

Review Article

**A REVIEW ARTICLE: CEREBELLUM AND EYESIGHT****Rengin Kosif**

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**ABSTRACT**

The cerebellum plays a significant role in the maintenance of equilibrium and the coordination of head and eye movements. The cerebellum receives extensive information from visual, somesthetic, vestibular and auditory sensory systems, as well as from motor and nonmotor areas of the cerebral cortex. The cerebellum was more active during independent rather than coordinated eye and hand tracking. Performance when tracking with the hand alone was worse than in the coordinated eye and hand condition. Cerebellum was significantly activated in coordinated eye-hand tracking compared to isolated eye and hand movements. Patients with cerebellar disease, eye movements, limb movements, gait and speech all may be affected. Bulbar muscles may also be affected, numerous disturbances of oculomotor activity, including nystagmus. In cerebellar disease decreased tone in postural muscles, Hypotonia in oculomotor muscles results in difficulty in maintaining the gaze. Studies investigating the relationship between the cerebellum and eyesight were revised in this manuscript.

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**INTRODUCTION**

Cerebellum is the region of the brain that is related to motor control, physical coordination and balance. Recent studies have also established that it is also associated with cognition and learning (Bauer *et al.* 2009). Cerebellum regulates motor activity and muscle tone and prompts cognitive behavior. In addition, it plays a key role in memory and learning in the cerebellar thalamic cortical circuit (Pierson *et al.* 2002). Cerebellar cortex regulates the interruption of preplanned fast movements, and in addition, cerebellar nuclei govern the continuance of fast movements.

Cognitive problems arise in persons with cerebellar cortical atrophy, and losses in verbal intelligence, visual-spatial ability, learning and memory and functional impairment in frontal system may additionally occur (Schmahmann 2004). An fMRI study showed that cerebellum plays an important role in hand and eye movement coordination. In the cases that necessitate a coordination between hand and eye movements (e.g. tennis), cerebellum is activated and provides the coordination between the two organs (Miall *et al.* 2001).

Cerebellar cortical atrophy demonstrates itself with asymmetry in saccadic movements of the eye. It is common that eye movements are represented in the median part of the vermis in cerebellum (Kornhuber *et al.* 1971).

Cerebellum is an important neural component that enables coordination in walking between the joints of an extremity, two extremities, the eye and the hand, and

the eye and the leg (van Donkelaar & Lee 1994; Vercher & Gauthier 1988). In his study, Miall established a significant activation increase in cerebellum in movements in which the hands and the eyes are used in combination compared with eye- or hand-only movements (Miall *et al.* 2001).

Eye-only movements create activation in the visual cortex, parietal cortex and vermis cerebelli (Petit & Haxby, 1999). Hand-only movements activate contralateral sensorimotor and premotor area, bilateral basal ganglion and ipsilateral cerebellum (Nishitani 1999). It is known that slow eye movements activate Purkinje cells in cerebellar ventral paraflocculus, and this demonstrates a correlation with the acceleration of eye movements (Shidara *et al.* 1993). Experimental tests have shown that cerebellum is the key field in the control of adaptive eye movements (vestibulo-ocular and optokinetic reflex) (Soichi 2000). Nucleus fastigii, flocculus, and paraflocculus are necessary for regular normal eye movements (Robinson & Fuchs 2001). When the inside and surface of cerebellum is stimulated in cats, horizontal, rotatory, upwards and downwards eye movements occur; it showed a reaction just as the stimulation of semicircular canals. Horizontal movements occur with the activation of tuber vermis and nucleus fastigii, and upwards and downwards eye movements happen with the activation of the median of anterior and posterior lobe and vermis. Downwards rotatory eye movements occur with the activation of the lateral regions of nodulus and uvula, and

the activation of nucleus dentatus leads to upwards rotatory eye movements. It was established that eye movements are topographically arranged in cerebellum and that they have neural organization (Cohen *et al.* 2004).

