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REVIEW ARTICLE

Recent Investigations on the Functional Role of Cerebellar Neural Networks in Motor Functions & Nonmotor Functions -Neurodegeneration

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Abstract: The cerebellum is a well-established primary brain center in charge of controlling sensorimotor functions and non-motor functions. Recent reports depicted the significance of cerebellum in higher-order cognitive functions, including emotion-processing, language, reward-related behavior, working memory, and social behavior. As it can influence diverse behavioral patterns, any defects in cerebellar functions could invoke neuropsychiatric diseases as indicated by the incidence of alexithymia and induce alterations in emotional and behavioral patterns. Furthermore, its defects can trigger motor diseases, such as ataxia and Parkinson's disease (PD). In this review, we have extensively discussed the role of cerebellum in motor and non-motor functions and how the cerebellum malfunctions in relation to the neural circuit wiring as it could impact brain function and behavioral outcomes in patients with neuropsychiatric diseases. Relevant data regarding cerebellar non-motor functions have been vividly described, along with anatomy and physiology of these functions. In addition to the defects in basal ganglia, the lack of activity in motor related regions of the cerebellum could be associated with the severity of motor symptoms. All together, this review delineates the importance of cerebellar involvement in patients with PD and unravels a crucial link for various clinical aspects of PD with specific cerebellar sub-regions.

Keywords: Cerebellum, emotions, behavior, motor and non-motor functions, cognition, neurodegeneration.

1. INTRODUCTION

Human behavior is apparently infinite in its functional complexity, as the intricacy and versatility of the human brain could confer to the sophisticated movements, motivations, emotions and fosters fluid continuity to distinctly recognizable behaviors. In addition, the major disruptions in the cerebellar neural networks can affect the extensive portions of the emotional, cognitive processing, and altered behaviour and these strategies could be beneficial for diagnosing a wide range of neurological and neuropsychiatric symptoms [1]. A full-fledged neuroscientific study is required to unravel robust behavioral changes accompanying these diseases by ascertaining the integration of sensorimotor and executive functions [1]. The cerebellum is considered as the central node for executing the integration of diverse neural circuit functions and it is considered as the initiating point to decipher how the brain computes and generates symphonic elegance, which exemplifies human behavior [1].

Furthermore, the cerebellum is traditionally considered as the main regulator of motor function [2-4]. Since the last few decades, a consensus has been forming to delineate the role of the cerebellum in nonmotor behavior; however, the significant role and nature in several motor and non-motor functions is yet to be completely unraveled [5-7]. Based on several clinical observations in literature, a crucial role of the cerebellum in cognition process has been reported [8, 9]. The motor dysfunction in relation to the cerebellar pathology was exemplified by clinical manifestations such as ataxia, dysto-

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nia, dysmetria, and tremors, whereas other manifestations such as cognitive defects are evident in pseudobulbar palsy, inattention, and psychosis [9].

Mirroring of motor dysfunction in terms of the cognitive sphere is a crucial concept often described as the dysmetria of thought [1]. The primary non-motor tasks of the cerebellum include executive functions, task performance and movement, balanced behavioral patterns and emotional activities. It plays a similar role as the cerebral cortex in certain functions, with diverse neural networks projecting onto the cortex during the execution of several executive functions, learning, memory, and cognitive process. Two intriguing questions are yet to be answered, for instance (a) what is the cerebellar circuit involved in mediating several non-motor functions? (b) whether cerebellar neural circuits are heterogeneous or not? By examining the cellular composition across neural circuits, and the anatomy of the cerebellum, we described how developmental, genetic, and mechanical cerebellar disruptions could influence neural circuit assembly that progressively influences motor and non-motor behavioral patterns [1].

Cellular composition and neural architecture of the cerebellar cortex have been reported to be more uniform than the neocortex even though they are variable anatomically, genetically, and electrophysiologically across several microdomains [10, 11]. Today's notion of human brain functioning has reached far beyond strict structure-function relationships. The integrative aspects of neuroscience are hereby prioritized. In this context, the studies of consciousness, memory, and social interaction mechanisms become more crucial [12, 13]. Taken together, this knowledge can be formalized into one consistent system [13, 14]. Systematization of knowledge allows to integrate acquired data into modern research and to provide novel applied technologies in order to develop novel cognitive behavioural therapies and therapeutic modalities to manage the neuropsychiatric diseases.

For many decades, the role of the cerebral cortex in higher mental functions has been studied [15]. Cognition-related functions of prefrontal, insular, and parietal cortex regions were extensively described and are now being further investigated [16]. On the other hand, sometimes, completely new properties of previously described brain regions are still being discovered. In this case, the role of cerebellum in cognitive and emotional processes can serve as a good example to unravel the executive functions of cerebellum [17, 18]. Cerebellar non-motor functions can be defined as properties that are not directly responsible for maintaining movement, coordination, and posture [19]. Usually, they are described as the executive functions (cognitive control, attention, mind flexibility, language), and functions that underlie social cognition (emotion recognition and decision-making) [20].

1.1. Literature Search

Cerebellar non-motor functions play a more complex role in human life than was previously believed. Systematization and formalization of knowledge become an important cue in providing a research concept to explore new paradigms in the study of neural structures. Pubmed/Medline, Google scholar, eMedicine, NLM database search was performed to derive suitable research reports and original articles for this review. We have used keywords such as 'cerebellum, emotions, behavior, motor and non-motor functions, cognition, neurodegeneration' for searching the peer-reviewed and published papers since the last 3 decades. The current review focuses on the recent updates in cerebellar motor & non-motor in a behavioral capacity; furthermore, this review discusses the microarchitecture of cerebellar regions evolved to exhibit specialized functions and progressive damage to these areas that sub-serve diverse cortical areas, which may invoke neurological diseases, and behavioral alterations in psychiatric disorders, and neurodegenerative diseases [1]. Furthermore, in this article, the current views on cerebellar non-motor functions have been discussed along with anatomical and physiological basis for these functions.

2. HISTORY OF CEREBELLUM RESEARCH

Cerebellar motor and non-motor functions were previously not delineated completely due to the lack of sophisticated data acquisition techniques. From the very beginning of history, the anatomical complexity of the cerebellum was obvious and its complex structure, including hemispheres, sulci and gyri were well described by morphologists [21]. Erasistratus is considered the first author to distinguish the cerebellum from other brain regions in the 4th century BC, followed by Galen, who proposed the idea of the cerebellum being a source of motor nerves with cerebellar vermis being a valve for body spirits [22]. Later, various functions of the cerebellum were discovered and suggested, such as memory, involuntary movement control, sensory integration, and even sexual function [23]. In some cases, scientists had contradictory results, although the general notion of cerebellar functions was poor; subsequently, several important functions of the cerebellum in many vital processes were postulated.

Ongoing investigation of cerebellar functions became possible after intense research based on animal models. During the 19th century, a number of great scientists, such as Rolando, Magendie, Luciani, Hammond studied how cerebellar lesions impacted animal's vital motor and non-motor functions [24]. It was found that the main symptoms of cerebellar lesion include motor function impairment: coordination, posture, and locomotor dysfunction. Clinical studies on patients with defects in the cerebellum were also described as they were accompanied by cerebellar ataxia [25]. At the same time, cerebellar histology was elucidated by Ramon YCajal and Purkinje. By the 20th century, on the basis of anatomical and physiological knowledge, the cerebellar function was formulated [26]. During the 20th century, the knowledge about cerebellar motor functions was established due to the acquisition of novel data about cerebellar dysfunctions [27]. Among them, the symptoms of cognitive deficit, emotional instability, speech impairment, and reading dysfunction are crucial manifestations of cerebellar cortex defects. As a result, the cognitive-affective syndrome, or Schmahmann syndrome has been reported to e associated with damage to the cerebellar cortex. In this disease, the attention deficit, impairment of social cognition, affective and cognitive dysfunctions occurred due to the cerebellar lesions of different etiology [28]. The importance of cerebellum in providing non-motor functions is yet to be unraveled and requires detailed research using modern neuroscience research techniques.

3. IMAGING STUDIES &THE CEREBELLUM

Modern neuroimaging techniques, such as fMRI, PET, MEG can allow efficient monitoring of the neural activity pertinent to different brain regions during a resting state and special tasks, thus illustrating the topography of brain activation [29]. A wide range of research is needed to delineate the specific cerebellar functions by transcranial direct current stimulation, which allows selective modulation of cerebellar activity [30]. Furthermore, coordinating movement and higher intellectual functions, the cerebellar neural networks have been playing a vital role in allowing neural programs to run automatically, like bicycle riding or piano playing, allowing the association of cortex to impose simultaneous functions during dual tasking [31, 32]. Taken together, these methods have shown cerebellar functional activity during cognitive tasks, emotional stimuli processing in evaluated subjects [33].

Several fMRI studies revealed that the cerebellum has been reported to be involved in integrating afferent sensory information perceived from the periphery, mainly sensory modalities including vestibular pathways, which are evolutionarily well-conserved. It is also possible that sensorimotor functions are also executed through the same neural circuits, which could modulate cognitive behaviors [34]. For instance, the heterogenous anatomical and functional aspects of the internal cerebellar microcircuitry can deliver such flexibility to potentiate this phenomenon [35, 36]. Therefore, basic neuroscientific and macro-evolutionary observations in several neurological and neurodegenerative diseases may help contextualize the current efforts for developing a highly sophisticated understanding of the role of the cerebellum in cognitive and affective human behavior.

4. BASIC NEURAL CIRCUITRY OF CEREBELLUM

The potential interactions between cell types across cerebellar cytoarchitecture were reported by Camillo Golgi [37]. Later, Cajal's findings on localization and morphology of cerebellar architecture were still relevant to the present day but novel significant features of neural circuits have been unveiled recently. For instance, the identification and elucidation of unipolar brush cells, and direct projections originating from Purkinje cells to granule cells and other nucleocortical circuit projections have suggested new insights in understanding both cellular and neural circuit heterogeneity in the cerebellum [24, 38-41].

Cerebellar circuitry involves the stereotypical connections with its surrounding neural networks (Fig. **1**).The cerebellum exhibits 3 layers in which the most superficial layer is the molecular layer associated with 'inhibitory interneurons' and 'excitatory climbing fibers'. The middle layer is the Purkinje cell layer onto which the superficial layer projects onto the dendritic arbors of the Purkinje cells, as these cells are involved in performing main computations within the cerebellum. In between the Purkinje cells, a very large Bergmann glia is found, but its functions are still poorly studied, although cerebellar glia is extensively heterogeneous [42-45]. The Purkinje cell layer is composed of interneurons, often referred to as *candelabrum cells*.

The deep layer is also referred to as the *granular layer* and it is composed of numerous excitatory neurons and referred to as granules. The terminals of excitatory mossy fibers are involved in generating sensory signals to the cerebellar cortex. The granular layer is composed of (a) inhibitory Golgi cell interneurons, (b) Laguro cells, and (c) unipolar brush cells also known as excitatory interneurons [1]. Unipolar brush cells are confined to the vermis of lobule IX and X and a smaller number are also confined to lobules VI and VII. Even though the primary afferent classes are composed of both climbing fibers and mossy fibers, the presence of "beaded" fibers terminates the majority of cerebellar cortical layers across the ten lobules of vermis and hemispheres [1]. Beneath the 3 layers, there is a dense network of fiber tracts. Cerebellar nuclei are confined to these networks. This nuclei consist of GABAergic, glycinergic, and glutamatergic cell types. In the case of primates, the anatomical descriptions of cerebellum: (a) the medial nucleus is also referred to as fastigial, (b) intermediate is composed of globose and emboliform nuclei, which together forms 'interposed nucleus', (c) lateral region is referred to as the dentate, a complex convoluted structure (Fig. **2**). Cerebellar nuclei is reported to link the cerebellar cortex to the brain and spinal cord [1].

