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CEREBELLAR NONMOTOR FUNCTIONS – APPROACHES AND SIGNIFICANCE

The cerebellum is involved in the control of motor and nonmotor functions. Refined and innovative experimental and clinical approaches, starting from anatomy and including functional magnetic resonance imaging (fMRI), have allowed researchers to store extensive information on the cerebellar contributions to motor control and also helped them to understanding cerebellar nonmotor functions. Does the cerebellum process exclusively cerebral information related to certain specific actions, or does it also process some forms of information independent of such relation? At present, researchers are close to evaluating how the cerebellum is active during resolution of cognitive tasks. Various therapy lines in perspective, from cerebellar stimulation to cerbellar grafts and artificial cerebellum, are of particular significance, as they can restore lost brain functions in animal models and repair insufficient brain processes in patients.

INTRODUCTION

The functions of the cerebellum are not restricted, as was traditionally believed within the past century, to the regulation of locomotion, muscle tone, equilibrium, and coordination of somatic motor activity. At present, it has been suggested that these functions are also related to tasks designed to assess attention, executive control, language, working memory, learning, pain, and emotions [1-4]. Dissection approaches in the research of cerebellar motor control were described in one of the first books on cerebellar physiology [5]; experimental and theoretical data on the structure and functions of the cerebellum are presented in the textbook [6], while a comprehensive handbook [7] provides immense amount of knowledge acquired on the cerebellar motor and nonmotor functioning. The purpose of our review is to point out the progress in various basic and clinical explorations, which enrich our understanding of cerebellar nonmotor functions and suggest possible therapeutic applications.

Experimental Approaches in the Studies of the Cerebellum. **Dissection Approaches.** Extensive data on the structure and functions of the cerebellum were obtained since the first description of cerebellar cortical cells at the light microscopy level [8]. Classic findings were the following: mossy fibers project to cerebellar granule cells, each of which gives rise to a long parallel fiber. Each such fiber forms synapses on the dendritic trees of 400-500 Purkinje cells (PCs), while each PC receives a strong synaptic input from a single climbing fiber [9]. There are divergent axonal projections of single catecholamine neurons, localized in the *locus coeruleus*, to the cerebellum, spinal cord, and frontal cortex [10]. Besides the well-known five types of cerebellar neurons, inhibitory units (stellate, basket, Golgi neurons, and PCs), excitatory units (granular cells), and also unipolar brush cells (small glutamatergic interneurons) and Lugaro GABAergic cells were discovered [11-13]. The cerebellum is connected not only to the motor cortex, but also to brain areas relevant to arousal, cognition, and behavioral phenomena. Among these structures, there are the reticular system [14, 15], dorsolateral prefrontal cortex, medial frontal cortex, parietal and superior temporal cortical areas, anterior cingulate cortex, and posterior hypothalamus [16, 17]. Quite later after the first electrophysiological recordings from the animal cerebellum [18], the first demonstration of the powerful climbing fiber-related responses in PCs, named complex spikes [19], and firing of PCs by simple spikes induced by volleys of

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parallel fibers [20], the hypothesis of the vestibulo-ocular reflex (VOR) control was proposed [21, 22]. It was suggested [23] that intricate neuronal circuitry of the cerebellum can encode internal models essential for movement control of body parts, and the cerebellum might also encode internal models that reproduce essential properties of mental representations in the cerebral cortex.

There is a new interpretation of the information flow through the granular layer in the cerebellar cortex of awake primates [24], in which mossy fiber input patterns drive the responses of granular-layer interneurons not only through excitatory but also through inhibitory network pathways. Weaker moderation of the excitability and action potential waveforms in granule cells of the Ts65Dn mouse strain (a model of Down's syndrome) by tonically active $GABA_A$ receptors is likely to contribute to the atypical transfer of information through the cerebellum [25]. Specific nonrandom connectivity patterns in interneuronal networks connected by both GABAergic chemical and electrical synaptic contacts are essential for the function of the cerebellar cortical network [26]. Defective leptin receptors affect the electrophysiological properties of cerebellar PCs in a rodent model for obesity and type-2 diabetes [27]. Motor memories are postulated to be stored in the form of long-term depression/potentiation not only at parallel fiber synapses with PCs, but also at several other synapses mostly dependent on calcium (reviewed in [28]). Purkinje cells disinhibit their climbing-fiber afferents via polysynaptic circuits and could take part in the regulation of cerebellar motor learning [29].

