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debate

Gavin J. Swanson
Editor

The following debate covers a long-standing controversy in neuroscience, namely, whether the cerebellum, which has traditionally been considered to participate only in motor functions, is involved in so-called higher functions, such as cognition and language. Henrietta Leiner, Alan Leiner and Robert Dow consider the evidence in favour of the latter view, by examining the evolutionarily enlarged dentate nucleus in humans.

The first debate in this new section of *TINS* covered another topic of higher cognitive processes, olfactory learning, and resulted in several letters from readers, many of which could not be published as a result of lack of space. Points of interest and comments from readers are always welcome, as are any suggestions for topics of interesting controversy for possible debate in future issues. Please contact the editor.

Cognitive and language functions of the human cerebellum

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Traditionally, the human cerebellum has been regarded as a motor mechanism, but this view of its function is being challenged by a growing body of data on the non-motor functions of the cerebellum. Some of these data are presented in this article, which reviews neuroanatomical, neuroimaging and behavioral reports of cerebellar involvement in cognitive and language functions. The article proposes that this functional expansion is a consequence of specific cerebellar structural changes that evolved during hominid evolution and that could have been a prerequisite for the evolution of human language.

In research on the neural basis of cognitive and language skills, one of the large structures in the human brain has often been overlooked. This structure is located in the lateral part of the human cerebellum, which enlarged enormously in the course of hominid evolution[1]. Why this part of the cerebellum grew to enormous size in humans has been a long-standing mystery. At first it was assumed that this part conferred a motor benefit on humans; but the motor assumption was thrown into doubt when functional imaging techniques made it possible to visualize cerebellar activity. These images showed that, even in the complete absence of any motor activity, the cerebellum was activated when humans performed certain cognitive and language tasks[2,3]. This cerebellar participation in mental tasks offers an explanation for the cerebellar enlargement: it may have provided the neural basis for a functional expansion of the cerebro-cerebellar system, in which the lateral cerebellum can improve certain cognitive and language functions[4–6]. How this functional expansion could occur as a consequence of the structural enlargement is discussed in this article.

The mystery of the human dentate nucleus

In the evolution of the human cerebellum, the most lateral part enlarged both its cortical and subcortical structures[7]. The lateral part of the cerebellar cortex sends its output to a lateral nucleus, called the dentate nucleus in humans, which is embedded in the white matter beneath the cortex (Fig. 1). During the evolution of this nucleus, a significant differentiation occurred, which contrasts with the evolution of the cerebellar cortex. While the newly-evolved part of the cortex is similar histologically to the older parts of the cortex, the newly-evolved part of the dentate nucleus is different from the older part of the nucleus. This differentiation between the newly-evolved part (ventrolateral) and the older part (dorsomedial) is based on morphological, histological, embryological, histochemical, and pathological evidence[7].

Because this neodentate part of the cerebellum grew to enormous size in humans, an obvious question has arisen about its function in the human brain. Neurosurgeons have provided a provocative piece of evidence by reporting that stereotaxic lesions, when placed in the neodentate, fail to produce some classical motor signs of cerebellar

dysfunction (ataxia or tremors)[8]. Such reports lead us to ask whether the neodentate might be performing a non-motor function[5].

Clues to its function are provided by the output connections through which the neodentate can send signals to other structures in the human brain. These target structures of the cerebellar signals are located in widely separated locations: in the brainstem, in the thalamus and (via the thalamus) in the cerebral cortex. Though dispersed in the brain, these structures are able to send signals to each other via the neural connections that evolved between them, which enable them to communicate with each other as parts of a coherent system (Fig. 2). The expanded connections from the cerebellum to the cerebral cortex, and from the cerebral cortex to the cerebellum, seem to provide this system with expanded cognitive and language capabilities[9,10].