5. MOTOR &NON-MOTOR FUNCTIONS OF THE CEREBELLUM: RECENT UPDATES

5.1. Cerebellum and Emotion Psychophysiology

The evolutionary purpose of emotions is still a topic of discussion. Undoubtedly, they represent a special adaptive mechanism by creating positive and negative motivations, thus maintaining goal-oriented behavior [46]. At the same time, it would be incorrect to consider emotions as only positive and negative fluctuations, since emotions could serve not only as a satisfactory mechanism, but also demonstrate the huge complexity of human psychological reactions [47]. Notably, the cerebellum has a significant role in providing emotional responses. The first suggestions about cerebellar involvement in the emotional functioning were made relatively long ago, but only a little knowledge about emotions is available [47]. According to the recent reports, the emotional mechanisms include perception, processing, and recognition.

Participation of the cerebellum in basic emotional responses became considerable after multiple cerebellar-limbic connections had been found [48]. The specific impact of cerebellar activity on the autonomic nervous system (ANS) functioning was also observed. Emotion-related psychophysiological processes can be well studied on animal models, mainly by observing negative emotional responses [49]. Commonly used behavioral tests for fear and anxiety (for example, maintaining conditioned reflexes for painful stimuli or exploration in the open field) have shown a cerebellar impact on animal behavior [50, 51]. For instance, cerebellar vermis stimulation has been reported to reduce stress and fear reactions in the open field [52]. Moreover, the emotional responses can be seen not only on behavioral, but on visceral level, by measuring heartbeat, respiratory rate, and vascular function [53-55]. The animal studies on psychophysiological responses revealed cerebellar participation in basic emotional reactions. Further studies on human subjects have revealed the cerebellar mechanisms of emotion recognition, emotional processing, and social cognition, which are discussed below.

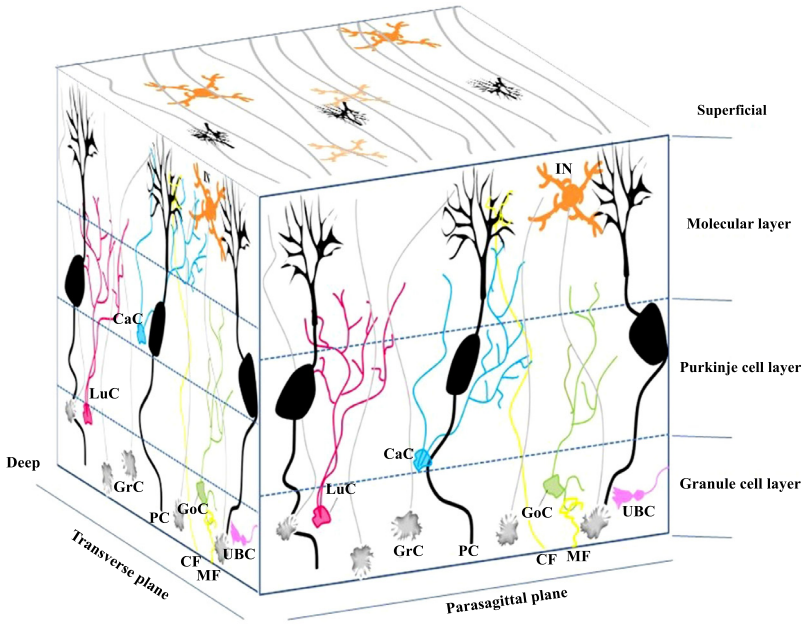

Fig. (1). Three-dimensional neural network microarchitecture confined to the cerebellar cortex. Afferent projections of the neuronal microarchitecture were indicated in yellow. Climbing fibers (CF indicated in yellow) are depicted to the molecular layer of the cerebellar cortex. These fibers further reach the dendritic tree of the Purkinje cell (PC indicated in black); Mossy fibers terminate in the granule cell layer. These fibers can form synaptic connections with other granule cells indicated as GrC in light black color. Granule cell layer is also composed of Golgi cells indicated as GoC, in light green as well as Lugaro cell indicated in LuC, pink, and unipolar brush cell-interneurons indicated in UBC, purple. Molecular layer has inhibitory interneurons (indicated as IN). The Purkinje cell layer is composed of cell bodies of Candelabrum cells. Transverse projections of parallel fibers foster the integration and afferent information through climbing. Purkinje cell soma, Bergmann axons, and the axon segments are coiled by the basket cell axons. These are innervated onto the molecular layer in the three-dimensional space. *(A higher resolution/colour version of this figure is available in the electronic copy of the article).*

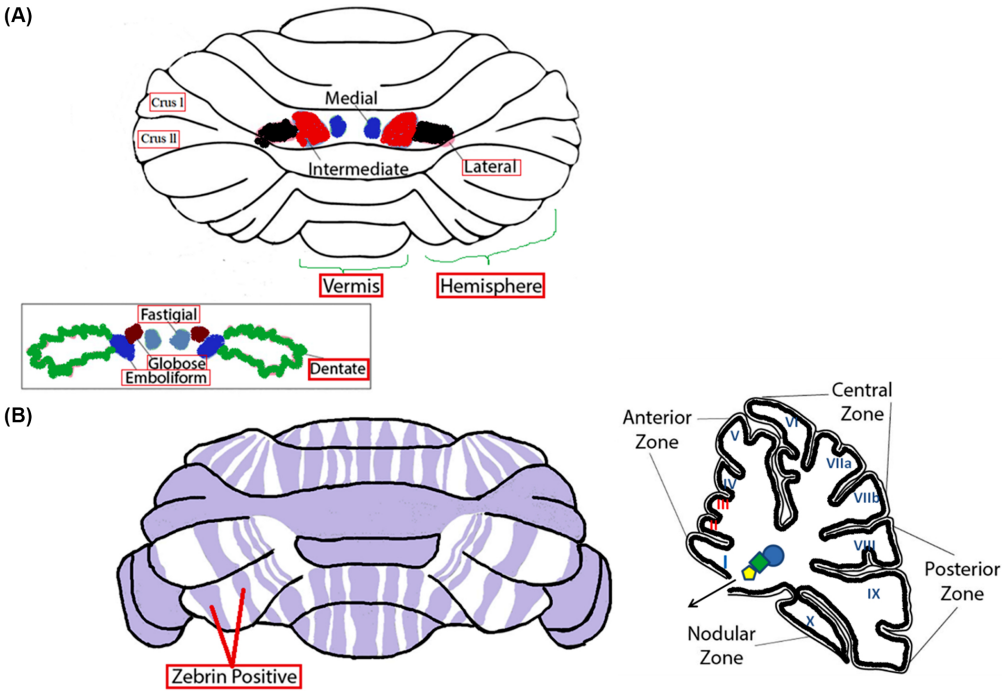

Fig. (2). (**A**). Cerebellum microarchitecture schematically represented from the dorsal view. The rostral view is superior, whereas the caudal view is inferior. The vermis is located at the midline. Different cerebellar nuclei are indicated in different colors; lateral nucleus - black, medial nucleus - blue, intermediate nucleus was indicated in red. (**B**). Zebrin patterning of cerebellar regions in dorsal view (left panel); Parasagittal view of the cerebellum indicated at midline. Different cerebellar nuclei are depicted across four different zones such as anterior zone, central zone, posterior zone, and nodular zone. *(A higher resolution/colour version of this figure is available in the electronic copy of the article).*

5.2. Emotion Recognition and Social Cognition

Emotion recognition is not only an essential mechanism of social interaction, but it is a way to adequately assess the environment [56]. The ability to successfully recognize basic and complex emotions can provide a fast and efficient evaluation of other's intentions to make a decision of whether to cooperate or not [57]. The early studies on emotion recognition are based on the face photo and video demonstrations, after which subjects are instructed to choose an appropriate emotion [58]. Further studies have been supplemented with simultaneous brain activity registration. In addition to the limbic system, the prefrontal cortex as well as visual system was reported to be involved in emotion recognition [59]. At the same time, a number of studies pertaining to cerebellar activity during emotion recognition are also seen. While the majority of research is dedicated to cortico-limbic relationships in emotion recognition, certain reports discuss the role of cerebellum in this process [60, 61].

When considering anatomy of the cerebellum, its participation in emotion recognition becomes more reasonable. Notably, there are multiple axon connections between cerebellar structures (fastigial nucleus, vermis, floculonodular lobe) and the limbic system (amygdala, hippocampus, septum, hypothalamus) [62]. Electrical stimulation of these cerebellar structures has been reported to induce neural activity in the limbic system [63]. Moreover, the projection fibers from 'cerebellum' to 'prefrontal cortex' provide bidirectional communications. In addition to that, the cerebellar activity itself is noticed during emotion recognition. This correlates with data obtained from patients with different cerebellar lesions: infarctions and degeneration. In these subjects, the emotion recognition was impaired with higher error rates while presented with basic emotions [64, 65]. It is also worth mentioning that cerebellar dysfunction has been observed in psychiatric diseases like autism spectrum disorder (ASD) and attention deficit hyperactive disease (ADHD), in which the social behavior and theory of mind (the ability to understand the others) mechanisms are impaired [66].

As mentioned above, there is evidence of cerebellar connections with the prefrontal cortex and limbic system, and these are crucial brain regions for emotion recognition [67]. According to the fMRI data, these connections are functionally active during the process of emotion recognition [68]. Cerebellar participation in the emotion recognition process is also shown using transcranial direct current stimulation (tDCS) with lower reaction time for negative emotions after cerebellar stimulation [67]. However, this effect is absent during positive and neutral emotion recognition, so that the involvement of cerebellum into the negative emotion recognition network is more evident. This may seem reasonable, since negative emotions are more important for individual survival; therefore, additional mechanisms underlying this emotional processing are yet to be unraveled. Thus, according to current reports, there is strong evidence of cerebellar participation in emotion recognition, including its multiple connections with the limbic system and cortex, and cerebellum activity alone during this process [67]. Since emotion recognition is an important mechanism of understanding others, the cerebellum can be considered as a structure involved in social cognition and social perception.

5.3. The Cerebellum and Emotion Processing

Emotion processing includes the generation of cognitive and behavioral responses to emotional stimuli so that positive or negative emotional stimuli can allow individuals to judge the desirability of such events in the future. Thus, the presentation of emotional stimuli can generate some affective state (mood) [69]. It is well known today that various neuropsychiatric diseases are characterized by 'affective disorders' [70]. For example, patients with 'depressive disorders' have been shown to pay more attention to negative emotional stimuli than to positive ones [71].

Emotion processing is considered a necessary aspect of survival. Notably, the processing of negative emotions is more essential, since ignorance of negative emotional stimuli causes a behavioral risk [72]. In laboratory conditions, various emotional stimuli can be used to induce a certain affective state: audio and video samples, narratives, face expressions [73]. Affective state induced by the stimuli is usually assessed by self-assessment scales or tests [74]. The disturbed emotion processing is also reported to be observed during the incidence of brain lesions in the cerebellar region [75]. Studies on cerebellar role in emotion processing have shown that cerebellar complex neural networks, including hypothalamus, hypophysis, and cerebral cortex, exhibit intricate roles in emotional processing. The fMRI data obtained in this research work demonstrate a higher activation in anterior and inferior posterior (tuber) regions of vermis, as well as in the limbic system to foster emotion processing [76, 77]. Cerebellum also seems to have more impact on emotion processing when dealing with negative stimuli [77]. In accordance with above mentioned data about psychophysiological reactions, the cerebellum can therefore be considered as an important participant to decipher the analysis of emotional information.

In cooperation with visual systems, limbic structures, and regions of the cerebral cortex, cerebellum could maintain a proper acquisition and analysis of emotional information. However, there are several other non-motor functions, in which cerebellum has been involved. Further in this review, cerebellum roles in speech, writing, and reading processes have been described.

5.4. Cerebellum and Linguistic Functions

Traditionally, cerebellum roles in linguistic functions, such as reading, writing, and speech are investigated by means of neuropsychological characteristics in the patients with cerebellum lesions [6]. Writing and speech disorders are associated with intricate pathophysiology among all language skills in the context of cerebellum dysfunction. As a rule, such disorders are related to motor aspects of these processes, for example, cerebellar ataxia and dysarthria, in which muscular contraction synchronization is reported to be disturbed [78].

