

The cerebrocerebellar system: anatomic substrates of the cerebellar contribution to cognition and emotion

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Abstract

The contribution of the cerebellum to the modulation of cognition and emotion is facilitated by the connections between the cerebellum and brain structures known to be associated with a wide array of non-motor behaviors. The cerebellum has interconnections with brainstem and thalamic reticular systems that subserve arousal. Autonomic activity is supported by the reciprocal interconnections with the hypothalamus. Limbic and paralimbic connections include the hypothalamus, septal region, hippocampus, and cingulate gyrus. Associative connections consist of both feedforward and feedback limbs. The basilar pons receives inputs from the prefrontal, posterior parietal, superior temporal, parahippocampal, and cingulate cortices, as well as from the sensorimotor cortices. This information is conveyed from the pons to cerebellum, before it is relayed back via thalamus to the associative and paralimbic regions of the cerebral cortex. The anatomical arrangement of segregated loops of cerebral cortical connections stands in contrast to the cerebellar cortical architecture that is essentially uniform. This has theoretical and clinical ramifications. It is the anatomical basis for the dysmetria of thought hypothesis that postulates a universal cerebellar transform, in which the cerebellum performs its unique computation in a topographically precise manner on diverse streams of information relating to almost all aspects of behavior including cognition and emotion. It provides an anatomic basis for the observations of cerebellar activation by cognitive and affective paradigms in functional neuroimaging experiments. It helps explain the clinical phenomena that characterize the cerebellar cognitive affective syndrome, and it provides an anatomic basis for a causal relationship between cerebellar pathology and psychiatric and neurobehavioral conditions. Knowledge of these anatomical pathways is critical to the further development of hypotheses, experimental approaches, and clinical questions that can advance the understanding of the contribution of the cerebellum to cognition and to disorders of intellect and emotion.

Introduction

The cerebellar cortex is characterized by a repeating cytoarchitecture that, with a few exceptions, is essentially constant throughout the structure (Voogd & Glickstein, 1998). A repeating sequence is also seen in the chemoarchitectonic divisions within the cerebellar cortex that are identified by alternating bands of neuronal staining induced by monoclonal antibodies (Hawkes *et al.*, 1985). This pattern of organization has led to the development of a number of models in which the cerebellum performs a uniform computation. Clinical, experimental, and functional neuroimaging studies demonstrate that the cerebellum is involved in multiple different functions from arousal, to sensorimotor function and higher order processing (see Schmahmann, 1997), and preliminary evidence suggests that there is a topographic arrangement of these functions within the cerebellum (Schmahmann, 1991; Desmond & Fiez, 1998; Schmahmann *et al.*, 1998).

The evolving understanding of this broader role of the cerebellum has been facilitated and substantiated by new insights into the cerebellar connections with other brain regions. Given the uniformity of cerebellar cortical architecture, the connectional

specificity of the cerebrocerebellar pathways confers on the cerebellum the ability to modulate the wide array of behaviors attributed to it. The anatomic systems that support the cerebellar contribution to cognition and affect are important in understanding the cerebellar role in nervous system organization, and consequently in the neurologic and psychiatric manifestations of systemic and focal brain pathology. This paper therefore provides a brief overview of the afferent and efferent cerebellar interconnections with other brain areas, and emphasizes the connectional specificity of the different aspects of the cerebrocerebellar circuit.

There are cerebellar connections with the reticular system that support arousal; the hypothalamus, important for autonomic function; the limbic system that subserves the experience and expression of emotion; and the paralimbic and neocortical association areas crucial for cognitive processes and the cognitive dimensions of affect.

Reticular system

The vermis at the cerebellar midline and the fastigial nucleus are anatomically tightly linked and

functionally related (Haines, 1981). Reticular projections to the vermal-fastigial region arise from the pontine raphe and pontine reticular tegmental nucleus, and from the mesencephalic and medullary reticular formation (Noda *et al.*, 1990). The lateral reticular nucleus sends projections to all the cerebellar nuclei (Qvist, 1989; Gonzalo-Ruiz & Leichnetz 1990).

Fastigial nucleus projections to the reticular formation are directed to the medial, lateral and paramedian reticular nuclei, the vestibular nuclei, nucleus tractus solitarius, nucleus gigantocellularis, and to the nucleus pontis caudalis (Andreuzik *et al.*, 1984). The physiological significance of this projection is underscored by the fact that blood pressure and heart rate are increased following fastigial stimulation (Andreuzik *et al.*, 1984). The fastigial nucleus also sends efferents to the central mesencephalic reticular formation, the periaqueductal gray and the lateral reticular nucleus (Qvist, 1989).

Efferent projections are also directed through the superior cerebellar peduncle to the non-specific intralaminar thalamic nuclei, notably the central lateral, paracentral, paraventricular and parafascicular nuclei (Miller & Strominger, 1977; Person *et al.*, 1986; Qvist, 1989; Gonzalo-Ruiz & Leichnetz, 1990; Aumann & Horne, 1996) that project widely throughout the cerebral hemispheres and may play a role in arousal as well as in nociception.

Catecholaminergic and monoaminergic systems

Brainstem neurotransmitter systems in the raphe (serotonin), locus ceruleus (norepinephrine), ventral tegmental area (dopamine) and possibly histaminergic structures receive diffuse cerebral cortical input and in turn convey their efferents to widespread cerebellar regions (Snider, 1975; Dempsey *et al.*, 1983; Marcinkiewicz *et al.*, 1989). This may confer a background tone upon which the mossy fiber and climbing fiber systems in the cerebellum exert their more specific and topographically precise influence.

Autonomic system

The influence of cerebellar stimulation on the autonomic nervous system in cats was one of the earliest demonstrations of a cerebellar role in non-motoractivity. These autonomic phenomena included inhibition of respiratory and vasomotor carotid sinus reflexes by stimulation of the anterior vermis (Moruzzi, 1940), and bradycardia, hypotension, mydriasis, altered gastrointestinal motility, length of gestational period and piloerection induced by anterior lobe cortex or fastigial nucleus stimulation (Rasheed *et al.*, 1970; Doba & Reis, 1972; Martner, 1975). More recent studies of cerebellar influences on vasomotor tone (Andreuzik *et al.*, 1984; Paton & Spyer 1990; Reis & Golanov, 1997) and on vagally mediated respiratory reflexes (Xu & Frazier, 1997)

confirm and extend the earlier observations. Functional imaging studies that reveal cerebellar activation during painful stimulation (Coghill *et al.*, 1999; Ploghaus *et al.*, 1999), thirst (Parsons *et al.*, 2000), and hunger (Tataranni *et al.*, 1999) also implicate the cerebellum in these autonomic-limbic behaviors.

The anatomic basis of these physiological demonstrations was examined by investigations into the anatomic links between the cerebellum and those brain regions important for autonomic function. These are the hypothalamus, certain brainstem nuclei including those that subserve taste (the nucleus tractus solitarius), and structures concerned with pain modulation such as the periaqueductal gray, and the central lateral and paracentral intralaminar thalamic nuclei. Dietrichs (1984) and Haines & Dietrichs (1984) demonstrated that projections arise from multiple hypothalamic nuclei and terminate in all layers of the cerebellar cortex and in the deep cerebellar nuclei (Figure 1).

Further, all the cerebellar nuclei send efferents back to the hypothalamus (Haines *et al.*, 1997). The nucleus tractus solitarius receives heavy projections from the fastigial nucleus (Andreuzik *et al.*, 1984), and the fastigial projections to the intralaminar thalamic nuclei have been referred to above.

Limbic system

The evidence for cerebellar limbic interactions is presently derived from behavioral and physiologic studies, and from a smaller amount of direct anatomic evidence. The phenomenon of sham rage that is produced in cats by hypothalamic stimulation (Bard, 1928) was shown to be altered by stimulation of the anterior cerebellum Moruzzi (1947), and specifically by the vermis and fastigial nucleus (Zanchetti & Zocolini, 1954). Berntson *et al.* (1973) showed eating and grooming responses in cats by stimulation of fastigial nucleus and superior cerebellar peduncle. Complex oral behaviors were elicited in the rat by fastigial nucleus stimulation (Ball *et al.*, 1974), and self-stimulation (previously thought to be regulated by the amygdala) was induced by stimulation of the rostral anterior lobe and the fastigial nucleus (Micco, 1974). Reis *et al.* (1973) showed that low intensities of fastigial nucleus stimulation produced grooming and ingestive behaviors, but at higher intensities of stimulation, predatory attack, and sham rage were elicited.

Electrical stimulation of the cerebellum influences the physiology of limbic system structures, producing evoked responses in hippocampus and amygdala (Whiteside & Snider, 1953; Heath & Harper, 1974), and altered and/or arrested abnormal or epileptiform discharges in the hippocampus (Mutani, 1967; Babb *et al.*, 1974). Heath *et al.* (1978) demonstrated facilitation in the septal region, inhibition in the hippocampus, and a mixed pattern of responses in the

