Deficits of Grasping in Cerebellar Disorders 82

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Contents

Abstract

Given its stereotyped cytoarchitecture, the widespread connections with cortical and subcortical sensory-motor structures, and the neural activity of cerebellar Purkinje cells during sensory-motor tasks, the cerebellum is considered to play a major role in the control of grasping. The cerebellum is involved in the timing and coordination of hand transport, grasp formation, and isometric grip force when reaching for, grasping, and handling an object. In addition, there is evidence from

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human lesion and brain imaging studies that the cerebellum is essential for the establishment and maintenance of internal sensory-motor representations, so-called internal models, related to motor output and sensory input during grasping. These representations are necessary to predict the consequences of ones' own movements. This chapter summarizes theoretical aspects, data from brain imaging, and behavioral data obtained from patients with cerebellar lesions characterizing the specific role of the cerebellum for grasping movements.

Keywords

Internal model · Grip force · Cerebellar lesion · Cerebellar degeneration · International cooperative ataxia rate scale

Introduction

The cerebellum plays a major role for the control of grasping movements. The involvement of the cerebellum in the coordination of hand transport, grasp formation, and the establishment of accurate grip forces when handling objects originates from its role in tuning muscle activity during voluntary motor actions (Manto 2010). The output from the cerebellum is directed to all components of the motor system. The cerebellum coordinates the timing, duration, and magnitude of agonist–antagonist muscle discharges (Hore et al. 1991; Manto et al. 1994). It participates in the planning of motor actions, in the learning of novel skills, and in adjusting descending motor commands to environmental requirements based on motor experience. Here the pertinent theories on the role of the cerebellum to form *internal models*, data from brain imaging, and behavioral data obtained from patients with cerebellar lesions that characterize the specific role of the cerebellum for grasping movements are summarized.

Deficits of Reaching and Grasping

Impaired coordination of voluntary movement is a cardinal sign of cerebellar disorders (Manto 2010). Reaching and grasping an object is an important and most frequently practiced action in daily life. Clumsiness is a common complaint in cerebellar disorders; however, grasping movements are not systematically tested in clinical ataxia rating scales (Trouillas et al. 1997). Reaching for and grasping an object incorporates at least two different components: (1) a transport movement of the hand toward the object (hand transport) and (2) shaping of the hand and fingers according to the mechanical object characteristics (grasp formation) (Castiello 2005). Once the fingers make contact with the object, grasping forces are scaled according to the object's weight, shape, and surface friction and this scaling depends on the inertial loads arising from lifting and transport movements (Johansson and Westling 1988). In healthy subjects, all components of reaching and grasping movements are highly automatized with minimal variance. In cerebellar disorders,

several abnormalities of the hand transport and grasp formation components have been detected. Hand transport is commonly impaired by increased path curvatures, corrective movements, and variable and slowed wrist velocity profiles (Brandauer et al. 2008; Zackowski et al. 2002). Grasp aperture is exaggerated and reveals multiple peaks, and there is prolongation of finger-object contact when cerebellar patients grasp for an object (Brandauer et al. 2008; Zackowski et al. 2002). These pathologic features of reaching to grasp movements are illustrated for a representative cerebellar subject in Fig. 1.

Interestingly, deficits in the hand transport (movement time) and grasp formation components (grasp formation time, number of peaks in grasp formation) are significantly correlated with ataxia scores rated by the International Cooperative Ataxia Rating Score subscales according to Trouillas et al. (1997) (Brandauer et al. 2008). Significant correlations are also found between deficits in the kinematics of reaching and grasping and atrophy within the lateral and intermediate cerebellum as assessed by magnetic resonance imaging–based volumetry (Brandauer et al. 2008). Thus, kinematic measures of reaching and grasping may provide valuable adjunct information in addition to clinical scales and morphometric brain analysis in the assessment of subjects with cerebellar degeneration.

