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# Cerebrocerebellar Loops in the Rodent Brain

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## INTRODUCTION

If one compares the rodent and the human brains, their structure scales up quite differently: while the total number of neurons is multiplied by a factor of 400 between adult rats and humans, the number of hippocampal neurons is increased by a modest factor of 20 (West & Gundersen, 1990; West, Slomianka, & Gundersen, 1991). In contrast, the number of neurons in the cerebellum and in the cerebral cortex (which might represent up to respectively 80 and 19% of human brain neurons) scales up by keeping their ratio constant (Herculano-Houzel, 2010). A complex, polysynaptic circuit reciprocally connects the cerebellum and the cerebral cortex: several mesencephalic and pontine nuclei relay inputs from the cerebral cortex to the cerebellum, and the cerebellum returns projections to portions of the cerebral cortex via multiple diencephalic nuclei. Many behavioral and theoretical studies have led to the general notion that the corticocerebellar circuit subserves the formation of “internal models,” which provide representations of the expected outcome of actions or of actions required to obtain a desired outcome (Ito, 2008; Wolpert, Miall, & Kawato, 1998). However, the neurophysiological analysis of the processes that underlie these models has made limited progress since the early recognition of functional cerebrocerebellar and cerebellocerebral connections (reviewed in Allen & Tsukahara, 1974), and the degree of specific reciprocity in these connections has long been unclear. Still, major progress has been achieved in the analysis of the anatomical organization of this circuit and in deciphering the modular structure of the cerebellum; this knowledge, coupled to the

advent of massively parallel recordings and optogenetic approaches, shall revolutionize our understanding of the operations taking place between and within the cerebellum and the cerebral cortex. This chapter provides an overview of current knowledge and general principles that seem to govern the organization of these circuits, with a strong emphasis on data obtained from rats and mice.

## THE CORTICOCEREBELLAR PATHWAY

The cerebral cortex contributes to the two main types of inputs to the cerebellum, the mossy fibers and the climbing fibers. However, these projections are generally indirect and relayed by structures in the midbrain, pons, and medulla.

Cerebellar mossy fibers relaying cortical inputs emanate primarily from the pontine nuclei and to a lesser extent from a set of nuclei associated with the reticular formation (notably the basal pontine reticulotegmental and the lateral reticular nuclei). Retrograde and anterograde studies indicate that most cortical regions contribute to this descending pathway, although the frontal and parietal areas provide major contributions while the temporal regions provide more modest inputs (Leergaard & Bjaalie, 2007; Legg, Mercier, & Glickstein, 1989; Wiesendanger & Wiesendanger, 1982a, 1982b). The cortical projections to the pontine nuclei emanate from a specific set of glutamatergic pyramidal neurons in layer V. Early retrograde tracing experiments suggested a limited overlap between the pyramidal cell populations contributing to the four major corticopontine, corticorubral, corticostriatal, and corticospinal (pre)motor pathways (Akintunde & Buxton, 1992). Retrograde labeling experiments have revealed that corticopontine cells are found solely in layer Vb, while corticostriatal cells are mostly located in cortical layer Va (with some labeling in layer Vb). These downward projections may be quite divergent since a quarter of the rodent's barrel field corticopontine neurons was estimated to send collaterals to the superior colliculus (Mercier, Legg, & Glickstein, 1990). Single-axon reconstruction studies demonstrated that most pyramidal tract- (Mercier et al., 1990) and cerebral- (Donoghue & Kitai, 1981; Levesque, Charara, Gagnon, Parent, & Deschenes, 1996) projecting neurons in the rat emit collaterals to the striatum. Still, two separated downward-projection channels emanate from layer V of the cortex, projecting respectively either to the brain stem/spinal cord and ipsilateral striatum or bilaterally to the striatum. The cortical neurons projecting bilaterally to the striatum entrain, via excitatory collaterals, the pontine-projecting cortical neurons, suggesting a hierarchical order between these subcircuits, the corticostriatal circuit being situated upstream from the corticopontine circuit (Kiritani, Wickersham, Seung, & Shepherd, 2012;

Morishima & Kawaguchi, 2006; Morishima, Morita, Kubota, & Kawaguchi, 2011). It shall be noted that the brain-stem/spinal cord-projecting pathways in rodents are probably less differentiated in rodents than in primates (see the comment in Smith, Wichmann, & DeLong, 2014).

The corticopontine projections exhibit a high level of topographical organization (Leergaard & Bjaalie, 2007; Legg et al., 1989; Panto, Cicirata, Angaut, Parenti, & Serapide, 1995; Wiesendanger & Wiesendanger, 1982b). Pontine territories receiving from the motor and sensory cortices are generally distinct, even when they are related to the same body area: barrel field cortex terminals and vibrissae motor cortex terminate in separate fields (Leergaard et al., 2004; Mihailoff, Lee, Watt, & Yates, 1985; Proville et al., 2014; Schwarz & Mock, 2001); interestingly, the strength of corticopontine projections, measured as an estimated number of terminal varicosities, is higher for the vibrissae sensory cortex input than for the vibrissae motor cortex input. Cortical projections to the basal pontine nuclei are typically organized as predominantly ipsilateral lamellar structures organized by a combination of mediolateral and inside-out arrangement rules (Leergaard & Bjaalie, 2007). Whereas different cortical regions generally end up in different lamellae, evidence points toward some occasional convergence: projections from cortical barrels corresponding to a single row of vibrissae—but not to different rows (Hoffer, Arantes, Roth, & Alloway, 2005; Leergaard, Alloway, Mutic, & Bjaalie, 2000; Schwarz & Mock, 2001)—or from several anteroposterior regions in the medial prefrontal cortex (Moya et al., 2014) exhibit some degree of overlap in the same lamellae. Moreover, the primary and secondary sensory vibrissae cortices exhibit a strikingly high degree of convergence in the pontine nuclei (Leergaard et al., 2004).

The basal pontine nuclei also receive inputs from a number of subcortical brain structures (Mihailoff, Kosinski, Azizi, & Border, 1989), allowing the convergence of direct and indirect corticopontine pathways; evidence for such convergence has been observed in tracing studies for medial-prefrontal cortex and hypothalamic inputs to the pontine nuclei (Allen & Hopkins, 1998). Similarly, cuneo- and gracilopontine fibers partially overlap with corticopontine projections from forelimb sensory and hind-limb sensorimotor cortical regions, respectively (Kosinski, Azizi, & Mihailoff, 1988; Kosinski, Neafsey, & Castro, 1986). In contrast, while the superior colliculus receives inputs from the somatosensory and visual cortices, the colliculopontine projections reach different pontine compartments than the somatosensory and visual cortices (Schwarz, Horowski, Mock, & Thier, 2005). In monkeys, transsynaptic retrograde tracings have provided evidence for a corticosubthalamic-pontine pathway (Bostan, Dum, & Strick, 2010), but there has been so far little evidence for such a circuit in the rat brain, although projections from the subthalamic area to the pontine and reticulotegmental nuclei have been found to emanate from the zona

incerta and fields of Forel (Mihailoff et al., 1989; Ricardo, 1981; Torigoe, Blanks, & Precht, 1986b).

The nature of the integration taking place in the pontine nuclei is still unresolved. The functional integration of inputs from different cortical regions has been suggested by single-unit electrophysiological studies in the rat (Potter, Ruegg, & Wiesendanger, 1978). However, the dendritic trees of single pontine neurons rarely cross the borders of cortical afferent fields, suggesting that they remain within the terminal fields of a single cortical area (Schwarz et al., 2005; Schwarz & Thier, 1995), leaving the early electrophysiological data unexplained. Little coupling between pontine neurons seems to take place via pontopontic connections, but reciprocal connections between pontine and cerebellar nuclei neurons could permit the integration of information across pontine areas (Lee & Mihailoff, 1990; Mock, Butovas, & Schwarz, 2006; Watt & Mihailoff, 1983).