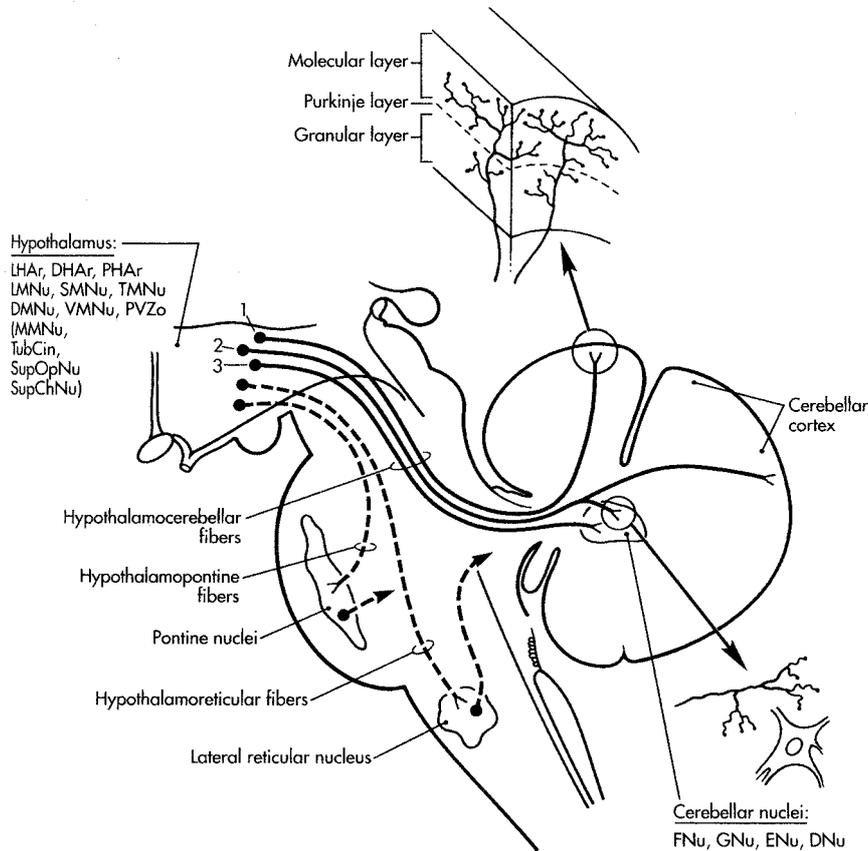


Figure 1. Diagram of efferent projections of hypothalamic nuclei to cerebellum, pontine nuclei, and lateral reticular nucleus. Cells number 1, 2 and 3 are indicative of (1) hypothalamic cells that project only to the cortex, (2) hypothalamic cells that project to the cortex and send collaterals into the cerebellar nuclei, and (3) hypothalamic cells that project only to the cerebellar nuclei. Hypothalamic nuclei listed in parenthesis give rise to relatively fewer projections. All cerebellar nuclei project back to hypothalamus (not shown) and terminate in lateral, posterior, and dorsal hypothalamic areas, and in dorsomedial and paraventricular hypothalamic nuclei. (DHA, dorsal hypothalamic area; DMN, dorsomedial hypothalamic nucleus; DNu, dentate nucleus; ENu, emboliform nucleus; FNu, fastigial nucleus; LHA, lateral hypothalamic area; LMN, lateral mammillary nucleus; MMN, medial mammillary nucleus; PHA, posterior hypothalamic area; PVZ, periventricular zone; SMN, supramammillary nucleus; SupChNu, supra-chiasmatic nucleus; SupOpNu, supraoptic nucleus; TMN, tuberomammillary nucleus; TubCin, tuber cinereum; VMN, ventromedial nucleus.) (From Haines *et al.*, 1997, with modified legend.) Reprinted with kind permission of Harcourt Inc.

amygdala in cats and rats following stimulation of the rostral vermis, fastigial nucleus, and intervening midline folia, but not following stimulation of the lateral cerebellar hemispheres and dentate nucleus.

Anatomic studies reveal projections from the fastigial nucleus of cat to the ventral tegmental area (VTA), interpeduncular nucleus, periaqueductal gray and locus ceruleus that are themselves interconnected with limbic regions (Snider & Maiti, 1976). The mesorhombencephalic component of the VTA also has a reciprocal projection back to the cerebellum (Oades & Halliday, 1987). The medial mammillary bodies are closely linked with the limbic anterior thalamic nuclei through the mammillothalamic tract, and they are also in communication with the cerebellum by way of their projections to the nuclei of the basilar pons (Haines & Dietrichs, 1984; Aas & Brodal, 1988). The hypothalamocerebellar connections discussed above are relevant in the consideration of the limbic cerebellum particularly in light of the phenomenon of sham rage produced originally by hypothalamic stimulation.

Finally, the cingulate gyrus implicated in depression

(Ebert & Ebmeier, 1996) and in obsessive compulsive disorder (Rauch *et al.*, 1994) has direct projections into the feedforward limb of the cerebrocerebellar circuits through the basilar pons (Vilensky & Van Hoesen, 1981; Brodal *et al.*, 1991). The rostral cingulate projects to medial pontine nuclei, the caudal cingulate to more lateral regions.

These studies together reveal that cerebellum is interconnected with multiple different elements of the limbic circuits that subserves emotion, although considerable detail is still missing from the understanding of these pathways.

Association and paralimbic cortices

The cerebral cortex is linked with the cerebellum via a two-stage feedforward limb in which the pontine nuclei serve as the obligatory synaptic step between the corticopontine pathway and the mossy fiber-mediated pontocerebellar pathway. The two-stage feedback system from cerebellum to cerebral cortex

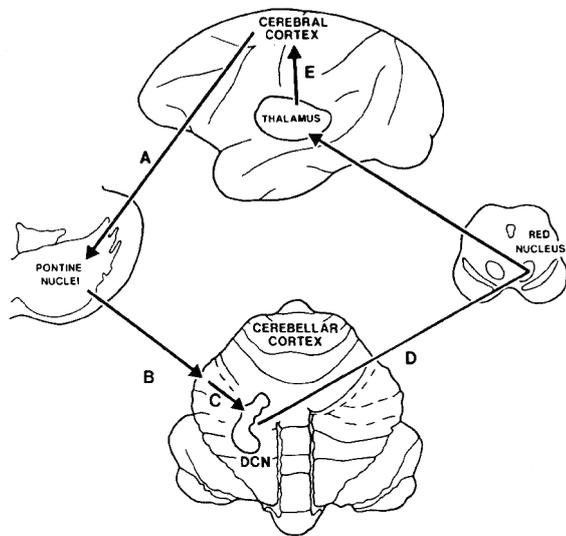


Figure 2. Diagram of the cerebrocerebellar circuit. Feedforward limb: the corticopontine pathway (A) carries associative, paralimbic, sensory, and motor information from the cerebral cortex to the neurons in the ventral pons. The axons of these pontine neurons reach the cerebellar cortex via the pontocerebellar pathway (B). Feedback limb: the cerebellar cortex is connected with the deep cerebellar nuclei (DCN, C), which project via the red nucleus to the thalamus (the cerebello-thalamic projection, D). The thalamic projection back to cerebral cortex (E) completes the feedback circuit. (From Schmahmann, 1994.) Reprinted by kind permission of the Johns Hopkins University Press.

has the thalamus as the obligatory synaptic step, between the cerebellothalamic pathway traveling in the superior cerebellar peduncle and the thalamocortical pathway (Figure 2).

Both the feedforward and feedback limbs are critical components of this circuit because of the specific information carried to the cerebellum by the inputs, and the cerebral regions that are the recipients of the cerebellar feedback. In the discussion concerning the role of the cerebellum in higher function, there are no pathways more critical than those linking the associative and paralimbic regions of the cerebral hemispheres with the cerebellum. These pathways provide the anatomic substrates that subserve the cerebellar involvement in cognitive operations.

Feedforward limb

It has long been known that neurons in layer Vb of the motor, premotor, and supplementary motor regions as well as primary somatosensory cortices and the rostral parietal lobe send their efferents to the cerebellum via the corticopontine pathway (Sunderland, 1940; Nyby & Jansen 1951; Brodal, 1978). Recent evidence, however, indicates that the corticopontine projections arise not only from these sensorimotor related regions, but considerable projections to pons are derived also from the prefrontal cortex, from multimodal regions of the posterior parietal and temporal lobes, from

paralimbic cortices in the cingulate and posterior parahippocampal gyrus, and from the visual association cortices in the parastriate region as well.

Prefrontal cortex

The prefrontal cortex is essential for such higher functions as planning, foresight, judgment, attention, language, and working memory (Milner, 1964; Luria, 1966; Fuster, 1980; Stuss & Benson, 1986). Anterograde tract tracing studies using tritiated amino acids (Schmahmann & Pandya, 1995, 1997a) reveal that prefrontal corticopontine projections arise most prominently from the dorsolateral and dorsomedial convexities, from areas concerned with attention as well as with conjugate eye movements (area 8), the spatial attributes of memory and working memory (area 9/46d), planning, foresight, and judgment (area 10), motivational behavior and decision-making capabilities (areas 9 and 32), and from areas considered to be homologous to the language area in human (areas 44 and 45) (Brodmann, 1909; Astruc, 1971; Künzle & Akert, 1977; Glickstein *et al.*, 1985; Stanton *et al.*, 1988; Goldman-Rakic & Friedman, 1991; Pandya & Yeterian, 1991; Petrides & Pandya, 1994; Petrides, 1995). The terminations in the pons are distributed in a topographically precise manner, favoring the median, paramedian, dorsomedial and medial part of the peripeduncular pontine nuclei (Schmahmann & Pandya, 1997a) (see Figure 3).

Posterior parietal cortex

The posterior parietal association cortices are critical for directed attention, visual-spatial analysis, and vigilance in the contralateral hemispace. When lesioned these areas are associated with complex behavioral manifestations (Critchley, 1953; Denny-Brown & Chambers, 1958; Mountcastle *et al.*, 1977; Lynch, 1980; Hyvarinen, 1982). The superior parietal lobule, more concerned with intramodality associative functions (multiple joint position sense, touch and proprioceptive impulses from similar regions) projects throughout the rostrocaudal extent of the pons focusing mostly on the nuclei in the central and lateral region of the basilar pons (Schmahmann & Pandya, 1989) [see Figure 3(right)]. The inferior parietal lobule, especially the most caudal region, is strongly implicated in the neglect syndrome, and is anatomically interconnected with other cortical association areas as well as with paralimbic cortical regions and limbic thalamic nuclei (Pandya & Yeterian, 1985; Cavada & Goldman-Rakic, 1989a, 1989b; Schmahmann & Pandya, 1990). The projections from the inferior parietal lobule favor the rostral half of the pons, terminations being located more at the lateral and dorsolateral pontine regions (Brodal, 1978; Glickstein *et al.*, 1985; May & Andersen, 1986; Schmahmann & Pandya, 1989).