Vercher *et al.* investigated the involvement of the cerebellum in coordination control during a visuo-oculo-manual tracking task. Experiments were conducted on baboons trained to track visual targets with the eyes and/or the hand. The role of the cerebellum was determined by comparing tracking performance defined in terms of delay, accuracy (position or velocity tracking errors) and maximal velocity, before and after lesioning the cerebellar dentate nucleus. Results showed that in the intact animal, ocular tracking was more saccadic when the monkey followed an external target than when it moved the target with its hand. After lesioning, eye-alone tracking of a visual target as well as eye-and-hand-tracking with the hand contralateral to the lesion was little if at all affected. Conversely, ocular tracking of the hand ipsilateral to the lesion side became more saccadic and the correlation between eye and hand movement decreased considerably while the delay between target and eyes increased. In normal animals, the delay between the eyes and the hand was close to zero, and maximal smooth pursuit velocity was around 100 degrees per second with close to unity gain; in eye-alone tracking the delay and maximal smooth pursuit velocity were 200 ms and 50 deg per second, respectively. After lesioning, delay and maximum velocity were respectively around 210 ms and 40 deg per second, that is close to the values measured in eye-alone tracking. Thus, after dentate lesioning, the oculomotor system was unable to use information from the motor system of the arm to enhance its performance. We conclude that the cerebellum is involved in the "coordination control" between the oculomotor and manual motor systems in visuo-oculo-manual tracking tasks (Vercher 1988).

Miall *et al.* tested using functional magnetic resonance imaging (fMRI) of the human brain during visually guided tracking tasks requiring varying degrees of eye-hand coordination. The cerebellum was more active during independent rather than coordinated eye and hand tracking. However, in three further tasks, we also found parametric increases in cerebellar blood oxygenation signal (BOLD) as eye-hand coordination increased. Thus, the cerebellar BOLD signal has a non-monotonic relationship to tracking performance, with high activity during both coordinated and independent conditions. These data provide the most direct evidence from functional imaging that the cerebellum supports motor coordination. Its activity is consistent with roles in coordinating and learning to coordinate eye and hand movement (Miall 2000).

Dysfunction of the cerebellum leads to significant deterioration of movements performed under visual guidance and of co-ordinated eye and hand movement. Visually guided tracking tasks combine both of these control features, as the eyes and hand together track a visual target. To better understand the involvement of the cerebellum in tracking tasks, we used functional magnetic resonance imaging to study the activation of cerebellar structures in visually guided tracking movements of the eye and hand. Subjects were tested performing ocular tracking, manual tracking without eye movement or combined eye and hand tracking of a smoothly moving visual target. Three areas were activated in the cerebellum: a bilateral

region in the ansiform lobule of the lateral hemisphere, a region in the ipsilateral paramedian lobule and a region in the oculomotor vermis. The ansiform and paramedian areas were most strongly activated by hand movement, although the vermal site was also active. The reverse was found for ocular tracking, with predominantly vermal activation. Activation of these cerebellar cortical areas related to movement of eyes or hand alone was significantly enhanced when the subjects performed co-ordinated eye and hand tracking of a visual target. These results provide the first direct evidence from a functional-imaging study for cerebellar activation in eye and hand co-ordination (Miall 2000).

The responses of neurones in the lateral cerebellar cortex to visual stimuli and to eye movements were recorded in rhesus monkeys trained to perform visually guided arm and eye movements in a tracking task. Thus most neurones were found to carry only visual, or eye movement, or limb movement information rather than combinations of these signals; they were located in different but overlapping regions of lateral cerebellar cortex. Visually responsive neurones are probably involved in planning the visual goal of movements, while eye and arm movement neurones probably help to create co-ordinative structures for executing voluntary eye and arm movements (Marple 1998).

Donkelaar *et al.* tested the hypothesis that interactions occur between eye and hand movements produced in conjunction. This was accomplished by having human subjects with cerebellar dysfunction and age-matched controls perform two tasks: 1) tracking a moving target with the hand and 2) performing a pointing movement to intercept the target. Their prediction was that the inaccuracies that are characteristic of eye and hand movements generated in isolation by cerebellar subjects would be accentuated in each system during combined eye-hand tasks. The cerebellar subjects took longer to respond to the onset of target motion in both tasks. This was true for both the eyes and hand, regardless of whether the eye and hand movements were generated in isolation or in conjunction with each other. The cerebellar subjects also displayed a larger degree of error and/or variability in their hand movements than the control subjects. A significant amount of this increased variability was due to systematic changes in the trajectory of the hand during the critical periods leading up to and after each ocular saccade. These systematic changes were consistent with an overestimation of target velocity in the perifoveal visual field. The increased variability of the cerebellar subjects' hand movements was markedly reduced by restricting eye movements. A similar reduction in variability occurred when vision of the hand was restricted in the tracking task. This effect was accompanied by improved eye movements. For both sets of subjects the eye movements were affected by the hand movements produced in the tracking task. In particular, eye movement accuracy was improved in the controls and degraded in the cerebellar subjects when compared with the eye movements generated in isolation. In contrast, no changes were observed in the interception task. Taken together, these results imply that a reciprocal interaction occurs between the eye and hand motor systems and/or that common "upstream" sites influence each of these (Donkelaar 1994).

