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Consensus Paper: The Cerebellum's Role in Movement and Cognition

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Abstract

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While the cerebellum's role in motor function is well recognized, the nature of its concurrent role in cognitive function remains considerably less clear. The current consensus paper gathers diverse views on a variety of important roles played by the cerebellum across a range of cognitive and emotional functions. This paper considers the cerebellum in relation to neurocognitive development, language function, working memory, executive function, and the development of cerebellar internal control models and reflects upon some of the ways in which better understanding the cerebellum's status as a “supervised learning machine” can enrich our ability to understand human function and adaptation. As all contributors agree that the cerebellum plays a role in cognition, there is also an agreement that this conclusion remains highly inferential. Many conclusions about the role of the cerebellum in cognition originate from applying known information about cerebellar contributions to the coordination and quality of movement. These inferences are based on the uniformity of the cerebellum's compositional infrastructure and its apparent modular organization. There is considerable support for this view, based upon observations of patients with pathology within the cerebellum.

Keywords

Cerebellum; Cognitive; Neurodevelopment; Cognition; Movement; Motor; Language; Executive Function

Introduction

Historically, the cerebellum's role in cognition has been a matter of debate. Most people in the fields of neurology and mental health in particular have been taught that the cerebellum functions primarily as a co-processor of movement in concert with the cortex and basal ganglia. Until fairly recently, it had been generally accepted that the cerebellum played little to no role in cognition, whereas those who argued otherwise were sometimes even considered to be “on the fringe” in their beliefs. However, particularly following Jeremy Schmahmann's landmark publication of *The Cerebellum and Cognition* in 1997 [1], there has been rapidly increasing interest in the cerebellum's role in emotion and cognition in addition to movement [2–6]. Nevertheless, despite these advances, the mainstream viewpoint has largely continued to place the neocortex as “the king on the chess-board,” the primary human brain region supporting and generating thought processes. To some degree, this has been due to a persisting arbitrary separation of movement and thinking left over from archaic, dualistic models of “mind” versus “body.” While no longer dismissed entirely, the cerebellum's role in cognitive function has continued to remain largely on the periphery in favor of cortico-centric models [7].

At the same time, over the past few decades, neuroscientific thinking about the cerebellum has changed dramatically, in large part thanks to technological advances in investigative imaging techniques and concurrent development of computational modeling systems [8–10]. These technical improvements have allowed for repeated demonstrations that the cerebellum plays important roles in both motor and non-motor functions [4, 11–14]. This journal volume has thus assembled a number of experts in the field in an attempt to find current

areas of consensus in relation to the cerebellum's increasingly appreciated roles in cognition and emotion in addition to motor function.

This special edition volume of *The Cerebellum* therefore presents an over-view of current thinking regarding the cerebellum's role in both movement *and* thought. The general consensus no longer concerns whether or not the cerebellum plays a role in cognition, but instead, concerns *how* the cerebellum contributes to both movement and thought. The issue begins with Dr. Ramnani's paper, which introduces the idea that the cerebellum relies upon analogous mechanisms to support both skilled motor and cognitive operations. Dr. Schmahmann then provides a succinct, elegant summary of how the cerebellum contributes to nearly all higher-level behavioral functions by what he terms the Universal Cerebellar Transform. Dr. Riva and her colleagues speak to the cerebellum's critical role as an associative center for higher cognitive and emotional functions in the developing brain. Drs. Manto, Parker and Andreasen address what can be learned about cerebellar contributions to cognition through studying patients with cerebellar pathology. Drs. Marvel and Vandervert discuss the role of the cerebellum in working memory and language. Dr. Pezzulo emphasizes the cerebellum's role in the development of executive functioning via sensorimotor interaction with the environment. Dr. Imamizu reviews laboratory studies that demonstrate a modular organization of motor behavior and cognition within the cerebellum in relation to development of cerebellar control models. This is followed by Dr. Ito's systematic review of how conceptual and computational models of investigation contribute to our understanding of cerebellar functioning. The volume closes with Dr. Yamazaki's computational modeling perspective on how the cerebellum develops internal control models by actually learning the complete waveform of neural activity through the supervisory/instructional activity of the cerebellum's climbing fiber system.

Cerebellar Plasticity and the Automation of Cognitive Processing (N. Ramnani)

It has long been known that the cerebellum plays important roles in the acquisition of motor skills. The process often involves a transition from “controlled” to “automatic” processing in which movements that initially require problem-solving and attention become increasingly efficient, stereotyped, resistant to online feedback, and importantly, require much less attention (they become immune to the distracting effects of concurrently executed tasks) [15]. Here, I argue that analogous processes support skilled *cognitive* operations using comparable mechanisms, and that both situations in which operations become skilled and automatic require cerebellar mechanisms.

Computational theories that are grounded in the anatomy and physiology of cerebellar circuitry suggest that these circuits can store motor memories with such properties. Some models suggest, for example, that the storage is achieved through plasticity at the synapses between Purkinje cells and their inputs. Marr's (1969) model, perhaps the most influential, places importance on cerebellar interactions with the cerebral cortex [16, 17]. He suggested that high-level commands from the cerebral cortex could access low-level cerebellar representations, “so that when [movements] have been learned a simple or incomplete message from the cerebrum will suffice to provoke their execution.” In essence, the

cerebellar cortex could be trained to run routine operations that result in skilfully executed movements, and these could be triggered by relatively sparse high-level command from cerebral cortical areas. Albus (1971) proposed similar mechanisms, suggesting that motor memory is encoded through decreases in synaptic strengths [18]. His model predicts that learning should be accompanied by decreasing trial-to-trial activity. Such models have substantial empirical support [19–22].

Information from the motor cortex reaches the cerebellar cortex via monosynaptic pathways in the pontine nuclei [23–25]. They play important roles in motor learning, and their organization is well understood, particularly in non-human primates. However it is now well known that similarly organized afferents to the cerebellum also arise from the prefrontal cortex and posterior parietal cortex [24, 26–36]. (There are other cortico-cerebellar routes, such as those that convey neocortical information via the inferior olive, but not much is known about their organization; for a brief discussion see [37]). Neurons in both areas are engaged by cognitive demands. Although the activity in some posterior parietal areas reflect visual and motor demands, their activity also reflects the processing of higher order information [38]. For instance, Platt and Glimcher [39] recorded from neurons in the lateral intraparietal cortex in monkeys, and demonstrated activity related to reward-related decisions (a cognitive demand). They were able to show that this activity was not explained by visual processing demands or movement dynamics. The prefrontal cortex is better known for its contributions to higher cognitive function than for its role in motor control. Although information from area 46 of the prefrontal cortex reaches the primary motor cortex via the ventral premotor cortex, neural activity in area 46 responds in relation to the rules that govern actions rather than to the details of how movements are organized. The processing in such areas is concerned with cognitive demands rather than with movement kinematics (see Ramnani [28] for a review of these issues). The existence of pathways that send information from prefrontal and posterior parietal areas to the cerebellum provide compelling evidence that the cerebellum processes information beyond the motor domain, from areas concerned with higher cognitive functions (e.g., implementing rules that govern actions rather than the kinematic details of motor control [40–42]). In one influential study, Kelly and Strick [30] used trans-synaptic viral tracers to identify the parts of the cerebellar cortex that receive projections from the primary motor cortex and prefrontal area 46. Their findings showed that afferents from the primary motor cortex terminated mainly in lobules IV, V, VI, and parts of HVIIB and HVIII. Their roles in skilled motor control are well established. Interestingly, afferents from the prefrontal area 46 terminated in cerebellar cortical Crus I and Crus II and not in areas connected with the primary motor cortex.

I have suggested that these anatomical findings confer a specific benefit to functional neuroimaging studies: they permit the generation of anatomically specific hypotheses about cerebellar contribution to cognition [36]. If the organization of the cortico-cerebellar system in humans is similar to that in monkeys [43], and if cerebellar contributions to automating movement control are similar to its contributions to automating cognitive function, then these functional neuroimaging experiments should reveal activity in Crus I and Crus II when human subjects acquire and use cognitive skills. We have tested the hypothesis that these specific parts of the cerebellar cortex are activated when human subjects execute skilled cognitive operations [36].

Recent functional neuroimaging studies from our lab have shown that these areas of the human cerebellar cortex demonstrate activity related to the execution of abstract rules that govern action (first-order rules) [14]. One might argue that these involve motor control at an abstract level, but the experimental designs in these studies ensure that activity is related to rules rather than movements. Nevertheless, we recently tested a more rigorous variant of the hypothesis, that demonstrated rule-related activity in these areas of the cerebellar cortex regardless of whether rules governed the selection of actions, or whether they govern the selection of other response rules. This approach is more rigorous: it tests for cerebellar engagement in rule-processing regardless of whether or not rules guide action selection. The theoretical framework set out above also predicts that the process of learning should be accompanied by excitability changes that signal cerebellar plasticity. We scanned subjects as they learned rules during training, and systematically manipulated the rate at which different rules came to be executed automatically during learning. We found that faster transitions to automaticity were accompanied by faster excitability changes in Crus I [44].

For the last few years, discussions in the literature have focussed on *Whether* the cerebellum is involved in cognition. The evidence progresses the discussion beyond this into enquiries about *how* the cerebellum participates in cognitive function. To answer this question properly, the framework described above demands a systematic analysis of how the information exchange between cerebellum and the neocortex contributes to transitions between automatic and controlled processing, in both motor and cognitive domains. Work in our lab is currently using neuroimaging to achieve this. Of course, much of the progress that neuroimaging can make is underpinned by what is understood about the connective organization in the cortico-cerebellar system. The fact remains that most of this system remains unmapped—we are only just beginning to understand the topographical distribution of connections from association cortex in the cerebellar cortex.

Dysmetria of Thought: A Unifying Hypothesis for the Cerebellar Role in Sensorimotor Function, Cognition, and Emotion (J. Schmahmann)

The dysmetria of thought theory postulates that the cerebellum is critical for the modulation of sensorimotor, cognitive, and limbic functions [45]. The theory is predicated upon the duality of the repeating paracrystalline structure of cerebellum versus the topographic organization of cerebellar connections with cerebral cortex and other extracerebellar structures and the differential arrangement within cerebellum of motor, cognitive, and limbic functions [46]. In this view, the architecture of the corticonuclear microcomplexes [47] subserves a computation unique to the cerebellum, the universal cerebellar transform (UCT) [48], by which the cerebellum integrates internal representations with external stimuli and self generated responses in an implicit (automatic/non-conscious) manner, serving as an oscillation dampener which optimizes performance according to context [45, 48–50]. Evidence for functional heterogeneity of the cerebellum is derived from anatomical tract tracing studies in monkey [30, 51] (Fig. 1), functional imaging investigations [52] and resting state functional connectivity mapping studies in humans [43, 53, 54], and from clinical studies in patients [55–58]. The UCT is applied to these multiple loops of afferent and efferent cerebellar connections, modulating diverse streams of information underlying a

wide range of functional domains. The cerebellar contribution to these different anatomical and functional subsystems permits the ultimate production of harmonious motor, cognitive and affective/autonomic behaviors. The corollary of the notion of the UCT is that lesions of the cerebellum should produce a similar pattern of deficits in all domains (the Universal Cerebellar Impairment (UCI)) in which maintenance of behavior around a homeostatic baseline is impaired. The resulting loss of cerebellar modulation of interoception, perception and action thus leads to dyscontrol, instability, and erratic responses to context. Restated, if the cerebellum performs the same computation/does the same thing throughout (applied to different streams of information processing), then lesions of the cerebellum should result in the same fundamental pattern of deficits/i.e., it should break the same way, in all domains of behavior. The UCI concept provides a conceptual framework in which hypo- and hypermetria in the motor system can be extended to the nonmotor domain.