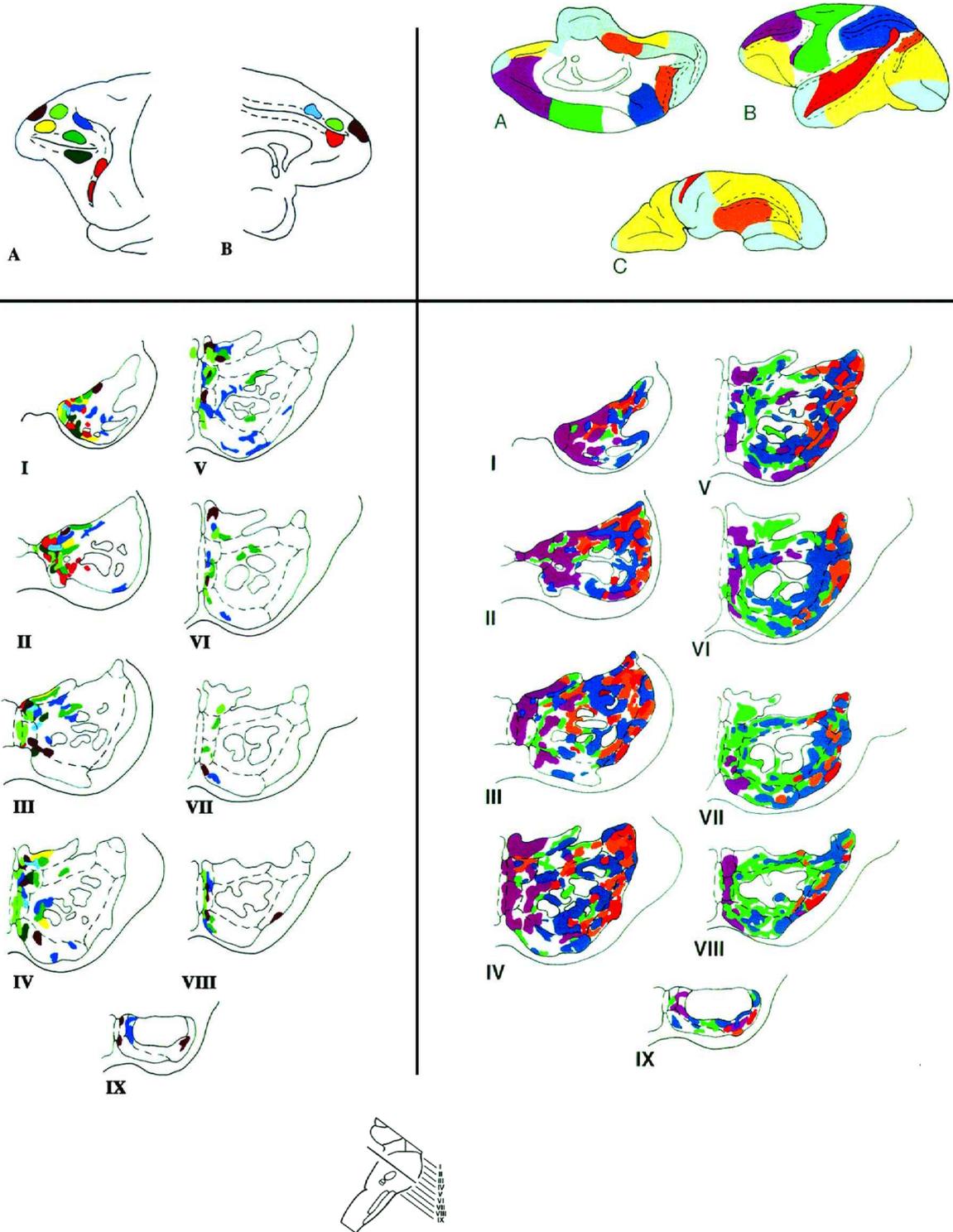


Figure 3. (Left) Shows the distribution within the basilar pons of the rhesus monkey of projections derived from the prefrontal cortices. Injections of anterograde tracers in the medial (A) and lateral (B) surfaces of the cerebral hemisphere result in terminations (color-coded) in rostrocaudal levels of the pons I-IX. The plane of section through the basilar pons for both left and right figures is at the bottom of the diagram. The prefrontopontine projection is characterized by a complex mosaic of terminations. Each cerebral cortical region has preferential sites of pontine terminations. There is considerable interdigitation of the terminations from some of the different cortical sites, but almost no overlap. (From Schmahmann & Pandya, 1997a.) © 1997 Society for Neuroscience. Reprinted with kind permission of the Journal of Neuroscience.

(Right) This figure is a color-coded summary diagram illustrating the distribution within the basilar pons (levels I-IX) of the rhesus monkey of projections derived from association and paralimbic cortices in the prefrontal (purple), posterior parietal (blue), temporal (red), and parastriate and parahippocampal regions (orange), and from motor, premotor and supplementary motor areas (green). The medial (A), lateral (B) and ventral (C) surfaces of the cerebral hemisphere are shown above. Cerebral areas that have been shown to project to the pons by other investigators using either anterograde or retrograde tracers are depicted in white. Areas that have no pontine projections (according to anterograde and retrograde studies) are shown in yellow; those with no pontine projections according to retrograde studies are in gray. Dashed lines on the hemispheres represent sulcal cortices. Dashed lines in the pons represent pontine nuclei, and solid lines demarcate corticospinal fibers. (From Schmahmann, 1996.) Reprinted with kind permission of Human Brain Mapping.

Temporal lobe

The superior temporal gyrus and supratemporal plane, which are auditory association areas, are connected with the lateral and dorsolateral pontine nuclei. The cortex in the upper bank of the superior temporal sulcus has neurons that are activated during face recognition tasks, and they are further selectively activated depending on the direction of gaze of the presented face (Perrett *et al.*, 1987). The lateral, dorsolateral, and extreme dorsolateral pontine nuclei receive most of the terminations from these temporal lobe regions (Schmahmann & Pandya, 1991) [Figure 3(right)]. Other temporal lobe cortices that are responsive to motion and direction of movement (areas MT, FST, and MST) also have pontine connections (Ungerleider *et al.*, 1984), but the inferotemporal cortex including the rostral lower bank of the superior temporal sulcus which is relevant for feature discrimination (Desimone & Ungerleider, 1989; Felleman & Van Essen, 1991) has no pontine efferents (Brodal, 1978; Glickstein *et al.*, 1985; Schmahmann & Pandya, 1991, 1993). There is thus a dichotomy in the temporal lobe pontine connections between visual motion (where) versus visual feature discrimination (what) systems (Ungerleider & Mishkin, 1982). The temporal lobe is known to be important for linguistic processing, and these temporopontine connections, along with those from the monkey homologue of Broca's area, are interesting in the light of cerebellar activation during functional neuroimaging studies of cerebellum (Fiez & Raichle, 1997) and in disorders of language in individuals with cerebellar lesions (Silveri *et al.*, 1994; Pollack *et al.*, 1995; Schmahmann & Sherman, 1998; Leggio *et al.*, 2000).

Parastriate cortices

The dorsal-ventral dichotomy seen in the temporopontine connections is also seen in the projections arising from the parastriate cortices in the occipitotemporal and occipitoparietal regions. The medial and dorsal prelunate regions project to the pons (dorsolateral nucleus, lateral nucleus, and lateral aspect of the peripeduncular nucleus most heavily), but the ventral prelunate cortices and the inferotemporal regions do not (Glickstein *et al.*, 1985; May & Andersen, 1986; Fries, 1990; Schmahmann & Pandya, 1993). The dorsal visual stream concerned with motion analysis and visual-spatial attributes of motion therefore participates in the cerebrotocerebellar interaction, but the ventral visual stream governing visual object identification does not.

Paralimbic cortices

The posterior parahippocampal gyrus is responsive to visual stimuli in the peripheral lower quadrant (Boussaoud *et al.*, 1991) and has been identified as part of the substrate for spatial attributes of memory

(Nadel, 1991). Pontine connections arising from this region are directed to the lateral, dorsolateral, and lateral aspects of the peripeduncular pontine nuclei (Schmahmann & Pandya, 1993). The cingulate cortex projections to the pons have been mentioned above, and these arise not only from the motor related areas in the depth of the cingulate sulcus (Picard & Strick, 1996), but also from regions of the cingulate gyrus thought to be concerned with motivation and drive (Devinsky *et al.*, 1995; Paus, 2001). The anterior insular cortex, an important cortical component of autonomic and pain modulation systems (Mesulam & Mufson, 1985) has been shown in retrograde anatomical studies to have pontine connections (Glickstein *et al.*, 1985), although the precise ordering of the projections from this region in the basilar pons is not yet established.

Specificity of connections

It is apparent from the foregoing discussion that the corticopontine projections are highly organized within the basilar pons. The associative and paralimbic projections together constitute a considerable extent of the pontine nuclear territory. Quantitative comparisons have not yet been performed, but these higher order anatomic connections are not at all overwhelmed but the motor corticopontine projections. The motor terminations have their own separate and distinct location, mostly in the caudal half of the pons, whereas the associative projections are found throughout the pons, with a rostral predominance (Schmahmann, 1996) [Figure 3(right)].

Each cortical area also has its own focus of predilection within the basilar pons. Thus, for example, the prefrontopontine terminations are present mostly in the medially situated nuclei within the rostral half of the pons (Schmahmann, 1996; Schmahmann & Pandya, 1997a) [see Figure 3(right)]. Moreover, each prefrontal area projects to a unique set of terminations within this general 'prefrontal' pontine territory (Schmahmann & Pandya, 1997a) [see Figure 3(left)]. The corticopontine terminations thus comprise a patchwork mosaic of interdigitating but highly specific terminations.

The trajectories of the corticopontine fiber systems are also discretely organized within the cerebral white matter. Whereas, for example, all the post-Rolandic corticopontine fibers descend abruptly into the cerebral peduncle above the mid-point of the lateral geniculate nucleus, they adopt a unique course both as they move (rostrally or caudally) towards the lateral geniculate nucleus, and as they hover above it prior to their descent (Schmahmann & Pandya, 1992). Similar organizing principles apply to the prefrontopontine fibers that traverse the anterior limb of the internal capsule *en route* to the cerebral peduncle (Schmahmann & Pandya, 1994). Thus the corticopontine projections are distinguishable at each

point, from origin, through trajectory, to termination, and appear to be organized in parallel. Each cortical locus has a unique complement of pontine neurons to which it directs its efferent volleys. In this sense the organization of the cerebrocerebellar system resembles the multiple parallel loops that characterize the cortico-subcortical interactions with the basal ganglia (Goldman-Rakic & Selemon, 1990).

Climbing fibers

The interaction between the pontine mossy fiber system input to the cerebellum, and the climbing fibers derived exclusively from the inferior olivary nucleus, has served as the substrate for hypotheses concerning the cerebellar role in both motor and non-motor behaviors (Marr, 1969; Albus, 1971; Ito, 1993; Thach, 1997). The inferior olive receives little, if any, direct input from the cerebral cortex. Its major source of descending afferents arises from the red nucleus that carries mostly sensorimotor information (Kuypers & Lawrence, 1967; Humphrey *et al.*, 1984; Kennedy *et al.*, 1986). It does, however, also receive some associative cortical input indirectly from brainstem reticular nuclei and from the zona incerta (ZI) (Saint-Cyr & Courville, 1980). The ZI receives input from the rostral cingulate cortex (area 24); the prefrontal cortex (areas 9/46d at the dorsolateral convexity and area 9 at the medial convexity); the posterior parietal cortex (areas PF and PG in the inferior parietal lobule, and area PGm at the medial convexity of the superior parietal lobule); and from the medial prefrontal cortex (Shah *et al.*, 1997). The detection of associative projections to the zona incerta, that in turn projects to the inferior olivary nucleus, maintains the possibility that interaction between the mossy-fiber and climbing fiber systems may be relevant for higher function, in addition to tasks related to motor performance and motor learning.