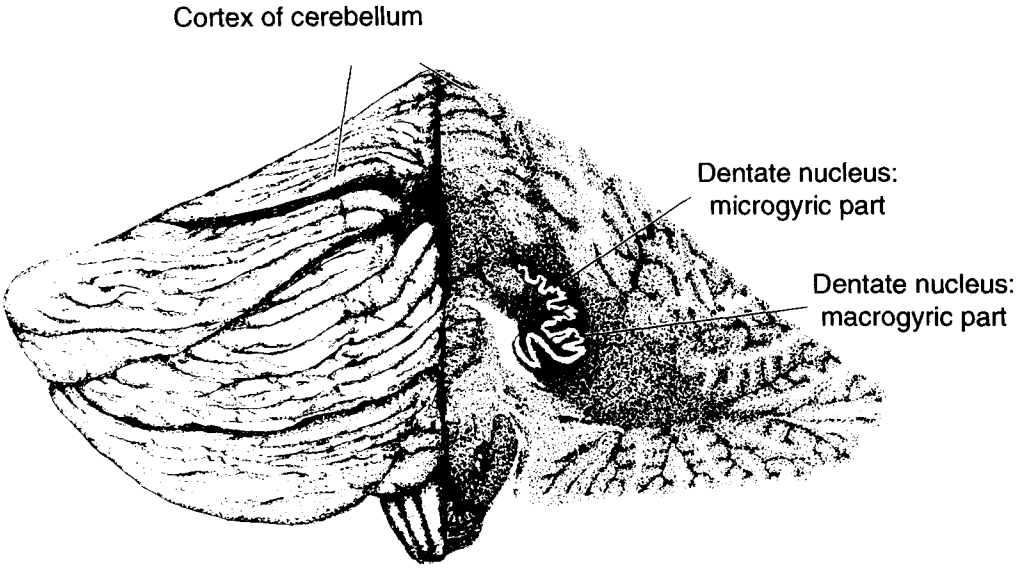

Fig. 1. *Newly-evolved structures in the human cerebellum, cortical and subcortical. On the left side of the figure, a surface view of the cerebellar cortex is shown; its most lateral part enlarged enormously in the course of hominid evolution, as did the subcortical dentate nucleus. On the right side of the figure, a cross-section (coronal slice) of the cerebellum reveals its inner core, where the dentate nucleus can be seen. Note the gross differences between the two parts of the dentate nucleus: the part that is phylogenetically new is located ventrolaterally and is characterized by wide gyri (macrogyric) while the phylogenetically older part is located dorsomedially and is characterized by narrow gyri (microgyric). The phylogenetically new part (the neodentate) enlarged enormously in the human brain. Its function remains undetermined, but we have proposed that it may be involved in some mental functions including language.* [Figure adapted from Angevine, J. B., *Mancall, E. L. and Yakovlev, P. I. (1961) The Human Cerebellum, An Atlas of Gross Topography in Serial Sections*, Little, Brown and Co.]

Expanded connections to the cerebral cortex

It has been difficult to investigate the neural connections that evolved between the neodentate and the cerebral cortex because the usual experimental animals cannot be used for this purpose. In the monkey, the neodentate is not yet fully differentiated; and in the apes it is not yet fully enlarged. The data that are available about these neodentate connections have therefore come from human patients whose brains were examined during their lifetimes by neurosurgeons, neurologists and neuroradiologists, or were examined post-mortem by neuropathologists. The picture that emerges from such examinations is at least consistent; it shows that in humans the primary target of the neodentate projection is the frontal lobe. This lobe is known to have enlarged in the course of hominid evolution, both in its posterior areas (motor areas) and in its anterior areas (prefrontal association areas), concomitantly with cerebellar enlargement[1].

Although it is generally recognized that the projection from the cerebellum reaches the motor areas of the frontal lobe (areas 4 and 6 of Brodmann), it is not widely recognized as yet that the cerebellar projection also reaches some prefrontal areas of the lobe. These particular prefrontal areas lie directly in front of the motor areas, which suggests that the enlargement of the frontal lobe made it possible for the cerebellar projection to expand into these forward territories. While the exact extent of this forward expansion is not yet known, there is evidence that (at the least) it reaches Broca's language area in the inferior prefrontal cortex (areas 44 and 45 of Brodmann), and area 8 in the superior prefrontal cortex. The neuroanatomical routes by which the cerebellum can send signals to these prefrontal areas are specified in our previous publications, to which the reader is referred for details[5,9,10].

What is interesting about these particular prefrontal areas is that their functions were initially thought to be motor ones, related to speech and eye movements, but now seem to be broader. This expanded view of their functions is based on imaging studies[11] and on neurosurgical reports[12]. Area 8, which was initially regarded as a motor area because it is involved in eye movements, seems to be activated (even with the eyes closed) when humans listen to verbal information[11]; and when surgical excisions of this area are performed, deficits in mentation are reported to ensue[12]. Broca's area also was initially thought to subserve a motor function because it is activated when humans express themselves verbally; but it is activated as well when no words are uttered[11]. Rather than subserving the motor function of word-articulation (which involves the motor cortex of the frontal lobe), Broca's prefrontal area and adjacent prefrontal areas seem to be involved in processes of word-finding[13], which are regarded as cognitive processes. In such cognitive word-processing, the lateral cerebellum evidently participates[2].