The primary sensorimotor region of the cerebellum is located in the anterior lobe and adjacent part of lobule VI; the second sensorimotor region is in lobule VIII [52, 59]. Damage to these regions results in features previously thought to be the only manifestation of cerebellar injury, namely, disequilibrium, gait ataxia, and impaired coordination (dysmetria) of the extremities, speech, and eye movements [57, 60]. Cognitive and limbic regions of cerebellum are located in the posterior lobe (lobule VI, lobule VIIA including Crus I and Crus II, lobule VIIB, and possibly lobule IX), with cognitive areas situated laterally whereas autonomic/affective/limbic functions are represented in the vermis [45, 52] (Fig. 2). Lesions of these cognitive or emotion loops lead to dysmetria of thought, with impairments of the cerebellar modulation of intellect and emotion manifesting as the cerebellar cognitive affective syndrome (CCAS) [56, 61].

It is worth noting that climbing fibers, originating from the inferior olive and terminating on proximal dendrites of Purkinje cells, are not usually considered to be anatomical substrates of the cerebellar contribution to higher function. This likely arises from the fact that olivary input from the cerebral cortex is largely indirect and is derived from sensorimotor cortices. These cortical projections are directed to the parvocellular red nucleus which sends efferents in the central tegmental tract to olivary subnuclei which receive spinal cord input and which are reciprocally interconnected with the cerebellar (motor) anterior lobe and deep nuclei engaged in motor control (mostly the interpositus nucleus). What has largely escaped notice, however, is that most of the principal olive (PO) is devoid of motor inputs either from the cerebral cortex or from the spinal cord, but is linked instead in tight parasagittal zones with the lateral cerebellum and the dentate nuclei which are involved in cognition (see Schmahmann [50]). There is some input to the olive from the zona incerta that receives afferents from prefrontal cortex [62], but it appears for the most part that the PO is engaged in tight reciprocal relationships with the cognitive cerebellum. This PO-cognitive cerebellar relationship could enable error detection, correction, and prevention in the cognitive domain that appears to be a critical function also of the olivocerebellar circuit in motor control. Cerebellar learning, implicit or otherwise, is essential to the UCT, and while the cerebro-cerebellar mossy fiber system conveys context dependent information, the olivocerebellar circuit is likely essential to optimal adaptation and refinement of both perception and action.

Evidence to date indicates that certain areas of cerebellar cortex and nuclei appear to be engaged in more than one function. This is exemplified best, perhaps, by the cerebellar vermis and fastigial nucleus, which has been implicated in balance/vestibular, visuomotor, autonomic, and limbic behaviors. It remains to be shown whether the anatomic signatures of each of these vermal–fastigial functions are indeed unique, or whether there is a shared neural substrate for related aspects of these different behaviors.

The net effect of these disturbances in cognitive functioning is a general lowering of overall intellectual function.

The cerebellar cognitive affective syndrome provides clinical underpinning to the role of the cerebellum in intellect and emotion. It is characterized by impairments in executive function, visual spatial processing, linguistic deficits, and affective dysregulation (Table 1). It can be prominent in developmental cerebellar disorders [63, 64] and following acute lesions such as stroke, hemorrhage, and cerebellitis [56], and it may be relatively subtle but still clinically relevant in late onset hereditary ataxias [58, 65].

Executive function deficits include problems with working memory, mental flexibility, and perseveration. Patients experience concrete thinking, poor problem-solving strategies, and impaired ability to multitask, with trouble planning, sequencing, and organizing their activities. Mental representation of visual spatial relationships is impaired (Fig. 3), with visuospatial dis-integration and simultanagnosia. Expressive language impairments include word finding difficulties and abnormal syntax with agrammatism, long latency and brief responses, reluctance to engage in conversation. Verbal fluency is decreased, affecting phonemic (letter) more than semantic (category) naming. Mutism occurs following acute injury such as surgery involving the vermis, mostly in children but also to varying degrees in adults. Poor control of volume, pitch, and tone can produce high-pitched, hypophonic speech. Short-term memory impairments include difficulty learning and spontaneously recalling new information, reflecting deficient encoding strategies, and difficulty locating information in memory stores. Conditional associative learning is also degraded, as previously shown in classical conditioning studies in patients and animal models [66].

The affective component of the CCAS occurs particularly when lesions involve the limbic cerebellum in the vermis and fastigial nucleus [56, 61, 64]. Patients have difficulty modulating behavior and personality style, with flattening of affect or disinhibition manifesting as overfamiliarity, flamboyant and impulsive actions, and humorous but inappropriate and flippant comments. Behavior may be regressive and childlike, sometimes with obsessive–compulsive traits. Patients can be irritable, impulsive, disinhibited, and with lability of affect and poor attentional and behavioral modulation. Pathological laughing and crying may occur when pontocerebellar circuits are damaged [67]. Acquired panic disorder has been described. Early evidence indicates that there are five domains of behavioral dysregulation caused by cerebellar damage—disorders of attentional control, emotional control, autism spectrum disorders, psychosis spectrum disorders, and social skill set (Table 2). Within each of these domains there are hypometric / diminished behaviors, and hypermetric/exaggerated behaviors, consistent with the UCT and UCI concepts embedded within the dysmetria of thought theory [68].

The paradigm shift in cerebellar function from movement to thought [62] and the notion embedded in the dysmetria of thought theory and the concept of the UCT that structure determines function, has relevance for understanding other cortical and subcortical nodes that comprise the distributed neural circuits governing neurological function [62], and for deciphering and treating mental illnesses such as autism, bipolar disorder, and schizophrenia [69].

Cognition and Cerebellar Pathology in Developmental Age (D. Riva, S. D'Arrigo, S. Bulgheroni)

The cerebellum, which was initially considered to be mainly involved in motor coordination and execution [70], is now recognized as an associative centre for higher cognitive and emotional functions even in the developing brain [11, 56, 71].

The specificity of functional processing is linked to an internal modular organization which repeats itself identically and which renders the harmonization of cognitive and emotional behaviors automatic. This is elaborated by a complex cerebro-cerebellar system of segregated connections between the cerebellum and various brain regions [11, 72], as confirmed by clinical and recent neuroimaging functional studies.

In adults, fMRI studies have reported cerebellar activation during a variety of tasks [52]. Lidzba et al. [73] have demonstrated not only supratentorial reorganization but also contralateral cerebellum one in five subjects with supratentorial congenital lesions. Riva et al. [74] have found a decreased lateralization in the operated cerebellar hemisphere correlated to decreased lateralization in the contralateral frontal lobe in six children undergoing cerebellar tumor resection.

Studies in animal models have demonstrated that the cerebellum receives input from many brain regions involved in cognition and emotions, including the hypothalamus, the parahippocampal gyrus, the cingulate gyrus, the superior temporal cortex, the posterior parietal cortex and the prefrontal cortex [25, 75]. In humans, these data have recently been confirmed by MRI and tractography studies [53, 76]. The development of functional networks is known to take place over an extended time window, first connecting sensory-motor and then associative areas [77]. These connections seem to be complete around the age of 9 years but they appear to be partially operative even before, as neurocognitive deficits have been described precociously even in children with congenital [78] or acquired cerebellar lesions [61, 79]. Cognitive impairments occur when posterior lobe lesions affect lobules VI and VII (including Crus I, Crus II, and lobule VIIIB), disrupting cerebellar modulation of cognitive loops involving cerebral associative cortices, while behavioural disorders manifest when vermis lesions disrupt cerebellar input in the cerebro-cerebellar- limbic loop [72].

The cerebellum develops over a relatively long time window, making it vulnerable to a spectrum of developmental insults, such as genetic mutations, toxic and vascular lesions. It is known that congenital or precocious cerebellar anomalies (hypoplasia, agenesis, etc.) are frequent in neurodevelopmental disorders [78, 80].

The incidence of posterior fossa malformations diagnosed in the newborn period is estimated to be 1 out of 5,000 live births [81]. Congenital cerebellar malformations are associated with neuropsychological impairments and/or different neurodevelopmental disorders, particularly intellectual disabilities, severe language disorders, and behavioral changes to the autistic phenotype [64, 72, 82].

Cerebellar malformations are reported in about 200 neurogenetic syndromes (Fragile X syndrome, Joubert syndrome-related disorders, Williams syndrome, Cokayne syndrome, etc.) as well as in several metabolic/degenerative diseases (CGH syndrome, neuroaxonal dystrophy, Ceroidlipofuscinosis, etc.). Cerebellar anatomical and volumetric abnormalities are consistently found in autistic children [83, 84] and, more rarely, in forms of acquired autism [85]. Cerebellar abnormalities prevent normal eye movements and interfere with the acquisition of lexical information in dyslexia [72]. Quantitative morphometry reveals smaller posterior lobes of the vermis in ADHD patients [72].

The study of acquired focal lesions in typically developing children represents the best way to investigate the functioning and connectivity of human cerebellum. Children with cerebellar tumors present deficits known as cerebellar cognitive affective syndrome [56]: lesions of the posterolateral hemispheres may cause cognitive disturbances, while vermis lesions may provoke behavioral and affective alterations [61, 79, 85, 86]. The right cerebellar hemisphere, through direct connections with the left cerebral hemisphere, is involved in verbal functions; conversely, the left cerebellar hemisphere is mainly involved in visual spatial information processing [79, 85, 87]. These data not only support the hypothesis of an internal cerebellar topography but also of a lateralized cerebellar organization of cognitive skills [53, 74]. The observation of mutism after removal of subtentorial tumours followed by long-term dysarthria is also interesting. A possible underlying pathophysiology could be a disturbed mental initiation before the programming of intentional bucco-phonatory movements probably due to a bilateral but not unilateral destruction of the dentate nuclei [88]. Mutism with subsequent dysarthria has also been reported following acute cerebellitis [89].

Children with vermian tumours present two profiles: post-surgical mutism, which evolves into speech disorder [79, 88] or true language disturbances similar to frontal agrammatism, suggesting that vermal connections with the supratentorial regions may be more complex [79].

As the cerebellum participates in many higher-order functions, its role is implicitly crucial in cognitive and emotional development [64, 78, 82]. But to what extent its contribution is essential during development depends on the type and the degree of mechanisms underlying cerebral reorganization, which influence a wide range of neuropsychological processes both immediately and as these fail to develop normally later on. The final outcome probably depends on many factors such as genetic mutations which alter gene expression pathways in different cerebellar (but perhaps also supratentorial) regions, the timing of expression and the reorganization of the relative circuit connections, as well as the individual's genetic background. All of these factors may account for the variability of clinical phenotypes, which range from mild clinical impairment, even in the presence of almost complete

cerebellar agenesis [90], to serious neurological, developmental, and functional disabilities [91].