Meanwhile, cerebellar dysfunction can contribute to the more complex problems related to writing and speech. A plethora of reports suggested that various impairments in perception of speech, motor planning, in the ability to predict and integrate speech stimuli can occur due to cerebellar pathology [79]. Cerebellar patients also demonstrated various agrammatic disorders and dysprosody [80, 81]. In patients with focal and degenerative cerebellar lesions, the non-motor

writing disorders (dysgraphia, agraphia) were also noticed [82]. In this case, cerebellum can serve as a coordination mechanism, which provides spatial and temporal harmonization for cognitive, linguistic, and motor processes [83]. These findings represent cerebellar function and maintain not only motor, but also cognitive control for speech and writing. Proper cerebellum functioning has been reported to be crucial for foreign language study [84].

Apart from clinical data, neuroimaging studies on healthy subjects are also available today. PET and fMRI data have shown increased functional activity of the cerebellum when executing linguistic tasks of sensory, motor, and cognitive modalities. Although the exact location is still unclear, the supporting role of cerebellum in maintaining metalinguistic functions is suggested with each cerebellar hemisphere connected with the cerebral hemisphere on the contralateral side [85]. These findings correlate with the fact that the right cerebellar hemisphere is more active at the time of performing 'linguistic functions', since, in most subjects, the left cerebral hemisphere is responsible for these processes [86].

For successful social interactions during an individual's life, more complex linguistic skills (metalinguistic skills) are required [87]. A number of studies have reported a link between cerebellar dysfunctions with metalinguistic skills impairment; For instance, the difficulties in constructing a sentence in given context, interpretation of ambiguous situations, finding word associations and synonym/antonym pairs [88]. Cerebellum lesions or blood flow disturbances can confer to the dysfunction of fronto-cerebellar connections (crossed cerebellar diaschisis) [89].

5.5. Cerebellum and Learning & Reading Skills Development

Several studies have reported the cerebellar role in reading skills development, which are related to a cerebellar deficit in the context of dyslexia. According to the studies made on healthy and dyslexic children, the dyslexic subjects demonstrated not only reading deficit, but also sensory-motor disorders like bad coordination and vestibular balance disorders [90]. According to this report, the cerebellar deficit hypothesis has been proposed, which links dysfunction of the cerebellum with the ability to learn and recognize printed words [91]. To date, the cerebellar deficit hypothesis has been defined, yet the mechanisms of these disorders have yet to be unraveled.

Further studies on the cerebellar deficit hypothesis, the cerebellar role in reading skills development has been suggested to occur *via* two processes: articulatory control and skills automatization [92]. These findings also correspond to the fact that speech processes contribute to the development of reading skills and decoding skills [93]. Thus, cerebellum provides not only 'motor control of speech', but also more complex properties. In this case, the cerebellar role in reading skills development can be explained *via* linguistic and sensory motor learning with cerebellar mechanisms of error correction [94]. Thus, disturbances in the cerebellum learning system can result in the impaired ability to recognize written text.

The cerebellar deficit hypothesis is complemented with neuroimaging data, which is still not excessive since reading is rarely studied in the context of cerebellar activity. According to the current data, several causes of cerebellar reading disorders have been observed: impaired functional activity, tissue atrophy, disturbance of frontal-cerebellar connections [95, 96]. Cerebellar lobules VI, VII are reported to be affected in dyslexic patients [97, 98]. Moreover, there are differences in frontal-cerebellar white matter integrity between healthy and dyslexic subjects [99]. This data represents the anatomical and physiological basis for cerebellar deficit-related dyslexia.

Thus, the cerebellar role points out the importance of this brain region in 'reading skills development' and 'sensory motor learning'. Since these processes are considered essential for all learning activities, the cerebellum can be thought to provide proper cognitive function development. Current studies on integrating the cerebellum into models of cognitive development are crucial for understanding the mechanisms underlying the learning process.

6. CEREBELLUM AND PSYCHIATRIC DISORDERS - RECENT UPDATES

The three cerebellar core projections, including the (1) cerebellar vermis projection into pons & reticular formation (2) intermediate zone projections to the red nucleus, & thalamus (3) lateral zone projection to the thalamus; have been suggested to influence emotions, behavioral patterns in several psychiatric disorders by intervening with neural fibers of frontal or motor cortex or parietal cortex [100-102].

6.1. Schizophrenia & Cerebellar Neural Networks

Several neuroimaging reports delineated the influence of cerebellar dysfunction in triggering cognitive abnormalities by intervening in the corticocerebellar connections [103, 104]. Predominantly, the imbalance in cortico-thalamic-cerebellar-cortical circuits could trigger alterations in cognition as well as task performance in schizophrenia patients.

Self-experience is one of the significant anomalies observed during schizophrenia, which has profound interlink with the aberrant brain malfunction controlled by cerebellum and cerebral cortex [105, 106]. The ventral premotor cortex (vPMC) and posterior insula (pIC) are associated with interconnecting neural networks with the posterior cingulate cortex, and these neural networks are involved in modulating self-experience during schizophrenia [106]. Functional connectivity is mitigated among cerebro-cerebellar neural networks. Predominantly, frontoparietal neural networks are affected, which subsequently provoke hallucinations, negative symptoms, and self-experience in schizophrenia patients. Malfunction of interconnected networks of cerebro-cerebellar circuitry could invoke changes in the behavioral patterns, indicating the cerebellum as a functional entity in schizophrenia patients. Furthermore, during the mirror neuron-driven simulation, the social cognition, and emotional cues are altered in schizophrenia patients and their underlying interaction with cerebellar networks is yet to be uncovered fully [107].

6.2. ADHD & Cerebellar Neural Networks

ADHD (Attention Deficit Hyperactivity Disorder) is prominently observed in 5% of children and the symptoms

are accompanied by attention defects, hyperactiveness, & impulsivity [108]. Defects in frontal-subcortical neural networks, mainly in the corpus callosum, basal ganglia, [109], could invoke the ADHD [109-113]. Furthermore, the changes in brain development could also trigger the incidence of ADHD. Changes in the volume of cerebrum and cerebellum, vermis & caudate nucleus are also reported to be one of the major causes of ADHD in childhood, but these changes disappear as the individual age increases [114].

6.3. Autism Spectrum Disorders (ASD) & Cerebellar Neural Networks

ASD is another psychiatric disease could be produced by the changes in cerebellar neural networks projected onto the motor cortex and prefrontal cortex [115]. Altered cognition, emotions, and stereotypic movements could cause ASD-like behavior during any damage to the cerebellum. Mitigation in the GABAergic neural networks could foster the rise in activity of cerebellar-cortical neural pathway, which cause repetitive behavior in individuals with ASD [116, 117]. Still, existing research gaps underline the need for studies addressing the relationship of Purkinje projections defects in triggering modulation in social behavior in ASD conditions.

6.4. Bipolar Disorder (BD) & Cerebellar Neural Networks

BD is significantly accompanied by the recurrent incidence of mania and depression with different behavioral patterns such as grandeur, defects in motivational behavior, and hyperactivity [115]. These bipolar symptoms are produced by the changes in cerebellar volume, and atrophy of cerebellum [118-120]. Furthermore, the low volume of V3 subregion of vermis could invoke changes in the behavioral patterns in bipolar disease [121]. However, the changes in the psychotic behavior in the Euthymic bipolar disorder type I (BD-I) in relation to the cerebellar neural networks require extensive scientific investigation [122].

6.5. Anxiety Disorders & Cerebellar Neural Networks

Alterations in the cerebellar function due to any functional damage of cerebellum could induce the occurrence of anxiety disorders. Disorders such as PTSD, generalized anxiety disorder, and social anxiety disorder are generated by the changes in the neural networks pertaining to the cerebellum. For instance, cerebellar hyperactivity can induce alterations in overall blood pressure and heart rate, which could be considered the possible explanation for the higher sympathetic activity in patients with anxiety disorders [123]. These investigations reveal the predominant high-glucose metabolism in these patients, mainly across pons, cerebellum, and amygdale, and midbrain [124]. Thus, the pathophysiology associated with alterations in the hyperactivity of cerebellum is yet to be explored significantly to fill the research gaps to prescribe suitable cognitive-behavioral therapies to these patients.

7. ALEXITHYMIA & CEREBELLAR NEURAL NETWORKS

A significant emotional regulation is a crucial process in daily life in order to promote effective psychological well being [125] and the psychological emotions are mainly controlled by the cerebellar neural networks along with other crucial parts of the brain such as prefrontal cortex–amygdale networks. Any damage to these brain areas could cause emotional dysregulation, mainly in individuals with psychomotor diseases. Individuals often with substance abuse could acquire alexithymia, which is accompanied by the induction of addictive behavior [126, 127]. Intricate cognitive and affective characteristics are referred to as alexythymia and these are most commonly observed in patients suffering from psychosomatic disorders [128]. For instance, alexythymia construct is reported to be multifaceted and exhibits divergent characteristics, including difficulty in expressing individual feelings and bodily sensations. Other divergent features of alexythymia are impairment of fantasy, and poor introspective thought process [129-131]. In patients with psychomotor diseases, the emotional regulation is typically poor due to alexithymia [132]. These patients with alexithymia exhibit predominantly higher instincts of psychological distress compared to the people without alexithymia subsequently, the patient acquire functional somatic symptoms and defects in emotional processing [133, 134]. Therefore, the behaviour patterns attain maladaptive in these individuals and other psychological problems emerge such as depression and anxiety [135]. Thus, alexithymia could induce the alterations in emotional regulation and induce suicidal thoughts [136]. Previous studies demonstrated the involvement of cerebellar neural networks along with amygdale, cigulate cortex, and fusiform gyrus in individuals with alexithymia. For instance, the neural networking in cerebellar gray matter exhibited a positive correlation with alexithymia scores and inversely correlated to the limbic and paralimbic neural networks suggesting a significant involvement of cerebellar networks in the functional modalities of emotional processing [137]. For instance, the patients with bipolar disorder type I (BD-I) are reported with negative emotional cues and alexithymia. This is characterized by the emotional dysregulation during acute and euthymic phases incurred by this diseases [138]. Thus, alexythymia has a significant impact on the 'mind-body connection' in the patients with psychomotor diseases, and is implicated as a prominent challenge for all the mental health care workers; therefore, these strategies could produce significant information to evaluate and develop possible therapeutic regimens for these patients [139].

8. MOTOR DETECTS & CEREBELLUM

A plethora of scientific evidence from converging modalities delineates that there is a certain functional topography of the cerebellar neural networks for overt control of movement with respect to higher functions. Therefore, the cerebellum is divided into sensorimotor cortices and multimodal association cortices. A study performed by Catherine J. Stoodley *et al.* (2012) reported the presence of different cerebro-cerebellar circuits depending on the demands of tasks being performed [140]. Overt movement activates both sensorimotor cortices as well as contralateral cerebellar lobules IV-V and VIII. In addition, the more cognitively demanding tasks have been reported to engage with prefrontal and parietal cortices along with cerebellar lobules VI and VII [140]. Thus, the cerebellum is vividly described in both motor and cognitive task performance [140].

Patients who have cerebellar damage often experience cerebellar motor syndrome such as dysmetria, dysarthria, and ataxia. In addition, the cerebellar cognitive affective syndrome could be produced from the cerebellar damage accompanied by the defects in executive, visual, spatial, and linguistic task performances. There is a topographic organization reported in the human cerebellar region such that the anterior lobe and lobule VIII consist of the sensorimotor region, whereas the lobules VI and VII of the posterior lobe consist of cognitive cerebellum [140]. For instance, the cerebellar motor syndrome could be caused due to lesions across the cerebellum, mainly across the anterior lobe and lobule VI, which consequently interrupts neural circuits associated with cerebral and spinal motor systems [140]. Therefore, neuropsychiatric disorders manifest when the vermis lesions are deprived of cerebro-cerebellar-limbic loops in cerebellar input. Furthermore, this kind of functional topography is a consequence of differential arrangement of the connections pertaining to the cerebellar region onto the spinal cord, brain stem, and cerebral hemispheres; these neural circuits reflect cerebellar incorporation into the innervations of wide neural networks subserving movement, cognition, and emotion [75].