Properties of the vermis and fastigial nuclei ("limbic cerebellum") are significant for therapeutic strategies [30]. It has been emphasized [4] that the cerebellum output affects multiple motor and nonmotor areas of the cerebral cortex, and that these cerebral cortical areas represent a major source of inputs to the cerebellar channels. A closed-loop circuit represents the major architectural unit of cerebro-cerebellar interactions capable of modulating movements and cognition. The effects of a repetitive typing task on the amplitude changes in somatosensory evoked potentials (SSEPs) implied the reduced inhibition at the level of the cuneate nucleus and/or inferior olives leading to alterations in cerebellar-cortical processing [31]. Morphological alterations in the prefrontal cortex following bilateral electrolytic lesions of the rat cerebellar dentate nuclei implicate a cerebellar role in nonmotor (visuospatial and motivational)

processes [32]. Insights are provided into the neural dynamics of the reciprocally connected networks underpinning fastigio-cerebellar and fronto-cerebellar communications [33]. Information on contributions of the cerebellar interposed nucleus is collected in a review [34].

There is a lot of evidence that brain systems generate a number of rhythmic activities, and the cerebellum is not an exception [35]. Analysis of electrocortical activity of the cerebellum revealed that this brain structure in humans can express all series of the rhythms [36, 37]. Estimations of relative mean power spectra, spectral entropy, and fractal dimensions can be successfully used to describe cerebellar activity in various pathophysiological states and also in anesthesia states in animal models [38-40]; the respective information could be useful for improving diagnostic procedures. A reanalysis of the human intracranial electrocerebellograms (see reports from the Soviet Union published in 1949-1951 and those from Belgium published in 1964) [41] demonstrated that there are electrical rhythms in the human cerebellar cortex having frequencies up to 250 Hz, which can bridge the cerebellar oscillatory networks with those of the cerebral cortex in mediating perception, actions, and cognition.

Destruction Approaches to the Cerebellum. The destruction experimental approaches used within the last decades give an indication of cerebellar functions subserved by damaged cerebellar tissue. The neuropsychological study describing survivors of childhood cerebellar tumours [42] indicated that the cerebellar cognitive affective syndrome is evident in both children and adults. The detailed neuropsychological examination of patients with cerebellar lesions due to a tumor or a hematoma and of adequate controls [43] indicated that cerebellar lesions lead to a "dysmetria of thought." Moreover, voxelwise statistical analysis confirmed somatopic representation within the superior cerebellum in patients with focal cerebellar lesions. Somatotopic localization was also found in the cerebellar nuclei. Lesions of the fastigial nuclei were described to be related to ataxia of stance and gait, while lesions of the interposed and adjacent dentate nuclei were related to limb ataxia and dysarthria [44]. Human lesion studies showed evidence that the cerebellum is involved in motor, emotional, and cognitive associative learning (reviewed in [45]). The involvement of the cerebellum and its functional interaction with the basal ganglia in proactive control of behavior and error monitoring was

reported in the study of patients with focal cerebellar damage [46].

Genetic Approaches to the Cerebellum. Genetic experimental approaches help to understand cerebellar functions and the nature of human diseases, which have their roots in the developmental processes [47]. Concentrated c-Fos expression in the medial vestibulocerebellum after exposure to a strong head velocity spatial signal suggested that granule and unipolar brush cells participate in a neuronal network for estimating the velocity of head movements, irrespective of the signal source [48].

The number of genes that, when mutate, cause disruption in cerebellar functioning is increased, and studies on spontaneous and engineering mouse mutants were crucial to this progress [49]. A study on an animal models of *sclerosis tuberous* (a genetic disorder characterized by autistic features) [50] showed that loss of the function of the gene *TSC1* in cerebellar PCs in mice induces an autism-like phenotype, which can be prevented by treatment with rapamycin (an immunosuppressive drug). Despite good graft survival and the presence of graft-derived Purkinje cells in a type-2 transgenic mice model of spinocerebellar ataxia, the structure of the graft did not show any significant specific functional effects. Nonetheless, further search for ways of enhancement of connections between the graft and the host is promising [51].