The reticulotegmental nucleus of the pons is another relay of cortical inputs to the cerebellum, mostly from ipsilateral prefrontal, sensorimotor, and cingular cortices (Torigoe, Blanks, & Precht, 1986a). The rostro-medial part of the lateral reticular nucleus also provides a (modest) relay of inputs mostly from the contralateral sensorimotor cortex (Rajakumar, Hryciyshyn, & Flumerfelt, 1992; Shokunbi, Hryciyshyn, & Flumerfelt, 1986). The vestibulocerebellum may receive cortical inputs via the pontine nuclei and potentially via reticular areas (Eisenman & Noback, 1980; Ruigrok, 2003), and via the vestibular nuclei, which receive direct projections from a parietotemporal region and a few more sensorimotor areas (Nishiike, Guldin, & Baurle, 2000) their.

Overall, the available evidence suggests that these descending pathways from the cortex are organized into numerous parallel channels, with occasional convergence for specific inputs allowing a limited degree of integration.

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## MOSSY FIBERS

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Mossy fibers carrying cerebral cortex information emanate primarily from the pontine, reticulotegmental, and lateral reticular nuclei. The topography of these projections is complex and its connection with the modular organization of the cerebellum (e.g., Apps & Hawkes, 2009) is not yet fully understood.

In the pontine nuclei, retrograde tracing from the cerebellar cortex often results in patchy patterns reminiscent of the lamellar organization of corticopontine terminal fields, each cerebellar area receiving inputs from distinct pontine sources, which relay separate cortical inputs (e.g., Eisenman, 1981; Leergaard, Lillehaug, De Schutter, Bower, & Bjaalie, 2006; Odeh, Ackerley, Bjaalie, & Apps, 2005; Pijpers & Ruigrok, 2006). In the

rat, the pontine nuclei project predominantly to the posterior cerebellar cortex (Serapide, Panto, Parenti, Zappala, & Cicirata, 2001). Projections from the pontine, reticulotegmental, and lateral reticular nuclei produce bilateral patterns of terminals with various degrees of preference: mostly contralateral for the pontine and reticulotegmental nuclei and ipsilateral for the lateral reticular nucleus. Ipsi- and contralateral projections emanate from largely distinct pools of pontine neurons (Herrero, Pardoe, & Apps, 2002; Mihailoff, 1983; Serapide, Zappala, Parenti, Panto, & Cicirata, 2002; Wu, Sugihara, & Shinoda, 1999). Small retrograde tracer injections in the cerebellum-labeled cells spread over relatively extended territories, which are more densely populated by larger tracer injections at the same site, suggesting that pontocerebellar projections are specified between territories rather than in a point-to-point manner (Mihailoff, Burne, Azizi, Norell, & Woodward, 1981).

The mapping of the cerebral cortex on the cerebellar cortex is not fully resolved. Transsynaptic retrograde labeling from various target areas in the posterior cerebellum of the rat revealed that each area receives inputs from widespread albeit different sets of cortical regions. Paravermal and hemispheric portions of lobules VIII (copula), VII (paramedian lobule), and crus II receive convergent inputs from motor and sensory areas of the cortical regions involved respectively in hind-limb, forelimb, and face sensorimotor processing, corresponding broadly to the distribution of peripheral inputs to these lobules; a mediolateral gradient of sensory versus motor cortex inputs was also noted in these lobules (Suzuki, Coulon, Sabel-Goedknecht, & Ruigrok, 2012). The posterior cerebellum also receives peripheral inputs via the mossy fiber system, and electrophysiological mapping demonstrated that they are distributed in patches with substantial redundancy, but little somatotopy (Shambes, Gibson, & Welker, 1978). This segmentation is conditioned by the modular, mediolateral, zonal organization of the cerebellum characterized by zebrin immunoreactivity, but also by a supplementary anteroposterior segmentation (Hallem et al., 1999): the same zebrin band may thus receive peripheral inputs from different body parts in different lobules. Electrophysiological recordings have documented the convergence of peripheral and cerebral inputs: recordings from the granular layer of crus II following various facial sensory stimuli revealed topographically organized, spatially confined, biphasic responses with an early component due to direct trigeminal inputs and a late component relayed by the corresponding facial part of the sensory cortex (Morissette & Bower, 1996). Superior colliculus inputs may also converge with these sensory inputs with a high degree of specificity (Kassel, 1980). Convergence at the level of single Golgi cells (i.e., interneurons of the granular layer) of inputs from the trigeminal nucleus and sensory and motor cortices of the mystacial vibrissae have been observed in the lateral hemisphere of

crus I; a similar sensorimotor convergence for the perioral cortical regions was also found in crus II (Proville et al., 2014). Anatomical reconstruction also revealed that single granule cells may integrate peripheral and pontine inputs (Huang et al., 2013). All these elements argue for a strong convergence of peripheral and cerebral sensorimotor inputs in the cerebellar hemispheres.

Injections of anterograde tracers in the pons occasionally reveal an organization of mossy fiber terminals from the pontine nuclei arrayed in sagittal stripes extending across more than one lobule (Mihailoff, 1993). These stripes are often bilateral and symmetric, with a preference for the side contralateral to the tracer injection site; pairs of small injections may reveal complementary terminal stripes, while wider injection sites produce diffuse labeling as expected if multiple sets of stripes were targeted (Serapide et al., 2001). Stripes are also observed for reticulotegmental projections (Serapide, Parenti, Panto, Zappala, & Cicirata, 2002) and for lateral reticular projections (Wu et al., 1999). Autoradiographic mapping of glucose uptake following stimulation of the vibrissae or the forelimb motor cortices revealed an increased metabolism in a large network encompassing distinct subterritories of the pontine nuclei, different patterns in the cerebellar nuclei, and distinct stripes in the granule layer of the lobules crus I and II and (for the forelimb motor cortex) copula (Sharp & Evans, 1982; Sharp & Ryan, 1984).

One of the best markers of the modular zonation of the cerebellar cortex is provided by the climbing fiber receptive fields and by their anatomical origin (Apps & Hawkes, 2009). Injections of retrograde tracers in defined zones of the copula, paramedian lobule, and crus II showed that the topography of the pontocerebellar projections is not only constrained by the zonal target, but is also distributed according to the lobules, with pontine areas relaying hind-limb, forelimb, and face sensory cortices projecting respectively to the copula, lateral paramedian lobule, and crus II/medial paramedian lobule (Odeh et al., 2005; Pijpers & Ruigrok, 2006). Interestingly, the redundancy of climbing fiber receptive fields is not reflected in the pontocerebellar projections: injections of retrograde tracers in the forelimb C1 zone of distant lobules (simplex and paramedian) reveals overlapping climbing fiber origin in the inferior olive but very limited shared pontine inputs (Herrero et al., 2002). Small injections of retrograde tracers, targeting individual zebrin zones of the copula, provided a finer description of the topography of pontocerebellar projections and demonstrated that pontine afferents to different zebrin zones (either positive or negative) emanate from largely distinct territories and cell populations (Cerminara, Aoki, Loft, Sugihara, & Apps, 2013). Similarly, retrograde injections from the C and D2 zone of the vibrissae-related area of crus I emanate from largely distinct (but intermingled) pontine populations (Proville et al., 2014).