9. CEREBELLUM & NEURODEGENERATIVE DISEASES

Previous imaging studies depicted that the insults to cerebellar damage due to neuropathological lesions could induce neurodegenerative diseases such as Alzheimer's diseases (AD), Parkinson's disease (PD) [141-144]. Mutations associated with C9orf72 in neuropathological lesions can induce the neurodegeneration of cerebellar neurons, consequently, provoking neurodegenerative diseases [145, 146]. Thus, the atrophy of cerebellar neural networks could cause changes in the functional intrinsic activity and promote the neurodegenerative disease, including AD and PD. In addition, the cerebellar-thalamic overactivity in PD tremor generation is one of the significant symptoms; and it is also evident that the underactivity of cerebellar-thalamic projections appears to play a major role in the manifestation of genetic dystonias [147].

For instance, Parkinson's disease (PD) is a neurodegenerative disease exemplified by the clinical manifestations such as tremors, bradykinesia, rigidity, and imbalance in posture [148]. Non-motor functions such as cognitive, sensory, emotional and social abilities are being affected during PD [149-151], and these symptoms sometimes precede the appearance of motor symptoms [152]. Although the non-motor symptoms are detrimental to the patient's quality of life, still, they have not been fully studied in clinical settings. Several studies delineated the neurological damage underlying PD incidence is confined to the damage to dopaminergic neural networks across basal ganglia, mainly in substantia nigra pars compacta. Neurodegeneration of dopaminergic neurons could invoke hyperactivity in the globus pallidus of basal ganglia [153-155]. These events could confer to the increased inhibition from thalamocortical and brain stem motor regions, consequently invoking impaired motor movements. Even though the dysfunction in basal ganglia can explain several motor symptoms observed in PD, it has not adequately delineated the non-motor symptoms underlying the disease; therefore, other than brain structures, cerebellum also typically may be involved in enhancing the pathophysiology of PD. Some of the PD motor symptoms like tremors have been reported to link to the abnormal functional connectivity confined to the basal ganglia and cerebellum through the thalamus [156, 157]. Despite the fact that cerebellum has significance in motor functioning and fine-tuning movements, it has been reported that it is also involved in modulating behavioral performances [158, 159]. Some investigations have reported that the basal ganglia and cerebellum together work synergistically to generate motor and non-motor functions [160]. Subcortical structures have been reported in reinforcement learning and reward-related behavior, and motor planning [161-164]. These findings suggest that cerebellar regions are instrumental in non-motor symptoms in PD. Neuroimaging studies reported that ^{18}F-fluorodesoxyglucosein positron emission tomography can enhance the metabolism in the cerebellum, which is further linked to cognitive impairment in PD [165-169]. Yet, it is not clear whether some cerebellar parts are more implicated than others to foster motor and non-motor symptoms during PD and several quantitative studies along with the systematic review of cerebellar findings in PD should be studied.

CONCLUSION

Research of the human brain is characterized by complexity and continued birth of new concepts and expansion of current knowledge on the structure of the brain. The integrative approaches in modern day neuroscience outline new functional connections, roles and architectonics in well known regions of the brain, including the cerebellum. New techniques for brain studying provide new data with the precision dedication to elemental evaluation of diverse regions in the brain. Such studies provide new insight into the function and vast connectivity of the cerebellum, as well as its role in non-motor function. The cerebellum should not be further considered a region responsible for only motor functions, but also for a large specter of important non-motor functions. Current research shows cerebellar activity in a number of non-motor functions playing a crucial role in cognitive function, social cognition, linguistic skills, and learning. Thus, the cerebellum plays a role in the maintenance of proper cognitive and behavioral functioning and remains an important element of the brain's integrative system, with evident dyfunction during several neuropsychiatric diseases. Knowledge of cerebellar non-motor functions is not only important for elaborating new research concepts but is crucial for the development of novel clinical implications.

AUTHORS' CONTRIBUTIONS

Narasimha M. Beeraka (NMB), Zakirov F. Khaidarovich (ZFK), Oganesyan M. Valikovna (OMV), Rizaeva N. Aliagayevna (RNA), Zharashueva L. Arturovna (ZLA), Krasilnikov A. Alexandrovich (KAA), Vladimir N. Nikolenko (VNN), Liudmila M. Mikhaleva (LMM), Mikhail Y Sinelnikov (MYS) conceptualized and designed the study. NMB, ZFK, OMV, RNA, ZLA, KAA, MYS, and LMM performed the literature analysis, and wrote the original manuscript draft. NMB, VNN, MYS, LMM revised, edited and extended the final draft. All authors have reviewed and approved the manuscript before submission. All authors have reviewed and approved the manuscript before submission.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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REFERENCES

[1] Gill, J.S.; Sillitoe, R.V. Functional outcomes of cerebellar malformations. *Front. Cell. Neurosci.,* **2019**, *13*, 441. http://dx.doi.org/10.3389/fncel.2019.00441 PMID: 31636540

[2] Manto, M.; Bower, J.M.; Conforto, A.B.; Delgado-García, J.M.; da Guarda, S.N.F.; Gerwig, M.; Habas, C.; Hagura, N.; Ivry, R.B.; Mariën, P.; Molinari, M.; Naito, E.; Nowak, D.A.; Oulad Ben Taib, N.; Pelisson, D.; Tesche, C.D.; Tilikete, C.; Timmann, D. Consensus paper: roles of the cerebellum in motor control--the diversity of ideas on cerebellar involvement in movement. *Cerebellum,* **2012**, *11*(2), 457-487. http://dx.doi.org/10.1007/s12311-011-0331-9 PMID: 22161499

[3] Perciavalle, V.; Apps, R.; Bracha, V.; Delgado-García, J.M.; Gibson, A.R.; Leggio, M.; Carrel, A.J.; Cerminara, N.; Coco, M.; Gruart, A.; Sánchez-Campusano, R. Consensus paper: current views on the role of cerebellar interpositus nucleus in movement control and emotion. *Cerebellum,* **2013**, *12*(5), 738-757. http://dx.doi.org/10.1007/s12311-013-0464-0 PMID: 23564049

[4] Lang, E.J.; Apps, R.; Bengtsson, F.; Cerminara, N.L.; De Zeeuw, C.I.; Ebner, T.J.; Heck, D.H.; Jaeger, D.; Jörntell, H.; Kawato, M.; Otis, T.S.; Ozyildirim, O.; Popa, L.S.; Reeves, A.M.; Schweighofer, N.; Sugihara, I.; Xiao, J. The roles of the olivocerebellar pathway in motor learning and motor control. A consensus paper. *Cerebellum,* **2017**, *16*(1), 230-252. http://dx.doi.org/10.1007/s12311-016-0787-8 PMID: 27193702

[5] Koziol, L.F.; Budding, D.; Andreasen, N.; D'Arrigo, S.; Bulgheroni, S.; Imamizu, H.; Ito, M.; Manto, M.; Marvel, C.; Parker, K.; Pezzulo, G.; Ramnani, N.; Riva, D.; Schmahmann, J.; Vandervert, L.; Yamazaki, T. Consensus paper: the cerebellum's role in movement and cognition. *Cerebellum,* **2014**, *13*(1), 151-177. http://dx.doi.org/10.1007/s12311-013-0511-x PMID: 23996631

[6] Mariën, P.; Ackermann, H.; Adamaszek, M.; Barwood, C.H.; Beaton, A.; Desmond, J.; De Witte, E.; Fawcett, A.J.; Hertrich, I.; Küper, M.; Leggio, M.; Marvel, C.; Molinari, M.; Murdoch, B.E.; Nicolson, R.I.; Schmahmann, J.D.; Stoodley, C.J.; Thürling, M.; Timmann, D.; Wouters, E.; Ziegler, W. Consensus paper: Language and the cerebellum: an ongoing enigma. *Cerebellum,* **2014**, *13*(3), 386-410. PMID: 24318484

[7] Baumann, O.; Borra, R.J.; Bower, J.M.; Cullen, K.E.; Habas, C.; Ivry, R.B.; Leggio, M.; Mattingley, J.B.; Molinari, M.; Moulton, E.A.; Paulin, M.G.; Pavlova, M.A.; Schmahmann, J.D.; Sokolov, A.A. Consensus paper: the role of the cerebellum in perceptual processes. *Cerebellum,* **2015**, *14*(2), 197-220. http://dx.doi.org/10.1007/s12311-014-0627-7 PMID: 25479821

[8] Schmahmann, J.D. An emerging concept. The cerebellar contribution to higher function. *Arch. Neurol.,* **1991**, *48*(11), 1178-1187. http://dx.doi.org/10.1001/archneur.1991.00530230086029 PMID: 1953406

[9] Schmahmann, J.D. Disorders of the cerebellum: ataxia, dysmetria of thought, and the cerebellar cognitive affective syndrome. *J. Neuropsychiatry Clin. Neurosci.,* **2004**, *16*(3), 367-378. http://dx.doi.org/10.1176/jnp.16.3.367 PMID: 15377747

[10] Cerminara, N.L.; Lang, E.J.; Sillitoe, R.V.; Apps, R. Redefining the cerebellar cortex as an assembly of non-uniform Purkinje cell microcircuits. *Nat. Rev. Neurosci.,* **2015**, *16*(2), 79-93. http://dx.doi.org/10.1038/nrn3886 PMID: 25601779

[11] Apps, R.; Hawkes, R.; Aoki, S.; Bengtsson, F.; Brown, A.M.; Chen, G.; Ebner, T.J.; Isope, P.; Jörntell, H.; Lackey, E.P.; Lawrenson, C.; Lumb, B.; Schonewille, M.; Sillitoe, R.V.; Spaeth, L.; Sugihara, I.; Valera, A.; Voogd, J.; Wylie, D.R.; Ruigrok, T.J.H. Cerebellar modules and their role as operational cerebellar processing units. *Cerebellum,* **2018**, *17*(5), 654-682. http://dx.doi.org/10.1007/s12311-018-0952-3 PMID: 29876802

[12] Stern, P. Neuroscience: In search of new concepts. *Science,* **2017**, *358*, 464-465.

[13] Leshinskaya, A.; Caramazza, A. For a cognitive neuroscience of concepts: Moving beyond the grounding issue. *Psychon. Bull. Rev.,* **2016**, *23*(4), 991-1001. http://dx.doi.org/10.3758/s13423-015-0870-z PMID: 27294420

[14] Ren, F. Influence of cognitive neuroscience on contemporary philosophy of science. *Transl. Neurosci.,* **2019**, *10*, 37-43. http://dx.doi.org/10.1515/tnsci-2019-0007 PMID: 31098310

[15] Yuan, P.; Raz, N. Prefrontal cortex and executive functions in healthy adults: a meta-analysis of structural neuroimaging studies. *Neurosci. Biobehav. Rev.,* **2014**, *42*, 180-192. http://dx.doi.org/10.1016/j.neubiorev.2014.02.005 PMID: 24568942

[16] Ball, G.; Stokes, P.R.; Rhodes, R.A.; Bose, S.K.; Rezek, I.; Wink, A-M.; Lord, L-D.; Mehta, M.A.; Grasby, P.M.; Turkheimer, F.E. Executive functions and prefrontal cortex: a matter of persistence? *Front. Syst. Neurosci.,* **2011**, *5*, 3. http://dx.doi.org/10.3389/fnsys.2011.00003 PMID: 21286223

[17] Reeber, S.L.; Otis, T.S.; Sillitoe, R.V. New roles for the cerebellum in health and disease. *Front. Syst. Neurosci.,* **2013**, *7*, 83. http://dx.doi.org/10.3389/fnsys.2013.00083 PMID: 24294192

[18] Lawrenson, C.; Bares, M.; Kamondi, A. Seeking a unified framework for cerebellar function and dysfunction: from circuit operations to cognition. *Front. Neural. Circuits,* **2013**, 6, 116.