The pontocerebellar pathway

Comprehensive anatomical details now exist for the corticopontine projections, but the details of the pontocerebellar system remain unclear, beyond some general organizing principles.

Information derived from physiological and anatomical studies indicates that both central and peripheral auditory and visual inputs are received in vermal lobules VI and VII, conveyed mostly via the dorsolateral pons and the nucleus reticularis tegmenti pontis (Snider, 1950; Allen & Tsukahara, 1974; Brodal, 1979, 1980; Stein & Glickstein, 1992; Glickstein *et al.*, 1985). The dorsal paraflocculus also receives visual input from the dorsolateral pontine nucleus (Glickstein *et al.*, 1994).

The parietal and prefrontal cortices are functionally related mainly to crus I, crus II and the paramedian lobule in the neocerebellar hemispheres, according to

physiological studies (Allen & Tsukahara, 1974; Sasaki *et al.*, 1975). The pontocerebellar studies of Brodal (1979) revealed that the anterior lobe receives input from medial parts of the caudal pons; the vermal visual area from the dorsomedial and dorsolateral pons; vermal lobule VIIIB from the intrapeduncular nucleus; crus I of the ansiform lobule from medial parts of the rostral pons, and crus II from the medial, ventral, and lateral pons. These studies, taken together with the investigations of the corticopontine pathways (Brodal, 1978; Schmähmann & Pandya 1997b), suggest the following. The anterior lobe in particular receives afferents from motor, premotor, and rostral parietal cortices. Prefrontal cortices are linked with crus I of the ansiform lobule, and with crus II to a lesser extent. Parietal association cortices are linked with crus I, crus II and lobule VIIIB. A more complete exploration of the pontocerebellar pathways is still needed in order to better understand the relationship between cerebral cortex and cerebellum.

There is a high degree of order in the pontocerebellar projection. Each cerebellar folium receives input from a unique complement of pontine cell groups, some of which are widely separated (Brodal, 1979; Schmähmann, 1996) (Figure 4).

The pattern of diverging corticopontine projections, and converging pontocerebellar projections has led to the suggestion that information from one cerebral cortical area is distributed to numerous sites in the cerebellar cortex (Brodal, 1979). Preliminary trans-synaptic anterograde tracer experiments in the prefrontal cortex, however (Strick, 1999), reveal that the anterograde projections through the medial pons are directed to focal areas in crus I and crus II, and are not widely distributed. This is an important detail that needs further clarification as it relates directly to the issue of connectional and functional topography in the cerebellum.

Feedback limb

The cerebellar cortical feedback to the cerebral cortex originates in the projection from the Purkinje cell layer to the deep cerebellar nuclei (the fastigial, globose, emboliform, and dentate). These projections are arranged in an orderly manner with medial cortical areas committing efferents mostly to the midline nuclei fastigial nucleus, and lateral cerebellar cortices projecting to the lateral, or dentate, nucleus (Jansen & Brodal, 1940; Chambers and Sprague, 1955; Haines, 1989) (see Figure 4). The dentate nucleus itself has for some time been recognized to be architectonically heterogeneous, and Dow (1942) elaborated upon this by defining a dorsomedial part with minimal gyration and large neurons, and a ventrolateral part that is heavily folded and contains small neurons. This distinction is readily apparent on light microscopy. Dow recognized that the dorsomedial part was phylogenetically older, whereas the ventrolateral part

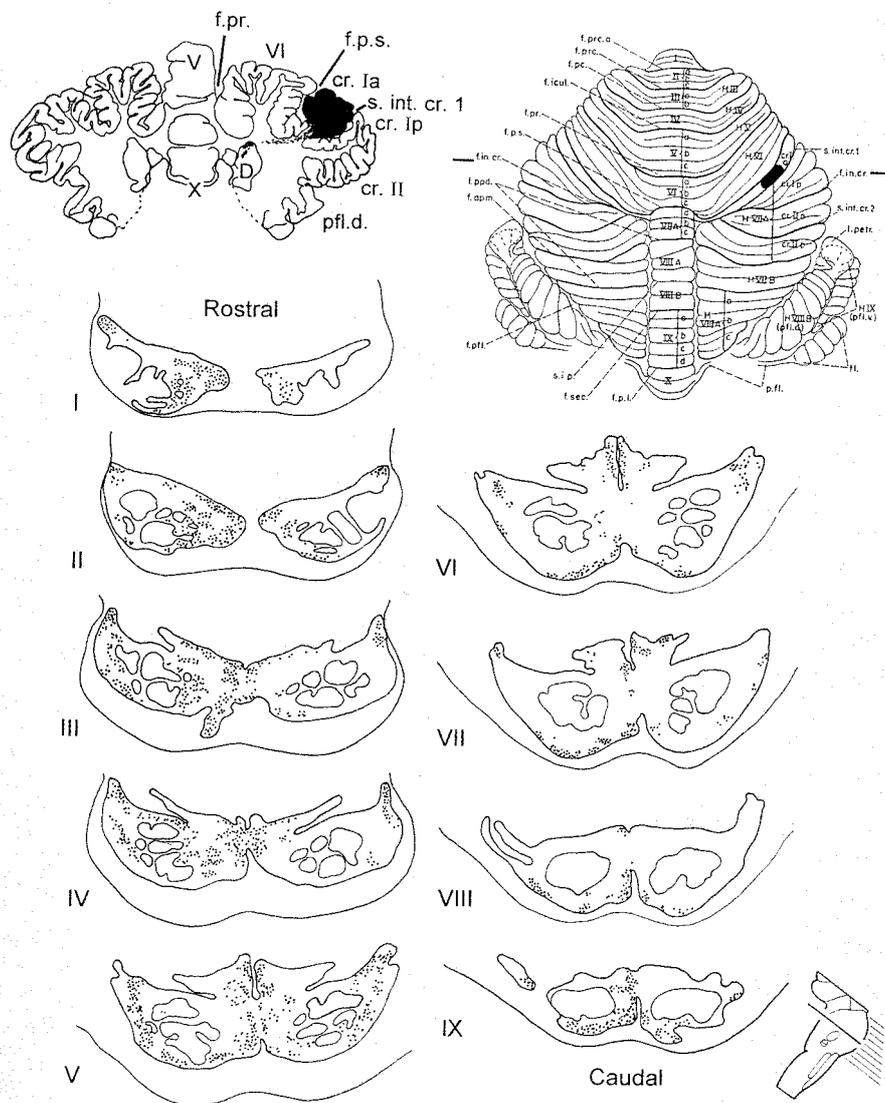


Figure 4. Diagram illustrating the distribution of labeled neurons (black dots) in the basilar pons following injection of tracer (WGA-HRP, black shading) into crus I anterior of rhesus monkey cerebellum [top left—transverse section; top right—flattened map (Larsell, 1970)]. Rostrocaudal levels of the pons I–IX are depicted in the diagram at lower right. Pontine nuclear subdivisions are not shown. Retrogradely labeled neurons are seen bilaterally in the pons, with a contralateral predominance, in multiple, distinct regions. Anterograde label is seen within the dentate nucleus. [cr. Ia = crus I anterior; cr. Ip = crus I posterior; cr. II = crus II; D = dentate nucleus; f.pr. = primary fissure; f.p.s. = superior posterior fissure; s.int.cr. I = internal sulcus of crus I. Roman numerals V, VI and X refer to the cerebellar lobules according to Larsell (1970).] (Schmahmann & Pandya, from Schmahmann, 1996.) © 1997 Society for Neuroscience. Reprinted with kind permission of *The Journal of Neuroscience*.

was more recently evolved. Leiner *et al.* (1986) later postulated that the newer ventrolateral dentate developed along with the expanded neocerebellar hemispheres, and evolved in concert with the cerebral association areas (prefrontal cortex in particular), thus facilitating a cerebellar role in language processing. This prediction has been supported by subsequent clinical (e.g. Leggio *et al.*, 2000; Levisohn *et al.*, 2000) and functional imaging studies (see Desmond & Fiez, 1998).

The conventional understanding has been that the cerebellar dentate nucleus projects via motor thalamic nuclei back to the motor related cortices. However, the cerebellar nuclear projections to thalamus arise not only from the dentate nucleus but from the fastigial and the interpositus nuclei as well (Brodal,

1981). Further, the thalamic input is directed not only to the classic cerebellar recipient 'motor' thalamic nuclei [subdivisions of VL, VPL and nucleus X of Olszewski (1952)], but the 'non-motor' thalamic nuclei have considerable cerebellar input as well. These include the intralaminar nuclei, particularly centralis lateralis (CL), as well as the paracentralis (Pcn) and centromedian-parafascicular (CM-Pf) complex, and the medial dorsal nucleus (Strick, 1976; Batton *et al.*, 1977; Thach & Jones, 1979; Stanton, 1980; Kalil, 1981; Wiesendanger & Wiesendanger, 1985; Ilinsky & Kultas-Ilinsky, 1987; Orioli & Strick, 1989). The CL nucleus, like other intralaminar nuclei, has widespread cortical connections including the posterior parietal cortex, the multimodal regions of the upper bank of the superior temporal sulcus, the

prefrontal cortex, the cingulate gyrus, and the primary motor cortex (Kieviet & Kuypers, 1977; Yeterian & Pandya, 1985, 1989; Vogt & Pandya, 1987; Schmahmann & Pandya, 1990; Siwek & Pandya, 1991), and the Pcn nucleus projections include the parahippocampal gyrus (G. Blatt, D.L. Rosene, D.N. Pandya, 1991, personal communication). The medial dorsal (MD) thalamic nucleus receives projections from the cerebellum mainly in its paralaminar parts, that is, in the pars multiformis (MDmf), and pars densocellularis (MDdc) (Stanton, 1980; Ilinsky & Kultas-Ilinsky, 1987). The MDmf and MDdc nuclei have reciprocal connections with the prefrontal cortex in area 8, area 46 at both banks of the principal sulcus, and area 9 (Giguere & Goldman-Rakic, 1988; Barbas *et al.*, 1991; Siwek & Pandya, 1991), as well as with the cingulate gyrus, posterior parietal cortex, and multimodal parts of the superior temporal sulcus (Yeterian & Pandya, 1985, 1989; Vogt & Pandya, 1987; Schmahmann & Pandya, 1990). Furthermore, the traditionally motor thalamic nuclei are reciprocally interconnected with the prefrontal periaruate areas (Kieviet & Kuypers, 1977; Stanton *et al.*, 1988; Künzle & Akert, 1977), the multimodal cortex (area TPO) in the upper bank of the superior temporal sulcus (Yeterian & Pandya, 1989), and the posterior parietal cortex including both the upper and lower banks of the intraparietal sulcus (Schmahmann & Pandya, 1990).

