P., CIOFI F. A. Transient 'cerebellar mutism' in lesions of the mesencephalic-cerebellar region. *Acta Neurol. (Napoli)*, 1993, **15** : 289-296.

DECETY J., SJOHOLM H., RYDING E., STENBERG G., INGVAR D. H. The cerebellum participates in mental activity : tomographic measurements of regional cerebral blood flow. *Brain Res.*, 1990, **535** : 313-317.

DEGUCHI K., TAKEUCHI H., YAMADA A., TOUGE T., NISHIOKA M. Crossed cerebello-cerebral diaschisis in olivopontocerbellar atrophy. Rinsho-Shinkeigaku, 1994, **34** : 851-853.

DRONKERS F. A new brain region for coordinating speech articulation. *Nature*, 1996, **384** : 159-61.

ENGELBORGHS S., MARIËN P., MARTIN J. J., DE DEYN P. P. Functional anatomy, vascularisation and pathology of the human thalamus. *Acta Neurol. Belg.*, 1998, **98** : 252-265.

ENGELBORGHS S., PICKUT B. A., MARIËN P., OPSOMER F., DE DEYN P. P. Crossed cerebellar diaschisis and hemiataxia after thalamic haemorrhage. *J. Neurol.*, 2000, **247** : 476-478.

ERSAHIN Y., MUTLUER S., SAYDAM S., BARÇIN E.. Cerebellar mutism : report of two unusual cases and review of the literature. *Clin. Neurol. Neurosurg.*, 1997, **99** : 130-134.

FABBRO F., MORETTI R., BAVA A. Language impairments in patients with cerebellar lesions. *Journal of Neurolinguistics*, 2000, **13** : 173-188.

FERRANTE L., MASTRONARDI L., ACQUI M., FORTUNA A. Mutism after posterior fossa surgery in children : report of three cases. *J. Neurosurg.*, 1990, **72** : 959-963.

FIEZ J. A., PETERSON S. E., CHENEY M. K., RAICHLE M. E. Impaired non-motor learning and error detection associated with cerebellar damage. A single case study. *Brain*, 1992, **115** : 155-178.

FIEZ J. A., RAICHLE M. E. Linguistic processing. In : *The cerebellum and cognition* (International Review of Neurobiology, Vol 41). SCHMAHMANN J. D. (ed.). San Diego CA, Academic Press, 1997, 233-254.

FOX P. T., RAICHLE M. E., TACH W. T. Functional mapping of the human cerebellum with positron emission tomography. *Proc.. Natl. Acad. Sci.*. USA, 1985, 7462-7466.

FRANK J., LEVINSON H. N. Dysmetria, dyslexia and dyspraxia : hypothesis and study. *J. Am. Acad. Child Psychiatry*, 1973, **12** : 690-701.

FRIM D. M., OGILVY C. S. Mutism and cerebellar dysarthria after brain stem surgery : case report. *Neurosurgery*, 1995, **36** : 854-857.

GASPARINI M., DI PIERO V., CICCARELLI O., CACIOPPO M. M., PANTANO P. *et al.* Linguistic impairment after right cerebellar stroke : a case report. *Eur. J. Neurol.*, 1999, **6** : 353-356.

GRABOWSKI T. J., FRANK R. J., BROWN C. K., DAMASIO H., BOLES-PONTO L. L. *et al.* Reliability of PET activation across statistical methods, subject groups, and sample sizes. *Hum. Brain Mapp.*, 1996, 23-46.

GRAFMAN J., LITVAN I., MASSAQUOI S., STEWART M., SIRIGU A. *et al.* Cognitive planning deficit in patients with cerebellar atrophy. *Neurology*, 1992, **42** : 1493-1496.

GRAFTON S. T., HAZELTINE E., IVRY R. Functional mapping of sequence learning in normal humans. *J. Cogn. Neurosci.*, 1995, **7** : 497-510.

HALLETT M., GRAFMAN J. Executive function and motor skill. In : *The cerebellum and cognition* (International Review of Neurobiology, Vol 41). SCHMAHMANN J. D. (ed.). San Diego CA, Academic Press, 1997, 297-323.

HASSID E. I. A case of language dysfunction associated with cerebellar infarction. *J. Neuro. Rehab.*, 1995, **9** : 157-160.

HOLMES G. The symptoms of acute cerebellar injuries due to gunshot injuries. *Brain*, 1917, **40** : 401-534.