[19] Klein, A.P.; Ulmer, J.L.; Quinet, S.A.; Mathews, V.; Mark, L.P. Nonmotor functions of the cerebellum: an introduction. *AJNR Am. J. Neuroradiol.,* **2016**, *37*(6), 1005-1009. http://dx.doi.org/10.3174/ajnr.A4720 PMID: 26939633

[20] Barkley, R.A. The executive functions and self-regulation: an evolutionary neuropsychological perspective. *Neuropsychol. Rev.,* **2001**, *11*(1), 1-29. http://dx.doi.org/10.1023/A:1009085417776 PMID: 11392560

[21] Schmahmann, J.D. A brief history of the cerebellum. In: *Essentials of cerebellum and cerebellar disorders*; Springer, **2016**; pp. 5-20. http://dx.doi.org/10.1007/978-3-319-24551-5_2

[22] Glickstein, M.; Strata, P.; Voogd, J. Cerebellum: history. *Neuroscience,* **2009**, *162*(3), 549-559. http://dx.doi.org/10.1016/j.neuroscience.2009.02.054 PMID: 19272426

[23] Manto, M.; Huisman, T.A.G.M. The cerebellum from the fetus to the elderly: history, advances, and future challenges. *Handb. Clin. Neurol.,* **2018**, *155*, 407-413. http://dx.doi.org/10.1016/B978-0-444-64189-2.00027-5 PMID: 29891075

[24] Voogd, J.; Koehler, P.J. Historic notes on anatomic, physiologic, and clinical research on the cerebellum. *Handb. Clin. Neurol.,* **2018**, *154*, 3-26. http://dx.doi.org/10.1016/B978-0-444-63956-1.00001-1 PMID: 29903448

[25] Ashizawa, T.; Xia, G. Ataxia. *Continuum (Minneap. Minn.),* **2016**, *22*, 1208-1226. http://dx.doi.org/10.1212/CON.0000000000000362 PMID: 27495205

[26] Vožeh, F. Jan Evangelista Purkyně and the cerebellum then and now. *Physiol. Res.,* **2015**, *64*(Suppl. 5), S567-S584. http://dx.doi.org/10.33549/physiolres.933231 PMID: 26674295

[27] Koeppen, A.H. The neuropathology of the adult cerebellum. *Handb. Clin. Neurol.,* **2018**, *154*, 129-149.

http://dx.doi.org/10.1016/B978-0-444-63956-1.00008-4 PMID: 29903436

[28] Argyropoulos, G.P.; van Dun, K.; Adamaszek, M.; Leggio, M.; Manto, M.; Masciullo, M.; Molinari, M.; Stoodley, C.; Van Overwalle, F.; Ivry, R. The cerebellar cognitive affective/Schmahmann syndrome: a task force paper. *Cerebellum,* **2020**, *19*, 102-125. PMID: 31522332

[29] Vožeh, F. Cerebellum—from JE Purkyně up to contemporary research. *Cerebellum,* **2017**, *16*(3), 691-694. http://dx.doi.org/10.1007/s12311-016-0835-4 PMID: 27858255

[30] Thair, H.; Holloway, A.; Newport, R.; Smith, A. Transcranial direct current stimulation (tDCS): A beginner's guide for design and implementation. *Front Neurosci.,* **2017**, *11*, 641. http://dx.doi.org/10.3389/fnins.2017.00641 PMID: 29213226

[31] Szameitat, A.J.; Schubert, T.; Müller, K.; Von Cramon, D.Y. Localization of executive functions in dual-task performance with fMRI. *J. Cogn. Neurosci.,* **2002**, *14*(8), 1184-1199. http://dx.doi.org/10.1162/089892902760807195 PMID: 12495525

[32] Bellebaum, C.; Daum, I. Cerebellar involvement in executive control. *Cerebellum,* **2007**, *6*(3), 184-192. http://dx.doi.org/10.1080/14734220601169707 PMID: 17786814

[33] D'Angelo, E. Physiology of the cerebellum. *Handb. Clin. Neurol.,* **2018**, *154*, 85-108. http://dx.doi.org/10.1016/B978-0-444-63956-1.00006-0 PMID: 29903454

[34] Diedrichsen, J.; King, M.; Hernandez-Castillo, C.; Sereno, M.; Ivry, R.B. Universal transform or multiple functionality? Understanding the contribution of the human cerebellum across task domains. *Neuron,* **2019**, *102*(5), 918-928. http://dx.doi.org/10.1016/j.neuron.2019.04.021 PMID: 31170400

[35] Reeber, S.L.; White, J.J.; George-Jones, N.A.; Sillitoe, R.V. Architecture and development of olivocerebellar circuit topography. *Front. Neural Circuits,* **2013**, *6*, 115. http://dx.doi.org/10.3389/fncir.2012.00115 PMID: 23293588

[36] Sathyanesan, A.; Zhou, J.; Scafidi, J.; Heck, D.H.; Sillitoe, R.V.; Gallo, V. Emerging connections between cerebellar development, behaviour and complex brain disorders. *Nat. Rev. Neurosci.,* **2019**, *20*(5), 298-313. http://dx.doi.org/10.1038/s41583-019-0152-2 PMID: 30923348

[37] Herndon, R.M. The fine structure of the Purkinje cell. *J. Cell Biol.,* **1963**, *18*, 167-180. http://dx.doi.org/10.1083/jcb.18.1.167 PMID: 13953993

[38] Glickstein, M.; Voogd, J. Lodewijk Bolk and the comparative anatomy of the cerebellum. *Trends Neurosci.,* **1995**, *18*(5), 206-210. http://dx.doi.org/10.1016/0166-2236(95)93903-B PMID: 7610489

[39] Voogd, J.; Glickstein, M. The anatomy of the cerebellum. *Trends Cogn. Sci.,* **1998**, *2*(9), 307-313. http://dx.doi.org/10.1016/S1364-6613(98)01210-8 PMID: 21227226

[40] Oberdick, J.; Sillitoe, R.V. Cerebellar zones: history, development, and function. *Cerebellum,* **2011**, *10*(3), 301-306. http://dx.doi.org/10.1007/s12311-011-0306-x PMID: 21822545

[41] Ruigrok, T.J. Ins and outs of cerebellar modules. *Cerebellum,* **2011**, *10*(3), 464-474. http://dx.doi.org/10.1007/s12311-010-0164-y PMID: 20232190

[42] Sotelo, C.; Alvarado-Mallart, R.M. Embryonic and adult neurons interact to allow Purkinje cell replacement in mutant cerebellum. *Nature,* **1987**, *327*(6121), 421-423. http://dx.doi.org/10.1038/327421a0 PMID: 3587363

[43] Buffo, A.; Rossi, F. Origin, lineage and function of cerebellar glia. *Prog. Neurobiol.,* **2013**, *109*, 42-63. http://dx.doi.org/10.1016/j.pneurobio.2013.08.001 PMID: 23981535

[44] Goertzen, A.; Veh, R.W. Fañanas cells-the forgotten cerebellar glia cell type: Immunocytochemistry reveals two potassium channel-related polypeptides, Kv2.2 and Calsenilin (KChIP3) as potential marker proteins. *Glia,* **2018**, *66*(10), 2200-2208. http://dx.doi.org/10.1002/glia.23478 PMID: 30151916

[45] Wizeman, J.W.; Guo, Q.; Wilion, E.M.; Li, J.Y. Specification of diverse cell types during early neurogenesis of the mouse cerebellum. *eLife,* **2019**, *8*, e42388. http://dx.doi.org/10.7554/eLife.42388 PMID: 30735127

[46] Derouesné, C. Qu'est-ce qu'une émotion? Une introduction à l'étude des émotions. *Gériatr. Psychol. Neuropsychiatr. Vieil.,* **2011**, *9*(1), 69-81. PMID: 21586380

[47] Strata, P.; Scelfo, B.; Sacchetti, B. Involvement of cerebellum in emotional behavior. *Physiol. Res.,* **2011**, *60*(Suppl. 1), S39-S48. http://dx.doi.org/10.33549/physiolres.932169 PMID: 21777033

[48] Blatt, G.J.; Oblak, A.L.; Schmahmann, J.D. Cerebellar connections with limbic circuits: Anatomy and functional implications. *Handbook of the cerebellum and cerebellar disorders*, **2013**, pp. 479-496.

[49] Moreno-Rius, J. The cerebellum in fear and anxiety-related disorders. *Prog. Neuropsychopharmacol. Biol. Psychiatry,* **2018**, *85*, 23-32. http://dx.doi.org/10.1016/j.pnpbp.2018.04.002 PMID: 29627508

[50] Lange, I.; Kasanova, Z.; Goossens, L.; Leibold, N.; De Zeeuw, C.I.; van Amelsvoort, T.; Schruers, K. The anatomy of fear learning in the cerebellum: A systematic meta-analysis. *Neurosci. Biobehav. Rev.,* **2015**, *59*, 83-91. http://dx.doi.org/10.1016/j.neubiorev.2015.09.019 PMID: 26441374

[51] Utz, A.; Thürling, M.; Ernst, T.M.; Hermann, A.; Stark, R.; Wolf, O.T.; Timmann, D.; Merz, C.J. Cerebellar vermis contributes to the extinction of conditioned fear. *Neurosci. Lett.,* **2015**, *604*, 173-177. http://dx.doi.org/10.1016/j.neulet.2015.07.026 PMID: 26219987

[52] Strata, P. The emotional cerebellum. *Cerebellum,* **2015**, *14*(5), 570-577. http://dx.doi.org/10.1007/s12311-015-0649-9 PMID: 25626523

[53] Ernst, T.M.; Brol, A.E.; Gratz, M.; Ritter, C.; Bingel, U.; Schlamann, M.; Maderwald, S.; Quick, H.H.; Merz, C.J.; Timmann, D. The cerebellum is involved in processing of predictions and prediction errors in a fear conditioning paradigm. *eLife,* **2019**, *8*, e46831. http://dx.doi.org/10.7554/eLife.46831 PMID: 31464686

[54] Leaton, R. Fear and the cerebellum. *Mol. Psychiatry,* **2003**, *8*(5), 461-462. http://dx.doi.org/10.1038/sj.mp.4001286 PMID: 12808422

[55] Sakakibara, R. The cerebellum seems not a 'little brain' for the autonomic nervous system. *Clin. Neurophysiol.,* **2019**, *130*(1), 160. http://dx.doi.org/10.1016/j.clinph.2018.08.021 PMID: 30219271

[56] Shu, L.; Xie, J.; Yang, M.; Li, Z.; Li, Z.; Liao, D.; Xu, X.; Yang, X. A review of emotion recognition using physiological signals. *Sensors (Basel),* **2018**, *18*(7), 2074. http://dx.doi.org/10.3390/s18072074 PMID: 29958457

[57] Yang, D.; Alsadoon, A.; Prasad, P.C.; Singh, A.K.; Elchouemi, A. An emotion recognition model based on facial recognition in virtual learning environment. *Procedia Comput. Sci.,* **2018**, *125*, 2-10. http://dx.doi.org/10.1016/j.procs.2017.12.003

[58] Tarnowski, P.; Kołodziej, M.; Majkowski, A.; Rak, R.J. Emotion recognition using facial expressions. *Procedia Comput. Sci.,* **2017**, *108*, 1175-1184. http://dx.doi.org/10.1016/j.procs.2017.05.025

[59] Ferretti, V.; Papaleo, F. Understanding others: Emotion recognition in humans and other animals. *Genes Brain Behav.,* **2019**, *18*(1), e12544. PMID: 30549185

[60] Sokolov, A.A. The cerebellum in social cognition. *Front. Cell. Neurosci.,* **2018**, *12*, 145. http://dx.doi.org/10.3389/fncel.2018.00145

[61] Hoche, F.; Guell, X.; Sherman, J.C.; Vangel, M.G.; Schmahmann, J.D. Cerebellar contribution to social cognition. *Cerebellum,* **2016**, *15*(6), 732-743. http://dx.doi.org/10.1007/s12311-015-0746-9 PMID: 26585120

[62] Qi, Z.; An, Y.; Zhang, M.; Li, H-J.; Lu, J. Altered cerebro-cerebellar limbic network in AD spectrum: a resting-state fMRI study. *Front. Neural Circuits,* **2019**, *13*, 72. http://dx.doi.org/10.3389/fncir.2019.00072 PMID: 31780903

[63] Boothe, A.C. *Resting state functional connectivity of the limbic cerebellum in ASD: vermis lobules IV, VII, and IX*; The University of Texas at Austin, **2019**.