The evolution of diversity of the cerebellar nuclei in amniotes may, hence, reflect a heterochronic adaptation of gene expression with respect to the sequential production of the rhombic lip derivatives resulting in altered axonal targeting [52]. In order to investigate the roles of plasticity at cerebellar inhibitory synapses *in vivo*, transgenic mice were generated; these mice express GABA$_A$ receptor-associated protein fused to a fluorescent protein selectively in PCs [53]. Furthermore, the PC-specific vesicular GABA transporter-knockout mice (that express GABA$_A$ receptor-associated protein fused selectively to a fluorescent protein in PCs using the PC-specific L7 promoter) are introduced as a novel model of ataxia with no PC degeneration, and the respective research would also be useful for studying the role of PCs in cognition and emotions [54].

Genetic strategies for achieving specific and robust labeling of neurons (including cerebellar cells) in mice result in recapitulation of the expression pattern of an endogenous gene with that of exogenous marker genes [55]. The respective approach uses genetic elements and techniques to label subsets of neurons in a large-scale scheme. There is a need for evaluation of the *C9orf72* promoter hypermethylation in a larger group of c9FTD patients suffering from amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) and for assessing whether DNA methylation variation across brain regions could reflect the disease phenotype [56].

Cerebellar Neuroimaging. Since the first published functional mapping of the human cerebellum [57], there is a great body of evidence for the cerebellar involvement in motor and nonmotor activities by a powerful experimental approach of functional imaging. It has been pointed out that, due to the relatively small spatial size, functional heterogeneity, and susceptibility to physiological artifacts, the human cerebellum in MRI research is far from clear concerning what neurophysiological processes drive the cerebellar BOLD (blood oxygenation level-dependent) signal [58]. It is known that, in the cerebrum, neural activity correlates with increase in the cerebral metabolic rate of oxygen consumption (CMRO$_2$); this initially increases the local concentration of deoxyhemoglobin and then leads to a compensatory increase in the intensity of cerebral blood flow (CBF). In the neocortex, the BOLD signal appears to reflect mostly postsynaptic activity caused by efferent regional and recurrent excitatory inputs to the cortical region. At the level of single cerebellar dentate neurons, firing patterns of the cells excluded sufficient alternations in the flow of oxyhemoglobin to produce measurable signals [59]; it does not necessarily mean that working memory exerts a weak influence on dentate neurons [60]. Cerebellar BOLD signals depend on how much energy (and, hence, oxygen) these processes require, and how they influence the local blood flow. Recent calculations led to the estimation that granule cells use 67% of energy, while PCs use only 18% of metabolic energy in the rat cerebellar cortex [61]. If blood flow increases proportionally to the energy use, it means that activity-dependent BOLD signal changes are mainly caused by increased signaling in the mossy fiber or parallel fiber systems. For the mossy fiber system, there is a tight coupling between the intensities of activity of this system and blood flow. For the climbing fiber systems, this relationship is, however, not clear. Climbing fiber inputs provide a major source of blood flow modulation. After inferior olive lesion, whisker stimulation produced only 42% of the blood flow increase observed in sham-lesioned rats [62]. Increasing complex- and simple-spike firing rates in PCs under conditions of

pharmacologically removed inhibitory inputs from interneurons increase $CMRO_2$ but not CBF [63]. According to these results, increases in the complex-spike rates would lead to a decrease in the BOLD signal.

Neurostimulation Techniques and the Cerebellum. The possibility that feedback relations between the cerebellum, septal region, and hippocampus are involved in epilepsy and emotional disorders has been considered [64]. It was found that stimulation through the cerebellar vermis inhibited epileptiform EEG activity in monkeys. Stimulation of the lateral cerebellar nucleus in an acute rat model of generalized epilepsy [65] resulted in decrease in the mean total EEG power spectra. It was suggested [66] that stimulation of the superior cerebellar peduncle can change the convulsive manifestation expression of amygdalar kindling in rats. Low-frequency electrical stimulation of the cerebellar cortex was effective in decreasing motor seizures and in reduction of generalized tonico-clonic seizures in the double-blind study [67]. A review of the terms "cerebellar," "epilepsy," "stimulation," "treatment," and all their combinations in the PubMed medical database [68] gave the conclusion that cerebellar stimulation is still worth exploring for defining its potential in the treatment of medically intractable epilepsy. With the use of repetitive transcranial magnetic stimulation (rTMS), it was found that the cerebellum is essential in explaining temporal processing of millisecond-range time intervals [69]. The experiments showed that it is a useful non-invasive technique for exploring cerebellar physiology and functions in humans [70]. An fMRI study and anodal transcranial direct-current stimulation of the right cerebellum showed that the latter structure interacts with the posterior parietal cortex, especially during late stages of verbal encoding, when verbal information enters the phonological storage [71]. A review of studies of the cerebellar role in nonmotor functions using noninvasive brain stimulation suggests methodological improvements for the establishment of standards for the location of cerebellar stimulation targets and appropriate levels of stimulation [72]. Noninvasive neurostimulation techniques can modulate human cognitive and motor functions, and new studies should be useful for patients with cerebellar dysfunction, psychiatric disorders, and those undergoing neurorehabilitation to enhance neuroplasticity [73, 74].