HOLMES G. Clinical symptoms of cerebellar disease and their interpretation. *Lancet*, 1922, **2** : 59-65.

HUMPHREYS R. P. Mutism after posterior fossa tumor surgery. In : *Concepts in pediatric neurosurgery*. MARLIN E. D. (ed.). Basel, Karger, 1989.

IVRY R. B., DIENER H. C. Impaired velocity perception in patients with lesions of the cerebellum. *J. Cogn. Neurosci.*, 1991, **3** : 355-366.

IVRY R., KEELE S. W. Timing functions of the cerebellum. *J. Cogn. Neurosci.*, 1989, **1** : 136-152.

JANOWSKI J. S., SHIMAMURA A. P., KRITCHEVSKY M., SQUIRE L. R. Cognitive impairment following frontal lobe damage and its relevance to human amnesia. *Behav. Neurosci.*, 1989, **103** : 548-560.

JENKINS I. H., BROOKS D. J., NIXON P. D., FRACKOWIAK R. S. J., PASSINGHAM R. E. Motor sequence learning : a study with positron emission tomography. *J. Neurosci.*, 1994, **14** : 3775-3790.

JEREMA G., KADZIELAWA D., WAITE J. On comprehension of active/passive sentences and language processing in a Polish agrammatic aphasic. *Brain and Language*, 1987, **32** : 215-232.

KEELE S. W., IVRY R. Does the cerebellum provide a common computation for diverse tasks ? A timing hypothesis. In : *The developement and neural basis of higher cognitive functions.* DIAMOND A. (ed.). New York, New York Academy of Sciences, 1991, 179-211.

KIMURA S., NAKAMURA H., MATSUMURA K., MOROHASHI S., UEOKA Y. *et al.* Crossed 'cerebral' diaschisis ? Seven cases with unilateral cerebellar vascular lesion which showed decreased perfusion in the contralateral cortex. Kaku-Igaku, 1989, **26** : 1259-1266.

KOLK H. H. J., VANGRUNSVEN M. J. F., KEYSER A. On parallelism between production and comprehension in agrammatism. In : *Agrammatism.* KEAN M. L. (ed.). New York, Academic Press, 1985, 165-206.

LEBRUN Y. Apraxia of speech : a critical review. *Journal of Neurolinguistics*, 1990, **5** : 379-406.

LECHTENBERG R., GILMAN S. Speech disorders in cerebellar disease. *Ann. Neurol.*, 1978, **3** : 285-290.

LEGGIO M. G., SOLIDA A., SILVERI M. C., GAINOTTI G., MOLINARI M. Verbal fluency impairments in patients with cerebellar lesions. *Soc. Neurosci. Abstr.*, 1995, **21** : 917.

LEINER H. C., LEINER A. L., DOW R. S. Does the cerebellum contribute to mental skills ? *Behav. Neurosci.*, 1986, **100** : 443-454.

LEINER H. C., LEINER A. L., DOW R. S. Reappraising the cerebellum : What does the hindbrain contribute to the forebrain ? *Behav. Neurosci.*, 1989, **103** : 998-1008.

LEVISOHN L., CRONIN-GOLOMB A., SCHMAHMANN J. D. Neuropsychological consequences of cerebellar tumour resection in children : cerebellar cognitive affective syndrome in a paediatric population. *Brain*, 2000, **123** : 1041-1050.

LURIA A., TSVETKOVA L. Towards the mechanisms of 'dynamic aphasia'. *Acta Neurol. Psychiatr. Belg.*, 1967, 67 : 1045-1057.

LURIA A. Neuropsychological studies in aphasia. Lisse, Swets & Zeitlingen, 1977.

MARIËN P., ENGELBORGHS S., PICKUT B. A., DE DEYN P. P. Aphasia following cerebellar damage : fact of fallacy ? *Journal of Neurolinguistics*, 2000, **13** : 145-171.

MARIËN P., PICKUT B. A., ENGELBORGHS S., MARTIN J.-J., DE DEYN P. P. Phonological agraphia following a focal anterior insulo-opercular infarction. *Neuropsychologia*, 2001, **39** : 845-855.

MARIËN P., SAERENS J., NANHOE R., MOENS E., NAGELS G. *et al.* Cerebellar induced aphasia : case report of cerebellar induced prefrontal aphasic language phenomena supported by SPECT findings. *J. Neurol. Sci.*, 1996, **144** : 34-43.