[64] Adamaszek, M.; D'Agata, F.; Steele, C.J.; Sehm, B.; Schoppe, C.; Strecker, K.; Woldag, H.; Hummelsheim, H.; Kirkby, K.C. Comparison of visual and auditory emotion recognition in patients with

cerebellar and Parkinson´s disease. *Soc. Neurosci.,* **2019**, *14*(2), 195-207. http://dx.doi.org/10.1080/17470919.2018.1434089 PMID: 29375013

[65] Gold, A.K.; Toomey, R. The role of cerebellar impairment in emotion processing: a case study. *Cerebellum Ataxias,* **2018**, *5*, 11. http://dx.doi.org/10.1186/s40673-018-0090-1 PMID: 30345063

[66] Stoodley, C.J. The cerebellum and neurodevelopmental disorders. *Cerebellum,* **2016**, *15*(1), 34-37. http://dx.doi.org/10.1007/s12311-015-0715-3 PMID: 26298473

[67] Ferrucci, R.; Giannicola, G.; Rosa, M.; Fumagalli, M.; Boggio, P.S.; Hallett, M.; Zago, S.; Priori, A. Cerebellum and processing of negative facial emotions: cerebellar transcranial DC stimulation specifically enhances the emotional recognition of facial anger and sadness. *Cogn. Emotion,* **2012**, *26*(5), 786-799. http://dx.doi.org/10.1080/02699931.2011.619520 PMID: 22077643

[68] Fusar-Poli, P.; Placentino, A.; Carletti, F.; Landi, P.; Allen, P.; Surguladze, S.; Benedetti, F.; Abbamonte, M.; Gasparotti, R.; Barale, F.; Perez, J.; McGuire, P.; Politi, P. Functional atlas of emotional faces processing: a voxel-based meta-analysis of 105 functional magnetic resonance imaging studies. *J. Psychiatry Neurosci.,* **2009**, *34*(6), 418-432. PMID: 19949718

[69] Lin, L.C.; Qu, Y.; Telzer, E.H. Intergroup social influence on emotion processing in the brain. *Proc. Natl. Acad. Sci. USA,* **2018**, *115*(42), 10630-10635. http://dx.doi.org/10.1073/pnas.1802111115 PMID: 30282742

[70] Green, M.J.; Waldron, J.H.; Coltheart, M. Emotional context processing is impaired in schizophrenia. *Cogn. Neuropsychiatry,* **2007**, *12*(3), 259-280. http://dx.doi.org/10.1080/13546800601051847 PMID: 17453905

[71] Zhang, L.; Fan, H.; Wang, S.; Li, H. The effect of emotional arousal on inhibition of return among youth with depressive tendency. *Front. Psychol.,* **2019**, *10*, 1487. http://dx.doi.org/10.3389/fpsyg.2019.01487 PMID: 31312156

[72] Zinchenko, A.; Obermeier, C.; Kanske, P.; Schröger, E.; Villringer, A.; Kotz, S.A. The influence of negative emotion on cognitive and emotional control remains intact in aging. *Front. Aging Neurosci.,* **2017**, *9*, 349. http://dx.doi.org/10.3389/fnagi.2017.00349 PMID: 29163132

[73] Smith, R.; Parr, T.; Friston, K.J. Simulating emotions: An active inference model of emotional state inference and emotion concept learning. *Front. Psychol.,* **2019**, *10*, 2844. http://dx.doi.org/10.3389/fpsyg.2019.02844 PMID: 31920873

[74] Vergallito, A.; Mattavelli, G.; Gerfo, E.L.; Anzani, S.; Rovagnati, V.; Speciale, M.; Vinai, P.; Vinai, P.; Vinai, L.; Lauro, L.J.R. Explicit and implicit responses of seeing own *vs*. Others' emotions: An electromyographic study on the neurophysiological and cognitive basis of the self-mirroring technique. *Front. Psychol.,* **2020**, *11*, 433. http://dx.doi.org/10.3389/fpsyg.2020.00433 PMID: 32296363

[75] Stoodley, C.J.; Schmahmann, J.D. Evidence for topographic organization in the cerebellum of motor control *versus* cognitive and affective processing. *Cortex.,* **2010**, *46*(7), 831-844. http://dx.doi.org/10.1016/j.cortex.2009.11.008 PMID: 20152963

[76] Snow, W.M.; Stoesz, B.M.; Anderson, J.E. The cerebellum in emotional processing: Evidence from human and non-human animals. *AIMS Neuroscience,* **2014**, *1*(1), 96-119. http://dx.doi.org/10.3934/Neuroscience.2014.1.96

[77] Park, I.S.; Lee, N.J.; Rhyu, I.J. Roles of the declive, folium, and tuber cerebellar vermian lobules in sportspeople. *J. Clin. Neurol.,* **2018**, *14*(1), 1-7. http://dx.doi.org/10.3988/jcn.2018.14.1.1 PMID: 29141275

[78] Sidtis, J.J.; Ahn, J.S.; Gomez, C.; Sidtis, D. Speech characteristics associated with three genotypes of ataxia. *J. Commun. Disord.,* **2011**, *44*(4), 478-492. http://dx.doi.org/10.1016/j.jcomdis.2011.03.002 PMID: 21592489

[79] Teive, H.A.G.; Arruda, W.O. Cognitive dysfunction in spinocerebellar ataxias. *Dement. Neuropsychol.,* **2009**, *3*(3), 180-187. http://dx.doi.org/10.1590/S1980-57642009DN30300002 PMID: 29213626

[80] Schwartze, M.; Kotz, S.A. Contributions of cerebellar event-based temporal processing and preparatory function to speech perception. *Brain Lang.,* **2016**, *161*, 28-32. http://dx.doi.org/10.1016/j.bandl.2015.08.005 PMID: 26362972

[81] Mariën, P.; Manto, M. Cerebellum as a master-piece for linguistic predictability. *Cerebellum,* **2018**, *17*(2), 101-103. http://dx.doi.org/10.1007/s12311-017-0894-1 PMID: 29071518

[82] van Dun, K.; Vandenborre, D.; Mariën, P. Cerebellum and Writing. In: *The Linguistic Cerebellum*; Elsevier, **2016**; pp. 149-198. http://dx.doi.org/10.1016/B978-0-12-801608-4.00008-6

[83] Hertrich, I.; Mathiak, K.; Ackermann, H. The role of the cerebellum in speech perception and language comprehension. In: *The linguistic cerebellum*; Elsevier, **2016**; pp. 33-50. http://dx.doi.org/10.1016/B978-0-12-801608-4.00002-5

[84] Srivastava, P. The cerebellum: Learning movement, language, and social skills. *Indian J. Med. Res.,* **2015**, *141*, 847-848. http://dx.doi.org/10.4103/0971-5916.160740

[85] Ang, C.; Zhang, J.; Chu, M.; Li, H.; Tian, M.; Feng, X.; Zhang, M.; Liu, L.; Meng, X.; Ding, G. Intrinsic cerebro-cerebellar functional connectivity reveals the function of cerebellum VI in reading-related skills. *Front. Psychol.,* **2020**, *11*, 420. http://dx.doi.org/10.3389/fpsyg.2020.00420 PMID: 32265778

[86] Riès, S.K.; Dronkers, N.F.; Knight, R.T. Choosing words: left hemisphere, right hemisphere, or both? Perspective on the lateralization of word retrieval. *Ann. N. Y. Acad. Sci.,* **2016**, *1369*(1), 111-131. http://dx.doi.org/10.1111/nyas.12993 PMID: 26766393

[87] Guell, X.; Hoche, F.; Schmahmann, J.D. Metalinguistic deficits in patients with cerebellar dysfunction: empirical support for the dysmetria of thought theory. *Cerebellum,* **2015**, *14*(1), 50-58. http://dx.doi.org/10.1007/s12311-014-0630-z PMID: 25503825

[88] De Smet, H.J.; Paquier, P.; Verhoeven, J.; Mariën, P. The cerebellum: its role in language and related cognitive and affective functions. *Brain Lang.,* **2013**, *127*(3), 334-342. http://dx.doi.org/10.1016/j.bandl.2012.11.001 PMID: 23333152

[89] Lin, D.D.; Kleinman, J.T.; Wityk, R.J.; Gottesman, R.F.; Hillis, A.E.; Lee, A.W.; Barker, P.B. Crossed cerebellar diaschisis in acute stroke detected by dynamic susceptibility contrast MR perfusion imaging. *AJNR Am. J. Neuroradiol.,* **2009**, *30*(4), 710-715. http://dx.doi.org/10.3174/ajnr.A1435 PMID: 19193758

[90] Nicolson, R.I.; Fawcett, A.J.; Dean, P. Developmental dyslexia: the cerebellar deficit hypothesis. *Trends Neurosci.,* **2001**, *24*(9), 508-511. http://dx.doi.org/10.1016/S0166-2236(00)01896-8 PMID: 11506881

[91] Nicolson, R.I.; Fawcett, A.J. Development of dyslexia: The delayed neural commitment framework. *Front. Behav. Neurosci.,* **2019**, *13*, 112. http://dx.doi.org/10.3389/fnbeh.2019.00112 PMID: 31178705

[92] Bryant, B.R.; Bryant, D.P.; Shih, M.; Seok, S. Assistive technology and supports provision: A selective review of the literature and proposed areas of application. *Exceptionality,* **2010**, *18*, 203-213. http://dx.doi.org/10.1080/09362835.2010.513925

[93] Peterburs, J.; Blevins, L.C.; Sheu, Y-S.; Desmond, J.E. Cerebellar contributions to sequence prediction in verbal working memory. *Brain Struct. Funct.,* **2019**, *224*(1), 485-499. http://dx.doi.org/10.1007/s00429-018-1784-0 PMID: 30390152

[94] Arsenault, J.S.; Buchsbaum, B.R. Distributed neural representations of phonological features during speech perception. *J. Neurosci.,* **2015**, *35*(2), 634-642. http://dx.doi.org/10.1523/JNEUROSCI.2454-14.2015 PMID: 25589757

[95] Ashburn, S.M.; Flowers, D.L.; Napoliello, E.M.; Eden, G.F. Cerebellar function in children with and without dyslexia during single word processing. *Hum. Brain Mapp.,* **2020**, *41*(1), 120-138. http://dx.doi.org/10.1002/hbm.24792 PMID: 31597004

[96] Richards, T.L.; Berninger, V.W. Abnormal fMRI connectivity in children with dyslexia during a phoneme task: Before but not after treatment. *J. Neurolinguist.,* **2008**, *21*(4), 294-304. http://dx.doi.org/10.1016/j.jneuroling.2007.07.002 PMID: 19079567

[97] van Ermingen-Marbach, M.; Grande, M.; Pape-Neumann, J.; Sass, K.; Heim, S. Distinct neural signatures of cognitive subtypes of dyslexia with and without phonological deficits. *Neuroimage Clin.,* **2013**, *2*, 477-490. http://dx.doi.org/10.1016/j.nicl.2013.03.010 PMID: 24936406

[98] Cruz-Rodrigues, C.; Barbosa, T.; Toledo-Piza, C.M.; Miranda, M.C.; Bueno, O.F.A. Neuropsychological characteristics of dyslexic children. *Psicol. Reflex. Crit.,* **2014**, *27*, 539-546. http://dx.doi.org/10.1590/1678-7153.201427315

[99] Takahashi, E.; Hayashi, E.; Schmahmann, J.D.; Grant, P.E. Development of cerebellar connectivity in human fetal brains revealed by high angular resolution diffusion tractography. *Neuroimage,* **2014**, *96*, 326-333. http://dx.doi.org/10.1016/j.neuroimage.2014.03.022 PMID: 24650603

[100] Phillips, J.R., Jr; Hewedi, D.H.; Eissa, A.M.; Moustafa, A.A. The cerebellum and psychiatric disorders. *Front. Public Health,* **2015**, *3*, 66. http://dx.doi.org/10.3389/fpubh.2015.00066 PMID: 26000269

[101] Baldaçara, L.; Borgio, J.G.F.; Lacerda, A.L.; Jackowski, A.P. Cerebellum and psychiatric disorders. *Rev. Bras. Psiquiatr.,* **2008**, *30*(3), 281-289. http://dx.doi.org/10.1590/S1516-44462008000300016 PMID: 18833430

[102] Middleton, F.A.; Strick, P.L. Anatomical evidence for cerebellar and basal ganglia involvement in higher cognitive function. *Science,* **1994**, *266*(5184), 458-461. http://dx.doi.org/10.1126/science.7939688 PMID: 7939688