These studies indicate that the cerebellum projects back to the higher order cerebral areas from which the inputs are derived (Schmahmann, 1991, 1996). This conclusion is supported and further clarified by more direct trans-synaptic retrograde tracer studies using attenuated herpes virus that replicates in synaptic neurons and amplifies the detectable signal at second order sites (Ugolini *et al.*, 1987; Kuypers & Ugolini, 1990). Middleton & Strick (1994, 1997) demonstrated that the cerebellar dentate nucleus sends projections through thalamus to different areas of the frontal lobe in the monkey (Figure 5).

The dorsomedial part of the dentate nucleus sends its projections to the motor cortex, whereas the ventrolateral and ventromedial parts of the dentate nucleus are connected with the prefrontal cortex, including area 9/46. It is likely that this degree of organization in the feedback from the cerebellum to the cerebral hemispheres is reproduced throughout the cerebrocerebellar system, but this remains to be demonstrated.

Clinical corroboration

The reciprocal anatomic connections between the cerebral hemispheres and the cerebellum have been shown to be directly relevant in the experimental, clinical, and functional neuroimaging domains.

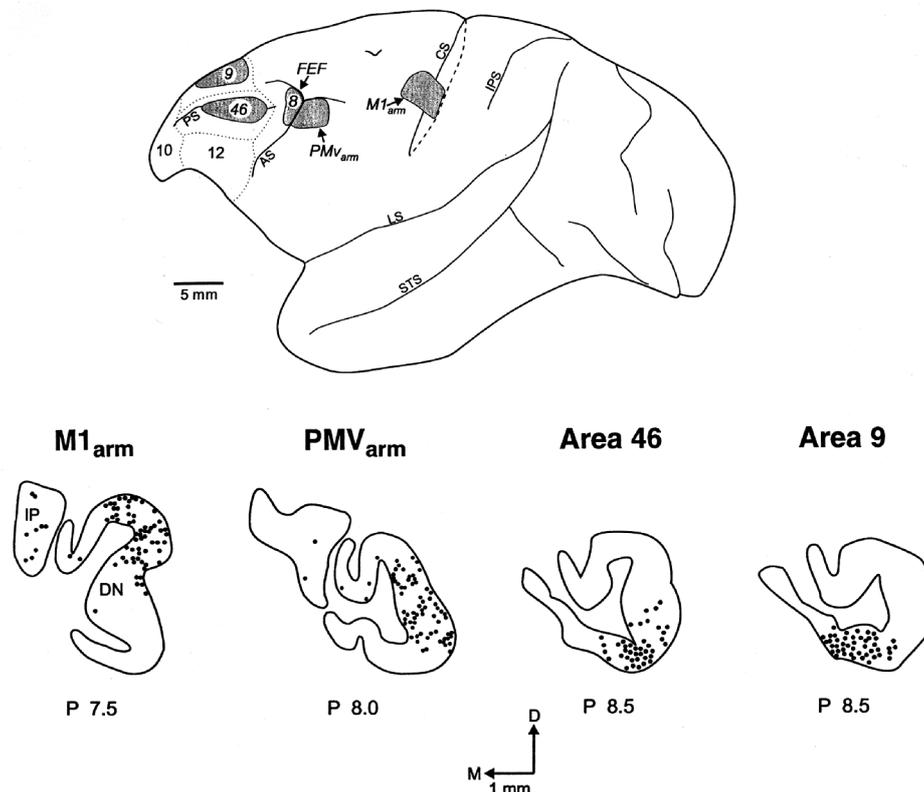


Figure 5. Lateral view of a cebus monkey brain (top) to show the location of injections of McIntyre-B strain of *Herpes simplex virus type 1* in the arm representation of the primary motor cortex ($M1_{arm}$), arm representation of the ventral premotor cortex (PMV_{arm}), and areas 9 and 46 of the prefrontal cortex. The resulting retrogradely labeled neurons in the cerebellar dentate and interpositus nuclei (bottom) are indicated by solid dots. Relative anteroposterior locations of the labeled neurons within the dentate nucleus are indicated below each section. (Adapted from Middleton & Strick, 1997.) Reprinted with kind permission of Harcourt Inc.

The cerebrocerebellar interactions appear to be important in recovery from cerebellar injury. When sensory cortex is removed prior to an induced cerebellar lesion, the cerebellar deficits are exaggerated and recovery is limited (Mackel, 1987). When sensory cortex lesions are made subsequent to a cerebellar lesion, and after recovery from the cerebellar deficits, the initially recovered cerebellar deficits reappear. Furthermore, the effects of combined sequential cerebellar and sensory cortical lesions appear worse than expected if the two lesions were merely additive. These results indicate a functional interrelationship dependent upon the cerebrocerebellar system, which facilitates compensation following injury.

The phenomenon of cerebellar diaschisis—functional deactivation at a distance following damage to an interconnected region, has been documented following lesions of the cerebral hemispheres, including language related cortex in the frontal lobe (Metter *et al.*, 1987). Conversely, reversed cerebellar diaschisis has also been observed. Lesions of cerebellum are associated with decreased activation in the contralateral cerebral hemisphere, in both sensorimotor as well as association cortices (Schmahmann, 1991; Botez-Marquard & Botez, 1997; Schmahmann & Sherman, 1998). These findings provide imaging support for the anatomic connections described here. They are also relevant in the genesis of the cerebellar cognitive affective syndrome (Schmahmann & Sherman, 1998) that results following focal cerebellar injury, and are consistent with the suggestion that the syndrome results from the removal of the cerebellar component of the distributed neural circuits responsible for cognition and affect (Schmahmann, 1991, 1996).

The cerebellar cognitive affective syndrome (CCAS) is most apparent when the lesion involves the posterior lobe of the cerebellum (Schmahmann & Sherman, 1998; Levisohn *et al.*, 2000; Riva & Giorgi *et al.*, 2000; Neau *et al.*, 2000), whereas the motor phenomena typically ascribed to cerebellar dysfunction are more related to lesions of the anterior lobe. This is in agreement with the anatomic connections described above, where the rostral pons receives more associative input and projects to the posterior lobe, whereas the caudal pons receives more sensorimotor inputs and projects to the anterior lobe. The more detailed characterization of the anatomic correlates of the different elements of the CCAS (executive, visual spatial, linguistic) remain to be determined, although the midline location of the affective changes (Schmahmann & Sherman, 1998; Levisohn *et al.*, 2000; Riva & Giorgi, 2000) is certainly consistent with the vermal-fastigial region interaction with the limbic system—giving rise to the notion of a limbic cerebellum (Heath, 1977; Schmahmann, 1991, 2000).

Initial attempts at characterization of the functional topography within cerebellum, consistent with the apparent specificity of the cerebrocerebellar loops, has been carried out in meta-analyses of functional

neuroimaging studies (Desmond & Fiez, 1998; Schmahmann *et al.*, 1998). The results are in agreement with the notion that the anterior lobe is the sensorimotor cerebellum, and the posterior lobe is the cognitive cerebellum. Executive and linguistic tasks activated lobule VI and crus I on the right, attentional modulation was more heavily concentrated in lobule VI on the left, and non-motor learning was focused particularly in crus I and crus II. The cerebellar vermis and paravermian regions are activated preferentially in studies of pain, hunger and thirst.

Synthesis

There is an evolving body of anatomic information that links the cerebellum with systems that subservise every level of behavior, from arousal to autonomic function, motivation, emotion, and the highest forms of cognitive processing. The cerebrocerebellar loops are topographically organized, linking specific cerebral areas with different regions of the cerebellum. The topographic arrangement in the cerebellar connections is superimposed upon an essentially constant pattern of intrinsic cerebellar cortical circuitry. This dichotomy provides support for the dysmetria of thought hypothesis (Schmahmann, 1991, 1996, 2000), predicated on the notion that the cerebellum performs its unique computations in a topographically precise manner on diverse streams of information relating to almost all aspects of behavior including cognition and emotion. The recognition of the anatomic, clinical and functional neuroimaging evidence suggesting a cerebellar role in higher order function has heralded a theoretical paradigm shift in clinical and cognitive neuroscience. It is necessary to explore the nature of cerebellar psychopathology, and to develop instruments to measure and further understand the cerebellar component of diseases that have traditionally fallen within the psychiatric domain. Knowledge of the anatomic underpinnings of the cerebro-cerebellar interaction will surely continue to be crucial.

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References

- AAS, J.-E. & BRODAL, P. (1988). Demonstration of topographically organized projections from the hypothalamus to the pontine nuclei: an experimental study in the cat. *Journal of Comparative Neurology*, 268, 313–328.
- ALBUS, J.S. (1971). A theory of cerebellar function. *Mathematical Biosciences*, 10, 25–61.
- ALLEN, G.I. & TSUKAHARA, N. (1974). Cerebrocerebellar communication systems. *Physiological Reviews*, 54, 957–1008.