In humans, the topography of cerebrocerebellar functional connectivity has been examined in studies of resting state brain activity; these studies have revealed a multiplicity of cerebrocerebellar patterns of covariance in the blood oxygen-level-dependent (BOLD) signal (Bernard et al., 2012; Buckner, Krienen, Castellanos, Diaz, & Yeo, 2011; Habas et al., 2009; Kipping et al., 2013; Krienen & Buckner, 2009; O'Reilly, Beckmann, Tomassini, Ramnani, & Johansen-Berg, 2010; Sang et al., 2012). The meaning of these patterns is not fully known, but since the BOLD signal is probably dominated by the granular layer signal (Howarth, Peppiatt-Wildman, & Attwell, 2010; discussion in Diedrichsen, Verstynen, Schlerf, & Wiestler, 2010), these patterns probably reveal the topography of the mossy fiber inputs to the cerebellar cortex. They show both segregation and redundancy of cerebrocerebellar connections; moreover the cerebellar areas are coupled to whole cortical circuits, which could result from the convergence of cortical inputs from regions belonging to these defined circuits (sensorimotor, visual, default mode, etc.). Patterns of activations in the cerebellum during behavior also vary as a function of the task (e.g., see Stoodley & Schmahmann, 2009 for a meta-analysis); the comparison between the resting-state and the task-related cerebrocerebellar activation patterns supports that they both reflect preferential cerebrocerebellar connectivity patterns (Balsters, Laird, Fox, & Eickhoff, 2014; Buckner et al., 2011).

Overall, these studies point to a complex and refined topography of the pontocerebellar projections, which exhibit some degree of convergence but are constrained according to the zonal segmentation and the functional segmentation of the granular layer. It shall be noted that the cerebellar nuclei also receive direct projections: anterograde tracing from the pontine nuclei revealed a predominantly (~90%) contralateral projection to the lateral (or dentate) nucleus and to portions of the intermediate nucleus, while the reticulotegmental projections target areas distributed across all cerebellar nuclei with a more bilateral pattern (Mihailoff, 1993; Parenti, Zappala, Serapide, Panto, & Cicirata, 2002). Reconstruction of single pontocerebellar axons in the cat revealed that they systematically gave rise to mossy fibers in the granular layer but only half of them exhibited pontonuclear collaterals (Shinoda, Sugiuchi, Futami, & Izawa, 1992). Such a study has not been replicated in the rat. How these pontonuclear projections converge with Purkinje cell inputs in the cerebellar nuclei remains to be investigated.

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## CLIMBING FIBERS

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The cerebral cortex also exerts some control over the climbing fiber afferents to the cerebellum. However, the organization of the cerebroolivary pathways in the rat is far less characterized compared to the corticopontocerebellar mossy fiber pathway. Experiments conducted in the rat

paramedian lobule and crus II demonstrated that the activation of corticofugal fibers by stimulation in the pyramidal tract triggers, with diverse latencies, climbing fiber discharge throughout the explored hemispheric and paravermal portions of these lobules (Ackerley, Pardoe, & Apps, 2006; Baker, Javid, & Edgley, 2001). Anterograde tracing experiments suggested the existence of broad direct olivary projections from the sensorimotor cortices, with a labeling pattern in the inferior olive subnuclei depending heavily on the cortical region injected (Swenson, Sievert, Terreberry, Neafsey, & Castro, 1989). However, more recent tracing experiments failed to evidence direct afferents from the forelimb and hind-limb motor cortices and forelimb sensory cortex to the inferior olive (Ackerley et al., 2006; Lee & Kim, 2012), but revealed discrete direct projections from the dysgranular zone of the cortex, a region involved in processing deep somatic inputs, to the dorsal inferior olive (Lee & Kim, 2012). An area situated ventral to the dorsal column nuclei was found to relay motor cortex inputs to the inferior olive (Ackerley et al., 2006). This area could indeed correspond to the dorsal column nucleus relay to the C1 and C3 zones formerly identified in the cat (Andersson, 1984). The inferior olive also receives afferents from a number of brain structures, such as the red nucleus, situated around the mesodiencephalic junction (Ruigrok, 2004; Swenson & Castro, 1983), which receives input from the cerebral cortex. The convergence of mesodiencephalic inputs with cerebellar (GABAergic) inputs to single glomeruli has been reported in the rostral medial accessory and posterior olive (respectively innervating the C2 and D zones) of the rat (de Zeeuw, Holstege, Ruigrok, & Voogd, 1990). How ascending sensory inputs and cerebral (direct or indirect) inputs are combined in the inferior olive is unknown. Studies in cats and monkeys support a refined functional organization of the cerebro-olivary pathway (see the review in Voogd, 2014) but the detailed functional organization of the cerebro-olivary pathway in the rat remains still largely unexplored.

## PARALLEL FIBERS

The excitation provided by the mossy fibers to the granule cells is propagated to the Purkinje cells via the parallel fibers and entrains the simple spike firing of these cells. The parallel fibers may extend over the whole transverse axis of the hemispheres and therefore propagate the variety of granule cell inputs to all the Purkinje cells they encounter in the mediolateral axis. The Purkinje cells could be potentially entrained—via the parallel fibers—by all the mossy fiber inputs found in the mediolateral axis of the lobule and, therefore, the topography of the mossy fiber inputs to the granule cells could be totally absent in the overlying Purkinje cell layer.

The examination of sensory simple spike receptive fields of Purkinje cells in the rat hemisphere reveals instead a strong resemblance to the

granule cell layer receptive field underneath (Bower & Woolston, 1983). This has led to the proposal that simple spike responses are entrained by the ascending axon of granule cells (Gundappa-Sulur, De Schutter, & Bower, 1999). *Ex vivo* inspection of connections between single granule cells and Purkinje cells (in the vermis and paravermal areas) confirmed that most parallel fibers do not trigger measurable synaptic currents in the Purkinje cells they contact, but these data do not support the hypothesis of distinct inputs from the ascending axon (Isope & Barbour, 2002). The global mapping of granule cell layer inputs (stimulated by glutamate uncaging in the vermis) to neighboring Purkinje cells also supports a substantial entrainment by the local granule layer via the parallel fiber system but little bias in favor of the ascending axon (Walter, Dizon, & Khodakhah, 2009). In the C3 zone of the decerebrated cat cerebellum, there is a good correspondence only between the receptive fields of mossy fibers and climbing fibers impinging on the overlying Purkinje cells, but these are anticorrelated with—or spatially distant from—the simple spike receptive field (Ekerot & Jorntell, 2001), indicating a dominant contribution of distant granule cells located in a neighboring microzone in the modulation of Purkinje cell firing. The correspondence between mossy fiber and climbing sensory receptive fields is also observed in the rat cerebellum (Brown & Bower, 2001). The mapping of the single vibrissae sensory response in the mouse crus lobules demonstrated that the climbing fiber receptive fields exhibited no systematic relation with the simple spike receptive fields (Bosman et al., 2010), suggesting that the correspondence between mossy and climbing fiber receptive fields is valid only at the regional level. A regional confinement of incoming mossy fiber excitation following white matter stimulation was observed with voltage-sensitive dyes (Cohen & Yarom, 1998; Rokni, Llinas, & Yarom, 2007). Although the studies cited above do not single out the pontine inputs, the available evidence is consistent with the notion that Purkinje cells are primarily driven (as far as the receptive fields approach can reveal) by mossy fibers emanating from a neighboring territory. For pontine inputs, evidence indeed showed that in crus I of mice, the predominance of responses to the stimulation of the vibrissae sensory and motor cortices was observed in the granule and Purkinje cell layers in the lateral but not in the medial part of the lobule (Proville et al., 2014), consistent with the limited spread of pontine mossy fiber excitation to distant Purkinje cells via parallel fibers.