[103] Ueland, T.; Øie, M.; Inge Landrø, N.; Rund, B.R. Cognitive functioning in adolescents with schizophrenia spectrum disorders. *Psychiatry Res.,* **2004**, *126*(3), 229-239. http://dx.doi.org/10.1016/j.psychres.2004.02.014 PMID: 15157749

[104] Konarski, J.Z.; McIntyre, R.S.; Grupp, L.A.; Kennedy, S.H. Is the cerebellum relevant in the circuitry of neuropsychiatric disorders? *J. Psychiatry Neurosci.,* **2005**, *30*(3), 178-186. PMID: 15944742

[105] Shinn, A.K.; Baker, J.T.; Lewandowski, K.E.; Öngür, D.; Cohen, B.M. Aberrant cerebellar connectivity in motor and association networks in schizophrenia. *Front. Hum. Neurosci.,* **2015**, *9*, 134. http://dx.doi.org/10.3389/fnhum.2015.00134 PMID: 25852520

[106] Ebisch, S.J.; Mantini, D.; Northoff, G.; Salone, A.; De Berardis, D.; Ferri, F.; Ferro, F.M.; Di Giannantonio, M.; Romani, G.L.; Gallese, V. Altered brain long-range functional interactions underlying the link between aberrant self-experience and self-other relationship in first-episode schizophrenia. *Schizophr. Bull.,* **2014**, *40*(5), 1072-1082. http://dx.doi.org/10.1093/schbul/sbt153 PMID: 24191160

[107] Ferri, F.; Costantini, M.; Salone, A.; Ebisch, S.; De Berardis, D.; Mazzola, V.; Arciero, G.; Ferro, F.M.; Di Giannantonio, M.; Romani, G.L.; Gallese, V. Binding action and emotion in first-episode schizophrenia. *Psychopathology,* **2014**, *47*(6), 394-407. http://dx.doi.org/10.1159/000366133 PMID: 25277690

[108] Biederman, J. Attention-deficit/hyperactivity disorder: a selective overview. *Biol. Psychiatry,* **2005**, *57*(11), 1215-1220. http://dx.doi.org/10.1016/j.biopsych.2004.10.020 PMID: 15949990

[109] Biederman, J.; Faraone, S.V. Attention-deficit hyperactivity disorder. *Lancet,* **2005**, *366*(9481), 237-248. http://dx.doi.org/10.1016/S0140-6736(05)66915-2 PMID: 16023516

[110] Rajan, S.; McKee, M.; Rangarajan, S.; Bangdiwala, S.; Rosengren, A.; Gupta, R.; Kutty, V.R.; Wielgosz, A.; Lear, S.; AlHabib, K.F.; Co, H.U.; Lopez-Jaramillo, P.; Avezum, A.; Seron, P.; Oguz, A.; Kruger, I.M.; Diaz, R.; Nafiza, M.N.; Chifamba, J.; Yeates, K.; Kelishadi, R.; Sharief, W.M.; Szuba, A.; Khatib, R.; Rahman, O.; Iqbal, R.; Bo, H.; Yibing, Z.; Wei, L.; Yusuf, S. Association of symptoms of depression with cardiovascular disease and mortality in low-, middle-, and high-income countries. *JAMA Psychiatry,* **2020**, *77*(10), 1052-1063. http://dx.doi.org/10.1001/jamapsychiatry.2020.1351 PMID: 32520341

[111] Qiu, A.; Crocetti, D.; Adler, M.; Mahone, E.M.; Denckla, M.B.; Miller, M.I.; Mostofsky, S.H. Basal ganglia volume and shape in children with attention deficit hyperactivity disorder. *Am. J. Psychiatry,* **2009**, *166*(1), 74-82. http://dx.doi.org/10.1176/appi.ajp.2008.08030426 PMID: 19015232

[112] Valera, E.M.; Faraone, S.V.; Murray, K.E.; Seidman, L.J. Meta-analysis of structural imaging findings in attention-deficit/ hyperactivity disorder. *Biol. Psychiatry,* **2007**, *61*(12), 1361-1369. http://dx.doi.org/10.1016/j.biopsych.2006.06.011 PMID: 16950217

[113] Ivanov, I.; Murrough, J.W.; Bansal, R.; Hao, X.; Peterson, B.S. Cerebellar morphology and the effects of stimulant medications in youths with attention deficit-hyperactivity disorder. *Neuropsychopharmacology,* **2014**, *39*(3), 718-726. http://dx.doi.org/10.1038/npp.2013.257 PMID: 24077064

[114] Townsend, J.; Courchesne, E.; Covington, J.; Westerfield, M.; Harris, N.S.; Lyden, P.; Lowry, T.P.; Press, G.A. Spatial attention deficits in patients with acquired or developmental cerebellar abnormality. *J. Neurosci.,* **1999**, *19*(13), 5632-5643. http://dx.doi.org/10.1523/JNEUROSCI.19-13-05632.1999 PMID: 10377369

[115] American Psychiatric Association. *A. Diagnostic and statistical manual of mental disorders*; American Psychiatric Association: Washington DC, **1980**, 3.

[116] Wang, S.S.H.; Kloth, A.D.; Badura, A. The cerebellum, sensitive periods, and autism. *Neuron,* **2014**, *83*(3), 518-532. http://dx.doi.org/10.1016/j.neuron.2014.07.016 PMID: 25102558

[117] Skefos, J.; Cummings, C.; Enzer, K.; Holiday, J.; Weed, K.; Levy, E.; Yuce, T.; Kemper, T.; Bauman, M. Regional alterations in purkinje cell density in patients with autism. *PLoS One,* **2014**, *9*(2), e81255. http://dx.doi.org/10.1371/journal.pone.0081255 PMID: 24586223

[118] Brambilla, P.; Barale, F.; Caverzasi, E.; Soares, J.C. Anatomical MRI findings in mood and anxiety disorders. *Epidemiol. Psichiatr. Soc.,* **2002**, *11*(2), 88-99. http://dx.doi.org/10.1017/S1121189X00005558 PMID: 12212470

[119] Jurjus, G.J.; Weiss, K.M.; Jaskiw, G.E. Schizophrenia-like psychosis and cerebellar degeneration. *Schizophr. Res.,* **1994**, *12*(2), 183-184. http://dx.doi.org/10.1016/0920-9964(94)90076-0 PMID: 8043529

[120] Monkul, E.S.; Hatch, J.P.; Sassi, R.B.; Axelson, D.; Brambilla, P.; Nicoletti, M.A.; Keshavan, M.S.; Ryan, N.D.; Birmaher, B.; Soares, J.C. MRI study of the cerebellum in young bipolar patients. *Prog. Neuropsychopharmacol. Biol. Psychiatry,* **2008**, *32*(3), 613-619. http://dx.doi.org/10.1016/j.pnpbp.2007.09.016 PMID: 18272276

[121] Mills, N.P.; Delbello, M.P.; Adler, C.M.; Strakowski, S.M. MRI analysis of cerebellar vermal abnormalities in bipolar disorder. *Am. J. Psychiatry,* **2005**, *162*(8), 1530-1532. http://dx.doi.org/10.1176/appi.ajp.162.8.1530 PMID: 16055777

[122] Sepede, G.; Chiacchiaretta, P.; Gambi, F.; Di Iorio, G.; De Berardis, D.; Ferretti, A.; Perrucci, M.G.; Di Giannantonio, M. Bipolar disorder with and without a history of psychotic features: fMRI correlates of sustained attention. *Prog. Neuropsychopharmacol. Biol. Psychiatry,* **2020**, *98*, 109817-109817. http://dx.doi.org/10.1016/j.pnpbp.2019.109817 PMID: 31756418

[123] Critchley, H.D.; Corfield, D.R.; Chandler, M.P.; Mathias, C.J.; Dolan, R.J. Cerebral correlates of autonomic cardiovascular arousal: a functional neuroimaging investigation in humans. *J. Physiol.,* **2000**, *523*(Pt 1), 259-270. http://dx.doi.org/10.1111/j.1469-7793.2000.t01-1-00259.x PMID: 10673560

[124] Sakai, Y.; Kumano, H.; Nishikawa, M.; Sakano, Y.; Kaiya, H.; Imabayashi, E.; Ohnishi, T.; Matsuda, H.; Yasuda, A.; Sato, A.; Diksic, M.; Kuboki, T. Cerebral glucose metabolism associated with a fear network in panic disorder. *Neuroreport,* **2005**, *16*(9), 927-931. http://dx.doi.org/10.1097/00001756-200506210-00010 PMID: 15931063

[125] De Berardis, D.; Fornaro, M.; Orsolini, L.; Ventriglio, A.; Vellante, F.; Di Giannantonio, M. Emotional dysregulation in adolescents: implications for the development of severe psychiatric disorders, substance abuse, and suicidal ideation and behaviors. *Brain Sci.,* **2020**, *10*(9), 591. http://dx.doi.org/10.3390/brainsci10090591 PMID: 32858969

[126] Schweizer, S.; Gotlib, I.H.; Blakemore, S-J. The role of affective control in emotion regulation during adolescence. *Emotion,* **2020**, *20*(1), 80-86. http://dx.doi.org/10.1037/emo0000695 PMID: 31961183

[127] Compas, B.E.; Jaser, S.S.; Bettis, A.H.; Watson, K.H.; Gruhn, M.A.; Dunbar, J.P.; Williams, E.; Thigpen, J.C. Coping, emotion regulation, and psychopathology in childhood and adolescence: A

meta-analysis and narrative review. *Psychol. Bull.,* **2017**, *143*(9), 939-991.
http://dx.doi.org/10.1037/bul0000110 PMID: 28616996

[128] Sifneos, P.E.; Apfel-Savitz, R.; Frankel, F.H. The phenomenon of 'alexithymia'. Observations in neurotic and psychosomatic patients. *Psychother. Psychosom.,* **1977**, *28*(1-4), 47-57.
http://dx.doi.org/10.1159/000287043 PMID: 609697

[129] De Berardis, D.; Vellante, F.; Fornaro, M.; Anastasia, A.; Olivieri, L.; Rapini, G.; Serroni, N.; Orsolini, L.; Valchera, A.; Carano, A.; Tomasetti, C.; Varasano, P.A.; Pressanti, G.L.; Bustini, M.; Pompili, M.; Serafini, G.; Perna, G.; Martinotti, G.; Di Giannantonio, M. Alexithymia, suicide ideation, affective temperaments and homocysteine levels in drug naïve patients with post-traumatic stress disorder: an exploratory study in the everyday 'real world' clinical practice. *Int. J. Psychiatry Clin. Pract.,* **2020**, *24*(1), 83-87.
http://dx.doi.org/10.1080/13651501.2019.1699575 PMID: 31829763

[130] Serafini, G.; De Berardis, D.; Valchera, A.; Canepa, G.; Geoffroy, P.A.; Pompili, M.; Amore, M. Alexithymia as a possible specifier of adverse outcomes: Clinical correlates in euthymic unipolar individuals. *J. Affect. Disord.,* **2020**, *263*, 428-436.
http://dx.doi.org/10.1016/j.jad.2019.10.046 PMID: 31969274

[131] Taylor, G.J. Alexithymia: concept, measurement, and implications for treatment. *Am. J. Psychiatry,* **1984**, *141*(6), 725-732.
http://dx.doi.org/10.1176/ajp.141.6.725 PMID: 6375397

[132] Taylor, P. *The Return of the Multi-Generational Family Household*; Pew Research Center, **2010**.