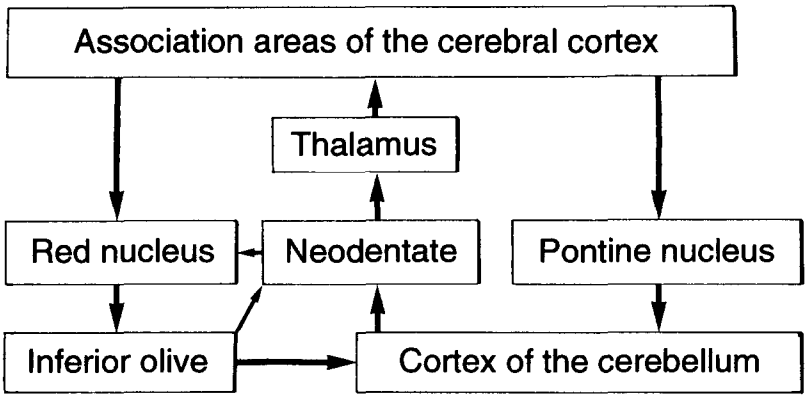

Fig. 2. *Newly-evolved connections between the cerebellum and cerebral cortex. Neural connections from the neodentate (via the thalamus) can reach cerebral association areas, including Broca's language area in the prefrontal cortex. Conversely, neural connections from cerebral association areas can reach the cerebellum, both via the pontine route and via the route from the red nucleus to the inferior olive. Note that the cortex of the cerebellum therefore receives a dual input of neural fibers: it receives mossy fibers from the pontine nuclei and climbing fibers from the inferior olive. Such a dual input of mossy fibers and climbing fibers is a basic characteristic of cerebellar input – characteristic of every module in the entire cerebellar cortex. The functional significance of the climbing fibers is still under debate. Also under debate is the function of the neural loop in the brainstem (formed by the connections from the inferior olive to the dentate nucleus to the red nucleus to the inferior olive), which we have proposed may be involved in language learning.*

Expanded connections from the cerebral cortex

From Broca's area in the prefrontal cortex, as well as from other areas of the cerebral cortex, a descending projection of nerve fibers can reach the red nucleus in the brainstem[14], where an interesting evolution of structure and function has taken place. In most mammals the red nucleus sends its major output to the spinal cord and it clearly subserves a motor function. But this projection to the spinal cord has diminished in the human brain[15] where the red nucleus sends its major output to the inferior olive in the brainstem. In turn, the inferior olive is connected to the dentate nucleus, which is connected to the red nucleus (Fig. 2). Thus, in the human brainstem a neural loop has evolved in which the red nucleus receives a projection from language areas of the cerebral cortex. This input to the red nucleus would enable the neural loop to participate in language functions as well as motor functions. It could participate both in the cognitive process of word-finding and in the motor process of expressing these words, perhaps functioning as a language-learning loop[6,9,10].

Far more massive than the projection from the cerebral cortex to the red nucleus is the cortical projection to the pontine nuclei in the brainstem, which also send information to the cerebellum (Fig. 2). Estimated to contain approximately 20 million nerve fibers on each side of the brain[16], this neural tract can convey a formidable amount of information. To appreciate fully its formidable power, the reader is invited to compare this tract with other effective tracts in the brain. Consider how much information the optic tract, with its one million fibers, can convey from the eyes to the brain; or consider how much information the pyramidal tract, with its one million fibers, can convey from the brain to the motor neurons. Such comparisons inevitably lead one to wonder why the cortex of the cerebellum receives this torrent of information from many lobes of the cerebral cortex, via the pons. What motor functions this information can subserve[17], and what non-motor functions it might subserve[18–20], are discussed in recent reviews. In the present review, we have concentrated only on the phylogenetically newest parts of the cerebro-cerebellar system, and have reached the following conclusions.