## CEREBELLOCEREBRAL CONNECTIONS

Purkinje cell inhibitory projections from the cerebellar cortex to the nuclei are highly organized following the zonal organization of the cerebellum as reviewed elsewhere (e.g., Ruigrok, 2011); injections of small

amounts of a retrograde tracer in to the cerebellar nuclei indeed label ipsilateral narrow bands of Purkinje cells, consistent with a precise mapping of cerebellar cortical microzones in the nuclei (Ruigrok, 2011; Sugihara et al., 2009). The cerebellum then projects to the cerebral cortex via nucleodiencephalic, primarily contralateral, excitatory projections. All the cerebellar nuclei contribute differentially to these projections, and a small subset of diencephalic structures concentrate most of the cerebellar inputs: ventrolateral and posterior medial thalamic nuclei, intralaminar nuclei (centrolateral, centromedial, parafascicular), zona incerta, ventromedial nuclei (Angaut, Cicirata, & Serapide, 1985; Aumann, Rawson, Finkelstein, & Horne, 1994; Teune, van der Burg, van der Moer, Voogd, & Ruigrok, 2000). The cerebellar inputs are never very abundant: even in the ventrolateral thalamus, which receives strong cerebellar projections, cerebellar synapses are estimated to represent less than 10% of the synapses, the others coming principally from the cerebral cortex and the reticular thalamus (Aumann & Horne, 1999; Sawyer, Tepper, & Groves, 1994). However, these inputs are rather powerful: cerebellar stimulations produce, in the ventrolateral thalamocortical neurons, relatively large excitatory synaptic potentials (several millivolts) with little gradation of the responses, suggesting that they emanate from few axons (Sawyer, Young, Groves, & Tepper, 1994). Cerebellar terminals exhibit a similar ultrastructural appearance (large boutons, packed with synaptic vesicles and mitochondria, with perforated synaptic densities) in all diencephalic structures examined so far (Aumann & Horne, 1996; Aumann et al., 1994), suggesting that they share the same functional properties.

Overall, the main diencephalic structures recipient of cerebellar inputs project primarily to the frontal cortex, dorsal striatum, and sensory cortex. Interestingly, while the cerebellum is, as the basal ganglia, a major afferent of the frontal cortex, the cerebellar and basal ganglia channels remain remarkably segregated in the ventrolateral thalamus (Deniau, Kita, & Kitai, 1992; Kuramoto et al., 2011). The ventrolateral thalamus projects to multiple layers in the cortex (II–V), with a dense innervation to layer VB where it excites pyramidal tract neurons (Kuramoto et al., 2009), therefore allowing the cerebro-ponto-cerebello-thalamo-cerebral loops to close.

The hierarchical structure of the cerebrostriatal and cerebrocerebellar circuit (see above) is not entirely respected: the cerebellum provides excitatory inputs to the striatum via the centrolateral (Chen, Fremont, Arteaga-Bracho, & Khodakhah, 2014) and possibly the parafascicular nuclei, which receive a cerebellar innervation from the lateral and medial nuclei. Moreover the ventromedial thalamus, which provides extensive projections to cortical layer I, might exhibit convergent inputs from the basal ganglia and cerebellum, although in contrast to the cat (Steriade, 1995), these afferents seem to be weak in the rat (Aumann et al., 1994; Deniau et al., 1992; Kuramoto et al., 2011). The zona incerta could also be an area of convergence with the basal ganglia

inputs, and a relay toward layer I of the cortex (Lin, Nicolelis, & Chapin, 1997), but very few data are available on these connections.

Single-axon tracing from the ventrolateral thalamus revealed wider projection patterns than found in sensory thalamocortical projections: each axon targets multiple motor and sensory cortical regions (Aumann, Ivanusic, & Horne, 1998; Kuramoto et al., 2009), suggestive of a broad divergence of this pathway. Similarly, single posterior thalamic neurons target multiple cortical regions (Ohno et al., 2012), consistent with a role of the cerebellum in the coordination of neuronal activity between distant cortical sites (Popa et al., 2013).

## FUNCTIONAL MAPPING OF THE CEREBELLOCEREBRAL CONNECTIONS

So far, there has been still little functional mapping of the cerebellar cortex onto the cerebral cortex. In the cat, microstimulations in the cerebellar nuclei at sites receiving from a distinct cerebellar microzone revealed wide but distinct patterns of activation in the motor cortex (Jorntell & Ekerot, 1999). In the monkey, transsynaptic retrograde tracing from cortical regions tend to label broad cerebellar territories (Kelly & Strick, 2003; Lu, Miyachi, Ito, Nambu, & Takada, 2007; Prevosto, Graf, & Ugolini, 2010), and functionally distinct cortical regions receive inputs from overlapping cerebellar territories (Lu et al., 2007). Testing the specificity of the connections requires functional approaches. The functional mapping of cerebellar projections to the cerebral cortex is complicated by the inhibitory nature of the projections from the cerebellar cortex. In mice, the functional input from crus I to the motor cortex has been investigated using the rebound activity taking place in the cerebellocerebral network following Purkinje cell optogenetic stimulation (Proville et al., 2014); stimulation of the Purkinje cells in the area receiving dense inputs from the vibrissae motor cortex, the lateral crus I, but not of the adjacent cerebellar areas triggered an activation of the vibrissae motor cortex; this demonstrates the existence of specific corticocerebrocortical loops, as suggested by transsynaptic viral tracing (Kelly & Strick, 2003).

Functional synchronization of population activity between the cerebral cortex and the cerebellar cortex and nuclei has indeed been reported in unanesthetized animals (O'Connor, Berg, & Kleinfeld, 2002; Ros, Sachdev, Yu, Sestan, & McCormick, 2009), but they exhibit a rather loose temporal relationship (100 ms time scale). Coherent activities are also found in anesthetized animals and directed transfer function analysis points rather toward an entrainment of the cerebellar circuit by the cerebral cortex than the reverse (Rowland, Goldberg, & Jaeger, 2010), but this might be due to the disruption of the mossy fiber excitation by anesthesia (Bengtsson & Jorntell,

2007), which would thus prevent cerebellar computations from being generated before being fed back to the cortex. Indeed, in the unanesthetized condition, the optogenetic interruption of the cerebrocerebellar loop resulted in a change in the whisking behavior, an effect that required an intact motor thalamus (Proville et al., 2014). Moreover, the selective disruption of a single parameter of whisking in this study suggests that, despite the apparent divergence of the cerebellocerebral pathways (see above), there is a rather sharp functional selectivity in the target of these pathways.

## CONCLUSION

One of the striking features of the cerebellocerebral connections is their asymmetry: most of the cortex projects to the cerebellum, but fewer cortical regions concentrate most of the inputs from the cerebellum. The studies of the sensorimotor system indicate that some of this reduction takes place in the cerebellar cortex where sensory and motor cortical inputs, together with peripheral and tectal inputs, may converge. However, the cerebellar cortex seems to primarily combine inputs of various origins but linked to the same body part. The ascending cerebellocerebral pathway is certainly less characterized and might seem to be more divergent. Indeed, the wide divergence of single thalamic cells relaying cerebellar inputs to the sensorimotor cortex contrasts with the functional evidence of selective cerebrocerebellar loops and with the discrete, specific, behavioral effects observed by the targeted disruption of these loops. Therefore the topographic divergence of the cerebellocerebral connections might rather reflect the topographically-distributed nature of sensorimotor representations in the cortex than a lack of specificity of cerebrocerebellar loops. In rodents, most of the principles of the functional organization of the cerebrocerebellar circuitry have been (and probably will continue to be) derived in the sensorimotor system. A major task now is to understand the computations performed in this circuit. Finally, a significant portion of the cerebrocerebellar loops in humans might be involved in higher-order, associative or cognitive functions (Buckner, 2013); finding and studying such loops in the rodent brain is certainly also an important challenge for the coming years.