[133] Meza-Concha, N.; Arancibia, M.; Salas, F.; Behar, R.; Salas, G.; Silva, H.; Escobar, R. Towards a neurobiological understanding of alexithymia. *Medwave.,* **2017**, *17*(4), e6960.
http://dx.doi.org/10.5867/medwave.2017.04.6960 PMID: 28622282

[134] Reeves, R.R.; Johnson-Walker, D. Alexithymia: Should this personality disorder be considered during treatment of patients with mental illness? *J. Psychosoc. Nurs. Ment. Health Serv.,* **2015**, *53*(8), 25-29.
http://dx.doi.org/10.3928/02793695-20150720-04 PMID: 26268478

[135] Orzechowska, A.; Denys, K.; Gałecki, P. Alexithymia--definition, causes and participation in the etiology of diseases. *Pol. Merkuriusz Lek.,* **2014**, *37*(218), 128-133.
PMID: 25252451

[136] Tolmunen, T.; Heliste, M.; Lehto, S.M.; Hintikka, J.; Honkalampi, K.; Kauhanen, J. Stability of alexithymia in the general population: an 11-year follow-up. *Compr. Psychiatry,* **2011**, *52*(5), 536-541.
http://dx.doi.org/10.1016/j.comppsych.2010.09.007 PMID: 21081227

[137] Laricchiuta, D.; Petrosini, L.; Picerni, E.; Cutuli, D.; Iorio, M.; Chiapponi, C.; Caltagirone, C.; Piras, F.; Spalletta, G. The embodied emotion in cerebellum: a neuroimaging study of alexithymia. *Brain Struct. Funct.,* **2015**, *220*(4), 2275-2287.
http://dx.doi.org/10.1007/s00429-014-0790-0 PMID: 24841618

[138] Sepede, G.; De Berardis, D.; Campanella, D.; Perrucci, M.G.; Ferretti, A.; Salerno, R.M.; Di Giannantonio, M.; Romani, G.L.; Gambi, F. Neural correlates of negative emotion processing in bipolar disorder. *Prog. Neuropsychopharmacol. Biol. Psychiatry,* **2015**, *60*, 1-10.
http://dx.doi.org/10.1016/j.pnpbp.2015.01.016 PMID: 25661850

[139] De Berardis, D.; Fornaro, M.; Orsolini, L. Editorial: "No words for feelings, yet!" exploring alexithymia, disorder of affect regulation, and the "mind-body" connection. *Front. Psychiatry,* **2020**, *11*, 593462.
http://dx.doi.org/10.3389/fpsyt.2020.593462 PMID: 33061929

[140] Stoodley, C.J.; Valera, E.M.; Schmahmann, J.D. Functional topography of the cerebellum for motor and cognitive tasks: an fMRI study. *Neuroimage,* **2012**, *59*(2), 1560-1570.
http://dx.doi.org/10.1016/j.neuroimage.2011.08.065 PMID: 21907811

[141] Guo, C.C.; Tan, R.; Hodges, J.R.; Hu, X.; Sami, S.; Hornberger, M. Network-selective vulnerability of the human cerebellum to Alzheimer's disease and frontotemporal dementia. *Brain,* **2016**, *139*(Pt 5), 1527-1538.
http://dx.doi.org/10.1093/brain/aww003 PMID: 26912642

[142] Dickson, D.W.; Wertkin, A.; Mattiace, L.A.; Fier, E.; Kress, Y.; Davies, P.; Yen, S-H. Ubiquitin immunoelectron microscopy of dystrophic neurites in cerebellar senile plaques of Alzheimer's disease. *Acta Neuropathol.,* **1990**, *79*(5), 486-493.
http://dx.doi.org/10.1007/BF00296107 PMID: 2158201

[143] Mattiace, L.A.; Davies, P.; Yen, S-H.; Dickson, D.W. Microglia in cerebellar plaques in Alzheimer's disease. *Acta Neuropathol.,* **1990**, *80*(5), 493-498.
http://dx.doi.org/10.1007/BF00294609 PMID: 2251906

[144] Chen, J.; Cohen, M.L.; Lerner, A.J.; Yang, Y.; Herrup, K. DNA damage and cell cycle events implicate cerebellar dentate nucleus neurons as targets of Alzheimer's disease. *Mol. Neurodegener.,* **2010**, *5*, 60.
http://dx.doi.org/10.1186/1750-1326-5-60 PMID: 21172027

[145] Mahoney, C.J.; Downey, L.E.; Ridgway, G.R.; Beck, J.; Clegg, S.; Blair, M.; Finnegan, S.; Leung, K.K.; Yeatman, T.; Golden, H.; Mead, S.; Rohrer, J.D.; Fox, N.C.; Warren, J.D. Longitudinal neuroimaging and neuropsychological profiles of frontotemporal dementia with C9ORF72 expansions. *Alzheimers Res. Ther.,* **2012**, *4*(5), 41.
http://dx.doi.org/10.1186/alzrt144 PMID: 23006986

[146] Whitwell, J.L.; Weigand, S.D.; Boeve, B.F.; Senjem, M.L.; Gunter, J.L.; DeJesus-Hernandez, M.; Rutherford, N.J.; Baker, M.; Knopman, D.S.; Wszolek, Z.K.; Parisi, J.E.; Dickson, D.W.; Petersen, R.C.; Rademakers, R.; Jack, C.R., Jr; Josephs, K.A. Neuroimaging signatures of frontotemporal dementia genetics: C9ORF72, tau, progranulin and sporadics. *Brain,* **2012**, *135*(Pt 3), 794-806.
http://dx.doi.org/10.1093/brain/aws001 PMID: 22366795

[147] Lewis, M.M.; Galley, S.; Johnson, S.; Stevenson, J.; Huang, X.; McKeown, M.J. The role of the cerebellum in the pathophysiology of Parkinson's disease. *Can. J. Neurol. Sci.,* **2013**, *40*(3), 299-306.
http://dx.doi.org/10.1017/S0317167100014232 PMID: 23603164

[148] Solstrand Dahlberg, L.; Lungu, O.; Doyon, J. Cerebellar Contribution to Motor and Non-motor Functions in Parkinson's Disease: A Meta-Analysis of fMRI Findings. *Front. Neurol.,* **2020**, *11*, 127.
http://dx.doi.org/10.3389/fneur.2020.00127 PMID: 32174883

[149] Pfeiffer, R.F. Non-motor symptoms in Parkinson's disease. *Parkinsonism Relat. Disord.,* **2016**, *22*(Suppl. 1), S119-S122.
http://dx.doi.org/10.1016/j.parkreldis.2015.09.004 PMID: 26372623

[150] Rana, A.Q.; Ahmed, U.S.; Chaudry, Z.M.; Vasan, S. Parkinson's disease: a review of non-motor symptoms. *Expert Rev. Neurother.,* **2015**, *15*(5), 549-562.
http://dx.doi.org/10.1586/14737175.2015.1038244 PMID: 25936847

[151] van Eijsden, P.; Veldink, J.H.; Linn, F.H.; Scheltens, P.; Biessels, G.J. Progressive dementia and mesiotemporal atrophy on brain MRI: neurosyphilis mimicking pre-senile Alzheimer's disease? *Eur. J. Neurol.,* **2008**, *15*(2), e14-e15.
http://dx.doi.org/10.1111/j.1468-1331.2007.02018.x PMID: 18093152

[152] Chaudhuri, K.R.; Healy, D.G.; Schapira, A.H. Non-motor symptoms of Parkinson's disease: diagnosis and management. *Lancet Neurol.,* **2006**, *5*(3), 235-245.
http://dx.doi.org/10.1016/S1474-4422(06)70373-8 PMID: 16488379

[153] Hinnell, C.; Chaudhuri, K.R. The effect of non-motor symptoms on quality of life in Parkinson's disease. *Eur. Neurol. Rev.,* **2009**, *4*, 29-33.
http://dx.doi.org/10.17925/ENR.2009.04.02.29

[154] Obeso, J.A.; Rodríguez-Oroz, M.C.; Rodríguez, M.; Lanciego, J.L.; Artieda, J.; Gonzalo, N.; Olanow, C.W. Pathophysiology of the basal ganglia in Parkinson's disease. *Trends Neurosci.,* **2000**, *23*(10)(Suppl.), S8-S19.
http://dx.doi.org/10.1016/S1471-1931(00)00028-8 PMID: 11052215

[155] Alexander, G.E.; Crutcher, M.D. Functional architecture of basal ganglia circuits: neural substrates of parallel processing. *Trends Neurosci.,* **1990**, *13*(7), 266-271.
http://dx.doi.org/10.1016/0166-2236(90)90107-L PMID: 1695401

[156] O'Doherty, J.P.; Dayan, P.; Friston, K.; Critchley, H.; Dolan, R.J. Temporal difference models and reward-related learning in the human brain. *Neuron,* **2003**, *38*(2), 329-337.
http://dx.doi.org/10.1016/S0896-6273(03)00169-7 PMID: 12718865

[157] Narabayashi, H.; Maeda, T.; Yokochi, F. Long-term follow-up study of nucleus ventralis intermedius and ventrolateralis thalamotomy using a microelectrode technique in parkinsonism. *Appl. Neurophysiol.,* **1987**, *50*(1-6), 330-337. PMID: 3329871

[158] Ebner, T.J.; Pasalar, S. Cerebellum predicts the future motor state. *Cerebellum,* **2008**, *7*(4), 583-588. http://dx.doi.org/10.1007/s12311-008-0059-3 PMID: 18850258

[159] Peterburs, J.; Desmond, J.E. The role of the human cerebellum in performance monitoring. *Curr. Opin. Neurobiol.,* **2016**, *40*, 38-44. http://dx.doi.org/10.1016/j.conb.2016.06.011 PMID: 27372055

[160] Suldo, S.M.; McMahan, M.M.; Chappel, A.M.; Loker, T. Relationships between perceived school climate and adolescent mental health across genders. *School Ment. Health,* **2012**, *4*, 69-80. http://dx.doi.org/10.1007/s12310-012-9073-1

[161] Caligiore, D.; Pezzulo, G.; Miall, R.C.; Baldassarre, G. The contribution of brain sub-cortical loops in the expression and acquisition of action understanding abilities. *Neurosci. Biobehav. Rev.,* **2013**, *37*(10 Pt 2), 2504-2515. http://dx.doi.org/10.1016/j.neubiorev.2013.07.016 PMID: 23911926

[162] Houk, J.C.; Wise, S.P. Distributed modular architectures linking basal ganglia, cerebellum, and cerebral cortex: their role in planning and controlling action. *Cereb. Cortex,* **1995**, *5*(2), 95-110. http://dx.doi.org/10.1093/cercor/5.2.95 PMID: 7620294

[163] Izawa, J.; Rane, T.; Donchin, O.; Shadmehr, R. Motor adaptation as a process of reoptimization. *J. Neurosci.,* **2008**, *28*(11), 2883-2891. http://dx.doi.org/10.1523/JNEUROSCI.5359-07.2008 PMID: 18337419

[164] Izawa, J.; Shadmehr, R. Learning from sensory and reward prediction errors during motor adaptation. *PLOS Comput. Biol.,* **2011**, *7*(3), e1002012. http://dx.doi.org/10.1371/journal.pcbi.1002012 PMID: 21423711

[165] Huang, C.; Mattis, P.; Tang, C.; Perrine, K.; Carbon, M.; Eidelberg, D. Metabolic brain networks associated with cognitive function in Parkinson's disease. *Neuroimage,* **2007**, *34*(2), 714-723. http://dx.doi.org/10.1016/j.neuroimage.2006.09.003 PMID: 17113310

[166] Eckert, T.; Tang, C.; Eidelberg, D. Assessment of the progression of Parkinson's disease: a metabolic network approach. *Lancet Neurol.,* **2007**, *6*(10), 926-932. http://dx.doi.org/10.1016/S1474-4422(07)70245-4 PMID: 17884682

[167] Huang, C.; Mattis, P.; Perrine, K.; Brown, N.; Dhawan, V.; Eidelberg, D. Metabolic abnormalities associated with mild cognitive impairment in Parkinson disease. *Neurology,* **2008**, *70*(16 Pt 2), 1470-1477. http://dx.doi.org/10.1212/01.wnl.0000304050.05332.9c PMID: 18367705

[168] Mentis, M.J.; Dhawan, V.; Nakamura, T.; Ghilardi, M.F.; Feigin, A.; Edwards, C.; Ghez, C.; Eidelberg, D. Enhancement of brain activation during trial-and-error sequence learning in early PD. *Neurology,* **2003**, *60*(4), 612-619. http://dx.doi.org/10.1212/01.WNL.0000044154.92143.DC PMID: 12601101

[169] Yu, H.; Sternad, D.; Corcos, D.M.; Vaillancourt, D.E. Role of hyperactive cerebellum and motor cortex in Parkinson's disease. *Neuroimage,* **2007**, *35*(1), 222-233. http://dx.doi.org/10.1016/j.neuroimage.2006.11.047 PMID: 17223579