Chapter 10
Visual Circuits

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Abstract The cerebellum receives substantial input from visual and eye movement-related areas by way of the pons. These signals are used to guide and refine motor behavior and to establish spatial orientation. Accordingly, damage to the cerebellum can lead to imprecise eye movements and deficits in visual perception. Here we discuss cerebro-cerebellar circuits supporting vision.

Keywords Cerebellum • Cerebellar anatomy • Visual perception • Sensory predictions • Forward models

10.1 Anatomical Considerations

Visual information processing in the cerebrum engages various areas that make up a large amount of cerebral cortex. Interestingly, many of these areas also project to the cerebellum. There, visual information, in combination with other kinds of inputs such as vestibular signals, is integrated in order to provide spatial orientation and to (visually) guide and refine motor behavior, such as eye movements (Thier and Möck 2006).

To allow for such close interaction, both cerebral and cerebellar cortices must share information. Hence, it is not surprising that the extensive projection system connecting these two structures by way of the pons constitutes one of the largest circuits in the human brain. Information from sensory and motor areas of the cerebral cortex, which accounts for the largest portion of pontine afferents, and also from additional subcortical structures such as the superior colliculus (Glickstein 2013), is sent to the cerebellum mainly via the pontine nuclei (PN) and another precerebellar nucleus, the nucleus reticularis tegmenti pontis (NRTP), which will not be further discussed here.

The PN are located around the cerebral peduncles in the ventral portion of the pons and are commonly subdivided into several nuclei based on their cytoarchitec-

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ture and their general location. They consist of roughly 20,000,000 neurons therewith accounting for almost 40 % of pontine brainstem volume (Matano et al. 1985; Tomasch 1969). The large majority of these neurons are believed to be projection neurons connecting cerebral and cerebellar cortex (Cooper and Fox 1976). Because of its intermediate position between the two cortices receiving cerebrocortical and collicular visual and eye movement-related signals, the PN are believed to be an important integrative relay of the visual and eye movement pathway on which we focus here.

10.1.1 Cerebrocortical Areas Projecting to the Pons

Using retrograde tracers injected into the PN to study the distribution and density of corticopontine projections, Glickstein and colleagues found labeled layer 5 pyramidal cells within a contiguous region covering parts of frontal, parietal, and temporal lobe (Glickstein et al. 1985) Fig. 10.1a. More precisely, the region containing substantial numbers of labeled cells ranged from the insular cortex within the sylvian fissure laterally to the ventral edge of the cingulate cortex medially and from the arcuate sulcus rostrally to the superior temporal sulcus caudally (Brodmann's areas 1–10, 13, 14, 19, 23–25; (Brodmann 1909)).

Importantly, this region found to project to PN comprises of all known cortical areas involved in providing visual and other signals necessary for eye movements such as saccades and smooth pursuit, but also for example the ocular following response. These visual and eye movement-related areas include the frontal eye fields (FEF; (Bruce et al. 1985; Gottlieb et al. 1994)), supplementary eye fields (SEF, (Heinen 1995; Schlag and Schlag-Rey 1985, 1987)), lateral intraparietal (LIP) and medial parietal areas (MP; (Andersen et al. 1990; Barash et al. 1991a, b; Thier and Andersen 1997, 1998)), medial superior temporal area (MST; (Newsome and Wurtz 1988; Thier and Erickson 1992; Kawano et al. 1994)), and middle temporal area (MT; (Dursteler and Wurtz 1988; Newsome et al. 1988)). Further analyses of the cerebro-pontine projections of these regions showed that most of them terminate in the dorsal part of the ipsilateral PN in several elongated lamellae often spanning several sub-nuclei. This suggests that the subdivision of the PN into several nuclei based on cytoarchitecture does not seem to correspond to the organization of afferent terminations (Thier and Möck 2006).

10.1.2 Ponto-Cerebellar Projections and Cerebellar Output

The pontine projection neurons' axons enter the cerebellum by way of the middle cerebellar peduncle and terminate as mossy fibers in the granular layer of the cerebellar cortex. From there they give rise to the parallel fibers, which connect to purkinje cells as the only output neurons of cerebellar cortex. While most of the ponto-cerebellar fibers terminate in the contralateral part of the cerebellum, there

seem to be also ipsilateral projections (Rosina et al. 1980). Major projection sites of these neurons that show an involvement in eye movements and will be discussed in the following chapter are the lobuli VII and VIc of the posterior vermis and the dorsal paraflocculus (Thier 2011) Fig. 10.1b.