Cerebellar Nonmotor Functions. The Cerebellum and Cognition. In consideration of the cognitive functions, speech is one of the most complex phenomena and tasks. A study of neural systems underlying translation and language switching [75] revealed contrasting patterns of activation for the above processes (translation and switching), suggesting at least partially independent mechanisms. Translation, but not switching, intensified activity in the anterior cingulate and subcortical structures and decreased activation in several other temporal and parietal language-related areas associated with the meaning of words. Translation also increased activation in the regions associated with articulation (anterior insula, cerebellum, and supplementary motor area). A study of the brain regions involved in overt production of vowels, monosyllables, and disyllables [76] showed that lateralized activity of the left premotor cortex supports predictions of the DIVA (Directions into velocities of articulators) model of speech production, and that the superior paravermal cerebellum was more active for consonant-vowel syllables compared with vowels. A recent study provided evidence of the significance of the neocerebellum in semantic associative computations [77].

The left hemisphere of the frontal lobes and the right side of the cerebellum are responsible for language comprehension [78]. Cerebellar asymmetry includes mirroring of the prominent cerebral asymmetries for language and attention [79]. Studies using a combination of fMRI and two simple cognitive tasks (silent counting forward and backward) [80-81] showed that, besides the conventional language areas, stronger activation in the right cerebellum in the task of counting forward than of counting backward was manifested. The hypothesis [83] was confirmed that the hippocampus interacts functionally with both hemispheres of the cerebellum to establish the spatiotemporal prediction of actual movements, but not of reactive motor tasks and imagery. Meta-analysis of the cerebellar contributions to higher cognition [84] showed a consistent cerebellar presence in the timing domain. It was revealed that the cerebellum is critically implicated in social cognition [85], particularly in a set of mental conditions when the level of abstraction is high. The role of the cerebellum in cognition originates from applying known information on cerebellar contributions to the coordination and quality of movements [86].

The Cerebellum in Affects, Psychoses, Drug Addiction, Pain, and Autonomic Functions. A great body of experimental and clinical data suggests the involvement of the cerebellum in modulation of affects

and emotions (reviewed in [87]). It was found that the cerebellar vermis is related to emotional memory consolidation, and a histamine H2 receptor antagonist, ranitidine, applied to the cerebellar vermis impaired this consolidation in mice re-exposed to the elevated plus maze [88].

The modulatory cerebellar "gate control" is impaired in the pseudobulbar affect, characterized by disparity between the patient's emotional expression and patient's emotional experience [89]. The potential role of the cerebellum in the control of emotions could be required for observing and reacting to another person's negative expressions in goal-directed behavior [90].

Cerebellar abnormalities occur in schizophrenia (reviewed in [91]). Cerebellar atrophy was suggested in patients with bipolar disorders or mania [92]. Autistic patients showed abnormalities typical of cerebellar and parietal-lobe dysfunction [93]. Cerebellar changes commonly observed in autism, schizophrenia, and other cognitive disorders could result in loss of the functionality of the cerebellar–medial prefrontal cortex circuitry manifested as aberrant dopaminergic activity in the medial prefrontal cortex (shown in the study on mice) [94]. The manner in which cerebellar pathology may contribute to the symptoms and characteristic features associated with autism-spectrum subtypes started to come into view [95]. Concerning drug addictions, it was suggested that verbal working memory in opioid-dependent individuals is impaired, and a disrupted cerebro-cerebellar circuit is involved [96].

Purkinje cells respond to nociceptive visceral and somatic stimulation in the form of early and delayed changes in their activity; it was proposed that a cerebellar negative feedback circuitry was involved in modulation of peripheral nociceptive events [97]. A supposition for the role of the cerebellum in affective aspects of pain perception was supported [98]. It was concluded that the cerebellum might play a potential antinociceptive role, probably through indirect activation of descending inhibitory pathways [99].