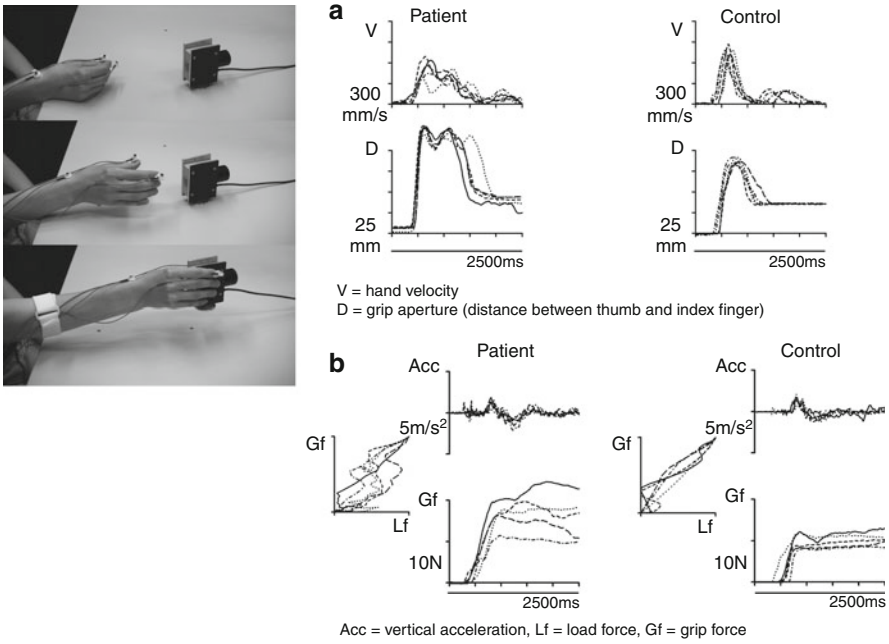

Fig. 1 (**a**) Traces of wrist velocity during hand transport and grasp formation (distance between index finger and thumb) during repetitive reaching to grasp movements performed by a cerebellar subject and a healthy control subject. (**b**) Traces of lifting acceleration and grip force during repetitive grip-lift movements performed by a representative patient with cerebellar degeneration and a healthy control subject. (Modified according to Brandauer et al. 2008)

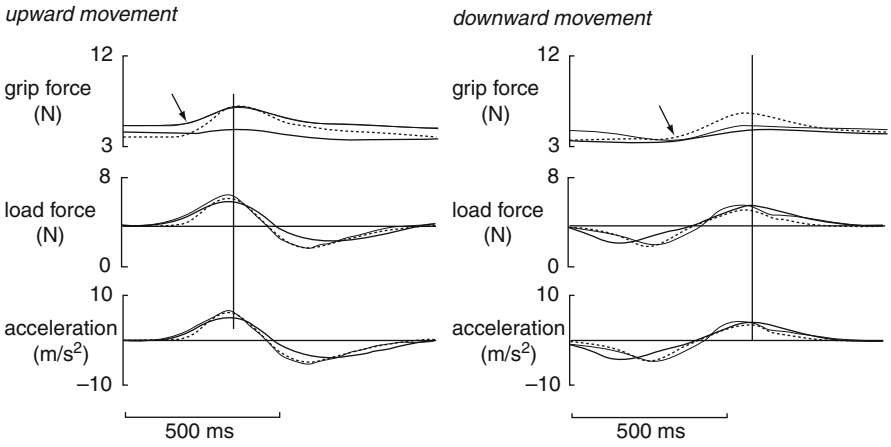

Fig. 2 Average data of grasping force, load force, and acceleration obtained from vertical movements performed by three healthy subjects. Subjects move a handheld instrumented object upward and downward. The handheld object incorporates a grasping force sensor and three linear accelerations sensors registering acceleration in three dimensions including gravity. The grasping and load force profiles change in parallel, suggesting predictive force planning. The *arrows* indicate the rise in grasping force from baseline

Predictive and Reactive Control of Grasping Forces

The exquisite control of grasping forces when manipulating objects is an essential part of the daily motor repertoire. Skilled control of grasping forces involves different modes of control which rely on prediction and sensory feedback to different extents (Wolpert and Flanagan 2001). When objects that exhibit stable properties are handled in the environment, predictive control mechanisms can effectively be exploited. When, for example, the load of a handheld object is increased by a self-generated action – such as moving the arm during a transport movement or dropping a weight from one hand into a receptacle held by the opposite hand – grasping forces increase in parallel with load forces without an obvious time delay (Flanagan and Wing 1993; Johansson and Westling 1988). When, on the other hand, objects are handled with unpredictable behavior, such as catching a weight that is unexpectedly dropped by another person into a handheld receptacle, sensory feedback provides the most useful source to signal a change in load with the consequence that grasping forces tend to lag behind load (Johansson and Westling 1988). Figure 2 illustrates the predictive and reactive mechanisms of grasping force control.