## References

- Ackerley, R., Pardoe, J., & Apps, R. (2006). A novel site of synaptic relay for climbing fibre pathways relaying signals from the motor cortex to the cerebellar cortical C1 zone. *The Journal of Physiology*, 576(Pt 2), 503–518.
- Akintunde, A., & Buxton, D. F. (1992). Origins and collateralization of corticospinal, corticopontine, corticorubral and corticostriatal tracts: a multiple retrograde fluorescent tracing study. *Brain Research*, 586(2), 208–218.

- Allen, G. V., & Hopkins, D. A. (1998). Convergent prefrontal cortex and mamillary body projections to the medial pontine nuclei: a light and electron microscopic study in the rat. *Journal of Comparative Neurology*, 398(3), 347–358.
- Allen, G. I., & Tsukahara, N. (1974). Cerebrocerebellar communication systems. *Physiological Reviews*, 54(4), 957–1006.
- Andersson, G. (1984). Demonstration of a cuneate relay in a cortico-olivo-cerebellar pathway in the cat. *Neuroscience Letters*, 46(1), 47–52.
- Angaut, P., Cicirata, F., & Serapide, F. (1985). Topographic organization of the cerebellothalamic projections in the rat. An autoradiographic study. *Neuroscience*, 15(2), 389–401.
- Apps, R., & Hawkes, R. (2009). Cerebellar cortical organization: a one-map hypothesis. *Nature Reviews Neuroscience*, 10(9), 670–681.
- Aumann, T. D., & Horne, M. K. (1996). A comparison of the ultrastructure of synapses in the cerebello-rubral and cerebello-thalamic pathways in the rat. *Neuroscience Letters*, 211(3), 175–178.
- Aumann, T. D., & Horne, M. K. (1999). Ultrastructural change at rat cerebellothalamic synapses associated with volitional motor adaptation. *Journal of Comparative Neurology*, 409(1), 71–84.
- Aumann, T. D., Ivanusic, J., & Horne, M. K. (1998). Arborisation and termination of single motor thalamocortical axons in the rat. *Journal of Comparative Neurology*, 396(1), 121–130.
- Aumann, T. D., Rawson, J. A., Finkelstein, D. I., & Horne, M. K. (1994). Projections from the lateral and interposed cerebellar nuclei to the thalamus of the rat: a light and electron microscopic study using single and double anterograde labelling. *Journal of Comparative Neurology*, 349(2), 165–181.
- Baker, M. R., Javid, M., & Edgley, S. A. (2001). Activation of cerebellar climbing fibres to rat cerebellar posterior lobe from motor cortical output pathways. *The Journal of Physiology*, 536(Pt 3), 825–839.
- Balsters, J. H., Laird, A. R., Fox, P. T., & Eickhoff, S. B. (2014). Bridging the gap between functional and anatomical features of cortico-cerebellar circuits using meta-analytic connectivity modeling. *Human Brain Mapping*, 35(7), 3152–3169.
- Bengtsson, F., & Jorntell, H. (2007). Ketamine and xylazine depress sensory-evoked parallel fiber and climbing fiber responses. *Journal of Neurophysiology*, 98(3), 1697–1705.
- Bernard, J. A., Seidler, R. D., Hassevoort, K. M., Benson, B. L., Welsh, R. C., Wiggins, J. L., et al. (2012). Resting state cortico-cerebellar functional connectivity networks: a comparison of anatomical and self-organizing map approaches. *Frontiers in Neuroanatomy*, 6, 31.
- Bosman, L. W., Koekkoek, S. K., Shapiro, J., Rijken, B. F., Zandstra, F., van der Ende, B., et al. (2010). Encoding of whisker input by cerebellar Purkinje cells. *The Journal of Physiology*, 588(Pt 19), 3757–3783.
- Bostan, A. C., Dum, R. P., & Strick, P. L. (2010). The basal ganglia communicate with the cerebellum. *Proceedings of the National Academy of Sciences of the United States of America*, 107(18), 8452–8456.
- Bower, J. M., & Woolston, D. C. (1983). Congruence of spatial organization of tactile projections to granule cell and Purkinje cell layers of cerebellar hemispheres of the albino rat: vertical organization of cerebellar cortex. *Journal of Neurophysiology*, 49(3), 745–766.
- Brown, I. E., & Bower, J. M. (2001). Congruence of mossy fiber and climbing fiber tactile projections in the lateral hemispheres of the rat cerebellum. *Journal of Comparative Neurology*, 429(1), 59–70.
- Buckner, R. L. (2013). The cerebellum and cognitive function: 25 years of insight from anatomy and neuroimaging. *Neuron*, 80(3), 807–815.
- Buckner, R. L., Krienen, F. M., Castellanos, A., Diaz, J. C., & Yeo, B. T. (2011). The organization of the human cerebellum estimated by intrinsic functional connectivity. *Journal of Neurophysiology*, 106(5), 2322–2345.
- Cerminara, N. L., Aoki, H., Loft, M., Sugihara, I., & Apps, R. (2013). Structural basis of cerebellar microcircuits in the rat. *Journal of Neuroscience*, 33(42), 16427–16442.