Neurocognitive long-term sequelae after congenital versus acquired lesions are obviously different because the former affect evolving systems while the latter act on networks that are at least partially functionally specialized. Follow-up studies on effect of cerebellar tumour resection in childhood indicate that there is a general improvement despite persistent cognitive and affective deficits with different degrees of seriousness up to adulthood [92].

The cerebellum acts as a homeostatic orchestrator integrating complex behaviors even in the developing brain. Functional specificity is ensured by segregated sub-circuits connecting the cerebellum to specific supratentorial areas. Although both congenital and acquired lesions may cause complex cognitive and affective deficits, a correlation with the internal cerebellar topography is more frequently observed in acquired lesions.

Cognitive Deficits in Autosomal Dominant Ataxias: What did we Learn? (M. Manto)

Autosomal dominant ataxias (ADCAs or SCAs: spinocerebellar ataxias) represent a group of disorders characterized by clinical and genetic heterogeneity [93]. More than 35 types have been identified. Current taxonomy is based on molecular findings; the numbering corresponding to the order of gene discovery. The most common forms in the world are SCA1, SCA2, SCA3, SCA6 and SCA7. All these SCAs result from an expansion of repeated trinucleotides encoding a polyglutamine repeat. The average onset of symptoms is between 30 and 40 years but there is a large variability amongst subtypes and even within affected families. A cerebellar motor syndrome is usually the predominating phenotypic manifestation, often combined with extra-cerebellar signs during the course of the disease. Pure cerebellar involvement is uncommon in SCAs. Non cerebellar tissues most often involved are the retina and the optic nerves, the brainstem, basal ganglia, cerebral cortex, spinal cord and peripheral nervous system. Many patients exhibit cognitive deficits, but they may be subtle at the beginning of the disease and are therefore often overlooked at an early stage, unless a detailed neuropsychological assessment is performed. SCAs share the feature of progressive degeneration of brain structures leading to atrophy. MRI-based volumetry allows the quantification of regional atrophy and has now entered in routine practice. From the neuropathological point of view, neuronal loss affects nearly invariably -but at various degrees- the cerebellar cortex, dentate nuclei and the inferior olivary nuclei. In SCA1, SCA2 and SCA7, the pons is affected, hence a picture of olivopontocerebellar atrophy.

The prevalence of cognitive deficits varies considerably [94]. Table 3 summarizes the deficits reported in the literature for the SCAs which have been studied in detail. Executive dysfunction is common. In SCA6, which is considered as one of the “pure cerebellar forms” amongst SCAs, and which is characterized by neuropathological changes nearly restricted to the cerebellar cortex, the majority of reports point out the lack of cognitive impairment, although verbal memory may be slightly defective. Noticeably, attention and fronto-executive functions are spared. In SCA17, which is one of the SCAs with prominent psychiatric/behavioural manifestations, correlations with the psychiatric course show gray

matter degeneration patterns in the frontal and temporal lobes, the cuneus and the cingulum, and there is a clear correlation between the MMSE score and the atrophy of the nucleus accumbens, likely accounting for neuropsychiatric manifestations [95]. In SCA17, the contribution of cerebellar atrophy per se in the constellation of behavioural/psychiatric symptoms remains a matter of debate.

Extra-cerebellar involvement impacts clearly on cognition in several SCAs and one would expect a more uniform pattern of cognitive deficits if cerebellar circuitry would be the sole key-structure behind the cognitive manifestations in SCAs [94]. Rather than a genuine and isolated cerebellar contribution, SCAs illustrate the major role of the parallel cerebello-cerebral networks between the cerebellum, the sensorimotor cortex, the prefrontal cortex and the paralimbic regions of the cerebral cortex [96]. The literature indicates that behavioural deficits observed in SCAs are suggestive of a disruption of the cerebellar modulation of the neural circuits that link prefrontal, posterior parietal, superior temporal and limbic cortices [56]. An open question which remains in autosomal dominant ataxias is to determine the impact of the temporal and spatial distribution of the neurodegenerative processes evolving in the brain upon cognitive operations, taking into account the modular organization of the cerebellar connections and the consequences of ageing on brain circuits. Rodent models of dominant ataxias are characterized by deficits in spatial orientation, in working memory and by behavioural disinhibition [97]. Several authors have underlined the lack of correlation between the extent of cerebellar damage and the cognitive capacities amongst the various cerebellar mutants [98]. The malfunction of the cerebellum could have a more dramatic impact upon cognitive operations than no functioning at all [99].

There is an agreement that executive dysfunction is common in SCAs, but again no clear demonstration that it results from errors within cerebellar micro-circuits, even if functional imaging studies show a clear cerebellar activation during executive tasks. Degeneration of the frontal lobes or involvement of subcortical structures such as basal ganglia per se cause dysexecutive symptoms. Visuo-spatial deficits can be explained by impaired feed-forward and feedback links between the cerebellum and the parietal cortex [31].

A definite statement that cognitive or behavioural deficits in SCAs have their origin in cerebellar pathological changes cannot be made at this stage. Further studies are required to better delineate our knowledge of the cerebello-cerebral connectivity in SCAs. Isolated cerebellar lesions (stroke, tumor resection, etc.) keep a clear advantage over disorders such as SCAs for the procedure of symptom-lesion mapping, including for the elucidation of the mechanisms sub-serving cognitive operations. Overall, SCAs provide a clinical model to address the consequences of various combinations of cerebellar and extra-cerebellar neurodegeneration upon cognitive and behavioural symptoms. One of the core features of SCAs is the progressive atrophic damage affecting diffusely the cerebellar circuits. As such, SCAs are a unique group of disorders to address the link between neurodegenerative diseases of the cerebellum and plasticity changes in the brain. Recent studies on social emotion recognition in SCAs illustrate the validity of studying this group of disorders to elucidate cerebello-cortical networks and extract the cerebellar contribution [100].

The Cortico-Cerebellar-Thalamic-Cortical Circuit / Cognitive Dysmetria Model of Schizophrenia: The Role of the Cerebellum (K. Parker, N. Andreasen)

Emerging evidence suggests that in addition to motor functions, the normal cerebellum plays a significant role in cognition in the healthy human brain. It has an active role in a variety of mental activities, including facial recognition, emotion attribution, theory of mind attributions, directed attention, and many types of memory [49, 117–123]. In functional imaging studies, cerebellar activations occur even when motor components of the tasks are well-controlled. It is now widely accepted that many normal cognitive functions are performed by using distributed circuits that include cerebellar and thalamic components, with cortical components that vary depending on the nature of a given mental activity.

Illustrations from several representative PET studies of healthy volunteers, chosen to demonstrate the occurrence of cerebellar activations in “cognitive tasks,” are shown in Fig. 4a (areas of increased flow in red). Therefore, we have hypothesized that “synchrony,” or fluidly coordinating sequences of thought and action, occurs as a consequence of very rapid on-line processing and feedback between the cerebral cortex and the cerebellum, mediated through the thalamus [124]. The substrate of synchrony is the cortico-cerebellar-thalamic-cortical circuit (CCTCC).

Schizophrenia is a disease that is characterized by poor coordination, or dysmetria, in both motor and cognitive functions. Although schizophrenia is not considered to be a “motor disease,” many indicators of motor dysfunction are present, suggesting that the basic abnormality in the disorder could be a brain system that mediates both motor and cognitive functions.

As our PET paradigms used to study normal cognition were applied to the study of patients suffering from schizophrenia, the evidence for cerebellar abnormalities became compelling. We found that the cerebellum has structural abnormalities including decreased volume or thickness when compared with the normal adult brain [125, 126], as well as a relatively consistent pattern of abnormal blood flow. Like a negative mirror image of normal brain function, we found that patients with schizophrenia have lower blood flow in the cerebellum and thalamus in a broad range of tasks that tap into diverse functional systems of the brain, including memory, attention, social cognition, and emotion [122, 125, 127–136]. These decreases in cerebellar flow are found in a variety of tasks, including recall of complex narratives, episodic memory, memory for word lists, and dichotic listening. Furthermore, most of these studies identify consistent abnormalities in the entire CCTCC, including the thalamus and prefrontal cortex. Sample PET images are shown in Fig. 4b illustrating this lower flow, as compared with healthy comparison subjects (areas of lower flow in schizophrenia shown in blue).

Recent studies using diffusion tensor imaging (DTI) reveal reduced fractional anisotropy (FA) in the white matter fiber tracts located between the cerebellum and the thalamus in patients with schizophrenia compared with normal controls. Specifically, there was reduced

FA within the superior cerebellar peduncle but not along the tract from the cerebellum to the thalamus [137]. Although it is impossible to infer the underlying cause of the reduced fiber anisotropy in the white matter, these results may imply an underlying developmental abnormality in schizophrenia.

We have therefore hypothesized that the symptoms and cognitive impairments of schizophrenia arise because of malfunctions in a group of distributed brain regions and that the cerebellum is a central node in this malfunctioning group of regions. This abnormality underlies the “fundamental deficit” and the “functional misconnections” of schizophrenia: “cognitive dysmetria,” defined as a difficulty in coordinating mental activity. Cognitive dysmetria is the “cognitive expression” of the underlying CCTCC neural circuit abnormality. The malfunctioning circuits are point-to-point feedback loops between the cerebral cortex, thalamus, and the cerebellum. These deficits in brain circuitry cause misconnections between percepts and their meanings, in turn causing errors in perceptual binding and misinterpretations of many kinds (e.g., delusions and hallucinations); it also leads to inefficient or inaccurate information processing; this forms the basis of the multiple types of cognitive impairments observed in schizophrenia.

The Cerebellum and Inner Speech (C. Marvel)

Verbal working memory (VWM) involves the ability to temporarily hold in mind information that is verbalizable, such as letters, words, or nameable objects. It is widely believed that VWM consists of a passive phonological storage process lasting 1–2 seconds, followed by an active rehearsal process that continues to maintain this information [138]. This active “phonological loop” may have evolved from primitive vocal sounds as phonemes were combined and lengthened to represent meanings [139, 140]. It is possible, therefore, that a working memory cache evolved alongside language. On a local scale, working memory capacity correlates to language acquisition and vocabulary in children [139, 141, 142]. Thus, expansion of working memory and speech during evolution and development suggests a natural coupling of the two systems.

On a neurobiological level, working memory systems are strongly associated with the dorsolateral prefrontal cortices and other cortical regions [143]. However, motor-related brain regions are also involved; for example, neuroimaging studies of VWM consistently activate motor preparation and planning areas that include the premotor cortex (mainly in the left hemisphere), inferior frontal gyrus, supplementary motor area (SMA), and pre-SMA [144–149]. Notably absent, however, is primary motor cortex activation, indicating that overt motor response (i.e., overt speech) is not a primary strategy used during working memory. In the cerebellum, motor planning regions are also activated during working memory (e.g., cerebellar lobule VI and Crus I) in the absence of activation in the primary motor cerebellar cortex (e.g., cerebellar lobules IV/V) [150, 151]. Therefore, during working memory, motor planning and preparation regions are strategically recruited.

One explanation for secondary-specific motor activity during VWM is that this system supports inner speech mechanisms to facilitate VWM rehearsal [144–149, 152]. Neuroimaging studies have shown that the cerebellum is an integral part of this process.