The cerebellum is involved in basic autonomic functions and primary emotions. A review [100] points out that the cerebellum exerts noticeable influence not only on the defense reactions and feeding phenomena, but also on cardiovascular, gastrointestinal, and urinary bladder adjustments. The involvement of the cerebellum in thirst was confirmed [101]; the cerebellum was activated during changes in the thirsty satiation state when the brain was

"vigilant." Investigation of cerebellar-conditioned anticipatory activity in the state of a visceral aversive fear in healthy humans showed that the cerebellum is involved in the abdominal pain-related associative learning processes [102].

The Cerebellum in Aging and Dementia. There was a 10 to 40% decrease in the PC layer [103] and a reduction in the area of the dorsal vermis [104] with aging; this suggests a possibility that any cerebellar functions (motor and nonmotor) may be affected, to some degree, by the aging process. Not only frontal lobe atrophy is implicated in the patterns of age-related cognitive decline, but other brain areas, including the cerebellum, are also sensitive to the effects of aging. It was shown [105] that the gray matter volume in the cerebellum predicts general cognitive ability, even when the total intracranial volume and volumes of the gray matter in the frontal lobes are statistically controlled. Males, as compared to females, show a stronger relationship between the volume of the cerebellum and cognitive ability. The relationship between the gait speed and volume of the cerebellar gray matter in older adults [106] is influenced by information-processing ability, and this relationship is stronger in subregions ascribed to cognitive functions than to vestibular or sensorimotor ones.

The cerebellum might be more resistant to some neurodegenerative disorders, such as stroke or Alzheimer's disease (AD), as this brain part appears to be "equipped with more tools" necessary to protect itself against these types of assaults [107]. However, the balance and mobility dysfunction may be intensified in individuals suffering from AD, and pathological changes found within the cerebellum may contribute to the decline in motor performance in AD [108]. It was also suggested that the cerebellum may have a direct influence on cholinergic dysfunction in AD [109]. A significant induction of apoptosis of cerebellar granule cells treated with amyloid β-peptide was found; the addition of 17β-estradiol reduced this effect. These findings may be important in further research of pharmacological AD treatment [110].

Can the Cerebellum Contribute to Cognitive Control Independent of the Motor One? The possible way how the cerebellum functions in cognition [111] assumes that this brain part develops a mechanism predicting internal conditions for a particular motor or mental operation and that cerebellar damage will not eliminate the functions but increase the variability in responses and conscious efforts. It is not clear which cognitive domains are involved, and why and

to what extent the cerebellum contributes to cognitive processing [112]. Distinct networks of the individual lobules were found to be clearly divided into "motor" and "nonmotor" regions, and an anatomically-driven connectivity atlas of the cerebellar lobules was created for the right hemisphere and vermis [113].

An attempt was made to address the extent to which the cerebellum could process abstract information originating from the prefrontal cortex [114]. The first hypothesis was that activity within the prefrontally projected cerebellar lobules could only be evoked by first-order rules (rules that specify an action), while the second hypothesis was that activity within prefrontally projecting cerebellar lobules could be evoked by both rules specifying the action and rules specifying another rule (i.e., second-order rules). The authors demonstrated, for the first time, that cerebellar circuits engage both first- and second-order rules and, in doing so, showed that the cerebellum could contribute to cognitive control independent of motor control.

Theoretical and Modeling Considerations of Cerebellar Functioning. The earliest "performance" theory (Braitenberg and Atwood, 1958 [115], and a modified version, Braitenberg et al. 1997 [116]) proposed that slow propagation of the signals along parallel fibers, which imposes predictable delays, allows the cerebellum to detect time relationships within a certain window. The "learning" theories" [117, 118] predicted motor learning in the system of parallel fiber synapses mediated by a concurrent climbing fiber input.

