EC NEUROLOGY
Conceptual Paper

Cerebellum - Ataxias of Motor System, Affect and Higher Cognition- A Unified Approach

Gautam Ullal*

Department of Neuroscience, American University of the Caribbean School of Medicine, Sint Maarten

***Corresponding Author:** Gautam Ullal, Department of Neuroscience, American University of the Caribbean School of Medicine, Sint Maarten.

Received: August 01, 2018; **Published:** November 29, 2018

Background

Understanding of functions of cerebellum the "*Little Brain*" of Leonardo Da Vinci has evolved in leaps and bounds. Although anatomy of cerebellum was studied in extensive details as early as 1500s [1,2] it took several centuries before investigators got interested in its functions. The 18th century investigators such as Gall and Spurzheim's "amativeness", love and sexuality in a patient associated with a bump on her skull in the region of cerebellum [3] was silenced by the scientific uproar raised against the topologists thereafter.

In Post-topology era, looking at the cerebellum with a different lens, neuroscientists were led to believe that cerebellum was merely a vestigial piece of neuronal tissue compressed in the posterior cranial fossa, that they then thought sub-served very little motor and hardly any sensory functions [4]. This further perpetuated the concept of the little brain of Leonardo Da Vinci. It is true, cerebellar lesions do not cause muscle paralysis or conscious sensory loss. However, subsequent close clinical observations and animal experimentations revealed that there is indeed loss of motor coordination accompanying cerebellar lesions [5-7]. We know now for several decades, that every single muscle movement be it a fine movement in the extraocular eye muscles, lumbricals of the hand or the large, posture-related movements of the trunk and the limbs; coordination of every action requires cerebellum and that loss of cerebellar control led to clinical signs such as ataxias, asynergia and dysdiadochokinesia [6-14].

In order to be able to be a "master-coordinator" of actions, cerebellum constantly receives neuronal inputs from the cerebral cortex containing information about the intended actions that are to be performed by the muscles as well as the unconscious kinesthetic sensory inputs from the limbs about the movements performed by them [10,12-14]. Using this information the cerebellum makes quick, on-the-go error-corrections via the "Servo mechanisms" thus bringing about precisely coordinated movements in terms of range, sequence, direction, force and speed [11]. Cerebellar synapses undergo constant modifications through long-term potentiation and long-term depression thus facilitating motor learning [10,12,15].

It is known now that cerebellum not only has 3 - 4 times more neurons than its much larger counterpart, the cerebral cortex but also, that the ratio of cerebellar neurons to cerebral cortical neurons has increased with the evolution of nervous system [16]. Further, the cerebellar granule cell neurons are the most populous of all the neurons in the entire nervous system [12] and the Purkinje dendrites have one of the most prolific branching patterns [17]. Cerebellum has neuronal maps and representations for every single region of the nervous system not just the pyramidal motor system but also the sensory cortex, association areas, hippocampus, basal ganglia and the limbic system [10].

Disturbance in any of the cerebellar pathways or in the working of cerebellum leads to a variety of truncal and limb ataxias [6-14].