During the encoding phase, when verbalizable content, such as letters, is visually presented to participants, cerebellar lobule VI activity climbs [145, 147]. Such activity then declines as the information is maintained across a delay. This suggests that the cerebellum is involved in creating an internal code for motor sequences related to the vocalization of information [149, 151, 153, 154]. It would also suggest that the cerebellum is not involved in the ongoing rehearsal phase since activity drops off at this point. However, cerebellar behavior can be affected by the nature of the working memory demands. Following encoding, if information needs to be manipulated in some way (e.g., by thinking two alphabetical letters forward of each original target letter, such that “f”→“h”), cerebellar lobule VI activity remains elevated relative to activity during straightforward (non-manipulated) rehearsal of information [149]. This behavioral pattern indicates that as long as the cerebellum is encoding new information—whether real or imagined—new motor traces continue to be created, and activity levels remain high.

One might infer that increased cerebellar activity reflects better VWM performance. Data suggest this may be true up to a point (Fig. 5). Yet Marvel and Desmond [149] found that increased lobule VI cerebellar activity in VWM correlates to lower overall accuracy. What this means is that cerebellar involvement in inner speech may serve a generalized purpose that is not necessarily tied to successful performance. For example, the cerebellum may contribute to the timing and sequencing of motor traces of inner speech, as has been proposed by Ackermann and colleagues [155]. Cerebellar activity related to temporal sequencing of inner speech may adjust to increasing working memory demands, yet continue to increase when a person struggles—and fails—to keep up with working memory demands.

Overall, it seems that the more effortful a VWM task is, the more one engages an inner speech neural mechanism. One might expect, therefore, that this effect would be observed in clinical populations with working memory deficits. The literature consistently reports that working memory-impaired populations exhibit abnormal cerebellar activity during VWM. Some populations show cerebellar *hyperactivity* (e.g., addiction [156, 157], cancer patients treated with chemotherapy [158]), while others show *hypoactivity* (e.g., multiple sclerosis [159], attention deficit/hyperactivity disorder [160], and dyslexia [161]). There can also be discordant results within populations (e.g., schizophrenia may show hyperactivity [162] or hypoactivity [163]). Such differences across and within patient populations may be linked to differences in the stage (or subtypes) of the disorder, in tasks used across studies, in compensatory strategies used to accomplish tasks, or any combination of these factors. The general message, however, is that clinical populations with VWM deficits generally show abnormal cerebellar function (increased or decreased) when challenged by high working memory demands.

In summary, the cerebellum is an integral component of a secondary motor system that supports VWM. The specific contribution of the cerebellum may be to temporally sequence inner speech information by creating internal motor traces that help maintain that information. Cerebellar activity intensifies with increasing working memory demands. However, intense recruitment can signify one's struggle to keep up with those demands.¹

How the Cerebro-cerebellar Blending of Visual–Spatial Working Memory with Vocalizations Supports Leiner, Leiner & Dow's Explanation of the Evolution of Thought and Language (L. Vandervert)

In two watershed articles, Leiner, Leiner and Dow proposed that the three- to fourfold increase in the size of the cerebellum over the last million years, particularly its phylogenetically newest parts, gave rise to the “skillful manipulation of ideas” ([164], p. 444), and made it “possible for the cerebellum to improve language dexterity” ([165], p. 1006). The purpose of this essay is to show how Imamizu et al.'s [166] findings on how cerebellar internal models are *blended* in the cerebral cortex, when combined with research on working memory, supports and extends Leiner, Leiner and Dow's evolutionary proposals in some detail. Before going on to Imamizu et al., it is necessary to provide pertinent background from research on working memory.

What Leiner, Leiner and Dow's Referred to as the Skillful Manipulation of Ideas and Language Dexterity is Now Called Working Memory

The manipulations of ideas and language are subsumed under what would now be called *working memory* [138, 167, 168]. According to Baddeley, working memory “provides temporary storage and manipulation of information for such complex cognitive tasks as language comprehension, learning and reasoning” [138], and consists of three components: (a) an attentional controlling system or “central executive,” (b) a visual–spatial sketchpad which manipulates visual images, and (c) a phonological loop which manipulates speech-based information.

From What Pre-existing Working Memory Was the Working Memory of Modern Humans Selected?

If existing non-human primates are any indication, all early hominins (notably *Homo habilis* a million and half years ago) had well-developed *visual–spatial* working memories. The visual–spatial working memories of monkeys have been found to be well-structured in spatial reasoning [169] and in sequences of abstract reasoning [170]. Therefore, as Aboitiz et al. [140], Vandervert [171–174], and Vandervert et al. [175] have suggested, the evolution of language would be most profitably studied as a direct adaptive extension of structured and sequential brain mechanisms which sub-serve cognitive visual–spatial working memory in nonhuman primates and early hominins.

Why Was the Phonological Loop Added to Visual–Spatial Working Memory?

Baddeley et al. (see [139], p. 159) argued that the primary function of the phonological loop (both in silent and overt speech) is to learn the sound patterns of *new* words and new syntactical sequences and, thereby, to mediate language learning. In their conclusion, Baddeley et al. extended the phonological loop's function of learning new sounds to the *evolution* of language: “the primary purpose for which the phonological loop evolved is to store unfamiliar sound patterns while more permanent memory records are being

¹Marvel note: funding source for this study: K01 DA030442 (NIH)

constructed (in long-term memory)” [171]. The storage and rehearsal processes of the phonological loop involve the lateral cerebellum and speech-related areas of the cerebral cortex in both overt and silent speech used in solving problems [149, 151]. According to Baddeley et al., then, the phonological loop was gradually added to working memory because it bestowed an advantage by incorporating *new* sound patterns *with* the manipulation of visual–spatial images.

The Contention of This Essay

Extending the findings of Imamizu et al. [171] on the *blending* of cerebellar internal models to meet new challenges, the contention of this essay is that cerebro-cerebellar mechanisms blended visual–spatial working memory *with* vocalizations of early hominins to produce the above adaptive emergence of the phonological loop. Specifically, it is proposed that during approximately the last million years of cerebro-cerebellar *co-evolution* [37, 164, 165] language evolved from the cerebral *blending of multiple cerebellar internal models* [166, 176] of (a) decomposed/re-composed contexts or “moments” [177, 178] of visual–spatial experience *with* (b) those of *new* sound patterns decomposed/-re-composed from parallel context-appropriate vocalizations (calls or previously acquired embryonic “words”). It is further proposed that the adaptive value of this blending was the progressively rapid access in working memory to the control of detailed cause-and-effect relationships for application in new and challenging environments.

Details of the Cerebro-cerebellar Blending Mechanism and Its Application to the Evolution of Human Language

Imamizu et al. [179, 180] demonstrated the learning of multiple cognitive internal models in the lateral cerebellum. Figure 6 shows the location of two sites of this cognitive modularity in the lateral posterior cerebellum. Subsequently, Imamizu et al. [166] found that when confronting *new* situations, these cognitive internal models are *blended* in the cerebral cortex to negotiate the new challenges. Based upon these findings, they argued that cerebral blending of multiple cerebellar internal models bestowed several tightly interrelated advantages: (a) interference between different learning epochs (or “moments”) is reduced thereby enabling the rapid switching of skilled behaviors, (b) entirely new environments can be coped with by adaptively blending pre-existing motor and cognitive primitives as multiple internal models, (c) multiple internal models are blended *in proportion* to the requirements of the current new context, and (d) as blending is proportionate to the specific requirements of changing contexts, an enormous, perhaps limitless, repertoire of behavior can be generated even when the number of internal models might be limited.²

²It is proposed that this feature of the nearly limitless blending of internal models of sound patterns *with* visual-spatial imagery explains the origin of what Hockett (1955) referred to as the “duality of patterning” feature of language (meaningless sounds or symbols can be rearranged to produce an unlimited number of messages, e.g., Hockett described how Morse Code exemplifies this feature). Hockett argued that duality of patterning is unique to human language. However, since monkeys have shown fronto-cerebellar action in switching tools [170] indicating an open-ended synthesis of multiple *visual-spatial* internal models, duality of patterning appears to be shared, at least in nascent form, with other primate species, and, therefore, that duality patterning originates not in the tags that place moments of visual-spatial working memory in long-term memory, but in the limitless potential of internal models of those visual spatial moments themselves.

Combining Baddeley et al. with Imamizu et al.

When applied to Baddeley et al.'s [139] conclusion that the phonological loop evolved to learn new sound patterns, Imamizu et al.'s findings can be interpreted to mean that an enormous number of sound forms of new words were adaptively mixed or blended with an equally enormous number of newly decomposed/re-composed visual–spatial contexts or moments. That is, as new “moments” of visual–spatial working memory were gradually “fractioned,” and tagged (with likewise newly fractioned sound forms), an enormous (perhaps limitless) number of new, rapidly learned and, later, rapidly accessible (from long-term memory) cause-and-effect strategies became available.

According to this model, syntax in Chomsky's [181] brain-based generative grammar was the direct result of the cerebrocerebellar blending of visual–spatial working memory with the sound patterns in utterances and calls in early humans. The blending of visual–spatial information with the selection of phonological working memory squares with Chomsky's generative grammar: “A generative grammar, ideally, specifies a pairing of phonetic and semantic representations (the meanings inherent in visual–spatial information) over an infinite range” [181], p. 75). This blending toward brain circuitry for generative grammar is believed to have been selected into the human brain over tens of thousands of years during which models in working memory guided the manipulation of stone-tool sequences [171]. Baddeley and Andrade [182] referred to such rapidly and *consciously* manipulated strategies as “mental models,” and, Tooby and DeVore [183] and Pinker [184] referred to this cause-and-effect modeling advantage as the “cognitive niche” which gave evolving humans dominant control over other species.

Conclusions

It is concluded that the evolutionary blending of cerebellar internal models of visual–spatial working memory *with* those of vocalizations gave rise to the following: (a) the gradual fractioning of visual–spatial working memory into *cause-and-effect* sequences and, simultaneously, systems of coordinated sound patterns (the phonological loop) for the former's rapid storage and retrieval, (b) the selection of *generative grammar* into the structure of the brain, (c) the selective evolution of human advancements in the *conscious* manipulation cause-and-effect relationships, and (d) *thereby*, the distinctive “cognitive niche” of early humans proposed by Tooby and DeVore [183] and supportively elaborated by Pinker [184]. This four-part conclusion directly supports and extends Leiner, Leiner and Dow's proposal that the phylogenetically newest parts of the recent three- to fourfold expansion in the size of the cerebellum sub-served the evolution of the skillful manipulation of ideas and language.

The Role of the Cerebellum in Movement and Cognition (G. Pezzulo)

According to grounded and motor theories of cognition, the brain of living organisms evolved for adaptive action in the real world, not for cognition and thought. The complex decisions and plans we do in our everyday life, and our “executive functions,” essentially reuse in more sophisticated and flexible ways the basic action control mechanisms of our earlier ancestors. The brain orchestrates these cognitive processes using widely distributed

(cortical and sub-cortical) brain networks, with no “central locus” of cognition [96, 186–189].