MARR D. A theory of the cerebellar cortex. *J. Physiol.*, 1969, **202** : 437-470.

MARTIN A., HAXBY J. V., LALONDE F. M., WIGGS C. L., UNGERLEIDER L. G. Discrete cortical regions associated with knowledge of color and knowledge of action. *Science*, 1995, **270** : 102-105.

MCCORMICK D. A., LAVOND D. G., CLARK G. A., KETTNER R. E., RISING C. E. *et al.* The engram found ? Role of the cerebellum in classical conditioning of nictitating and eyelid response. *Bull. Psychonom. Soc.*, 1981, **18** : 103-105.

MESULAM M. M. A cortical network for directed attention and unilateral neglect. Annals of Neurology, 1981, 10 : 309-315.

MICELI G., MAZZUCCHI A., MENN L., GOODGLASS H. Contrasting cases of Italian agrammatic aphasia without comprehension disorder. *Brain and Language*, 1983, **19** : 65-97.

MOLINARI M., LEGGIO M., SOLIDA A., CIORRA R., MISCIAGNA S. *et al.* Cerebellum and procedural learning : evidence from focal cerebellar lesion. *Brain*, 1997, **120** : 1753-1763.

NADEAU S. E. Impaired grammar with normal fluency and phonology. Implications for Broca's aphasia. *Brain*, 1988, **111** : 1111-1135.

NADEAU S. E., GONZALEZ ROTHI L. J. Morphological agrammatism following a right hemisphere stroke in a dextral patient. *Brain and Language*, 1992, **43** : 642-667.

NAGATANI K., WAGA S., NAKAGAWA Y. Mutism after removal of vermian medulloblastoma : cerebellar mutism. *Surg. Neurol.*, 1991, **36** : 307-309.

PANTANO P., BARON J. C., SAMSON Y., BOUSSER M. G., DEROUESNE C. *et al.* Crossed cerebellar diaschisis. *Brain*, 1986, **109** : 677-694.

PASCUAL-LEONE A., GRAFMAN J., CLARK K., STEWART M., MASSAQUOI S. *et al.* Procedural learning in Parkinson's disease and cerebellar degeneration. *Ann. Neurol.*, 1993, **34** : 594-602.

PAULESU E., FRITH C. D., FRACKOWIAK R. S. J. The neural correlates of the verbal component of working memory. *Nature*, 1993, **362** : 342-345.

PETERSEN S. E., FOX P. T., POSNER M. I., MINTUN M. A., RAICHLE M. E. Positron emission tomographic studies of the cortical anatomy of single-word processing. *Nature*, 1988, **331** : 585-589.

PETERSEN S. E., FOX P. T., POSNER M. I., MINTUN M. A., RAICHLE M. E. Positron emission tomographic studies of the processing of single words. *J. Cogn. Neurosci.*, 1989, **1** : 153-170.

POLLACK I. F. Posterior fossa syndrome. In : *The cerebellum and cognition* (International Review of Neurobiology, Vol 41). SCHMAHMANN J. D. (ed.). San Diego CA, Academic Press, 1997, 411-432.

POLLACK I. F., POLINKO P., ALBRIGHT A. L., TOWBIN R., FITZ C. Mutism and pseudobulbar symptoms after resection of posterior tumors in children : incidence and pathophysiology. *Neurosurg.*, 1995, **37** : 885-893.

POSNER M. I., PETERSEN S. E. The attention system of the human brain. *Annu. Rev. Neurosci.*, 1990, **13** : 25-42.

RAICHLE M. E., FIEZ J. A., VIDEEN T. O., MACLEOD A. M., PARDO J. V. *et al.* Practice-related changes in human brain functional anatomy during nonmotor learning. Cereb. Cortex, 1994, **4** : 8-26.

REKATE H. L., GRUBB R. L., ARAM D. M., HAHN J. F., RATCHESON R. A. Muteness of cerebellar origin. *Arch. Neurol.*, 1985, **42** ; 697-698.

RIVA D. The cerebellar contribution to language and sequential functions : evidence from a child with cerebellitis. *Cortex*, 1998, **24** : 279-287.

RIVA D., GIORGI C. The cerebellum contributes to higher functions during development : evidence from a series of children surgically treated for posterior fossa tumours. *Brain*, 2000, **123** : 1051-1061.