The cerebellar volume of males and females with congenital visual impairment was found to be smaller

compared with healthy individuals. This finding was statistically significant in females but not in males. The relationship between cerebellum and the eyes is intensive and complicated. Since impulses that would normally need to come from the eyes and circulations that should occur do not reach their target from birth onwards, atrophy could be expected in cerebellum due to low usage. Atrophy may occur in cerebellum due to such reasons as the absence of stimulus that would normally come from the eyes, inability to have voluntary eye movements, or inactive midways. Asymmetry is non-existent between right and left lobes of cerebellum (Kosif 2013).

When patients with ocular motor deficits come to the clinic, in numerous situations it is hard to relate their behavior to one or several deficient neural structures. We sought to demonstrate that neuromimetic models of the ocular motor brainstem could be used to test assumptions of the neural deficits linked to a patient's behavior. Patients exhibited unusual ocular motor disorders including increased saccadic peak velocities (up to 1000 deg/s), dynamic saccadic overshoot, left-right asymmetrical post-saccadic drift and saccadic oscillations. Daye et al show that their model accurately reproduced the observed disorders allowing us to hypothesize that those disorders originated from a deficit in the cerebellum. Their study suggests that neuromimetic models could be a good complement to traditional clinical tools. Their behavioral analyses combined with the model simulations localized four different features of abnormal eye movements to cerebellar dysfunction. Importantly, this assumption is consistent with clinical symptoms (Daye 2013).

Neuromimetic saccadic model of ocular motor control that integrates the current knowledge of the ocular motor brainstem, superior colliculus and cerebellar circuitry (Daye 2013).

The nucleus prepositus hypoglossi is a key structure in the brainstem to ensure that the eyes remain stationary between saccades (Lopez 1982). It receives drives from the burst neurons, integrates them (in the mathematical sense) and projects to the ocular motor nuclei. (Robinson 1989).

The brainstem connectivity reproduces as closely as possible (for a lumped model) the known anatomical connectivity and the functions of the ocular motor brainstem (Abel 1978).

## RESULTS

In conclusion, a lumped neuromimetic model of brainstem eye movement circuitry enabled us to propose that all of saccadic ocular motor deficit patients diverse deficits could be localized to a single structure, the cerebellum (Daye 2013).

Voluntary eye movements are particularly useful for investigating the specific mechanisms underlying cerebellar control. It is well known that patients affected by cerebellar disease have reduced capacities to control eye movement (saccade) (Veneri 2012).

Inactivation data showing that the posterior vermis and the caudal fastigial nucleus, to which it projects, provide a signal during horizontal saccades to make them fast, accurate, and consistent. The caudal fastigial nucleus also is necessary for the recovery of saccadic accuracy after actual or simulated neural or muscular damage causes horizontal saccades to be dysmetric. Saccade-related activity in the interpositus nucleus is related to vertical saccades. Both the caudal fastigial nucleus and the

flocculus/paraflocculus are necessary for the normal smooth eye movements that pursue a small moving spot (Robinson 2001).

Eye movements that follow a target (pursuit eye movements) facilitate high acuity visual perception of moving targets by transforming visual motion inputs into motor commands that match eye motion to target motion. The performance of pursuit eye movements requires the cerebellar flocculus, which processes both visual motion and oculomotor signals. Electrophysiological recordings from floccular Purkinje cells have allowed the identification of their firing patterns during generation of the image velocity and image acceleration signals used for pursuit. The flocculus encodes all the signals needed to guide pursuit (Krauslis 1991).

Cerebellum that provide coordination of balance, head and eye motion will continue to inspire a lot of researchers in the future.

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