- Chen, C. H., Fremont, R., Arteaga-Bracho, E. E., & Khodakhah, K. (2014). Short latency cerebellar modulation of the basal ganglia. *Nature Neuroscience*, 17(12), 1767–1775.
- Cohen, D., & Yarom, Y. (1998). Patches of synchronized activity in the cerebellar cortex evoked by mossy-fiber stimulation: questioning the role of parallel fibers. *Proceedings of the National Academy of Sciences of the United States of America*, 95(25), 15032–15036.
- Deniau, J. M., Kita, H., & Kitai, S. T. (1992). Patterns of termination of cerebellar and basal ganglia efferents in the rat thalamus. Strictly segregated and partly overlapping projections. *Neuroscience Letters*, 144(1–2), 202–206.
- Diedrichsen, J., Verstynen, T., Schlerf, J., & Wiestler, T. (2010). Advances in functional imaging of the human cerebellum. *Current Opinion Neurology*, 23(4), 382–387.
- Donoghue, J. P., & Kitai, S. T. (1981). A collateral pathway to the neostriatum from corticofugal neurons of the rat sensory-motor cortex: an intracellular HRP study. *Journal of Comparative Neurology*, 201(1), 1–13.
- Eisenman, L. M. (1981). Pontocerebellar projections to the pyramis and copula pyramidis in the rat: evidence for a mediolateral topography. *Journal of Comparative Neurology*, 199(1), 77–86.
- Eisenman, L. M., & Noback, C. R. (1980). The ponto-cerebellar projection in the rat: differential projections to sublobules of the uvula. *Experimental Brain Research*, 38(1), 11–17.
- Ekerot, C. F., & Jorntell, H. (2001). Parallel fibre receptive fields of Purkinje cells and interneurons are climbing fibre-specific. *European Journal of Neuroscience*, 13(7), 1303–1310.
- Gundappa-Sulur, G., De Schutter, E., & Bower, J. M. (1999). Ascending granule cell axon: an important component of cerebellar cortical circuitry. *Journal of Comparative Neurology*, 408(4), 580–596.
- Habas, C., Kamdar, N., Nguyen, D., Prater, K., Beckmann, C. F., Menon, V., et al. (2009). Distinct cerebellar contributions to intrinsic connectivity networks. *Journal of Neuroscience*, 29(26), 8586–8594.
- Hallam, J. S., Thompson, J. H., Gundappa-Sulur, G., Hawkes, R., Bjaalie, J. G., & Bower, J. M. (1999). Spatial correspondence between tactile projection patterns and the distribution of the antigenic Purkinje cell markers anti-zebrin I and anti-zebrin II in the cerebellar folium crus IIA of the rat. *Neuroscience*, 93(3), 1083–1094.
- Herculano-Houzel, S. (2010). Coordinated scaling of cortical and cerebellar numbers of neurons. *Frontiers in Neuroanatomy*, 4, 12.
- Herrero, L., Pardoe, J., & Apps, R. (2002). Pontine and lateral reticular projections to the cl zone in lobulus simplex and paramedian lobule of the rat cerebellar cortex. *Cerebellum*, 1(3), 185–199.
- Hoffer, Z. S., Arantes, H. B., Roth, R. L., & Alloway, K. D. (2005). Functional circuits mediating sensorimotor integration: quantitative comparisons of projections from rodent barrel cortex to primary motor cortex, neostriatum, superior colliculus, and the pons. *Journal of Comparative Neurology*, 488(1), 82–100.
- Howarth, C., Peppiatt-Wildman, C. M., Attwell, D. (2010). The energy use associated with neural computation in the cerebellum. *Journal of Cerebral Blood Flow Metabolism*, 30(2), 403–414.
- Huang, C. C., Sugino, K., Shima, Y., Guo, C., Bai, S., Mensh, B. D., et al. (2013). Convergence of pontine and proprioceptive streams onto multimodal cerebellar granule cells. *Elife*, 2, e00400.
- Isope, P., & Barbour, B. (2002). Properties of unitary granule cell→Purkinje cell synapses in adult rat cerebellar slices. *Journal of Neuroscience*, 22(22), 9668–9678.
- Ito, M. (2008). Control of mental activities by internal models in the cerebellum. *Nature Reviews Neuroscience*, 9(4), 304–313.
- Jorntell, H., & Ekerot, C. F. (1999). Topographical organization of projections to cat motor cortex from nucleus interpositus anterior and forelimb skin. *The Journal of Physiology*, 514(Pt 2), 551–566.
- Kassel, J. (1980). Superior colliculus projections to tactile areas of rat cerebellar hemispheres. *Brain Research*, 202(2), 291–305.



- Kelly, R. M., & Strick, P. L. (2003). Cerebellar loops with motor cortex and prefrontal cortex of a nonhuman primate. *Journal of Neuroscience*, 23(23), 8432–8444.
- Kipping, J. A., Grodd, W., Kumar, V., Taubert, M., Villringer, A., & Margulies, D. S. (2013). Overlapping and parallel cerebello-cerebral networks contributing to sensorimotor control: an intrinsic functional connectivity study. *Neuroimage*, 83, 837–848.
- Kiritani, T., Wickersham, I. R., Seung, H. S., & Shepherd, G. M. (2012). Hierarchical connectivity and connection-specific dynamics in the corticospinal-corticostriatal microcircuit in mouse motor cortex. *Journal of Neuroscience*, 32(14), 4992–5001.
- Kosinski, R. J., Azizi, S. A., & Mihailoff, G. A. (1988). Convergence of cortico- and cuneopontine projections onto components of the pontocerebellar system in the rat: an anatomical and electrophysiological study. *Experimental Brain Res*, 71(3), 541–556.
- Kosinski, R. J., Neafsey, E. J., & Castro, A. J. (1986). A comparative topographical analysis of dorsal column nuclear and cerebral cortical projections to the basilar pontine gray in rats. *Journal of Comparative Neurology*, 244(2), 163–173.
- Krienen, F. M., & Buckner, R. L. (2009). Segregated fronto-cerebellar circuits revealed by intrinsic functional connectivity. *Cerebral Cortex*, 19(10), 2485–2497.
- Kuramoto, E., Fujiyama, F., Nakamura, K. C., Tanaka, Y., Hioki, H., & Kaneko, T. (2011). Complementary distribution of glutamatergic cerebellar and GABAergic basal ganglia afferents to the rat motor thalamic nuclei. *European Journal of Neuroscience*, 33(1), 95–109.
- Kuramoto, E., Furuta, T., Nakamura, K. C., Unzai, T., Hioki, H., & Kaneko, T. (2009). Two types of thalamocortical projections from the motor thalamic nuclei of the rat: a single neuron-tracing study using viral vectors. *Cerebral Cortex*, 19(9), 2065–2077.
- Lee, H. S., & Mihailoff, G. A. (1990). Convergence of cortical and cerebellar projections on single basilar pontine neurons: a light and electron microscopic study in the rat. *Neuroscience*, 39(3), 561–577.
- Lee, T., & Kim, U. (2012). Descending projections from the dysgranular zone of rat primary somatosensory cortex processing deep somatic input. *Journal of Comparative Neurology*, 520(5), 1021–1046.
- Leergaard, T. B., Alloway, K. D., Mutic, J. J., & Bjaalie, J. G. (2000). Three-dimensional topography of corticopontine projections from rat barrel cortex: correlations with corticostriatal organization. *Journal of Neuroscience*, 20(22), 8474–8484.
- Leergaard, T. B., Alloway, K. D., Pham, T. A., Bolstad, I., Hoffer, Z. S., Pettersen, C., et al. (2004). Three-dimensional topography of corticopontine projections from rat sensorimotor cortex: comparisons with corticostriatal projections reveal diverse integrative organization. *Journal of Comparative Neurology*, 478(3), 306–322.
- Leergaard, T. B., & Bjaalie, J. G. (2007). Topography of the complete corticopontine projection: from experiments to principal Maps. *Frontiers in Neuroscience*, 1(1), 211–223.
- Leergaard, T. B., Lillehaug, S., De Schutter, E., Bower, J. M., & Bjaalie, J. G. (2006). Topographical organization of pathways from somatosensory cortex through the pontine nuclei to tactile regions of the rat cerebellar hemispheres. *European Journal of Neuroscience*, 24(10), 2801–2812.
- Legg, C. R., Mercier, B., & Glickstein, M. (1989). Corticopontine projection in the rat: the distribution of labelled cortical cells after large injections of horseradish peroxidase in the pontine nuclei. *Journal of Comparative Neurology*, 286(4), 427–441.
- Levesque, M., Charara, A., Gagnon, S., Parent, A., & Deschenes, M. (1996). Corticostriatal projections from layer V cells in rat are collaterals of long-range corticofugal axons. *Brain Research*, 709(2), 311–315.
- Lin, R. C., Nicolelis, M. A., & Chapin, J. K. (1997). Topographic and laminar organizations of the intercortical pathway in rats. *Neuroscience*, 81(3), 641–651.
- Lu, X., Miyachi, S., Ito, Y., Nambu, A., & Takada, M. (2007). Topographic distribution of output neurons in cerebellar nuclei and cortex to somatotopic map of primary motor cortex. *European Journal of Neuroscience*, 25(8), 2374–2382.
- Mercier, B. E., Legg, C. R., & Glickstein, M. (1990). Basal ganglia and cerebellum receive different somatosensory information in rats. *Proceedings of the National Academy of Sciences of the United States of America*, 87(11), 4388–4392.