Internal Forward Models

The predictive coupling between grasping and load force profiles has been interpreted within the theoretical concept of internal models (Wolpert and Flanagan 2001). Figure 3 illustrates the theoretical concept of an *internal forward model* in the

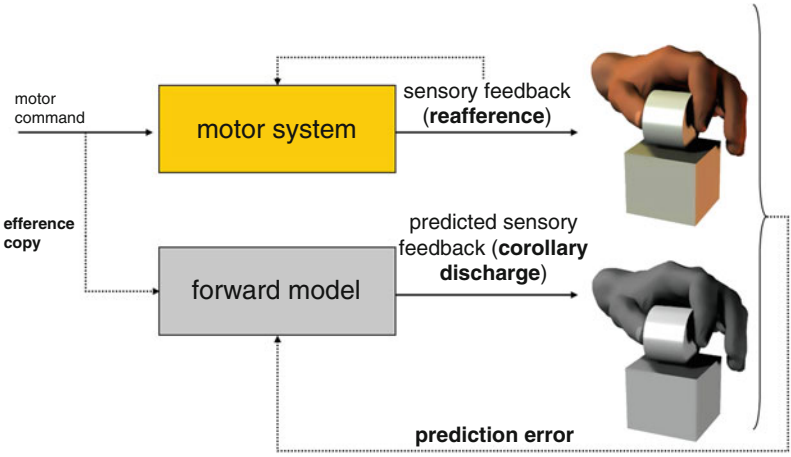

Fig. 3 Internal forward models enable a parallel modulation of gasping force with the movement-induced loads when transporting a handheld object. The motor system generates a descending motor command that results in sensory feedback (reafference). A forward model of this system uses a copy of the descending motor command (efference copy) and generates an estimate of the sensory feedback likely to result from the movement (corollary discharge). The cerebellum computes an estimate of the sensory feedback. A mismatch between the predicted and actual sensory outcomes (prediction error) triggers force corrections along with an updating of the relevant internal models

context of the control of grasping forces. Expectations and estimates of future motor states are essential for performing fast coordinated voluntary motor actions. Predictions are necessary as the cerebral motor cortex cannot respond on the basis of slowly evolving sensory and somatosensory feedback. The latter would produce essential time delays varying between 50 and 300 ms (Wolpert and Flanagan 2001). Given the regular anatomical cytoarchitecture of the cerebellar cortex and the well-characterized functional circuitry with only one output cell and four main classes of interneurons, the cerebellum has been considered to incorporate such internal forward models (Blakemore et al. 2001; Ito 2006; Ramnani 2006; Wolpert et al. 1998). Single cell recordings obtained from cerebellar Purkinje cells and deep cerebellar nuclei suggest that cerebellar activity is closely linked to predictive mechanisms of grasping (Monzee and Smith 2004). Behavioral data have demonstrated that predictive control of grasping forces is severely impaired while reactive mechanisms of force control appear to be well preserved in subjects with cerebellar disorders (Nowak et al. 2002; Rost et al. 2005). The cerebellum may function similarly to a *forward model* by using *efference copies* of motor commands to predict the sensory effects (*corollary discharge*) of voluntary actions. Accurate predictions reduce the dependence on time-delayed somatosensory feedback. Cerebellar circuitry would be necessary to learn how to establish accurate predictions using error information about the discrepancies between actual and predicted sensory consequences (*corollary discharge*) of voluntary actions. Given its anatomical connections, the cerebellum is well suited to compute expected sensory outcomes of voluntary motor actions. Some of the most convincing evidence that the central nervous system

uses internal forward models in human motor behavior comes from studies dedicated to the control of grasping forces during object manipulation (Fig. 3).

Data from functional brain imaging have provided additional support for the idea that the cerebellum is relevant for implementing the equivalent of internal forward models within the central nervous system (Boecker et al. 2005; Kawato et al. 2003). During pulling movements exerted by healthy subjects against a handheld, but fixed, object in a positron emission tomography scanner, grasping force-pull force coupling was found to be related to neural activity in the ipsilateral posterior cerebellum (Boecker et al. 2005). In addition, force coupling–related neural activation was recorded in the anterior cingulate and the frontal association regions of the brain, the ipsilateral right caudate nucleus, and the left lingual gyrus. A functional magnetic resonance imaging study examined healthy subjects performing cyclic vertical arm movements with a handheld load. The imaging data obtained suggest that the right ipsilateral anterior lobe and/or the left biventer of the posterior cerebellum represent the anatomical correlate of the functional coupling between grip and load forces (Kawato et al. 2003). Cerebellar neural activation shifted from right anterior cerebellum to the left posterior cerebellum. These data are in agreement with other brain imaging studies, suggesting that the cerebellum is a principal site involved in the storage, retrieval, and switching of internal models related to newly acquired motor representations (Imamizu et al. 2000). A recent neuro-computational model implies that a cerebellar network is optimally suited to serve predictive coupling between grasping and load forces (De Gruijl et al. 2009).