Visual and eye movement-related signals leave the cerebellum through the projection of purkinje cells to the deep cerebellar nuclei (DCN). The caudal fastigial and the posterior interposed nucleus have been studied the most with respect to oculomotor functions and both have been shown to connect to the PN (Thier and Möck 2006).

10.2 Cerebellum and Eye Movements

The previous section provided a rough overview about circuits underlying cerebrocerebellar information transfer with a focus on visual and eye movement related signals. Here we will focus on behaviorally and/or perceptually relevant cerebellar contributions to eye movements and visual perception.

The cerebellum is of utter importance for visual perception because it optimizes goal-directed eye movements such as saccadic and smooth pursuit eye movements as well as ocular reflexes stabilizing visual perception such as the vestibulo-ocular reflex (VOR) or the ocular following response (OFR) (Thier 2011). The ability to precisely direct gaze towards objects of interest as well as to perceive a stable visual word despite one's own movements lies at the heart of our visual perceptual abilities. At this point it is important to note, however, that the cerebellum is of course not only involved in directing and optimizing eye movements. It is, on the contrary, also involved in visually guiding limb movements, such as reaching, among many other tasks. Yet, discussing these cerebellar features goes beyond the scope of this chapter. Therefore, in the following section we will explore effects of damage to the cerebellum or the PN on eye movements.

10.2.1 Effects of Cerebellar Lesions on Saccades and Smooth Pursuit

Saccades are fast and goal-directed eye movements that serve to bring an object of interest onto the fovea, i.e., onto the part of the retina with highest visual acuity. Hence, being able to perform precise saccades is important to ensure proper object analysis. Likewise, in cases in which an object of interest is moving and/or the observer is moving, smooth pursuit eye movements are additionally engaged to track the object by matching eye velocity to target velocity and thereby keeping it on the fovea (often supported by head and body tracking).

Immediate insights into the importance of the cerebellum for eye movements are provided by lesion studies. Barash and colleagues showed that after lesioning small parts of the oculomotor vermis in macaque monkeys, visually guided saccades

became dramatically unreliable and hypometric, i.e., saccades fell too short relative to the saccade target (Barash et al. 1999). Similar effects, namely imprecise saccades with a high variability in saccade end points, can also be observed in human subjects suffering from cerebellar damage (Golla et al. 2005) Fig. 10.1c. Comparable problems in precision arise during smooth pursuit eye movements. While healthy subjects are capable of smoothly tracking a constantly moving visual target, patients and animals with cerebellar lesions fail in doing so (May et al. 1988; Haarmeier and Thier 1999). This is because their eye velocity is typically too small to match target velocity. Therefore, the distance between the tracked object and the fovea continuously increases during the course of a tracking movement and this "foveation error" then needs to be repeatedly compensated with (so-called) catch-up saccades (Fig. 10.1d).

10.2.2 Cerebellar Adaptation of Eye Movements

As we have seen in the previous paragraph, damage to certain parts of the cerebellum can lead to imprecise visually guided eye movements. The role of the cerebellum thus seems to be the optimization and coordination of movement. The lack of coordination and fine-grained motor abilities is indeed a typical symptom of (cerebellar) ataxias in a clinical context.

Such an involvement in refining motor output would be essential for learning new or for adapting already learned motor skills. Interestingly, in the study by Barash and colleagues referred to above, monkeys' saccades on average returned to pre-lesion amplitudes after some time, although displaying bigger variation. What was completely abolished, however, was the capacity to adapt saccade amplitude in an adaptation paradigm (Barash et al. 1999). This finding is in agreement with a large body of literature describing adaptation deficits of saccades and smooth pursuit in cerebellar disease, e.g. (Takagi et al. 2000; Straube et al. 2001). Furthermore, these deficits are also reported for skeletomotor movements in tasks that call for an adaptation of motor (and possibly sensory) output in response to altered sensorimotor relationships (Martin et al. 1996). In fact, motor learning and adaptation deficits are usually one of the strongest symptoms of patients suffering from cerebellar damage (Bastian 2011).