Theories of (optimal) control permit to look at the brain in terms of the mechanisms necessary to fulfill its adaptive functions: the selection and performance of actions. For the online control of action, the vertebrate brain realizes anticipatory control loops, using internal (inverse and forward) models. In this computational scheme, prediction (forward modeling) gives clear advantages in terms of compensation of noise and delay in sensory feedback, cancelation of self-generated stimuli, and better state estimation [190, 191]. The cerebellum plays a pivotal role in such anticipatory control loops. Its role in the temporal organization, coordination, and finessing of actions can be conceptualized in terms of adaptive filtering and internal modeling of the body, learned through adaptive processes dependent on sensory prediction errors [192–196].

What is the link between primitive control architectures and our modern cognitive abilities? I propose that predictive and internal modeling abilities originally acquired for adaptive motor control were exapted during evolution, and that the development of increasingly richer and far-reaching anticipatory control loops bootstrapped cognition and thought (and the same applies at developmental scale) [197].

According to this hypothesis, anticipatory control loops originated for on-line control of action, but gradually developed into more sophisticated (and offline) systems capable to predict distal and abstract consequences of actions, mentally rehearse entire sequences, imagine novel ones, monitor and evaluate them. This determined a passage from reactive to goal-directed and proactive systems, and from the selection of currently available affordances to the flexible realization of distal intentions detached from the here-and-now [198, 199]. The similarity of the neuronal substrate for motor preparation and imagery supports this idea [186].

Although the anticipatory control loop was primarily developed for the internal modeling of the body and the monitoring of action outcomes, it become accessible for other tasks. It has been proposed that bodily internal models can be re-enacted and used in simulation [200, 201], emulation [202], or other (Bayesian) generative schemes [203] to support higher cognition in individual and social domains. The reuse of existing internal models, together with the acquisition of novel models (not necessarily linked to bodily movements), enables many cognitive abilities, such as predicting and understanding external events [204], planning action sequences, understanding affordances, using tools [205], reading minds [206], imitating, performing joint actions [207], and controlling mental activities and thought processes [117].

The uniform structure of the cerebellum and its recurrent connections with multiple cortical areas (including not only the primary motor cortex, but also areas of premotor and prefrontal cortex [117, 208]) suggest that it could play a similar coordination and support role in the anticipatory control loops of motor and non-motor domains; this could explain why cerebellar deficits have consequences in both domains [72]. In short, this theory suggests that anticipatory control loops are not only used for the routinization and temporization of

action control programs, but are also re-enacted for supporting cognitive processing and thought. It is possible to speculate that the (evolutionary) recent expansion of posterior cerebellum and prefrontal areas could have supported increasingly more sophisticated overt and covert loops.

A more profound consequence of the proposed hypothesis is that there is not a separated realm for abstract or symbolic cognition; rather, thought consists in an internalized form of action that reuses and re-enacts the same anticipatory control loops supporting on-line action control and adaptive behavior. So-called executive functions are sophistications of these primitive control loops, which include more distal and abstract internal models and predictive mechanisms, and rely on more elaborated mechanisms of inhibition, monitoring, working memory, and event representation and learning, but also retain much of the original functioning of more primitive architectures [209]. This implies that all cognitive knowledge manipulation in the brain retains vestigial aspects of the anticipatory control loops, as revealed by many empirical studies [2, 210].

In sum, evolutionary and computational arguments suggest that thinking and executive functions could be covert forms of behavior and reuse anticipatory control loop originally developed for overt actions, and that cognitive processing remains ultimately grounded in sensorimotor anticipation. By linking sensorimotor and cognitive control domains, this hypothesis explains why the cerebellum (and other subcortical structures) can play the same role in the shaping, coordination and finessing of action, cognition, and thought.

Embodied Problem Solving and the Cerebellum (G. Pezzulo)

Grounded theories of cognition assume that both cognitive processing abilities (the “vehicle” of cognition) and the brain's knowledge (the “content” of cognition) derive from action and are grounded in sensorimotor processes of action prediction and control. An open research question is how grounded processes can support declarative forms of knowledge and higher cognitive abilities [211, 212].

I suggest that the cerebellum permits to capitalize on procedural learning (of internal models) to produce declarative knowledge that can be used in open-ended ways for complex cognitive tasks. This happens in two ways: via *embodied problem solving*, and via the *internalization of grounded knowledge* [197, 210].

1. Embodied Problem Solving

Although some cognitive theories link higher cognitive abilities to language and symbols, we hypothesize that most of them use *embodied representations*, which originate (and are grounded in) sensorimotor control loops, but can also be internally manipulated before or instead of acting in the external world [198, 199]. This could explain, for instance, the ability of humans (and other animals) to reason, plan for the future, and anticipate social interactions; for example, an interior designer can compare, in her mind, different possible arrangements of the furniture in a room by considering their shape, color and size, and anticipate if her clients will be satisfied or not. We all frequently mentally compare multiple

paths to get home and select the shortest one, or the one with less traffic (some animals, such as rats, have similar navigation skills).

How is this possible? Grounded theories of cognition assume that knowledge is mostly retained in modal and multi-modal brain areas, in the same format as used for action; e.g., verbal memory in articulatory control system [210]. Furthermore, internal models include extensive procedural knowledge, part of which (that can be called “tacit knowledge”) can be accessed by re-enacting these areas [210]. The off-line re-enactment of the cerebellum gives access to such tacit information, and makes it available for open-ended cognitive tasks and detached cognition. For instance, the internal models of hand movements contain useful information to calculate the closest, farthest, or biggest object in a room; the internal models encoding mine and your position can be used to understand if a given object, say, a wall or a newspaper, “shields” me from your sight; internal models of social interactions and preferences can tell the interior designer if the client will be happy with the new furniture arrangement.

Because these representations are used in open-ended ways and outside their original domains of acquisition (e.g., for reasoning and deliberation), they play the role of *declarative* representations in symbolic theories. We propose that we extensively use re-enactment processes and internal thought manipulations to perform complex forms of embodied problem solving, mostly unconsciously, but occasionally using conscious imagery as well [213]; see an example in Fig. 7. Although largely automatic, embodied problem solving is a controlled process, and requires the ability to (intentionally) steer internal simulations towards desired ends, to manipulate and reassemble tacit knowledge in open-ended ways. Mechanistically, this requires self-control [214] and inhibition [215] processes that guide the anticipatory control loops [209]. Furthermore, due to its origins within overt control loops, embodied problem solving might retain (part of) the same constraints as situated action.

2. Shaping of Cortical Cognition Through the Internalization of Grounded Knowledge

Several researchers have suggested that the cerebellum acquires internal models of the body, mimicking information processing in cortex, so that movements can become automatic. Furthermore, it has been proposed that it coordinates and automatizes thought processes in much the same way it does for movement control [117]. However, this can be only part of the story: cortico-cerebellar influences are *bidirectional*, and the cerebellum influences what memories the (motor) cortex retains.

As a consequence, not only do anticipatory control loops support actions and thought processes, they also permanently structure one's own knowledge of the world, and sculpt cortical representations. As increasingly more complex control and anticipation skills are learned, brain circuits are shaped and internalize knowledge of bodily processes, facts (and predictions) about objects and social interactions, and thought processes. This knowledge can be successively used in open-ended ways, for flexible cognitive processing, not necessarily re-enacting the whole anticipatory control loops which served to acquire them. This process ensures that even abstract knowledge and intellectual skills [216] remain ultimately grounded in anticipatory control loops [217]. The hypothesis advanced here can

be tested by performing memory, learning and extinction experiments that probe the linkage between procedural skill learning (or deprivation) and declarative knowledge (see [218] for preliminary evidence).

Rather than being disconnected, “embodied problem solving” and “internalization of grounded knowledge” are two expressions of the fact that procedural learning contributes to forming (grounded) declarative representations, and operate at two different timescales. Embodied problem solving operates at the shorter timescale of immediate goal achievement, while the permanent shaping of embodied representations reinforces this adaptive process at the developmental scale, by shaping brain representations and memories for later use. As a consequence, the cerebellum is not only implied in the automatization of behavior but also in flexible cognitive control. It emerges from our arguments that an intact cerebellum is necessary for (optimal) cognitive development, and the cerebellum actively participates in tasks requiring the elicitation of tacit information in the internal models. However, once cortical representations are shaped that encode grounded representations, they can be also used without the sustained activation of cerebellar (and subcortical) loops. This is a potential source of confounds in the empirical study of the cognitive roles of the cerebellum.

Internal Models for Dexterous use of Tools: The Border Between Cognitive and Motor Skills (H. Imamizu)

Humans have remarkable abilities to flexibly control their own bodies and such objects as tools. Because the sensorimotor feedback of movements is inevitably delayed by many factors including the delay of the transmission of motor commands from the brain to the muscles and the time for processing the sensory information, many studies have suggested that rapid and smooth movements are supported by neural mechanisms that can calculate the motor commands necessary for realizing intended motions and predict sensorimotor feedback from the motor commands before movements [219, 220]. Such neural mechanisms are called internal models. Although the concepts of internal models were originally proposed in studies on the control of body movements, many behavioral studies have suggested that the central nervous system (CNS) applies such models to the manipulation of external objects [221] as well as tools [222].

In a series of functional magnetic resonance imaging (fMRI) studies, we demonstrated possible mechanisms regarding how the CNS acquires and switches internal models for the dexterous use of many tools. In our seminal study [180], we investigated cerebellar activity when human subjects learned how to use a novel tool (a rotated mouse, whose cursor appears in a rotated position). As the learning proceeded, we found two types of activity in the lateral cerebellum: decreasing and increasing activities. The intensity of the former activity was precisely correlated with the size of the error made by subjects, suggesting that it is related to the error signals that guide the learning acquisition of an internal model of the tool. However, the intensity of the latter activity was not correlated with error size and probably reflects the acquired internal model. This was the first fMRI evidence for the existence of an internal model in the human cerebellum.

In a subsequent study [179], we investigated the internal-model activity after sufficient training for using two types of novel tools (the rotated mouse and a velocity mouse, whose cursor velocity was proportional to the mouse position) and found that the cerebellar activity for the two tools was spatially segregated and that the overlap was very small. This regional difference, which could not be explained by the difference in the hand movements or the size of the errors between the tools, suggests that internal models representing different input–output properties are acquired in different regions. Such modular organization of internal models is thought to support flexible adaptation to sudden changes of tools and environments by preserving and recalling previously acquired internal modes. In a related study [223], we also demonstrated the modularity of internal models for such common tools as scissors and chopsticks.

Our recent studies [224, 225] have focused on the switching mechanisms of internal models. The prefrontal (especially area 46) and parietal regions, and the functional connectivity between the lateral cerebellum and them, are particularly important for the switching of internal models. We found that two types of switching internal models are related to distinct neural mechanisms. One relies on contextual information (such as the color and the texture of objects) that can be obtained before the movements and enables rapid switching of the human behaviors, and the other is based on sensorimotor feedback that becomes available during or after the movements. Our results indicate that the prefrontal and the superior parietal regions contribute to predictive switching based on the contextual information, whereas the prefrontal and the inferior parietal regions contribute to post-hoc switching based on the sensorimotor feedback. Prediction of the feedback from the motor commands by internal models plays a crucial role in post-hoc switching because the switching mechanisms compare the prediction and the actual feedback and select an internal model with the least prediction error. These studies suggest that the predictive function of internal models is also essential for their own selection.