Living Without a Cerebellum

When discussing the question of how the cerebellum contributes to the control of grasping in daily life, it appears legitimate to follow a *lesion approach*, that is, to observe humans who live without a cerebellum. Human individuals with complete absence of the cerebellum are exceedingly rare with only a few cases reported in the world literature since its first description in 1831 (Rubinstein and Freeman 1940; for a review see Glickstein 1994 or Macchi and Bentivoglio 1977). Given the well-established notion that the cerebellum is an essential promoter and coordinator in motor control and motor learning (Nowak et al. 2007a; Topka and Massaquoi 2002), one might suggest that motor performance in general and manual dexterity in particular is commonly impaired in humans living without a cerebellum. This appears to be true, but it is remarkable that subjects with complete congenital absence of the cerebellum are able to reach a high level of motor performance in daily life.

H.K., who is presently a 67-year-old white female, is such an example. She exhibits clear motor abnormalities, such as upper limb ataxia, saccadic ocular pursuit, dysarthria, and gait disturbance when clinically tested; however, these deficits are less pronounced than expected given her almost complete absence of the cerebellum. H.K.'s motor development was delayed and she did not learn to walk unaided until 3 years of age (Timmann et al. 2003). She learnt to ride a bicycle and is

able to perform manual crafts, suggesting that her motor system was able to compensate a remarkable amount of dysfunction due to inherited cerebellar loss. At age 63, her manual dexterity was tested (Nowak et al. 2007b).

Case Description

H.K. is a right-handed white female who was born with almost complete absence of the cerebellum (Fig. 4). Her past medical and family histories have been described earlier in detail (Timmann et al. 2003). At age 63, her neurological examination reveals mild to moderate cerebellar dysarthria, mild to moderate ataxia of the upper and lower limbs, mild ataxia of stance, and impaired gait. Her gait disorder is aggravated by a marked shortening of the right leg following traumatic hip disorder. The finger-to-nose test reveals mild decomposition of movement, mild intention tremor, and mild to moderate dysmetria. Pronation-supination alternating movements are slightly irregular and slowed. Writing and drawing of the Archimedes' spiral are slowed with only mild impairment. In the International Cooperative Ataxia Rating Scale (Trouillas et al. 1997), she scores a total of 30.5 out of 100 points. The International Cooperative Ataxia Rating Score subscales are 3 out of 8 for speech disorders, 2.5 out of 6 for oculomotor disorders, 15.5 out of 52 for limb ataxia (right upper limb: 3; left upper limb 3.5; lower limbs: 9), and 9.5 out of 34 for postural and gait disturbance.

Predictive and reactive control of grasping forces was tested in H.K. in comparison to three age- and gender-matched healthy right-handed female subjects (aged 59, 63, and 65 years). A weight-catching task was used that allows separation of predictive and reactive mechanisms of grasping force control. When we drop a weight from one hand into a receptacle held with the other hand, predictive increase in grip force occurs prior to weight impact (Johansson and Westling 1988). When, however, another person drops the weight unexpectedly in the receptacle while we close our eyes, our grip force increase lags some 100 ms behind the perturbation at impact, suggesting long-loop reflexes that are initiated by sensory feedback

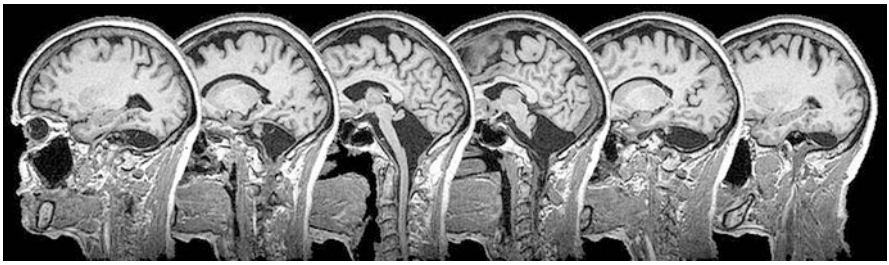

Fig. 4 Sagittal T1-weighted magnetic resonance imaging of H.K.'s brain revealed almost complete absence of the cerebellum, a small brainstem without protuberance of the pons and olives. Small cerebellar remnants are present (see Timmann et al. 2003 for a detailed anatomical description of K.K.'s brain abnormalities based on magnetic resonance imaging)