Adapting and recalibrating movements is not only required in experimental settings but, on the contrary, is a continuous process ensuring precise motor output and

Fig. 10.1 (continued) Note the wide spread of saccade endpoints of the patient (dysmetria) compared to the control (Modified from Golla et al. 2005). (**d**) Performance in smooth-pursuit of a patient suffering from cerebellar degeneration compared to a healthy control group. (**d1**) Eye movement traces (*red lines*) in a task where the subject was supposed to track a moving target at 8°/s (*black line*). The pursuit velocity is insufficient to stay on the target, which leads to compensatory corrective saccades. (**d2–d4**) Psychophysical evidence for impaired visual analysis of a moving object (**d2**) as a result of smooth pursuit deficits (**d3–d4**) in a cerebellar patient (*light grey*) compared to a healthy control group (Modified from Haarmeier and Thier 1999). *DPF* dorsal paraflocculus, *FL* flocculus, *PML* paramedian lobule

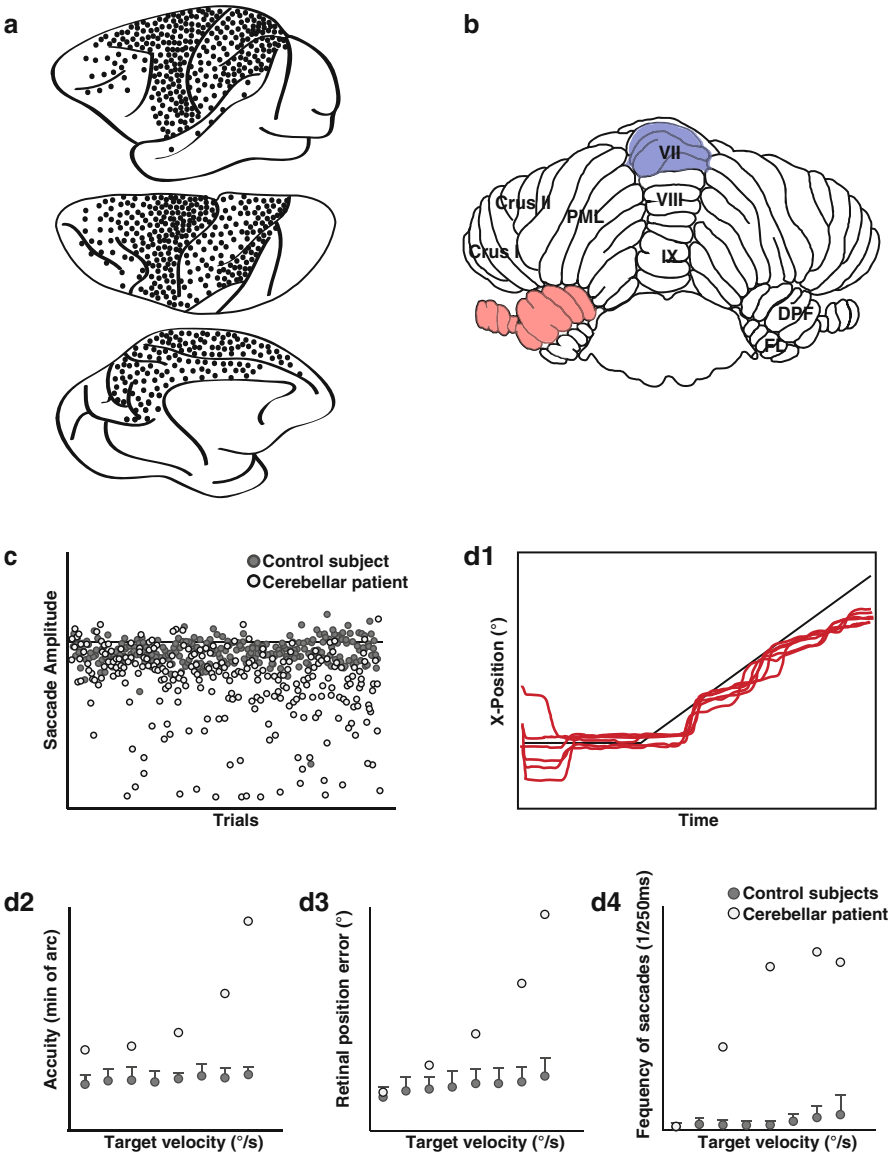

Fig. 10.1 (**a**) Location of cells (*black dots*) in the cortex that have been found to project to the PN using retrograde tracers in a monkey. Layer 5 pyramidal cells within a region involving parts of frontal, parietal, and temporal lobe, ranging from the insular cortex within the sylvian fissure laterally to the ventral edge of the cingulate cortex medially and from the arcuate sulcus rostrally to the superior temporal sulcus caudally project to the PN (Modified from Glickstein et al. 1985). (**b**) Schematic drawing of a caudal view of cerebellar cortex with the location of the two main oculomotor regions highlighted. The oculomotor vermis (OMV) is shown in *blue* and the dorsal paraflocculus in *red* (Adapted from Thier and Möck 2006). (**c**) Exemplary data on visually guided saccades of a cerebellar patient (*light grey*) and a control subject (*dark grey*).

self-motion perception despite the continuous changes of the motor plant due to aging, disease etc. (Haarmeier et al. 2001). It has been shown, for instance, that even the compensation of eye movement fatigue critically depends on the cerebellum (Golla et al. 2008).