ROSS E. D., MESULAM M.-M. Dominant language functions of the right hemisphere : prosody and emotional gesturing. *Arch. Neurol.*, 1979, **36** : 144-148.

ROUSSEAUX M., STEINLING M. Crossed hemispheric diaschisis in unilateral cerebellar lesions. *Stroke*, 1992, **23** : 511-514.

SALAMÉ P., BADDELEY A. D. Disruption of memory by unattended speech : implications for the structure of working memory. *J. Verb. Learn. Verb. Behav.*, 1982, **21** : 150-165.

SALVATI M., MISSORI P., LUNARDI P., ORLANDO E. R. Transient cerebellar mutism after posterior cranial fossa surgery in an adult. *Clin. Neurol. Neurosurg.*, 1991, **93** (4) : 313-316.

SILVERI M. C., LEGGIO M. G., MOLINARI M. The cerebellum contributes to linguistic production : a case of agrammatic speech following a right cerebellar lesion. *Neurology*, 1994, **44** : 2047-2050.

SILVERI M. C., MISCIAGNA S., LEGGIO M. G., MOLINARI M. Spatial dysgraphia and cerebellar lesion : a case report. *Neurology*, 1997, **48** : 1529-1532.

SILVERI M. C., MISCIAGNA S., LEGGIO M. G., MOLINARI M. Cerebellar spatial dysgraphia : further evidence. *J. Neurol.*, 1999, **246** : 321-323.

SÖNMEZOGLU K., SPERLING B., HENRIKSEN T., TFELT-HANSEN P., LASSEN N. A. Reduced contralateral hemispheric flow measured by SPECT in cerebellar lesions : crossed cerebral diaschisis. *Acta Neurol. Scand.*, 1993, **87** : 275-280.

TACH W. T. Context-response linkage. In : *The cerebellum and cognition* (International Review of Neurobiology, Vol 41). SCHMAHMANN J. D. (ed.). San Diego CA, Academic Press, 1997, 599-611.

THOMPSON R. F. The neurobiology of learning and memory. Science, 1986, **233** : 941-947.

THOMPSON R. F., BAO S., CHEN L., CIPRIANO B. D., GRETHE J. S. *et al.* Associative learning. In : *The cerebellum and cognition* (International Review of Neurobiology, Vol 41). SCHMAHMANN J. D. (ed.). San Diego CA, Academic Press, 1997, 151-189.

TISSOT R., MOUNIN G., LHERMITTE F. L'Agrammatisme. Paris, Dessart, 1973.

VALLAR G., PAPAGNO C. Neuropsychological impairments of short-term memory. In : *Handbook of memory disorders*. BADDELEY A. D., WILSON B. A., WATTS F. N. (eds.). Chichester, John Wiley, 1995, 135-165.

VALLAR G., DI BETTA A. M., SILVERI M. C. The phonological short-term store-rehearsal system : patterns of impairment and neural correlates. *Neuropsychologia*, 1997, **35** : 795-812.

VAN DONGEN H. R., CATSMAN-BERREVOETS C. E., VAN MOURIK M. The syndrome of "cerebellar" mutism and subsequent dysarthria. *Neurology*, 1994, **44** : 2040-2046.

YEO C., HARDIMAN M., GLICKSTEIN M. Classical conditioning of nictitating membrane response of the rabbit. II. Lesions of the cerebellar cortex. *Exp. Brain Res.*, 198, **60** : 99-113.

YOKOJI H., IDE Y., MATSUBARA S., TAKAMORI M. A case of cerebellar hemispheric venous malformation presenting crossed cerebello-cerebral diaschisis. Rinsho-Shinkeigaku, 1989, **29** : 1414-1416.

YOKOTA H., NAKAZAWA S., KOBAYASHI S., TANIGUCHI Y., YUKIHIDE T. Clinical study of two cases of traumatic cerebellar injury. No Shinkei Geka, 1990, **18** : 67-70.

ZETTIN M., CAPPA S. F., D'AMICO A., RAGO R., PERINO C. *et al.* Agrammatic speech production after a right cerebellar haemorrhage. *Neurocase*, 1997, **3** : 375-380.

Peter MARIËN,
A.Z. Middelheim,
Department of Neurology,
Lindendreef 1,
B-2020 Antwerp (Belgium).