Because tools are extensions of our own bodies [226], CNS tends to generalize the control principles for the body movements to use tools. On the other hand, using tools is one of the fundamental cognitive functions [227]. Therefore, the neural mechanisms for tool-use provide insights into common computational mechanisms between cognition and motor control. Our studies revealed the mechanisms of internal models that contribute to the flexible and dexterous use of tools. The organization principles of these mechanisms, modularity and the switching of modules based on prediction, are expected to be shared with other cognitive functions. However, such cognitive functions as language and thought are more complex than tool-use, and thus future studies are needed to understand how the cerebellum is involved in higher-order cognition.

What Can We Learn from Computational Models? (M. Ito)

1. Importance of computational models in brain research

To understand how the brain works, we may start from neuroscience studies including comparative anatomy, lesion studies, and brain imaging, which would tell us where in the brain certain functions are localized. In prevailing cellular/ molecular neuroscience, we further examine hardware (e.g., neurons, synapses, and genes) implemented in neuronal

circuits along with certain design principles. Computational modeling is another unique approach, in which we mathematically formulate an overall goal of a neuronal circuit and mechanisms to achieve it. Given such a computational model, its performance can be reproduced in computers (brain in silico), and with parameters adjusted, will closely mimic that of real brain tissues. Many may hopefully agree that this approach leads us to the development of an artificial brain.

2. Computational models for the cerebellum

In the cerebellum, whereas its major areas are linked with motor systems, the D2 zone is linked with the cerebral association cortex, the ultimate center of cognition [29, 36, 228]. No distinct difference has been found at hardware levels between these cerebellar areas. Some may consider that a crucial element is still missing from the hardware of the cerebellum in cognition. Others may consider, however, that the cerebellum utilizes similar local modular circuits for both movement and cognition, but whether the cerebellum serves either movement or cognition depends on the overall system structures involving these modules.

Two types of computational model of the cerebellum have been developed: network models (such as the Simple Perceptron [229] and adaptive filters [230, 231] and control system models (such as the adaptive control [232] and model-based control [194]). These models well apply to the cerebellum for movement, but how to apply them to the cerebellum for cognition is a matter of discussion (see below).

3. Conceptual model as precursor

Once a computational model is available in an analogous case of other fields (for example, adaptive filters in signal processing [233]), it may readily be introduced into studies of the cerebellum. Otherwise, it will not be an easy task to conceive a new computational model. In such a situation, a “conceptual” model is considered as a possible precursor. For example, Hebb's [234] “neuron assembly” is a conceptual model of learning, from which Rosenblat's [229] Simple Perceptron emerged as a computational model. Indeed, conceptual models are often used to explain hypotheses in psychology. Because conceptual models are based on qualitative arguments, we cannot test their behavior rigorously using computers. Nevertheless, we may agree that they would help us find or develop a new computational model.

4. Analogy between thought and movement

The computational model of model-based control well applies to voluntary movement [117, 194]. When we move a limb, the primary motor cortex acts as the controller, and the limb connected to segmental neuronal circuits provides the controlled object. The cerebellum provides the internal model that simulates the controlled object or its inverse. Using the internal model, the primary cortex can perform control without external feedback and, consequently, skillfully even without conscious attention. As a formalistic analogy to movement, we considered a conceptual model of the thought process as a typical example of cognition [36, 117, 235]. In this model, the prefrontal cortex may act as the controller, which manipulates an idea expressed in the temporoparietal cortex as a controlled object. When the

idea is further represented in a cerebellar internal model, thought will proceed without conscious concern, as in intuition.

The above consideration ultimately leads to the question of how an idea is encoded in neuronal circuits of the temporoparietal cortex and cerebellum to be manipulated by the prefrontal cortex. Such a representation may be achieved as something similar to Craik's [236] and Johnson-Laird's [237] mental model or a Piaget's schema [238, 239]. These psychological conceptual models, however, presently cannot be expressed computationally.

5. Perspectives

The above-stated problem has been continuously raised over the past half century in the effort to develop an artificial intelligence that could reproduce human's capabilities of using language and forming abstraction and concepts [240]. Despite the great efforts so far devoted, this attempt has not been successful. Note, however, that this does not mean that it is impossible. Indeed, the human brain does express and process both movement and thought. However, we do not know yet how ideas, abstraction, or concepts are expressed and processed in neuronal circuits. Here, we face one of the most profound challenges in science that should be addressed through studies of the cerebellum.

How Does the Cerebellum Acquire Internal Models? (T. Yamazaki)

An internal model is a neural representation of the external world [239], and such models are necessary for fast and smooth information processing. An internal model of a body part, for example, reproduces the dynamics of that body part, in either a direct or inverse relationship. Based on predictions generated by internal models, feedback signals from the environment or other brain areas, which may be delayed and noisy but are necessary to converge the current state to the goal state, may be cancelled or simply discarded. Thus, internal models can turn a feedback system into a feedforward circuit that works identically. This internal model hypothesis may explain how conscious, voluntary movements are gradually brought under automatic control through repetition, as described in prism adaptation of dart throwing [241]. In this sense, conscious control is the principal pattern generator, and automated control through internal models is simply a copy of the pattern generated by conscious control. Internal model hypothesis has been adopted to not just motor area but even cognitive area to explain how our conscious thoughts mediated by frontal cortices are translated to unconscious process such as intuition, where an internal model of “thought” represented as spatiotemporal neural signals in prefrontal cortices is assumed to be acquired in the cerebellum [239].

In their intriguing article [242], Koziol et al. propose that the scenario is rather opposite. They hypothesize that the cerebellum first acquires internal models through sensorimotor interactions with the environment, and then uses these internal models to provide predicted signals to the cerebral cortex so that executive functioning can be used to conduct mental simulation or rehearsal. Through these executive functions, semantic or declarative knowledge is formed in the frontal cortex. In this way, procedural learning mediated by the cerebellum encourages the formation of declarative knowledge and conscious control. This

hypothesis echoes a recent theory of motor sequence learning [243], and it is attractive because it provides a scaffold from which to tackle difficult brain-mind problems.

From a theoretical viewpoint, an internal model can be thought of as a table of input–output relations, where both input and output signals carry spatiotemporal information about the represented object, not just static information. The cerebellum therefore has to learn pairs of spatiotemporal signals. In Koziol et al.'s scenario, the cerebellum has to comprehend the complete waveform of spatiotemporal neural activity exerted by the target object for mental simulation or rehearsal. How might the cerebellum accomplish such tasks?

Behavioral and electrophysiological studies have demonstrated that the cerebellum seems to learn pairs of spatiotemporal signals fed by mossy fibers and climbing fibers, respectively. In Pavlovian delay eyeblink conditioning, Purkinje cells exhibit a timed “pause” just before the onset of an unconditioned stimulus in response to a conditioned stimulus that triggers the conditioned response: anticipatory eyeblink [244]. This means that the Purkinje cells learn a delta-function-like waveform provided by climbing fibers in response to a constant input fed by mossy fibers. In a study of gain adaptation of the vertical vestibulo-ocular reflex (VOR), Hirata et al. demonstrated that squirrel monkeys acquire different VOR gains (high and low) in the upward and downward directions of head movement, which implies that Purkinje cells may respond differently to upward versus downward head rotation [245]. In phase adaptation of VOR, eye rotation either lags or precedes head rotation, with a certain phase difference [246], suggesting that Purkinje cells in the flocculus may elicit spikes sinusoidally with the phase difference in response to sinusoidally modulating signals fed by semicircular canals via mossy fibers. In any case, if Purkinje cells are able to store the complete waveform instructed by climbing fibers in response to the paired mossy fiber inputs, these experimental results can be explained.

Now, the central question is how might these cells do that? Theoretical studies have proposed mechanisms for waveform learning based on different mathematical operations such as Fourier series expansion by a set of temporal filters [247], or random projection by a random recurrent network [248]. A theoretical study has attempted to unify cerebellar gain and timing control mechanisms into one single computational principle [249]. These theoretical results rely on a critical hypothesis, in which cerebellar granule cells show temporally fluctuating spike patterns in response to mossy fiber signals. Single-unit recordings of granule cells from awake animals in fine temporal resolution may be helpful to examine the activity of granule cells.

In sum, the cerebellum, a versatile supervised learning machine of spatiotemporal information, plays a key role in forming internal models (Fig. 8). The machine does not just learn scalar information such as gain or timing, but rather it learns the complete waveform of neural activity instructed by climbing fibers. These observations may shed new light on the role of the neuronal circuits within the cerebellum called microcomplexes, beyond the traditional Marr–Albus–Ito model.

Summary and Conclusions

A total of fourteen experts contributed to this twelve manuscript consensus paper on the topic of the role of the cerebellum in movement and cognition. The authors of each paper were provided copies of all other contributions and were asked to review and provide critical comments. The authors of six separate contributions responded with specific statements of agreement/disagreement. Most contributors were in complete agreement with the hypotheses generated in all papers. One contributor had reservations about how the actual “blending” of cerebellar control models might contribute to language development. However, overall, we are hard pressed to find any disagreement with respect to any contributor's position. Perhaps this was because the conclusions remain hypothetical while based upon accepted neuroscientific principles. Similarly, while experts in the investigation of the cerebellum and its pathologies were asked to participate, we were also hard pressed to find a potential contributor who disagreed with the proposed topic. The following summary and conclusions are justifiable based upon the aggregate of manuscripts that were collected.

First, there is unanimous agreement that the cerebellum plays a role in both movement and cognition. While historically, the cerebellum was considered solely as a co-processor of movement, working in concert with the basal ganglia and the cerebral cortex, this narrow viewpoint is no longer defensible. As Dr. Ramnani stated, the question posed today is not whether or not the cerebellum plays a role in cognition, but instead, how the cerebellum contributes to cognitive processes. This conclusion has been offered on the basis of evolutionary reviews of the cerebellum's developmental expansion, including an examination of the role of the cerebellum ascending along the phylogenetic scale [250]. Of particular interest is Dr. Vandervert's hypothesis concerning the neurobiologic co-evolution of the cerebellum and the neocortex coinciding with the development of tool use and language. This hypothesis was similarly proposed by Dr. Marvel. This simultaneous biologic and functional development appears to be reflected today in studies of tool use and cognitive processes, as described by Dr. Imamizu. Dr. Ito cautions that the role of the cerebellum in cognition remains a psychological conceptual model that has not yet been demonstrated computationally. However, he did not question the contributory role of the cerebellum in thinking. In fact, in previous papers, he developed a hypothesis as to how the cerebellum employs the same mechanisms in manipulating movements and thought [117]. Dr. Yamazaki has presented a preliminary review as to how computational modeling might contribute to understanding how the cerebellum might acquire internal models that govern both movement and thinking. The somewhat ambiguous concept of “blending” cerebellar control models is similar to the concept introduced by Dr. Schmahmann concerning the Universal Cerebellar Transformation, or UTC. This concept is analogous to Dr. Riva and colleague's characterization of the cerebellum as a “homeo-static orchestrator,” and Parker and Andreasen's concept of “synchrony” in the coordination of sequences of both action (movement) and thought. These viewpoints might also be considered foundational to conceptualizations of the cerebellum as a versatile “supervised learning machine” that constructs or generates internal models for the control and adaptation of behavior across contexts. This is also consistent with the view that the cerebellum is critical to motor and cognitive automation and adaptation as reviewed by Dr. Ramnani, and as supported by

others such as Nijokiktjien [251]. In other words, it is almost as if the contributors are describing extremely similar processes while using somewhat different vocabularies.