Motor updating is believed to depend on so called *forward models*, which predict the sensory consequences of movements on the basis of motor commands and (sensory) information about the current state of the system. Using these predictions, movements can be corrected on the fly and do not (only) depend on delayed sensory feedback, thereby guaranteeing fast and accurate movements (Wolpert and Ghahramani 2000; Wolpert and Flanagan 2001). Accordingly, it is currently believed that the cerebellum is responsible for predicting the sensory consequences of movement and/or, in particular, for keeping these forward model predictions precisely tuned (Wolpert et al. 1998; Bastian 2006; Tseng et al. 2007).

10.3 Deficits of Visual Perception in Cerebellar Patients

Up to this point, the reported influence of the cerebellum on perception/vision was an indirect one – one that is mediated by imprecise eye movements. In the following we will focus on seemingly isolated visual deficits and on visual functions that are informed by forward models. At least one purely visual deficit that is seemingly unrelated to motor action has been consistently reported over the last years. That is, deficits in detecting a global visual motion component embedded in randomly moving dots (Nawrot and Rizzo 1995; Thier et al. 1999; Jokisch et al. 2005; Händel et al. 2009). Compared to healthy controls, cerebellar patients need a much higher degree of coherently moving dots within a moving random dot pattern to establish a global visual motion percept (Fig. 10.2a).

10.3.1 Role of the Cerebellum in Global Visual Motion Perception

But why and how should the cerebellum influence such motion perception? A key for a better understanding of such findings could be provided by the fact that the causes for visual motion can either be a “true” motion in the environment, or an ego-motion (in light), which in itself can induce visual motion signals. This is, for instance, the case when one is moving her eyes. In order to extract the part of the incoming visual afference that is chiefly important to the brain, i.e., the exafference (von Holst and Mittelstaedt 1950) that has not been self-caused, the cerebellum is believed to predict the visual sensory consequences of performed movements by also resorting to forward models. In case of smooth pursuit eye movements, this prediction is then used to cancel out the self-induced (reafferent) visual motion to ensure perceptual stability (Haarmeier et al. 2001) Fig. 10.2b.