(Johansson and Westling 1988). Reactive grip force responses were maintained in all healthy subjects and H.K. (Fig. 4). In contrast, when the weight was dropped from the opposite hand, H.K. established a reactive rather than a predictive mode of force control (see Fig. 5; Nowak et al. 2007b). That is, she was unable to establish a predictive increase of grasping forces prior to impact when dropping the weight herself. These data imply that the cerebellum is essential for predictive force control

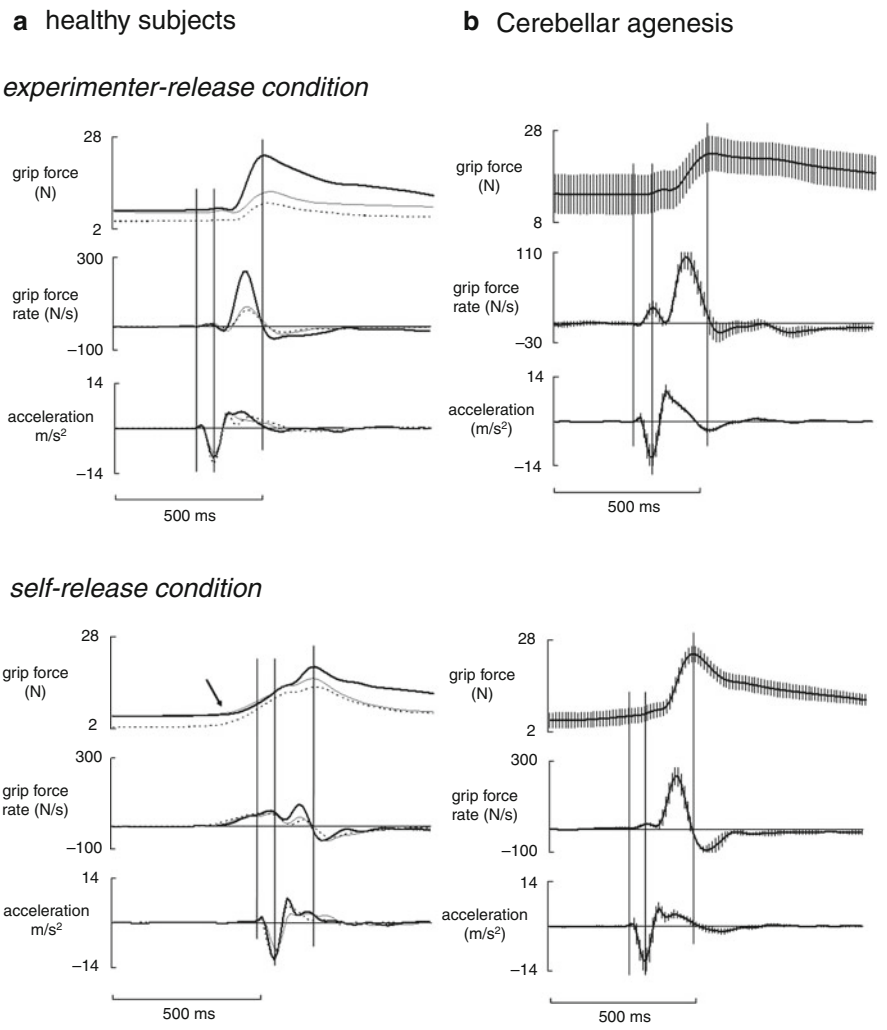

Fig. 5 Average grip force, grip force rate, and acceleration traces obtained from weight-catching trials in the experimenter- and self-release conditions of three healthy subjects (**a**) and a subject with cerebellar agenesis (**b**). The vertical lines indicate the times of weight impact, peak downward acceleration due to impact, and peak grasping force response. The *arrows* indicate the increase in grasping force

and one might interpret the data to reflect the existence of internal models implemented within the cerebellum.