In this regard, there is a general agreement that the cerebellum forms internal models for the coordination of movement and thought. These models appear to serve a modulatory or coordinative role in predicting sensorimotor feedback and/or thought and behavioral outcomes. Dr. Vandervert reviewed how this role can be considered in terms of anticipation, or the appreciation of cause-and-effect relationships. Dr. Pezzulo has summarized that these internal models appear to regulate movement and cognition in a similar way. This conclusion is further exemplified again in Drs. Ramnani's, Marvel's and Schmahmann's comments that the cerebellum generally performs a common function whether in support of movement or cognition. Furthermore, there is a generalized agreement that the cerebellum is topographically organized in regards to function, that the cerebellum assists working memory, perhaps by copying neocortical content [239], and that the cerebellum contributes to learning, automaticity, and behavioral adaptation through the cerebro-cerebellar circuitry system as described by Dr. Schmahmann. Dr. Schmahmann briefly but comprehensively described the cerebro-cerebellar and climbing fiber "olivary" circuitry systems, including his linking the Principal Olive (PO) with the lateral "cognitive" cerebellar hemispheres and those regions of the dentate nucleus specifically involved in cognition. He provided the analogy that the olivary system enables error detection and correction, critical functions for both motor and cognitive control. These systems, functioning in an integrated or "homeostatic" way, allow for generating hypotheses that the UCT plays a critical function even in the preparation, coordination, and adaptation of eye and limb movements, through posterior parietal-premotor connections, that are necessary for the development and automation of certain skills and cognitions. The fact that reductions in cerebellar activity accompany learning and automaticity and that increases in cerebellar activity accompany errors by comparing intended versus actual behavioral outcome also supports the proposal that the cerebral cortex stores or retains the most efficient representation of the behavior [252]. Similarly, this is consistent with Dr. Manto's conclusion that malfunction of the cerebellum could have a more dramatic impact upon cognitive operations than no cerebellar functioning at all, a viewpoint shared by Lalonde and Strazielle [99]. The previous hypotheses would be applicable to adults, while Dr. Riva and colleagues provide insights into how the role of the cerebellum in cognition is situated within a developmental process, likely dependent upon age and neurobiologic maturity.

While all contributors agree that the cerebellum plays a role in cognition, there is also agreement that this conclusion remains highly inferential. The study of cerebellum's role in cognition remains in its infancy. Many conclusions about the role of the cerebellum in cognition originate from applying known information about cerebellar contributions to the coordination and quality of movement. These inferences are based upon the uniformity of the cerebellum's compositional infrastructure and its apparent modular organization. There is considerable support for this view, based upon observations of patients with pathology within the cerebellum [49, 62, 68, 253–256]. Additionally, there are numerous studies of normal control subjects while comparing actual and imaginary tool use, as reviewed by Imamizu and others [179, 194, 219, 220, 223, 257]. Dr. Parker's and Andreasen's comments are particularly integrative in their review of cerebellar functions in thought in relation to

psychosis, a position also summarized in Dr. Schmahmann's succinct review of a cerebellar role in every domain of functioning through the cerebro-cerebellar circuitry system, and as exemplified in the Cerebellar Cognitive Affective Syndrome, or CCAS.

This overview of the cerebellum's role in cognition is very preliminary. However, progress has been made in acceptance of the general idea that the cerebellum is critical to cognition and its development. This progress comes within the context of a larger movement toward understanding the human brain as functioning as an ensemble, rather than a fragmented collection of regions and abilities [258–261]. In this way, the neocortex can no longer be viewed simply as the sole or primary driver of thinking and behavior, but instead, a new paradigm conceptualizing distinct brain regions as operating in an integrated way is a necessary model for investigating and understanding human cognitive and behavioral functions.

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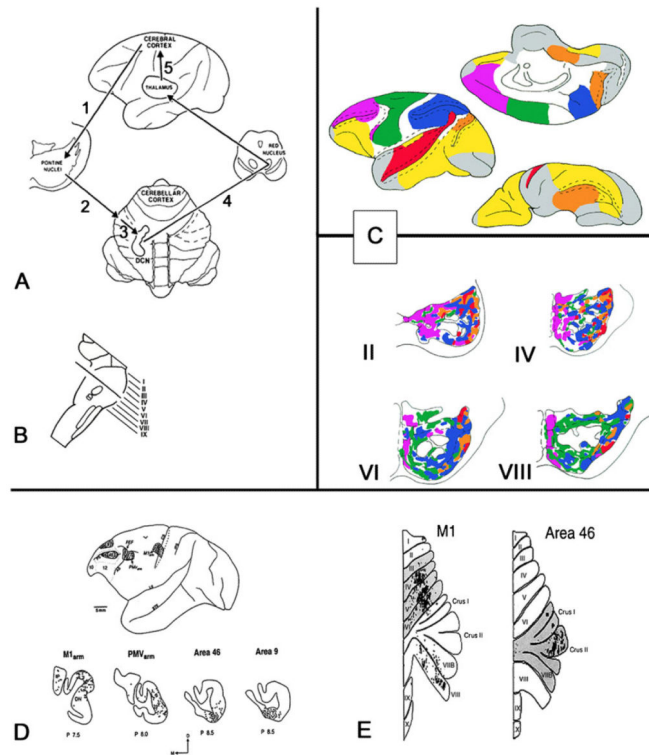
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**Fig. 1.**

a Diagram of the cerebro-cerebellar circuit. Feedforward limb: the corticopontine pathway (1) 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 (2). Feedback limb: the cerebellar cortex is connected with the deep cerebellar nuclei (3), which course through the midbrain in the vicinity of the red nucleus to terminate in the thalamus (the cerebello-thalamic projection, 4). The thalamic projection back to cerebral cortex (5) completes the feedback circuit. **b** Plane of section through the pons from which the rostrocaudal levels II through VIII are taken in the schematic (c). **c** Composite color-coded summary diagram illustrating the distribution within selected regions of the basis pontis of projections from association and paralimbic areas shown on medial, lateral, and orbital views of the cerebral hemisphere in the prefrontal (*purple*), posterior parietal (*blue*), superior temporal (*red*), and parastriate and parahippocampal regions (*orange*) and from motor, premotor, and supplementary motor areas (*green*). Other cerebral areas known to project to the pons are depicted in white. Cortical areas with no pontine projections are shown in *yellow* (from anterograde and retrograde studies) or *gray* (from retrograde studies). *Dashed lines* in the hemisphere diagrams represent sulcal cortices. *Dashed lines* in the pons diagrams represent pontine nuclei; *solid lines* depict corticofugal fibers. **d** Lateral view of monkey brain (*top*) shows the locations of viral tracer injections in the M1 arm, PMv arm, and prefrontal cortex areas 46 and 9. The resulting retrogradely labeled neurons in the cerebellar dentate nucleus (*bottom*) are indicated by solid dots. **e** Flattened representation of cerebellum to show the folia linked with M1 motor cortex (*left*) and prefrontal cortex area 46 (*right*) using viral tracers that travel in the anterograde direction (H129 strain of HSV1) and retrograde direction (rabies

virus). **a–c** reproduced and adapted from Schmahmann [62] and Schmahmann and Pandya [34, 35, 51]; **d** from Middleton and Strick [208]; **e** from Kelly and Strick [30]

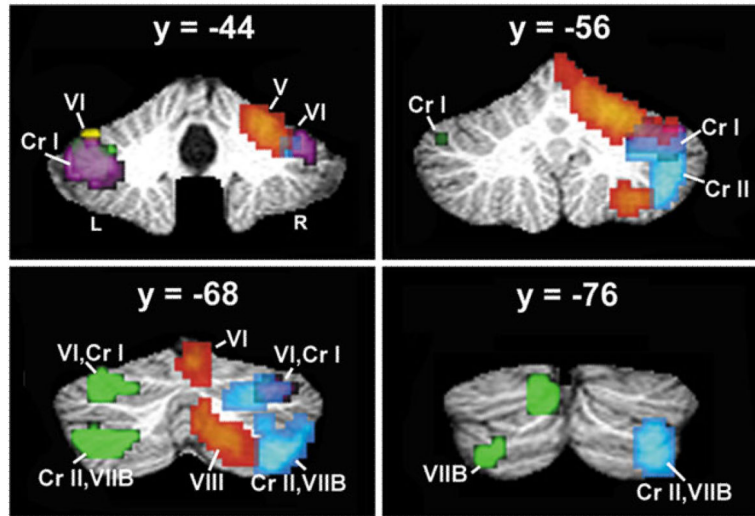


Fig. 2. Coronal slices through the cerebellum of a single individual showing topographic arrangement of fMRI activation patterns for tasks of finger tapping, color coded in *red-orange*; verb generation, *blue*; n-back, *purple*; mental rotation, *green*; and International Affective Picture Rating Scale, *yellow*. Left cerebellum is on the *left*, and coronal levels at $y=-44$, -56 , -68 , and -76 are shown. Activations are present in cerebellar lobules V, VI, Crus I, Crus II, VIIIB, and VIII, as labeled. (Reproduced from Stoodley et al. [262]. Nomenclature of cerebellar lobules as in Schmahmann et al. [263])

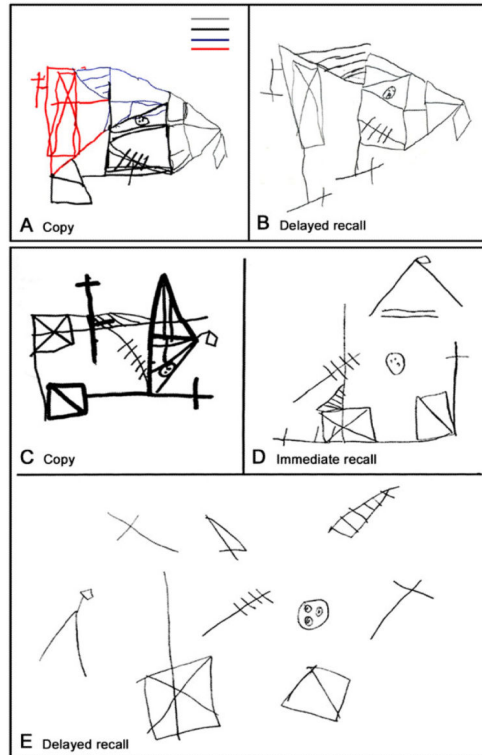


Fig. 3. Visual spatial disintegration in the cerebellar cognitive affective syndrome. **a** Copy of the Rey figure by a 15-year-old boy with near-total cerebellar agenesis showing piecemeal performance rather than overall conceptual understanding of the figure. Diagram drawn using pencil, then *black*, *blue*, and *red* pen sequentially. **b** Delayed recall of the figure showing impaired recall and design. Performance on the Rey figure by a 6-year-old boy after resection of a left cerebellar cystic astrocytoma is shown in **c** copy, **d** immediate recall, and **e** delayed recall. Concept, design, and recall are impaired, with fragmentation of the image in (e) reminiscent of loosening of associations as may be seen in a psychiatric context. (**a**, **b** from Chheda et al. [63]. **c**, **d** from Levisohn et al. [61])