The possibility

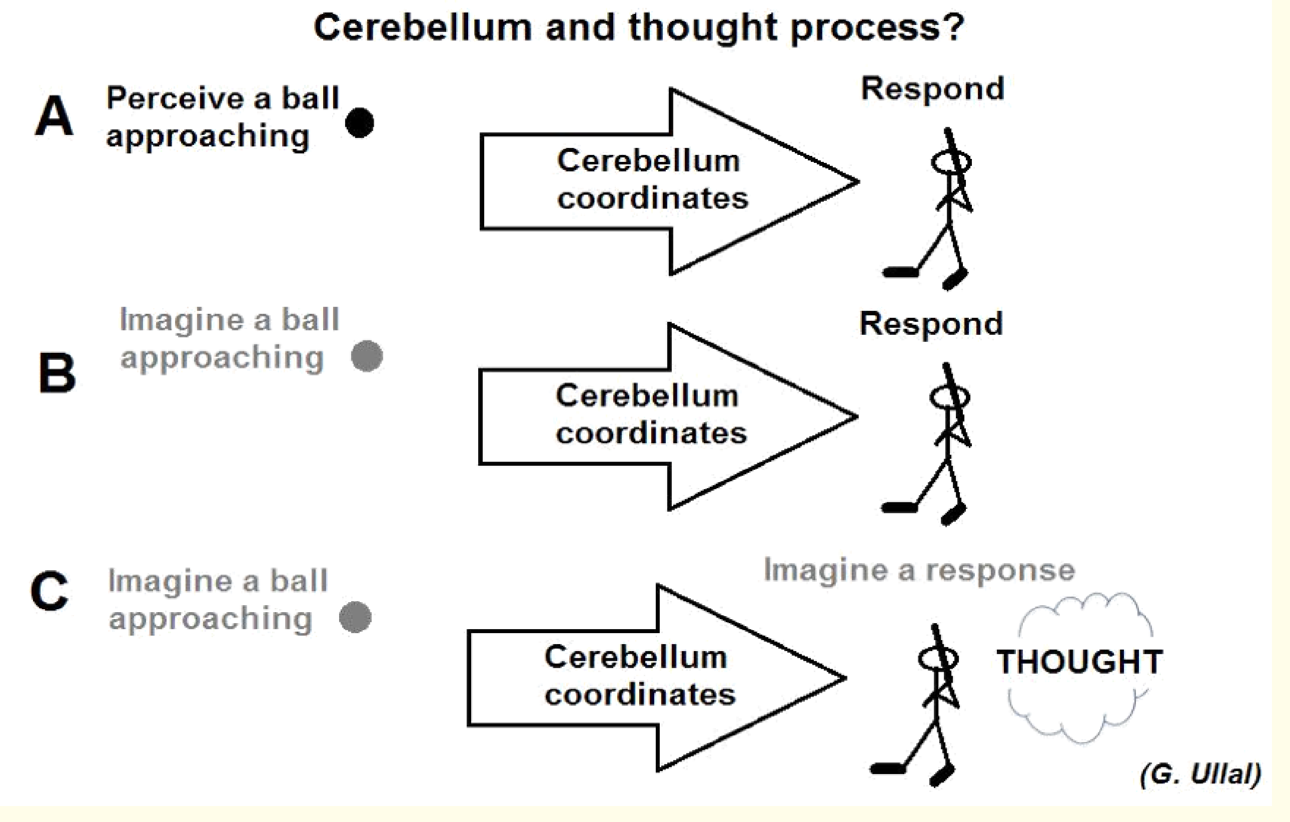
Considering the density of neurons the cerebellum has and its extensive connections with the entire nervous system and the complex topological maps the cerebellum has for the entire body, a logical progression of concepts emerges concerning the implications of cerebellum in not just basic motor coordination but also higher cognitive functions. The cartoon illustrates the concept.

Situation A: Ball approaches the batter the batter has to coordinate his actions in order to strike the ball- Cerebellum is involved in coordinating the motor response.

Situation B: The batter imagines that there is a ball approaching him although there is not any. He performs the movement of striking at the imaginary ball. Cerebellum is involved in coordinating this movement as well.

Situation C: The batter imagines that there is a ball approaching him although there is not any. He also imagines that he is performing the movement of striking at the imaginary ball without really performing a true action. Is cerebellum involved in this imaginary movement as well? Considering that cerebellum has all the motor plans the answer is, most likely yes.

There is no thought without the connecting action words. Thus, cerebellar functions might have ramifications into not just motor coordination but also co-ordination of thoughts. Extrapolating this concept even further onto clinical situations, disorders of cerebellum may be associated with dysmetria of thoughts as seen in schizophrenia.



Furthermore, affect and the autonomic responses need to be congruous with thoughts and external situations. Perhaps, cerebellum orchestrates these as well. Could, cerebellar lesions cause affective disturbances?