TABLE I. Cerebellar participation in human mental functions

Subjects	Published data	Refs
Normal adults, SPECT scans	Cerebellar activation during mental imagery	3
Normal adults, PET scans	Cerebellar activation during word-processing	2
Children whose cerebellum is normal but cerebrum is reduced	Good linguistic skills	31
Children with cerebellar damage due to surgical resection	Cognitive deficit in shifting attention rapidly between sensory modalities	29
Adult patient with cerebellar degeneration	Deficits in verbal and non-verbal intelligence, in verbal associative learning, and in visuospatial skills	29
Adult patient with a right-side cerebellar infarct	Impaired non-motor learning and error-detection	2
Patients with bilateral or unilateral cerebellar damage	Deficits in visuospatial organization, in cognitive planning and in speed of information-processing	24
Patients with cerebellar atrophy	Deficits in cognitive planning	26
	Deficits in word-retrieval	27
	Deficits in procedural learning	28
Patients with cerebellar lesions or atrophy	Deficits in verbal associative learning, in spatial and general intelligence	25
Patients with cerebellar lesions	Impaired in judging time intervals and in judging velocity of moving stimuli	19
Patients with lesions in the left neocerebellum	Deficits in cognitive operations in three-dimensional space	30

In this Table only the most recent references are given; in them can be found previous references that are pertinent to this topic.
Abbreviations: PET, positron emission tomography; SPECT, single photon emission computed tomography.

Expanded cerebro-cerebellar capabilities

We contend that, in the brains of all vertebrates, the cerebellum can improve the performance of any other parts of the brain to which it is reciprocally connected. Because the cerebellar connections to other parts of the brain are different in different species, the specific functions that the cerebellum can improve also differ. For example: when the cerebellum is connected to sensory parts of the brain (as it is conspicuously in an electric fish[20]), the cerebellum

can modulate sensory functions; when it is connected to limbic parts of the brain (as it is in mammals), the cerebellum can modulate emotional and vegetative functions[4]; when it is connected to some cognitive parts of the frontal cortex (as it is in humans), the cerebellum also can improve cognitive processes that are associated with human language. Exactly what operations the cerebellum carries out, in improving such functions, is still a matter of debate[17–23]. However, we have shown that the newly-evolved structures of the cerebellum can send signals via ascending connections to cerebral association areas and conversely that cerebral association areas can send signals via descending connections to the newly-evolved structures of the cerebellum (Fig. 2). Such two-way communications make it possible for these cerebro-cerebellar structures to work together in carrying out specific cognitive and language tasks.

Data on cerebellar participation in cognitive and language functions (Table I) have been produced in recent years both by the neuroimaging of normal adult brains[2,3,11] and by the neuropsychological testing of patients in whom the cerebellum is defective[19,24–30]. Also, a group of retarded children was tested in whom the volume of cerebral cortex is reduced but the cerebellum is normal. Despite their retardation these children exhibit remarkable linguistic competence[31].

Specific data on the participation of the lateral cerebellum in language functions (as distinct from speech) were obtained from normal adults whose brains were imaged by positron emission tomography (PET) scans[2]. These adults, who had no prior practice in the tasks assigned to them, were required to generate a cognitive association between words. A noun was presented to them and they had to think of a verb associated with the use of the noun (e.g. 'needle' associated with 'sew'). The neuroimaging revealed a striking activation in the inferior lateral part of the cerebellum, which was anatomically distinct from the activation in the paramedian part of the cerebellum during motor tasks, including speech[2].

Data on cerebellar participation in cognitive processing also were obtained from a different group of normal adults who were required to count silently and to imagine certain sequences of movements. This mental imagery was not accompanied by any sensory stimulation or any motor activity, and therefore was deemed to be purely cognitive. The inferior lateral part of the cerebellum was activated markedly during both the mental counting and the mental imagery[3].

In addition to these data on adults and children with normal cerebella, data have been obtained from patients with defective cerebella, who exhibit deficits in several cognitive domains. These include, for example, deficits in cognitive planning[24,26–28], in practice-related learning and error-detection[2], in learning arbitrary associations between words[25], in judging time intervals and the velocity of moving stimuli[19], in rapidly shifting attention between sensory modalities[29], and in cognitive operations in three-dimensional space[30]. See Table I for specific details.

In the light of these neuroanatomical, neuroimaging and behavioral data, the traditional view of the cerebellum as serving a purely motor function seems to be unduly narrow. So too do the proposed theoretical models of cerebellar function seem unduly narrow when their explanations are limited to the motor system. Fortunately, one of the models that was proposed to explain motor functions has now been expanded to include mental functions as well[21]. In the future, theoreticians may be able to expand other proposed models also, so that they reflect more adequately the actual scope of cerebro–cerebellar capabilities in the human brain. Such models could help to ensure that the connections of the neodentate will not be overlooked in future research on the neural basis of human cognitive and language functions.

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