Deficits of Grasping Force Control

Exaggerated grasping force levels have been found in subjects with cerebellar disorders when grasping, lifting, and transporting objects (Rost et al. 2005; Serrien and Wiesendanger 1999). The force overshoot observed in subjects with cerebellar pathologies has been interpreted to reflect an acquired strategy to ensure a stable grasp in situations in which the motor system works suboptimally. Consequently, the force overflow may be considered a strategic response of the motor apparatus to compensate for the deficit resulting from the lack of predictive control of motor actions. In addition, impaired timing in the establishment of grasping forces in relation to inertial loads arising when grasping and lifting an object has been found in cerebellar degeneration and focal cerebellar lesions (Brandauer et al. 2008; Fellows et al. 2001). In particular, subjects with cerebellar disorders exhibit prolonged grasp formation times and decoupling of the temporal coordination between grasping and load force profiles. However, correlation between these impairments and clinical ataxia rating scales, such as the International Cooperative Ataxia Rating Score subscales (Trouillas et al. 1997), was weak, implying that these kinetic measures may serve as a valuable adjunct measure for testing dexterity in cerebellar disorders (Brandauer et al. 2008).

Deficits of Higher-Order Motor Control Related to Grasping?

The debate on whether or not the cerebellum has a role in non-motor functions, such as perception, is still unsettled. Problems in weight perception have already been documented by Gordon Holmes in subjects suffering gun-shot wounds of the cerebellum during World War I (Holmes 1917). There are also data suggesting that cerebellar lesions cause a deficit in kinesthesia (Grill et al. 1994, but see Maschke et al. 2003). However, a recent study demonstrated that the size-weight illusion during object lifting is intact in patients with cerebellar degeneration (Rabe et al. 2009). The size-weight illusion is based on perceptual and higher-order cognitive processes. It refers to the fact that the smaller of two objects with identical weight, but different size, is judged to be heavier when grasped and lifted (Flanagan and Belttzner 2000). This *perceptive* size-weight illusion probably depends on the integrity of the ventral visual path, which is essential for object recognition (Goodale and Milner 1992). In contrast, the dorsal visual path is involved in predictive scaling of the hand and fingers to object size when grasping and the cerebellum has close connections to the dorsal visual path (Glickstein 2000).

This finding implies that the cerebellum is less actively involved in higher-order motor performance related to grasping.

References

Blakemore SJ, Frith CD, Wolpert DM (2001) The cerebellum is involved in predicting the sensory consequences of action. Neuroreport 12:1879–1884

Boecker H, Lee A, Mühlau M, Ceballos-Baumann AO, Ritzl A, Spilker M, Marquardt C, Hermsdörfer J (2005) Force level independent representation of predictive grip force-load force coupling: a PET activation study. NeuroImage 25:243–252

Brandauer B, Hermsdörfer J, Beck A, Aurich V, Gizewski ER, Marquardt C, Timmann D (2008) Impairments of prehension kinematics and grasping forces in patients with cerebellar degeneration and the relationship to cerebellar atrophy. Clin Neurophysiol 119(11):2528–2537

Castiello U (2005) The neuroscience of grasping. Nat Rev Neurosci 6:726–736

Fellows SJ, Ernst J, Schwarz M, Topper R, Noth J (2001) Precision grip in cerebellar disorders in man. Clin Neurophysiol 112:1793–1802

Flanagan JR, Belttzner MA (2000) Independence of perceptual and sensorimotor predictions in the size-weight illusion. Nat Neurosci 3:737–741

Flanagan JR, Wing AM (1993) Modulation of grip force with load force during point-to-point arm movements. Exp Brain Res 95:131–143

Glickstein M (1994) Cerebellar agenesis. Brain 117:1209–1212

Glickstein M (2000) How are visual areas of the brain connected to motor areas for the sensory guidance of movement. Trends Neurosci 23:613–617

Goodale MA, Milner AD (1992) Separate visual pathways for perception and action. Trends Neurosci 15:20–25

Grill SE, Hallett M, Marcus C, McShane L (1994) Disturbances of kinaesthesia in patients with cerebellar disorders. Brain 117:1433–1447

Gruijl D, von der Smagt P, De Zeeuw CI (2009) Anticipatory grip force control using a cerebellar model. Neuroscience 162:777–786

Holmes G (1917) The symptoms of acute cerebellar injuries due to gunshot injuries. Brain 40: 461–535

Hore J, Wild B, Diener HC (1991) Cerebellar dysmetria at the elbow, wrist and fingers. J Neurophysiol 65:563–571