Broader outcome- The least charted territory

The vermal region of cerebellum coordinate the truncal movements and the paravermal region the distal limb movements. Lesions in any of these anatomical regions causes "truncal" and "limb" ataxias respectively [6-14]. There is a much larger area namely the lateral neo-cerebellum that is connected widely with the entire cerebral cortex. We do not have a clear understanding about what this area does.

It is implicated with complex programming of movements. There are no defined neurological disorders associated with isolated lesions of this area s. Thus, this is a relatively uncharted territory.

However, more recent clinical, anatomical, neuroimaging and tractography studies suggest that cerebellum is engaged not just in motor coordination but also in cognitive functions and control of affect [18,19]. Studies in the past two decades have clearly demonstrated that cerebellar lesions particularly the lateral neo-cerebellum do manifest in the form of disorders such as "Cerebellar cognitive affective syndromes" (CCAS) where there is not just incoordination of thoughts but loss of control on emotions as well. They manifest in the form of loss of executive functions, linguistic processing and aphasias, spatial cognition, apraxias and disturbed executive functioning [18,20]. Memories particularly associated with verbal rehearsal and episodic information are quite often lost with cerebellar pathologies [21]. Cerebellar mutism syndrome and affective incoordination following surgeries in the posterior cranial fossa is well known [22].

More specific neuropsychological evaluations have further characterized these clinical features [20]. For instance, aphasias are more in the domain of fluency rather than semantics [21]. Executive functions are more affected in cognitive set shifting and verbalizing compared to semantic categorizations [20,21]. There was poorer performance of addition and subtraction tasks [20]. Children that had resections of cerebellar tumors developed difficulty in planning and sequencing, digit span and perseveration [22]. Furthermore, cerebellar cognitive functions are also revealing laterality in functions in tune with the cortical functions [22].

More specific neuropsychological evaluations have further characterized these clinical features [20]. For instance, aphasias are more in the domain of fluency rather than semantics [21]. Executive functions are more affected in cognitive set shifting and verbalizing compared to semantic categorizations [20,21]. There was poorer performance of addition and subtraction tasks [20]. Children that had resections of cerebellar tumors developed difficulty in planning and sequencing, digit span and perseveration [22]. Furthermore, cerebellar cognitive functions are also revealing laterality in functions in tune with the cortical functions [22].

Detailed investigations of cerebellar microcircuits has revealed stereotyped architecture throughout the cerebellum [25]. This strongly suggests that the computational algorithms used by the cerebellum are similar.

Eventually what parts of the nervous system are wired to cerebellum through its mossy fiber-climbing fiber-Purkinje cell-deep nuclei modules might determine the unified functional outcome and the disorders associated with it [26].

There is no surprise therefore in encountering more varieties of cognitive and affective syndromes as we get to know cerebellum further. Perhaps there are answers to several unsolved clinical puzzles in the field of neuropsychiatry in this "Little brain" of Leonardo Da Vinci.

Finally Cerebellum, an Ode to thee!

Oh! Servomechanism of the brain,
So enchanting thou are indeed!
Be it complex speech or a simple deed,
In every response, I see your need!
You silently guide my locomotion,
You coordinate my emotion.
You are perhaps the string of my higher cognition!
Perhaps we are looking elsewhere for answers on schizophrenia and bipolar disorders.
For disturbed attention, compulsions and obsessions.
Please reveal to us your complete manifestations.
So that we could wipe these various maladies!
Not only of ataxias of the body but also of mentation!
I remain your eternal admirer...