The cerebellum can be characterized as an internal timing system, contributing to the performance of a wide range of skilled behaviors, particularly when the tasks entail event timing [119]; it was expected that, similarly to the motor control, the functional domain of the cerebellum in cognition would be limited to situations that require real-time predictions. A spiking cerebellar model [120] embedded in different loop architectures (recurrent, forward, and forward/recurrent) is capable of controlling a robotic arm (three degrees of freedom) using a biologically inspired approach. The dendritic arborization of PCs behaves like a complex of high-threshold and low-frequency spatial electrical oscillators, while the axo-somatic trigger zone is characterized by a low threshold and is capable of providing a high firing frequency [121]. A "lock-and-key" hypothesis was formulated concerning cerebellum-dependent motor memory [122] in which neuronal plasticity *per se*

is necessary but not sufficient to modify motor behavior. It has been reviewed how the adaptive-filter model of the cerebellum, which fits very well with electrophysiological discoveries concerning the importance of molecular-layer interneurons, their plasticity, long-term potentiation, and the number of silent parallel-fiber synapses, may also be useful for automatic self-adjusting damage avoidance in the next generation of "soft" robots [123]. It has been emphasized that sensorimotor learning can occur at multiple levels. Adaptation provided by a cerebellar-based internal model improves action execution, while processes in the prefrontal cortex and basal ganglia improve action selection [124]. There is further evidence for the involvement of the cerebellum in predictive language processes, which suggests that the notion of cerebellar internal models may be extended toward the language domain [125].

A conceptual and operational framework was developed [126]; it is based on multiple interconnected levels, from cellular/molecular to network mechanisms providing generation of computational primitives, then to high-level cognitive/emotional processing, and finally to the sphere of mental functions and dysfunctions. An artificial cerebellum [127] may replace areas of damaged brain tissues or even enhance the healthy brain function and to restore learning processes that decline with age. In the project of these authors, brainstem signals fed into a real cerebellum are analyzed, and output signals are generated in response. The input-output function of neuronal circuits [128] was used for a synthetic version on a chip located outside the skull and wired into the brain using electrodes. This device is considered to be able to restore brain functions in rats by receiving sensory inputs from the brainstem and prompting motoneurons to initiate the appropriate movement. An acquired trigger for the well-timed conditioned eye-blink response, repetition of unpaired trials, and the extinction of the conditioned response trigger were compatible with natural cerebellar learning in awake animals. A programmable chip could replace the ability of the cerebellum to learn a timed eye-blink response to an auditory signal.

The virtual reality (VR)-based rehabilitation gaming system (RGS) was used in the study by Prochnow et al. [129]. The results supported the hypothesis that this novel neurorehabilitation approach engages human mirror mechanisms that can be employed for visuomotor training. A close relationship between movements and thoughts was examined [130]. A traditional serial-order

processing model of adaptation was rejected, while a model of behavior based upon continuous interaction with the environment, in which behaviors occur in "real" time with focus on the cerebellar role in these processing, was accepted. It was suggested that the cerebral cortex is "allowed" to retain the most efficient representation of a behavior type; without the cortex, the cerebellum might be "useless" because it would not obtain information, upon which the anticipatory control can be based. By contrast, with no involvement of the cerebellum, the cerebrum remains capable of storing experience and motor programs, but this process should be less efficient in the control of both motor and nonmotor executive functions.

Concluding Remarks. Further studies of the cerebellar involvement in the control of nonmotor functions using various approaches will show if the cerebellar cognitive control is independent of the motor control. The use of various experimental approaches in the studies of the cerebellum can help researchers to develop new strategies in diagnostics and therapy of cerebellar patients.

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НЕМОТОРНІ ФУНКЦІЇ МОЗОЧКА: ПІДХОДИ ДО ВИВЧЕННЯ ТА ЗНАЧЕННЯ

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Р е з ю м е

Мозочок залучений у контроль моторних та немоторних функцій. Вдосконалені та інноваційні експериментальні та клінічні підходи, починаючи від врахування даних анатомічних досліджень та аж до використання результатів функціональної магніто-резонансної томографії (fMRT), дозволили дослідникам отримати великий обсяг інформації щодо внесків мозочка в керування рухами і допомогли усвідомити, що мозочок також виконує функції немоторного контролю. Виникає питання: чи обробляє мозочок виключно церебральну інформацію щодо контролю певних специфічних дій, або він також має відношення до обробки деяких форм інформації, незалежних від таких відношень. Зараз дослідники вже підійшли до визначення того, яким чином мозочок є активним протягом вирішення когнітивних задач. Різні перспективні підходи в терапії (від стимуляції мозочка до використання імплантів мозочка та «штучного» мозочка) виглядають досить важливими, оскільки вони дозволяють відновити втрачені мозкові функції в модельних експериментах на тваринах та коригувати певні процеси мозкової недостатності у пацієнтів.

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