- ANDREZIK, J.A., DORMER, K.J., FOREMAN, R.D. & PERSON, R.J. (1984). Fastigial nucleus projections to the brain stem in beagles: pathways for autonomic regulation. *Neuroscience*, *11*, 497–507.
- ASTRUC, J. (1971). Corticofugal connections of area 8 (frontal eye field) in macaca mulatta. *Brain Research*, *33*, 241–256.
- AUMANN, T.D. & HORNE, M.K. (1996). Ramification and termination of single axons in the cerebellothalamic pathway of the rat. *Journal of Comparative Neurology*, *376*, 420–430.
- BABB, T.L., MITCHELL, A.G. JR. & CRANDALL, P.H. (1974). Fastigiobulbar and dentatothalamic influences on hippocampal cobalt epilepsy in the cat. *Electroencephalography and Clinical Neurophysiology*, *36*, 141–154.
- BALL, G., MICCO, D. JR. & BERNTSON, G. (1974). Cerebellar stimulation in the rat. Complex stimulation bound oral behaviors and self-stimulation. *Physiology Behavior*, *13*, 123–127.
- BARBAS, H., HASWELL HENION, T.H. & CERMON, C.R. (1991). Diverse thalamic projections to the prefrontal cortex in the rhesus monkey. *Journal of Comparative Neurology*, *313*, 65–94.
- BARD, P. (1928). A diencephalic mechanism for the expression of rage with special reference to the sympathetic nervous system. *American Journal of Physiology*, *84*, 490–515.
- BATTON, R.R. III, JAYARAMAN, A., RUGGIERO, D. & CARPENTER, M.B. (1977). Fastigial efferent projections in the monkey: an autoradiographic study. *Journal of Comparative Neurology*, *174*, 281–306.
- BERNTSON, G., POTOLICCHI, S. JR. & MILLER, N. (1973). Evidence for higher functions of the cerebellum: eating and grooming elicited by cerebellar stimulation in cats. *Proceedings of the National Academy of Sciences of the USA*, *70*, 2497–2499.
- BOTEZ-MARQUARD, T. & BOTEZ, M.I. (1997). Olivopontocerebellar atrophy and Friedreich's ataxia: neuropsychological consequences of bilateral versus unilateral cerebellar lesions. In: J.D. SCHMAHMANN (Ed.), *The cerebellum and cognition. International Review of Neurobiology*, *41*, 387–410.
- BOUSSAOU, D., DESIMONE, R. & UNGERLEIDER, L.G. (1991). Visual topography of area TEO in the macaque. *Journal of Comparative Neurology*, *306*, 554–575.
- BRODAL, A. (1981). *Neurological anatomy in relation to clinical medicine*. New York: Oxford University Press.
- BRODAL, P. (1978). The corticopontine projection in the rhesus monkey. Origin and principles of organization. *Brain*, *101*, 251–283.
- BRODAL, P. (1979). The pontocerebellar projection in the rhesus monkey: an experimental study with retrograde axonal transport of horseradish peroxidase. *Neuroscience*, *4*, 193–208.
- BRODAL, P. (1980). The projection from the nucleus reticularis tegmenti pontis to the cerebellum in the rhesus monkey. *Experimental Brain Research*, *38*, 29–36.
- BRODAL, P., BJAALI, J.G. & AAS, J.E. (1991). Organization of cingulo-ponto-cerebellar connections in the cat. *Anatomy and Embryology (Berlin)*, *184*, 245–254.
- BRODMANN, K. (1909). *Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues* (p. xii). Leipzig: J.A. BARTH.
- CAVADA, C. & GOLDMAN-RAKIC, P.S. (1989a). Posterior parietal cortex in rhesus monkey: I. Parcellation of areas based on distinctive limbic and sensory corticocortical connections. *Journal of Comparative Neurology*, *287*, 393–421.
- CAVADA, C. & GOLDMAN-RAKIC, P.S. (1989b). Posterior parietal cortex in rhesus monkey: II. Evidence for segregated corticocortical networks linking sensory and limbic areas with the frontal lobe. *Journal of Comparative Neurology*, *287*, 422–445.
- CHAMBERS, W.W. & SPRAGUE, J.M. (1955). Functional localization in the cerebellum. I. Organization in longitudinal corticonuclear zones and their contribution to the control of posture, both extrapyramidal and pyramidal. *Journal of Comparative Neurology*, *103*, 105–130.
- COGHILL, R.C., SANG, C.N., MAISOG, J.M. & IADAROLA, M.J. (1999). Pain intensity processing within the human brain: a bilateral, distributed mechanism. *Journal of Neurophysiology*, *82*, 1934–1943.
- CRITCHLEY, M. (1953). *The parietal lobes*. New York: Hafner Press.
- DEMPSEY, C.W., TOOTLE, D.M., FONTANA, C.J., FITZJARRELL, A.T., GAREY, R.E. & HEATH, R.G. (1983). Stimulation of the paleocerebellar cortex of the cat: increased rate of synthesis and release of catecholamines at limbic sites. *Biological Psychiatry*, *18*, 127–132.
- DENNY-BROWN, D. & CHAMBERS, R.A. (1958). The parietal lobe and behavior. *Research Publications of the Association for Research in Nervous and Mental Disease*, *36*, 35–117.
- DESIMONE, R. & UNGERLEIDER, L.G. (1989). Neural mechanisms of visual processing in monkeys. In: F. BOLLER & J. GRAFMAN (Eds), *Handbook of neurophysiology*, (Vol. 2, pp. 267–299). New York: Elsevier.
- DESMOND, J.E. & FIEZ, J.A. (1998). Neuroimaging studies of the cerebellum: language, learning and memory. *Trends in Cognitive Science*, *2*, 355–362.
- DEVINSKY, O., MORRELL, M.J. & VOGT, B.A. (1995). Contributions of anterior cingulate cortex to behaviour. *Brain*, *118*, 279–306.
- DIETRICH, E. (1984). Cerebellar autonomic function: direct hypothalamocerebellar pathway. *Science*, *223*, 591–593.
- DOBA, N. & REIS, D.J. (1972). Changes in regional blood flow and cardiodynamics evoked by electrical stimulation of the fastigial nucleus in the cat and their similarity to orthostatic reflexes. *Journal of Physiology*, *227*, 729–747.
- DOW, R.S. (1942). The evolution and anatomy of the cerebellum. *Biological Reviews*, *17*, 179–220.
- EBERT, D. & EBMEIER, K.P. (1996). The role of the cingulate gyrus in depression: from functional anatomy to neurochemistry. *Biological Psychiatry*, *39*, 1044–1050.
- FELLEMAN, D.J. & VAN ESSEN, D.C. (1991). Distributed hierarchical processing in the primate cerebral cortex. *Cerebral Cortex*, *1*, 1–47.
- FIEZ, J.A. & RAICHLE, M.E. (1997). Linguistic processing. In: J.D. SCHMAHMANN (Ed.), *The cerebellum and cognition. International Review of Neurobiology*, *41*, 233–254.
- FRIES, W. (1990). Pontine projection from striate and prestriate visual cortex in the macaque monkey: an anterograde study. *Visual Neuroscience*, *4*, 205–216.
- FUSTER, J.M. (1980). *The prefrontal cortex: anatomy, physiology and neuropsychology of the frontal lobe*. New York: Raven Press.
- GIGUERE, M. & GOLDMAN-RAKIC, P.S. (1988). Mediodorsal nucleus: areal, laminar, and tangential distribution of afferents and efferents in the frontal lobe of rhesus monkeys. *Journal of Comparative Neurology*, *277*, 195–213.
- GLICKSTEIN, M., MAY, J.G. & MERCIER, B.E. (1985). Corticopontine projection in the macaque: The distribution of labeled cortical cells after large injections of horseradish peroxidase in the pontine nuclei. *Journal of Comparative Neurology*, *235*, 343–359.
- GLICKSTEIN, M., GERRITS, N., KRALJ-HANS, I., MERCIER, B., STEIN, J. & VOOGD, J. (1994). Visual pontocerebellar