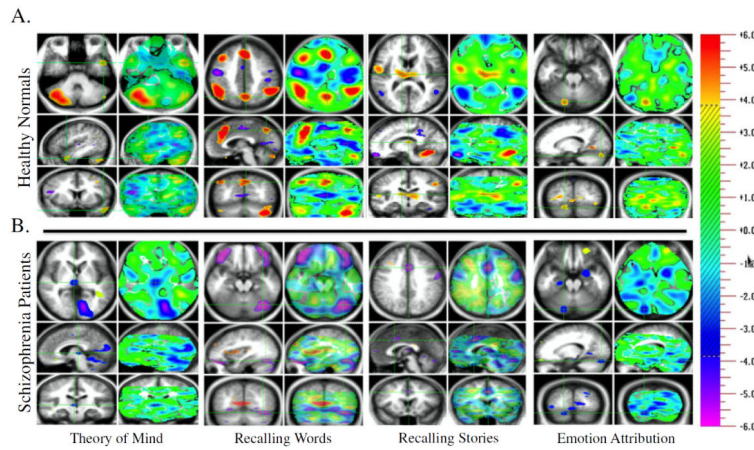


Fig. 4. Schizophrenia patients (a) have significantly less cerebellar blood flow than healthy normals (b) during several cognitive tasks: (1) theory of mind, (2) recalling words, (3) recalling stories, and (4) emotion attribution. Representative images from each task were chosen to illustrate cerebellar recruitment during each of these cognitive tasks. Images follow radiological convention. Regions in *red/yellow* tones indicate positive peaks and regions with *blue/purple* indicate negative peaks. Each cognitive task is organized by two columns containing a threshold on the right (significant differences at the 0.005 level) and global blood flow column subdivided by slice orientation axial (*top*), sagittal (*middle*), and coronal (*bottom*) on the *left*. Statistical results are portrayed using the value of the associated *t* statistic, which is shown on the *color bar on the right*

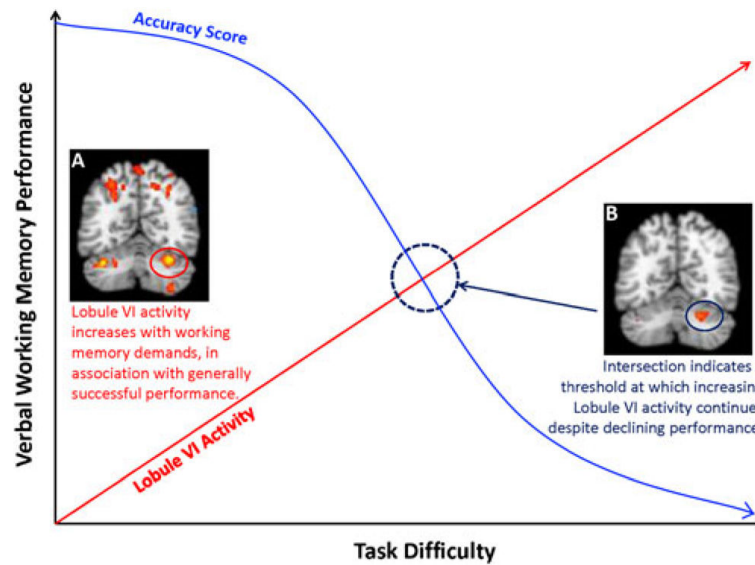


Fig. 5. Schematic illustrates the relationship between superior cerebellar lobule VI activity and verbal working memory performance. Neuroimaging results from young, healthy adults performing a high vs. low load VWM task (149) showed that (a) activity in superior cerebellar lobule VI increased specifically in response to high load working memory demands, and (b) that this activity was inversely correlated to overall performance accuracy ($r=-0.79$). Increased lobule VI activity may reflect the temporal sequencing of motor traces representing inner speech. This strategy continues even when performance begins to decline, indicating an ongoing struggle to keep up with working memory demands. In (a) and (b), $p<0.001-0.00001$

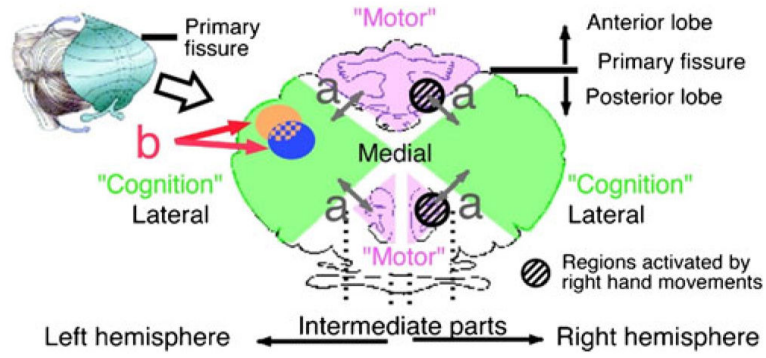


Fig. 6. Flattened view of cerebellar surface illustrating that the anterior lobe and intermediate parts of the posterior lobe are related to “motor and somatosensory functions,” whereas the lateral posterior cerebellum is related to “cognitive functions.” To orient properly to the anterior/posterior axis of the flattened view, the viewer should keep in mind that anterior/posterior refer to what is actually a substantially convex cerebellar surface (see smaller drawing to left). *Arrows in (a)* indicate difference between “motor” (note modularity of somatotopic maps at *top* and *bottom*) and “cognition” found in previous neuroimaging studies. *Arrows at (b)* indicate modularity within the lateral posterior cerebellum for two different cognitive functions. (Adapted from Imamizu et al. [179], p. 5461). Copyright 2003 by Hiroshi Imamizu. Reprinted with Permission



Fig. 7.

An example of *embodied problem solving*. During climbing competitions, before climbing an unknown route, athletes can pre-view it for some minutes; they typically mimic, imagine, and plan their future climbing movements (in the picture, they do this overtly, but this is not always the case). This is a complex problem solving, as (route settlers ensure that) the sequence of movements to reach the top of the wall is novel and far from trivial. It depends on goal state (the climbing hold to reach) and previous movements. Furthermore, it incorporates the athlete's embodied knowledge, as length of limbs, strength of fingers, affordances offered by the various kinds of climbing holds, possible or impossible kinematics, all constraint the problem solving process. Part of the athletes' skill is in the ability to anticipate relevant information (proprioceptive, body posture at critical points, how much force to use, etc.) prior to climbing, to form motor plans, and to maintain and refine them in memory before climbing. We reported in Pezzulo et al. [218] an advantage of expert climbers in a memory task (i.e., remembering sequences of holds in a route) but only when “climb-ability” constraints were respected (not when the sequences formed a nonclimbable route)

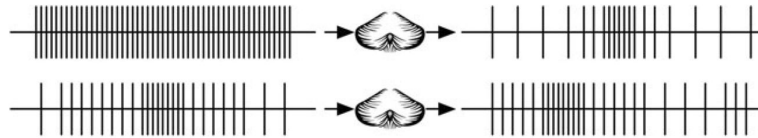


Fig. 8.

Schematic illustration of a cerebellar internal model learning spatiotemporal information. *Top* In eyeblink conditioning, the cerebellar internal model (drawing of the cerebellum in the middle) receives a spike train that is temporally constant (conditioned stimulus, left) and exerts another spike train that modulates in time maximally at the onset of an unconditioned stimulus (right). *Bottom* In phase adaptation of the vestibulo-ocular reflex, the internal model receives a spike train that modulates sinusoidally from semicircular canals and exerts another sinusoidally modulating spike train with a certain phase difference. In this way, an internal model is a general-purpose supervised learning machine of pairs of spatiotemporal signals. Horizontal bar, time axis; vertical bars, spikes

Table 1

Deficits that characterize the cerebellar cognitive affective syndrome

1. Executive function

Deficient planning, motor or ideational set-shifting, abstract reasoning, working memory. Decreased verbal fluency, sometimes to the point of telegraphic speech or mutism. Perseverative ideation in thought and/or action.

2. Spatial cognition

Visuospatial disintegration with impaired attempts to draw or copy a diagram. Disorganized conceptualization of figures. Impaired visual-spatial memory. Simultanagnosia in some.

3. Linguistic difficulties

Anomia, agrammatic speech, and abnormal syntactic structure, with abnormal prosody.

4. Personality change

Aberrant modulation of behavior and personality with posterior lobe lesions that involve midline structures. Manifests as flattening or blunting of affect alternating or coexistent with disinhibited behaviors such as over-familiarity, flamboyant and impulsive actions, and humorous but inappropriate and flippant comments. Regressive, childlike behaviors and obsessive-compulsive traits can be observed (see Table 2).

Table 2

Neuropsychiatric manifestations in patients with cerebellar disorders, arranged according to major domains, each with positive and negative symptoms

| | Positive (exaggerated) symptoms | Negative (diminished) symptoms |
|---------------------|---|--|
| Attentional control | Inattentiveness | Ruminativeness |
| | Distractibility | Perseveration |
| | Hyperactivity | Difficulty shifting focus of attention |
| | Compulsive and ritualistic behaviors | Obsessional thoughts |
| Emotional control | Impulsiveness and disinhibition | Anergy and anhedonia |
| | Lability and unpredictability | Sadness and hopelessness |
| | Incongruous feelings and pathological laughing/crying | Dysphoria |
| Autism spectrum | Anxiety, agitation, and panic | Depression |
| | Stereotypical behaviors | Avoidant behaviors and tactile defensiveness |
| | Self stimulation behaviors | Easy sensory overload |
| Psychosis spectrum | Illogical thought | Lack of empathy |
| | Paranoia | Muted affect and emotional blunting |
| | Hallucinations | Apathy |
| Social skill set | Anger and aggression | Passivity, immaturity, and childishness |
| | Irritability | Difficulty with social cues and interactions |
| | Overly territorial | Unawareness of social boundaries |
| | Oppositional behavior | Overly gullible and trusting |

From Schmahmann et al. [68]

Table 3

Cognitive/behavioral deficits observed in SCAs

| SCA subtype | Deficit | Selected references |
|-------------|---|---------------------|
| SCA1 | Mental deterioration | [101–104] |
| | Emotional lability | |
| | Perseveration | |
| | Defective verbal memory | |
| | Executive dysfunction | |
| SCA2 | Dementia | [105–108] |
| | Executive dysfunction | |
| | Impairment of verbal memory | |
| | Impulsiveness | |
| | Anxiety | |
| | Depression | |
| SCA3 | Executive dysfunction | [109–113] |
| | Impairment of verbal memory | |
| | Depression | |
| | Apathy | |
| SCA6 | Slight evidence of defective verbal memory and verbal fluency | [114] |
| SCA13 | Non progressive mental retardation | [115] |
| SCA17 | Prominent psychiatric and behavioural symptoms | [95] |
| | Executive dysfunction | |
| DRPLA | Dementia | [116] |
| | Seizures | |
| | Psychiatric symptoms | |

Only SCAs with detailed neuropsychological reports are considered