Imamizu H, Miyauchi S, Tamada T, Sasaki Y, Takino R, Putz B, Yoshiaka T, Kawato M (2000) Human cerebellar activity reflecting an acquired internal model of a new tool. Nature 403: 192–195

Ito M (2006) Cerebellar circuitry as a neuronal machine. Prog Neurobiol 78:272–303. Review

Johansson RS, Westling G (1988) Programmed and triggered actions to rapid load changes during precision grip. Exp Brain Res 71:72–86

Kawato M, Kuroda T, Imamizu H, Nakano E, Miyauchi S, Yoshioka T (2003) Internal forward models in the cerebellum: FMRI study on grip force and load force coupling. Prog Brain Res 142:171–188

Macchi G, Bentivoglio M (1977) Agenesis or hypoplasia of cerebellar structures. In: Vinken PJ, Bruyn GW (eds) Handbook of clinical neurology, vol 30. North-Holland, Amsterdam, pp 367–393

Manto MU (2010) Physiology of the cerebellum. In: Cerebellar disorders. A practical approach to diagnosis and management. Cambridge University Press, Cambridge, pp 23–35

Manto M, Godaux E, Jacquy J (1994) Cerebellar hypermetria is is larger when the inertial load is artificially increased. Ann Neurol 35:45–52

Maschke M, Gomez CM, Tuite P, Konczak J (2003) Dysfunction of the basal ganglia, but not the cerebellum, impaires kinaesthesia. Brain 126:2312–2322

Monzee J, Smith AM (2004) Responses of cerebellar interpositus neurons to predictable perturbations applied to an object held in a precision grip. J Neurophysiol 91:1230–1239

Nowak DA, Hermsdörfer J, Marquardt C, Fuchs HH (2002) Grip and load force coupling during discrete vertical movements in cerebellar atrophy. Exp Brain Res 145:28–39

Nowak DA, Topka H, Timmann D, Boecker H, Hermsdörfer J (2007a) The role of the cerebellum for predictive control of grasping. Cerebellum 6:7–17

Nowak DA, Timmann D, Hermsdörfer J (2007b) Dexterity in cerebellar agenesis. Neuropsychologia 45:696–703

Rabe K, Brandauer B, Li Y, Gizewski ER, Timmann D, Hermsdörfer J (2009) Size-weight illusion, anticipation and adaption of fingertip forces in patients with cerebellar degeneration. J Neurophysiol 101:569–579

Ramnani N (2006) The primate cortico-cerebellar system: anatomy and function. Nat Rev Neurosci 7:511–522

Rost K, Nowak DA, Timmann D, Hermsdörfer J (2005) Preserved and impaired aspects of predictive grip force control in cerebellar patients. Clin Neurophysiol 116:1405–1414

Rubinstein HS, Freeman W (1940) Cerebellar agenesis. J Nerv Ment Dis 92:489–502

Serrien JD, Wiesendanger M (1999) Grip-load coordination in cerebellar patients. Exp Brain Res 128:76–80

Timmann D, Dimitrova A, Hein-Kropp C, Wilhelm H, Dörfler A (2003) Cerebellar agenesis: clinical, neurophysiological and MR findings. Neurocase 9:402–413

Topka H, Massaquoi S (2002) Pathophysiology of clinical cerebellar signs. In: Manto M, Pandolfo M (eds) The cerebellum and its disorders. Cambridge University Press, Cambridge, pp 121–135

Trouillas P, Takayanagi T, Hallett M, Currier RD, Subramony SH, Wessel K, Bryer A, Diener HC, Massaquoi S, Gomez CM, Coutinho P, Ben Hamida M, Campanella G, Filla A, Schut L, Timmann D, Honnorat J, Nighoghossian N, Manyam B (1997) International cooperative ataxia rating scale for pharmacological assessment of the cerebellar syndrome. The Ataxia Neuropharmacology Committee of the World Federation of Neurology. J Neurol Sci 145:205–211

Wolpert DM, Flanagan JR (2001) Motor prediction. Curr Biol 11:R729–R732

Wolpert DM, Miall RC, Kawato M (1998) Internal models in the cerebellum. Trends Cogn Sci 2: 338–347

Zackowski KM, Thach WT Jr, Bastian AJ (2002) Cerebellar subjects show impaired coupling of reach and grasp movements. Exp Brain Res 146:511–522