Bibliography

1. Glickstein M., *et al*. "Cerebellum: History". *Neuroscience* 162.3 (2009): 549-559.
2. Varolio C. "De nervis opticis nonulisque aliis prater communem opinionem in humano capite observatis epistole". Padova: Metti (1573).
3. Whishaw IQ. "The development of neuropsychology". In Fundamentals of human neuropsychology. Sixth Edition, Worth (2008).
4. D'Angelo E and Casali S. "Seeking a unified framework for cerebellar function and dysfunction". *Frontiers in Neural Circuits* 6 (2013): 116.
5. Rolando L. "Saggio sopra le vera struttura del cervello dell'uomo e degli animali e sopra le funzioni del sistema nervosa". Sassari: Stamperia da S.S.R.M (1809).
6. Flourens P. "Rechérches expérimentales sur les propriétés et les fonctions du système nerveux dans les animaux vertébrés". Paris: Crevot (1824).
7. Babinski J. "Sur le rôle du cervelet dans les actes volitionnels necessitant une succession rapide de mouvements (diadococinésie)". *Revista de Neurología* 10 (1902): 1013-1015.
8. Holmes G. "The symptoms of acute cerebellar injuries due to gunshot injuries". *Brain* 40.4 (1917): 461-535.
9. Thach WT. "The cerebellum". In: Mountcastle, V (Ed). Medical Physiology. St. Lousi: C. V. Mosby Co. (1980): 837-858.
10. Kandel ER., *et al*. "The cerebellum". In: Principles of neural science. Fifth Edition. McGraw Hill (2013): 860-981.
11. Massaquoi SG and Topka H. "Models of cerebellar function". In: The Cerebellum and its disorders. Ed. Manto MU and Pandolfo M. Cambridge University Press (2002): 68-93.
12. Purves D., *et al*. "Modulation of movement by the cerebellum". In: Neuroscience. Sixth Edition. Sinauer Oxford University Press (2018): 427-445.
13. Ropper AH and Samuels MA. "Incoordination and other disorders of cerebellar function". In: Principles of neurology. Adams and Victor. Ninth Edition. McGraw Hill (2009): 78-88.
14. Blumenfeld H. "Cerebellum". In: Neuroanatomy through clinical cases. Second Edition. Sinauer Associates (2010): 698-736.
15. Ito M., *et al*. "Climbing fibre induced depression of both mossy fibre responsiveness and glutamate sensitivity of cerebellar Purkinje cells". *Journal of Physiology* 324 (1982): 113-134.
16. Herculano-Houzel S. "Coordinated scaling of cortical and cerebellar numbers of neurons". *Frontiers in Neuroanatomy* 4 (2010): 12.
17. Huang ZJ. "Subcellular organization of GABAergic synapses: role of ankyrins and L1 cell adhesion molecules". *Nature Neuroscience* 9.2 (2006): 163-166.
18. Schmahmann JD and Sherman JC. "The cerebellar cognitive affective syndrome". *Brain* 121.4 (1998): 561-579.
19. Desmond JE and Fiez JA. "Neuroimaging studies of the cerebellum: language, learning and memory". *Trends in Cognitive Sciences* 2.9 (1998): 355-362.
20. Hoche F., *et al*. "The cerebellar cognitive affective/Schmahmann syndrome scale". *Brain* 141.1 (2018): 248-270.
21. Bodranghien F., *et al*. "Consensus paper: Revisiting the symptoms and signs of cerebellar syndrome". *Cerebellum* 15.3 (2016): 369-391.
22. Wibroe M., *et al*. "Cerebellar mutism syndrome and other complications after surgery in the posterior fossa in adults: A prospective study". *World Neurosurgery* 110 (2018): e738-e746.
23. Hoche F., *et al*. "Cerebellar contribution to social cognition". *Cerebellum* 15.6 (2016): 732-743.

24. Bruchhage MMK., *et al*. "Cerebellar involvement in autism and ADHD". *Handbook of Clinical Neurology* 155 (2018): 61-72.

25. Valera AM., *et al*. "Stereotyped spatial patterns of functional synaptic connectivity in the cerebellar cortex". *Elife* 5 (2016): e09862.

26. Schmahmann JD. "Dysmetria of thought: clinical consequences of cerebellar dysfunction on cognition and affect". *Trends in Cognitive Sciences* 2.9 (1998): 362-371.

Volume 10 Issue 12 December 2018