- projections in the macaque. *Journal of Comparative Neurology*, 349, 51–72.
- GOLDMAN-RAKIC, P.S. & FRIEDMAN, H.R. (1991). The circuitry of working memory revealed by anatomy and metabolic imaging. In: H.S. LEVIN *et al.* (Eds), *Frontal lobe function and dysfunction* (pp. 72–91). Oxford: Oxford University Press.
- GOLDMAN-RAKIC, P.S. & SELEMON, L.D. (1990). New frontiers in basal ganglia research. *Trends in Neuroscience*, 13, 241–244.
- GONZALO-RUIZ, A. & LEICHNETZ, G.R. (1990). Connections of the caudal cerebellar interpositus complex in a new world monkey (*Cebus apella*). *Brain Research Bulletin*, 25, 919–927.
- HAINES, D.E. (1981). Zones in the cerebellar cortex. Their organization and potential relevance to cerebellar stimulation. *Journal of Neurosurgery*, 55, 254–256.
- HAINES, D.E. (1989). HRP study of cerebellar corticonuclear-nucleocortical topography of the dorsal culminate lobule—lobule V—in a prosimian primate (*Galago*): with comments on nucleocortical cell types. *Journal of Comparative Neurology*, 282, 274–292.
- HAINES, D.E. & DIETRICH, E. (1984). An HRP study of hypothalamo-cerebellar and cerebello-hypothalamic connections in squirrel monkey (*Saimiri sciureus*). *Journal of Comparative Neurology*, 229, 559–575.
- HAINES, D.E., DIETRICH, E., MIHAILOFF, G.A. & MCDONALD, E.F. (1997). The cerebellar-hypothalamic axis: basic circuits and clinical observations. In: J.D. SCHMAHMANN (Ed.), *The cerebellum and cognition. International Review of Neurobiology*, 41, 83–107.
- HAWKES, R., COLONNIER, M. & LECLERC, N. (1985). Monoclonal antibodies reveal sagittal banding in the rodent cerebellar cortex. *Brain Research*, 6, 359–365.
- HEATH, R.G. (1977). Modulation of emotion with a brain pacemaker. Treatment for intractable psychiatric illness. *Journal of Nervous and Mental Disease*, 165, 300–317.
- HEATH, R.G. & HARPER, J.W. (1974). Ascending projections of the cerebellar fastigial nucleus to the hippocampus amygdala and other temporal lobe sites: evoked potential and histological studies in monkeys and cats. *Experimental Neurology*, 45, 2682–2687.
- HEATH, R.G., DEMPSEY, C.W., FONTANA, C.J. & MYERS, W.A. (1978). Cerebellar stimulation: effects on septal region, hippocampus, and amygdala of cats and rats. *Biological Psychiatry*, 13, 501–529.
- HUMPHREY, D.R., GOLD, R. & REED, D.J. (1984). Sizes, laminar and topographic origins of cortical projections to the major divisions of the red nucleus in the monkey. *Journal of Comparative Neurology*, 225, 75–94.
- HYVARINEN, J. (1982). Posterior parietal lobe of the primate brain. *Physiological Reviews*, 62, 1060–1129.
- ILINSKY, I.A. & KULTAS-ILINSKY, K. (1987). Sagittal cytoarchitectonic maps of *Macaca mulatta*. *Journal of Comparative Neurology*, 173, 147–164.
- ITO, M. (1993). Movement and thought: identical control mechanisms by the cerebellum. *Trends in Neuroscience*, 16, 448–450.
- JANSEN, J. & BRODAL, A. (1940). Experimental studies on the intrinsic fibers of the cerebellum. II. The corticonuclear projection. *Journal of Comparative Neurology*, 73, 267–321.
- KALIL, K. (1981). Projections of the cerebellar and dorsal column nuclei upon the thalamus of the rhesus monkey. *Journal of Comparative Neurology*, 195, 25–50.
- KENNEDY, P.R., GIBSON, A.R. & HOUK, J.C. (1986). Functional and anatomic differentiation between parvicellular and magnocellular regions of red nucleus in the monkey. *Brain Research*, 364, 124–136.
- KIEVET, J. & KUYPERS, H.G.J.M. (1977). Organization of the thalamocortical connections to the frontal lobe in the rhesus monkey. *Experimental Brain Research*, 29, 299–322.
- KÜNZLE, H. & AKERT, K. (1977). Efferent connections of cortical area 8 (frontal eye lid) in *Macaca fascicularis*. A reinvestigation using the autoradiographic technique. *Journal of Comparative Neurology*, 173, 147–164.
- KUYPERS, H.G. & UGOLINI, G. (1990). Viruses as transneuronal tracers. *Trends in Neuroscience*, 13, 71–75.
- KUYPERS, H.G.J.M. & LAWRENCE, D.G. (1967). Cortical projections to the red nucleus and the brainstem in the rhesus monkey. *Brain Research*, 4, 151–188.
- LARSELL, O. (1970). The comparative anatomy and histology of the cerebellum from monotremes through apes. In: J. JANSEN (Ed.), Minneapolis, MN: The University of Minnesota Press.
- LEGGIO, M.G., SILVERI, M.C., PETROSINI, L. & MOLINARI, M. (2000). Phonological grouping is specifically affected in cerebellar patients: a verbal fluency study. *Journal of Neurology, Neurosurgery and Psychiatry*, 69, 102–106.
- LEINER, H.C., LEINER, A.L. & DOW, R.S. (1986). Does the cerebellum contribute to mental skills? *Behavioral Neuroscience*, 100, 443–454.
- LEVISOHN, L., CRONIN-GOLOMB, A. & SCHMAHMANN, J.D. (2000). Neuropsychological consequences of cerebellar tumor resection in children: cerebellar cognitive affective syndrome in a pediatric population. *Brain*, 123, 1041–1050.
- LURIA, A.R. (1966). *Higher cortical functions in man*. New York: Basic Books.
- LYNCH, J.C. (1980). The functional organization of posterior parietal association cortex. *Behavioral Brain Science*, 3, 485–534.
- MACKEL, R. (1987). The role of the monkey sensory cortex in the recovery from cerebellar injury. *Experimental Brain Research*, 66, 638–652.
- MARCINKIEWICZ, M., MORCOS, R. & CHRETIEN, M. (1989). CNS connections with the median raphe nucleus: retrograde tracing with WGA-apoHRP-gold complex in the rat. *Journal of Comparative Neurology*, 289, 11–35.
- MARR, D. (1969). A theory of cerebellar cortex. *Journal of Physiology*, 202, 437–470.
- MARTNER, J. (1975). Cerebellar influences on autonomic mechanisms. *Acta Physiologica Scandinavica, (Suppl.)*, 425, 1–42.
- MAY, J.G. & ANDERSEN, R.A. (1986). Different patterns of corticopontine projections from separate cortical fields within the inferior parietal lobule and dorsal prelunate gyrus of the macaque. *Experimental Brain Research*, 63, 265–278.
- MESULAM, M.-M. & MUFSON, E.J. (1985). The insula of reil in man and monkey. architectonics, connectivity, and function. In: A. PETERS & E.G. JONES (Eds), *Cerebral cortex* (Vol. 4, pp. 179–226). New York: Plenum Press.
- METTER, E.J., KEMPLER, D., JACKSON, C.A., HANSON, W.R., RIEGE, W.H., CAMRAS, L.R., MAZZIOTTA, J.C. & PHELPS, M.E. (1987). Cerebellar glucose metabolism in chronic aphasia. *Neurology*, 37, 1599–1606.
- MICCO JR, D.J. (1974). Complex behaviors elicited by stimulation of the dorsal pontine tegmentum in rats. *Brain Research*, 75, 172–176.
- MIDDLETON, F.A. & STRICK, P.L. (1994). Anatomical evidence for cerebellar and basal ganglia involvement in higher cognitive function. *Science*, 266, 458–451.
- MIDDLETON, F.A. & STRICK, P.L. (1997). Cerebellar output channels. In: J.D. SCHMAHMANN (Ed.), *The cerebellum and cognition. International Review of Neurobiology*, 41, 61–82.
- MILLER, R.A. & STROMINGER, N.L. (1977). An experimental study of the efferent connections of the superior cerebellar peduncle in the rhesus monkey. *Brain Research*, 133, 237–250.

- MILNER, B. (1964). Some effects of frontal lobectomy in man. In: J.M. WARREN & K. AKERT (Eds), *The frontal granular cortex and behavior* (pp. 313–334). New York: McGraw Hill.
- MISHKIN, M. & UNGERLEIDER, L.G. (1982). Contribution of striate inputs to the visuospatial functions of parieto-occipital cortex in monkeys. *Behavioral Brain Research*, 6, 57–77.
- MORUZZI, G. (1940). Paleocerebellar inhibition of vasomotor and respiratory carotid sinus reflexes. *Journal of Neurophysiology*, 3, 20–32.
- MORUZZI, G. (1947). Sham rage and localized autonomic responses elicited by cerebellar stimulation in the acute thalamic cat. *Proceedings of the XVII International Congress on Physiology*, Oxford, pp. 114–115.
- MOUNTCASTLE, V.B., TALBOT, W.H. & YIN, T.C.T. (1977). Parietal lobe mechanisms for directed visual attention. *Journal of Neurophysiology*, 40, 362–389.
- MUTANI, R. (1967). Cobalt experimental hippocampal epilepsy in the cat. *Epilepsia*, 8, 223–240.
- NADEL, L. (1991). The hippocampus and space revisited. *Hippocampus*, 1, 221–229.
- NEAU, J.P., ARROYO-ANLLO, E., BONNAUD, V., INGRAND, P. & GIL, R. (2000). Neuropsychological disturbances in cerebellar infarcts. *Acta Neurologica Scandinavica*, 102, 363–370.
- NODA, H., SUGITA, S. & IKEDA, Y. (1990). Afferent and efferent connections of the oculomotor region of the fastigial nucleus in the macaque monkey. *Journal of Comparative Neurology*, 302, 330–348.
- NYBY, O. & JANSEN, J. (1951). An experimental investigation of the corticopontine projection in macaca mulatta. *Skrifter utgitt av Det Norske Videnskaps-Akademi: Oslo; 1. Mat. Naturv. Klasse.*, 3, 1–47.
- OADES, R.D. & HALLIDAY, G.M. (1987). Ventral tegmental (A10) system: neurobiology. 1. Anatomy and connectivity. *Brain Research*, 434, 117–165.
- OLSZEWSKI, J. (1952). *The thalamus of the macaca mulatta*. Basel: S. Karger.
- ORIOLI, P.J. & STRICK, P.L. (1989). Cerebellar connections with the motor cortex and the arcuate premotor area: an analysis employing retrograde transneuronal transport of WGA-HRP. *Journal of Comparative Neurology*, 288, 621–626.
- PANDYA, D.N. & YETERIAN, E.H. (1985). Architecture and connections of cortical association areas. In: A. PETERS & E.G. JONES (Eds), *Cerebral cortex* (Vol. 4, pp. 43–61). New York: Plenum Press.
- PANDYA, D.N. & YETERIAN, E.H. (1991). Prefrontal cortex in relation to other cortical areas in rhesus monkey: architecture and connections. *Progress in Brain Research*, 85, 3–94.
- PARSONS, L.M., DENTON, D., EGAN, G., MCKINLEY, M., SHADE, R., LANCASTER, J. & FOX, P.T. (2000). Neuroimaging evidence implicating cerebellum in support of sensory/cognitive processes associated with thirst. *Proceedings of the National Academy of Sciences of the USA*, 97, 2332–2336.
- PATON, J.F. & SPYER, K.M. (1990). Brain stem regions mediating the cardiovascular responses elicited from the posterior cerebellar cortex in the rabbit. *Journal of Physiology*, (London) 427, 533–552.
- PAUS, T. (2001). Primate anterior cingulate cortex: where motor control, drive and cognition interface. *Nature Reviews Neuroscience*, 2, 417–424.
- PERRETT, D.I., MISTLIN, A.J. & CHITTY, A.J. (1987). Visual neurons responsive to faces. *Trends in Neuroscience*, 10, 358–364.
- PERSON, R.J., ANDREZIK, J.A., DORMER, K.J. & FOREMAN, R.D. (1986). Fastigial nucleus projections in the midbrain and thalamus in dogs. *Neuroscience*, 18, 105–120.
- PETRIDES, M. (1995). Impairments of nonspatial self-ordered and externally ordered working memory tasks after lesions of the mid-dorsal part of the lateral frontal cortex in the monkey. *Journal of Neuroscience*, 15, 359–375.
- PETRIDES, M. & PANDYA, D.N. (1994). Comparative architectonic analysis of the human and the macaque frontal cortex. In: F. BOLLER & J. GRAFMAN (Eds), *Handbook of neuropsychology* (Vol. 9, pp. 17–57). New York: Elsevier.
- PPICARD, N. & STRICK, P.L. (1996). Motor areas of the medial wall: a review of their location and functional activation. *Cerebral Cortex*, 6, 342–353.
- PLOGHAUS, A., TRACEY, I., GATI, J.S., CLARE, S., MENON, R.S., MATTHEWS, P.M. & RAWLINS, J.N. (1999). Dissociating pain from its anticipation in the human brain. *Science*, 284, 1979–1981.
- POLLACK, I.F., POLINKO, P., ALBRIGHT, A.L., TOWBIN, R. & FITZ, C. (1995). Mutism and pseudobulbar symptoms after resection of posterior fossa tumors in children: incidence and pathophysiology. *Neurosurgery*, 37, 885–893.
- QVIST, H. (1989). Demonstration of axonal branching of fibres from certain precerebellar nuclei to the cerebellar cortex and nuclei: a retrograde fluorescent double-labelling study in the cat. *Experimental Brain Research*, 75, 15–27.
- RASHEED, B.M., MANCHANDA, S.K. & ANAND, B.K. (1970). Effects of the stimulation of paleocerebellum on certain vegetative functions in the cat. *Brain Research*, 20, 293–308.
- RAUCH, S.L., JENIKE, M.A., ALPERT, N.M., BAER, L., BREITER, H.C., SAVAGE, C.R. & FISCHMAN, A.J. (1994). Regional cerebral blood flow measured during symptom provocation in obsessive-compulsive disorder using oxygen 15-labeled carbon dioxide and positron emission tomography. *Archives of General Psychiatry*, 1, 62–70.
- REIS, D.J. & GOLANOV, E.V. (1997). Autonomic and vasomotor regulation. In: J.D. SCHMAHMANN (Ed.), *The cerebellum and cognition. International Review of Neurobiology*, 41, 121–149.
- REIS, D.J., DOBA, N. & NATHAN, M.A. (1973). Predatory attack, grooming and consummatory behaviors evoked by electrical stimulation of cat cerebellar nuclei. *Science*, 182, 845–847.
- RIVA, D. & GIORGI, C. (2000). The cerebellum contributes to higher function during development: evidence from a series of children surgically treated for posterior fossa tumors. *Brain*, 123, 1051–1061.
- SAINT-CYR, J.A. & COURVILLE, J. (1980). Projections from the motor cortex, midbrain, and vestibular nuclei to the inferior olive in the cat: anatomical and functional correlates. In: J. COURVILLE, C. DEMONTIGNY & Y. LAMARRE (Eds), *The inferior olivary nucleus: anatomy and physiology* (pp. 97–124). New York: Raven Press.
- SASAKI, K., OKA, H., MATSUDA, Y., SHIMONO, T. & MIZUNO, N. (1975). Electrophysiological studies of the projections from the parietal association area to the cerebellar cortex. *Experimental Brain Research*, 23, 91–102.
- SCHMAHMANN, J.D. (1991). An emerging concept: the cerebellar contribution to higher function. *Archives of Neurology*, 48, 1178–1187.
- SCHMAHMANN, J.D. (1994). The cerebellum in autism: clinical and anatomic perspectives. In: M.L. BAUMAN T.L. KEMPER (Eds), *The neurobiology of autism* (pp. 195–226). Baltimore, MD: Johns Hopkins University Press.
- SCHMAHMANN, J.D. (1996). From movement to thought: anatomic substrates of the cerebellar contribution to cognitive processing. *Human Brain Mapping*, 4, 174–198.
- SCHMAHMANN, J.D. (1997). The cerebellum and cognition. *International Review of Neurobiology*, 41.