- Mihailoff, G. A. (1983). Intra- and interhemispheric collateral branching in the rat pontocerebellar system, a fluorescence double-label study. *Neuroscience*, 10(1), 141–160.
- Mihailoff, G. A. (1993). Cerebellar nuclear projections from the basilar pontine nuclei and nucleus reticularis tegmenti pontis as demonstrated with PHA-L tracing in the rat. *Journal of Comparative Neurology*, 330(1), 130–146.
- Mihailoff, G. A., Burne, R. A., Azizi, S. A., Norell, G., & Woodward, D. J. (1981). The pontocerebellar system in the rat: an HRP study. II. Hemispherical components. *Journal of Comparative Neurology*, 197(4), 559–577.
- Mihailoff, G. A., Kosinski, R. J., Azizi, S. A., & Border, B. G. (1989). Survey of noncortical afferent projections to the basilar pontine nuclei: a retrograde tracing study in the rat. *Journal of Comparative Neurology*, 282(4), 617–643.
- Mihailoff, G. A., Lee, H., Watt, C. B., & Yates, R. (1985). Projections to the basilar pontine nuclei from face sensory and motor regions of the cerebral cortex in the rat. *Journal of Comparative Neurology*, 237(2), 251–263.
- Mock, M., Butovas, S., & Schwarz, C. (2006). Functional unity of the ponto-cerebellum: evidence that intrapontine communication is mediated by a reciprocal loop with the cerebellar nuclei. *Journal of Neurophysiology*, 95(6), 3414–3425.
- Morishima, M., & Kawaguchi, Y. (2006). Recurrent connection patterns of corticostriatal pyramidal cells in frontal cortex. *Journal of Neuroscience*, 26(16), 4394–4405.
- Morishima, M., Morita, K., Kubota, Y., & Kawaguchi, Y. (2011). Highly differentiated projection-specific cortical subnetworks. *Journal of Neuroscience*, 31(28), 10380–10391.
- Morissette, J., & Bower, J. M. (1996). Contribution of somatosensory cortex to responses in the rat cerebellar granule cell layer following peripheral tactile stimulation. *Experimental Brain Research*, 109(2), 240–250.
- Moya, M. V., Siegel, J. J., McCord, E. D., Kalmbach, B. E., Dembrow, N., Johnston, D., et al. (2014). Species-specific differences in the medial prefrontal projections to the pons between rat and rabbit. *Journal of Comparative Neurology*, 522(13), 3052–3074.
- Nishiike, S., Guldin, W. O., & Baurle, J. (2000). Corticofugal connections between the cerebral cortex and the vestibular nuclei in the rat. *Journal of Comparative Neurology*, 420(3), 363–372.
- O'Connor, S. M., Berg, R. W., & Kleinfeld, D. (2002). Coherent electrical activity between vibrissa sensory areas of cerebellum and neocortex is enhanced during free whisking. *Journal of Neurophysiology*, 87(4), 2137–2148.
- Odeh, F., Ackerley, R., Bjaalie, J. G., & Apps, R. (2005). Pontine maps linking somatosensory and cerebellar cortices are in register with climbing fiber somatotopy. *Journal of Neuroscience*, 25(24), 5680–5690.
- Ohno, S., Kuramoto, E., Furuta, T., Hioki, H., Tanaka, Y. R., Fujiyama, F., et al. (2012). A morphological analysis of thalamocortical axon fibers of rat posterior thalamic nuclei: a single neuron tracing study with viral vectors. *Cerebral Cortex*, 22(12), 2840–2857.
- O'Reilly, J. X., Beckmann, C. F., Tomassini, V., Ramnani, N., & Johansen-Berg, H. (2010). Distinct and overlapping functional zones in the cerebellum defined by resting state functional connectivity. *Cerebral Cortex*, 20(4), 953–965.
- Panto, M. R., Cicirata, F., Angaut, P., Parenti, R., & Serapide, F. (1995). The projection from the primary motor and somatic sensory cortex to the basilar pontine nuclei. A detailed electrophysiological and anatomical study in the rat. *Journal für Hirnforschung*, 36(1), 7–19.
- Parenti, R., Zappala, A., Serapide, M. F., Panto, M. R., & Cicirata, F. (2002). Projections of the basilar pontine nuclei and nucleus reticularis tegmenti pontis to the cerebellar nuclei of the rat. *Journal of Comparative Neurology*, 452(2), 115–127.
- Pijpers, A., & Ruigrok, T. J. (2006). Organization of pontocerebellar projections to identified climbing fiber zones in the rat. *Journal of Comparative Neurology*, 496(4), 513–528.
- Popa, D., Spolidoro, M., Proville, R. D., Guyon, N., Belliveau, L., & Lena, C. (2013). Functional role of the cerebellum in gamma-band synchronization of the sensory and motor cortices. *Journal of Neuroscience*, 33(15), 6552–6556.

- Potter, R. F., Ruegg, D. G., & Wiesendanger, M. (1978). Responses of neurones of the pontine nuclei to stimulation of the sensorimotor, visual and auditory cortex of rats. *Brain Research Bulletin*, 3(1), 15–19.
- Prevosto, V., Graf, W., & Ugolini, G. (2010). Cerebellar inputs to intraparietal cortex areas LIP and MIP: functional frameworks for adaptive control of eye movements, reaching, and arm/eye/head movement coordination. *Cerebral Cortex*, 20(1), 214–228.
- Proville, R. D., Spolidoro, M., Guyon, N., Dugue, G. P., Selimi, F., Isope, P., et al. (2014). Cerebellum involvement in cortical sensorimotor circuits for the control of voluntary movements. *Nature Neuroscience*, 17(9), 1233–1239.
- Rajakumar, N., Hryciyshyn, A. W., & Flumerfelt, B. A. (1992). Afferent organization of the lateral reticular nucleus in the rat: an anterograde tracing study. *Anatomy and Embryology (Berlin)*, 185(1), 25–37.
- Ricardo, J. A. (1981). Efferent connections of the subthalamic region in the rat. II. The zona incerta. *Brain Research*, 214(1), 43–60.
- Rokni, D., Llinas, R., & Yarom, Y. (2007). Stars and stripes in the cerebellar cortex: a voltage sensitive dye study. *Frontiers in Systems Neuroscience*, 1, 1.
- Ros, H., Sachdev, R. N., Yu, Y., Sestan, N., & McCormick, D. A. (2009). Neocortical networks entrain neuronal circuits in cerebellar cortex. *Journal of Neuroscience*, 29(33), 10309–10320.
- Rowland, N. C., Goldberg, J. A., & Jaeger, D. (2010). Cortico-cerebellar coherence and causal connectivity during slow-wave activity. *Neuroscience*, 166(2), 698–711.
- Ruigrok, T. J. (2003). Collateralization of climbing and mossy fibers projecting to the nodulus and flocculus of the rat cerebellum. *Journal of Comparative Neurology*, 466(2), 278–298.
- Ruigrok, T. J. (2004). Precerebellar nuclei and red nucleus. In G. Paxinos (Ed.), *The rat nervous system* (3rd ed.) (pp. 167–204). San Diego: Elsevier/Academic Press.
- Ruigrok, T. J. (2011). Ins and outs of cerebellar modules. *Cerebellum*, 10(3), 464–474.
- Sang, L., Qin, W., Liu, Y., Han, W., Zhang, Y., Jiang, T., et al. (2012). Resting-state functional connectivity of the vermal and hemispheric subregions of the cerebellum with both the cerebral cortical networks and subcortical structures. *Neuroimage*, 61(4), 1213–1225.
- Sawyer, S. F., Tepper, J. M., & Groves, P. M. (1994). Cerebellar-responsive neurons in the thalamic ventroanterior-ventrolateral complex of rats: light and electron microscopy. *Neuroscience*, 63(3), 725–745.
- Sawyer, S. F., Young, S. J., Groves, P. M., & Tepper, J. M. (1994). Cerebellar-responsive neurons in the thalamic ventroanterior-ventrolateral complex of rats: in vivo electrophysiology. *Neuroscience*, 63(3), 711–724.
- Schwarz, C., Horowski, A., Mock, M., & Thier, P. (2005). Organization of tectopontine terminals within the pontine nuclei of the rat and their spatial relationship to terminals from the visual and somatosensory cortex. *Journal of Comparative Neurology*, 484(3), 283–298.
- Schwarz, C., & Mock, M. (2001). Spatial arrangement of cerebro-pontine terminals. *Journal of Comparative Neurology*, 435(4), 418–432.
- Schwarz, C., & Thier, P. (1995). Modular organization of the pontine nuclei: dendritic fields of identified pontine projection neurons in the rat respect the borders of cortical afferent fields. *Journal of Neuroscience*, 15(5 Pt 1), 3475–3489.
- Serapide, M. F., Panto, M. R., Parenti, R., Zappala, A., & Cicirata, F. (2001). Multiple zonal projections of the basilar pontine nuclei to the cerebellar cortex of the rat. *Journal of Comparative Neurology*, 430(4), 471–484.
- Serapide, M. F., Parenti, R., Panto, M. R., Zappala, A., & Cicirata, F. (2002). Multiple zonal projections of the nucleus reticularis tegmenti pontis to the cerebellar cortex of the rat. *European Journal of Neuroscience*, 15(11), 1854–1858.
- Serapide, M. F., Zappala, A., Parenti, R., Panto, M. R., & Cicirata, F. (2002). Laterality of the pontocerebellar projections in the rat. *European Journal of Neuroscience*, 15(9), 1551–1556.