- SCHMAHMANN, J.D. (2000). The role of the cerebellum in affect and psychosis. *Journal of Neurolinguistics*, 13, 189–214.
- SCHMAHMANN, J.D. & PANDYA, D.N. (1989). Anatomical investigation of projections to the basis pontis from posterior parietal association cortices in rhesus monkey. *Journal of Comparative Neurology*, 289, 53–73.
- SCHMAHMANN, J.D. & PANDYA, D.N. (1990). Anatomical investigation of projections from thalamus to the posterior parietal association cortices in rhesus monkey. *Journal of Comparative Neurology*, 295, 299–326.
- SCHMAHMANN, J.D. & PANDYA, D.N. (1991). Projections to the basis pontis from the superior temporal sulcus and superior temporal region in the rhesus monkey. *Journal of Comparative Neurology*, 308, 224–248.
- SCHMAHMANN, J.D. & PANDYA, D.N. (1992). Fiber pathways to the pons from parasensory association cortices in rhesus monkey. *Journal of Comparative Neurology*, 326, 159–179.
- SCHMAHMANN, J.D. & PANDYA, D.N. (1993). Prelunate, occipitotemporal, and parahippocampal projections to the basis pontis in rhesus monkey. *Journal of Comparative Neurology*, 337, 94–112.
- SCHMAHMANN, J.D. & PANDYA, D.N. (1994). Trajectories of the prefrontal, premotor, and precentral corticopontine fiber systems in the rhesus monkey. *Society for Neuroscience Abstracts*, 20, 985.
- SCHMAHMANN, J.D. & PANDYA, D.N. (1995). Prefrontal cortex projections to the basilar pons: implications for the cerebellar contribution to higher function. *Neuroscience Letters*, 199, 175–178.
- SCHMAHMANN, J.D. & PANDYA, D.N. (1997a). Anatomic organization of the basilar pontine projections from prefrontal cortices in rhesus monkey. *Journal of Neuroscience*, 17, 438–458.
- SCHMAHMANN, J.D. & PANDYA, D.N. (1997b). The cerebrotocerebellar system. In: J.D. SCHMAHMANN (Ed.), *The cerebellum and cognition. International Review of Neurobiology*, 41, 31–60.
- SCHMAHMANN, J.D. & SHERMAN, J.C. (1998). The cerebellar cognitive affective syndrome. *Brain*, 121, 561–579. (See Editorial, *Brain*, (1998); 121, 545–546.)
- SCHMAHMANN, J.D., LOEBER, R.T., MARJANI, J. & HURWITZ, A.S. (1998). Topographic organization of cognitive functions in the human cerebellum. A meta-analysis of functional imaging studies. *Neuroimage*, 7, S721.
- SHAH, V.S., SCHMAHMANN, J.D., PANDYA, D.N. & VAHER, P.R. (1997). Associative projections to the zona incerta: Possible anatomic substrates for extension of the Marr-Albus hypothesis to non-motor learning. *Society for Neuroscience Abstract*, 23, 1829.
- SILVERI, M.C., LEGGIO, M.G. & MOLINARI, M. (1994). The cerebellum contributes to linguistic production: a case of agrammatic speech following a right cerebellar lesion. *Neurology*, 40, 2047–2050.
- SIWEK, D.F. & PANDYA, D.N. (1991). Prefrontal projections to the mediodorsal nucleus of the thalamus in the rhesus monkey. *Journal of Comparative Neurology*, 312, 509–524.
- SNIDER, R.S. (1950). Recent contributions to the anatomy and physiology of the cerebellum. *Archives of Neurology and Psychology*, 64, 196–219.
- SNIDER, R.S. (1975). A cerebellar-cereuleus pathway. *Brain Research*, 88, 59–63.
- SNIDER, R.S. & MAITTI, A. (1976). Cerebellar contributions to the Papez circuit. *Journal of Neuroscience Research*, 2, 133–146.
- STANTON, G.B. (1980). Topographical organization of ascending cerebellar projections from the dentate and interposed nuclei in Macaca mulatta: an anterograde degeneration study. *Journal of Comparative Neurology*, 190, 699–731.
- STANTON, G.B., GOLDBERG, M.E. & BRUCE, C.J. (1988). Frontal eye field efferents in the macaque monkey: II. Topography of terminal fields in midbrain and pons. *Journal of Comparative Neurology*, 271, 493–506.
- STEIN, J.R. & GLICKSTEIN, M. (1992). Role of the cerebellum in visual guidance of movement. *Physiological Reviews*, 72, 967–1017.
- STRICK, P.L. (1976). Anatomical analysis of ventrolateral thalamic input to primate motor cortex. *Journal of Neurophysiology*, 39, 1020–1031.
- STRICK, P.L. (1999). Symposium: basal ganglia, cerebellum and motor control. *Society for Neuroscience Abstracts*, 25, 528.
- STUSS, D.T. & BENSON, D.F. (1986). *The frontal lobes*. New York: Raven Press.
- SUNDERLAND, S. (1940). The projection of the cerebral cortex on the pons and cerebellum in the macaque monkey. *Journal of Anatomy*, 74, 201–226.
- TATARANNI, P.A., GAUTIER, J.F., CHEN, K., UECKER, A., BANDY, D., SALBE, A.D., *et al.* (1999). Neuroanatomical correlates of hunger and satiation in humans using positron emission tomography. *Proceedings of the National Academy of Sciences of the USA*, 96, 4569–4574.
- THACH, W.T. (1997). Context-response linkage. In: J.D. SCHMAHMANN (Ed.), *The cerebellum and cognition. International Review of Neurobiology*, 41, 599–611.
- THACH, W.T. & JONES, E.G. (1979). The cerebellar dentatothalamic connection: Terminal field, lamellae, rods and somatotopy. *Brain Research*, 169, 168–172.
- UGOLINI, G., KUYPERS, H.G. & SIMMONS, A. (1987). Retrograde transneuronal transfer of herpes simplex virus type 1 (HSV 1) from motoneurons. *Brain Research*, 422, 242–256.
- UNGERLEIDER, L.G. & MISHKIN, M. (1982). Two cortical visual systems. In: D.J. INGLE, M.A. GOODALE & R.J.W. MANSFIELD (Eds), *Analysis of visual behavior* (pp. 549–586). Cambridge, MA: MIT Press.
- UNGERLEIDER, L.G., DESIMONE, R., GALKIN, T.W. & MISHKIN, M. (1984). Subcortical projections of area MT in the macaque. *Journal of Comparative Neurology*, 223, 368–386.
- VILENSKY, J.A. & VAN HOESEN, G.W. (1981). Corticopontine projections from the cingulate cortex in the rhesus monkey. *Brain Research*, 205, 391–395.
- VOGT, B.A. & PANDYA, D.N. (1987). Cingulate cortex of the rhesus monkey: II. Cortical afferents. *Journal of Comparative Neurology*, 262, 271–289.
- VOOGD, J. & GLICKSTEIN, M. (1998). The anatomy of the cerebellum. *Trends in Neuroscience*, 21, 370–375.
- WHITESIDE, D.G. & SNIDER, R.S. (1953). Relation of cerebellum to upper brain stem. *Journal of Neurophysiology*, 16, 397–413.
- WIESENDANGER, R. & WIESENDANGER, M. (1985). The thalamic connections with medial area 6 (supplementary motor cortex) in the monkey (*Macaca fascicularis*). *Experimental Brain Research*, 59, 91–104.
- XU, F. & FRAZIER, T. (1997). Involvement of the fastigial nuclei in vagally mediated respiratory responses. *Journal of Applied Physiology*, 82, 1853–1861.
- YETERIAN, E.H. & PANDYA, D.N. (1985). Corticothalamic connections of the posterior parietal cortex in the rhesus monkey. *Journal of Comparative Neurology*, 237, 408–426.
- YETERIAN, E.H. & PANDYA, D.N. (1989). Thalamic connections of the cortex of the superior temporal sulcus in the rhesus monkey. *Journal of Comparative Neurology*, 282, 80–97.
- ZANCHETTI, A. & ZOCCOLINI, A. (1954). Autonomic hypothalamic outbursts elicited by cerebellar stimulation. *Journal of Neurophysiology*, 17, 475–483.

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