- Shambes, G. M., Gibson, J. M., & Welker, W. (1978). Fractured somatotopy in granule cell tactile areas of rat cerebellar hemispheres revealed by micromapping. *Brain, Behavior, and Evolution*, 15(2), 94–140.
- Sharp, F. R., & Evans, K. (1982). Regional ( $^{14}\text{C}$ ) 2-deoxyglucose uptake during vibrissae movements evoked by rat motor cortex stimulation. *Journal of Comparative Neurology*, 208(3), 255–287.
- Sharp, F. R., & Ryan, A. F. (1984). Regional ( $^{14}\text{C}$ ) 2-deoxyglucose uptake during forelimb movements evoked by rat motor cortex stimulation: pons, cerebellum, medulla, spinal cord, muscle. *Journal of Comparative Neurology*, 224(2), 286–306.
- Shinoda, Y., Sugiuchi, Y., Futami, T., & Izawa, R. (1992). Axon collaterals of mossy fibers from the pontine nucleus in the cerebellar dentate nucleus. *Journal of Neurophysiology*, 67(3), 547–560.
- Shokunbi, M. T., Hryciyshyn, A. W., & Flumerfelt, B. A. (1986). A horseradish peroxidase study of the rubral and cortical afferents to the lateral reticular nucleus in the rat. *Journal of Comparative Neurology*, 248(3), 441–454.
- Smith, Y., Wichmann, T., & DeLong, M. R. (2014). Corticostriatal and mesocortical dopamine systems: do species differences matter? *Nature Reviews Neuroscience*, 15(1), 63.
- Steriade, M. (1995). Two channels in the cerebello-thalamo-cortical system. *Journal of Comparative Neurology*, 354(1), 57–70.
- Stoodley, C. J., & Schmahmann, J. D. (2009). Functional topography in the human cerebellum: a meta-analysis of neuroimaging studies. *Neuroimage*, 44(2), 489–501.
- Sugihara, I., Fujita, H., Na, J., Quy, P. N., Li, B. Y., & Ikeda, D. (2009). Projection of reconstructed single Purkinje cell axons in relation to the cortical and nuclear aldolase C compartments of the rat cerebellum. *Journal of Comparative Neurology*, 512(2), 282–304.
- Suzuki, L., Coulon, P., Sabel-Goedknecht, E. H., & Ruigrok, T. J. (2012). Organization of cerebral projections to identified cerebellar zones in the posterior cerebellum of the rat. *Journal of Neuroscience*, 32(32), 10854–10869.
- Swenson, R. S., & Castro, A. J. (1983). The afferent connections of the inferior olivary complex in rats. An anterograde study using autoradiographic and axonal degeneration techniques. *Neuroscience*, 8(2), 259–275.
- Swenson, R. S., Sievert, C. F., Terreberry, R. R., Neafsey, E. J., & Castro, A. J. (1989). Organization of cerebral cortico-olivary projections in the rat. *Neuroscience Research*, 7(1), 43–54.
- Teune, T. M., van der Burg, J., van der Moer, J., Voogd, J., & Ruigrok, T. J. (2000). Topography of cerebellar nuclear projections to the brain stem in the rat. *Progress in Brain Research*, 124, 141–172.
- Torigoe, Y., Blanks, R. H., & Precht, W. (1986a). Anatomical studies on the nucleus reticularis tegmenti pontis in the pigmented rat. I. Cytoarchitecture, topography, and cerebral cortical afferents. *Journal of Comparative Neurology*, 243(1), 71–87.
- Torigoe, Y., Blanks, R. H., & Precht, W. (1986b). Anatomical studies on the nucleus reticularis tegmenti pontis in the pigmented rat. II. Subcortical afferents demonstrated by the retrograde transport of horseradish peroxidase. *Journal of Comparative Neurology*, 243(1), 88–105.
- Voogd, J. (2014). What we do not know about cerebellar systems neuroscience. *Frontiers in Systems Neuroscience*, 8, 227.
- Walter, J. T., Dizon, M. J., & Khodakhah, K. (2009). The functional equivalence of ascending and parallel fiber inputs in cerebellar computation. *Journal of Neuroscience*, 29(26), 8462–8473.
- Watt, C. B., & Mihailoff, G. A. (1983). The cerebellopontine system in the rat. I. Autoradiographic studies. *Journal of Comparative Neurology*, 215(3), 312–330.
- West, M. J., & Gundersen, H. J. (1990). Unbiased stereological estimation of the number of neurons in the human hippocampus. *Journal of Comparative Neurology*, 296(1), 1–22.
- West, M. J., Slomianka, L., & Gundersen, H. J. (1991). Unbiased stereological estimation of the total number of neurons in the subdivisions of the rat hippocampus using the optical fractionator. *Anatomical Record*, 231(4), 482–497.

- Wiesendanger, R., & Wiesendanger, M. (1982a). The corticopontine system in the rat. I. Mapping of corticopontine neurons. *Journal of Comparative Neurology*, 208(3), 215–226.
- Wiesendanger, R., & Wiesendanger, M. (1982b). The corticopontine system in the rat. II. The projection pattern. *Journal of Comparative Neurology*, 208(3), 227–238.
- Wolpert, D. M., Miall, R. C., & Kawato, M. (1998). Internal models in the cerebellum. *Trends in Cognitive Science*, 2(9), 338–347.
- Wu, H. S., Sugihara, I., & Shinoda, Y. (1999). Projection patterns of single mossy fibers originating from the lateral reticular nucleus in the rat cerebellar cortex and nuclei. *Journal of Comparative Neurology*, 411(1), 97–118.
- de Zeeuw, C. I., Holstege, J. C., Ruigrok, T. J., & Voogd, J. (1990). Mesodiencephalic and cerebellar terminals terminate upon the same dendritic spines in the glomeruli of the cat and rat inferior olive: an ultrastructural study using a combination of [<sup>3</sup>H]leucine and wheat germ agglutinin coupled horseradish peroxidase anterograde tracing. *Neuroscience*, 34(3), 645–655.