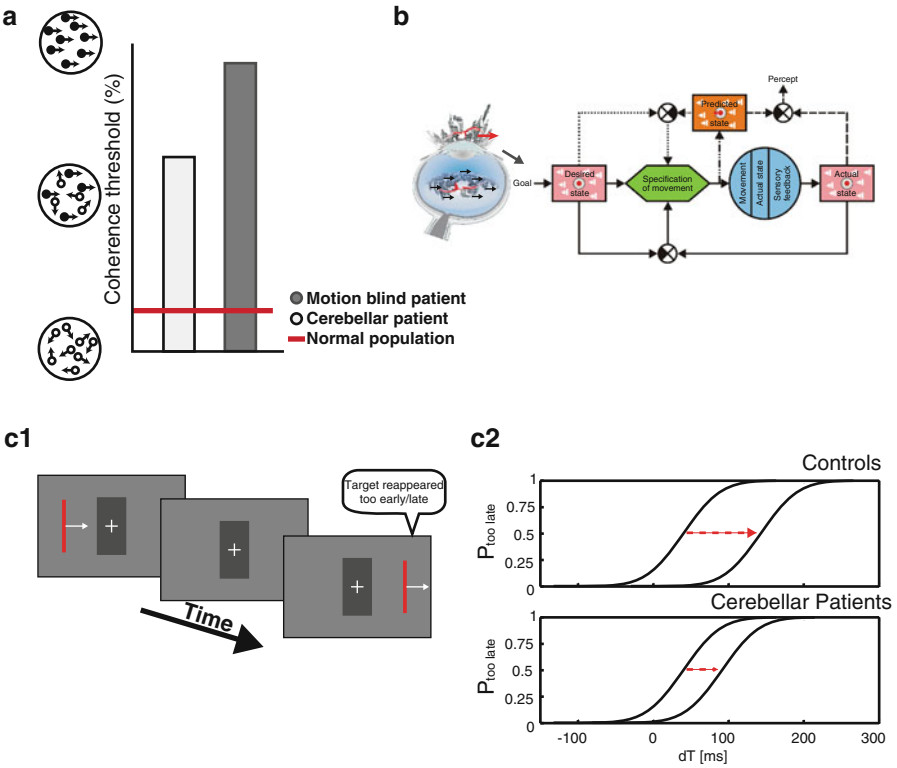

Fig. 10.2 (a) Deficits of a cerebellar patient suffering from spinocerebellar ataxia type 6 (SCA6) in global visual motion perception. When measuring the percentage of coherently moving dots necessary to evoke a percept of global motion in a display of otherwise randomly moving dots, this SCA6 patient (light grey bar) has not only a strongly elevated threshold compared to a healthy population (red line), but her perceptual threshold is in fact closer to the one of a motion blind patient due to cortical lesions (Zihl et al. 1983). (b) Depiction of a comparator model used to predict and possibly subtract self-induced motion, for example in the case of smooth pursuit eye movements. If one is tracking a moving object with the eyes in order to stabilize the retinal image, a motor command is generated to achieve this desired state. This desired state is then compared with the actual state and a possible motor error can be fed back into the system to improve its function (solid lines). Furthermore, the system forms a prediction about the sensory outcome of the behavior based on the motor command (predicted state). This prediction can then be used for feedforward movement control, but also to remove or attenuate self-caused sensory afference, e.g. the self-caused retinal image slip during smooth pursuit (dotted lines; Adapted from Lindner et al. 2005). (c) Deficit of cerebellar patients in recalibrating a spatiotemporal prediction in response to altered stimulus statistics. (c1) Subjects had to predict the time of reappearance of a constantly moving visual target that disappeared behind an occluder for a part of its movement trajectory. The time the visual target spent behind the occluder was manipulated in such a way, that in half of the trials the target reappeared too late, denoted by a positive deltaT (dT). (c2) While healthy controls recalibrated their prediction about when the target should reappear in response to the target reappearing too late (dT>0) in half of the trials, as indicated by a shift of the psychometric function towards more positive deltaT, cerebellar patients did not show this recalibration. Hence, cerebellar patients show a deficit in adapting perceptual predictions that is similar to the reported deficits in motor tasks (Adapted from Roth et al. 2013)

As already discussed in the section on (motor) adaptation, also such *sensory predictions* need to undergo constant recalibration in order to match not only the changing properties of the motor plant but also the ever-changing sensory environment (brightness, contrast etc.). These forward models therefore need to incorporate information on actual body states, issued motor commands, as well as incoming sensory information (and probably context information), a job that fits to the integrative position the cerebellum holds in the brain. Furthermore, its unique cellular architecture is best suited for the comparison of a predicted with an actual sensory afference that is necessary for recalibration.

In the case of the discussed global visual motion deficit, the precise forward model input to cortical areas involved in motion perception could be missing due to the cerebellar damage and thereby explain deficits in motion perception of these patients.

Support for this idea comes from work on the suprasylvian cortex of cats, in a region that contains cells that seem to represent the homolog of primate area MT responsible for motion perception. The cerebellar input to this area of cortex via the thalamus is as large as the purely visual afference. Given this tremendous cerebellar input to this part of cortex it stands to reason that the missing (predictive) cerebellar input could corrupt motion processing. A hint that this could also be the case in humans comes from an MEG study that found altered parieto-occipital activity of cerebellar patients in a coherent motion task, paralleling patients' perceptual impairment (Händel et al. 2009). Furthermore, in a recent study Sultan and colleagues have used electrical stimulation of the cerebellar output combined with functional magnetic resonance imaging and found connections between the cerebellar output and areas involved in motion processing (Sultan et al. 2012).

10.3.2 Are There Other Deficits in Visual Perception?

In the last decades many studies have been trying to identify other perceptual or cognitive deficits in cerebellar patients (Baumann et al. 2015). In fact, the idea of forward models predicting upcoming sensory afference based on current state and contextual information can be theoretically easily transferred to the cognitive/perceptual domain without the explicit need for motor behavior (Ito 2005, 2008). But separating motor from perceptual or cognitive effects can be hard and often experimentally impossible because the ability to move and therefore explore ones environment is the basis for much of our perceptual system.

However, the notion to use a system like the cerebellum that is mostly used for optimizing (visually guided) actions and therefore has all the necessary information and computational abilities to predict upcoming sensory events on the basis of current state information in combination with internally stored models and to update these models also for closely related perceptual tasks, seems parsimonious. Especially since such sensory events are usually important for subsequent movements (Baumann et al. 2015). A study by Roth and colleagues recently investigated

the question whether the cerebellum also plays a role in forward models about external motion, which likewise need to undergo adaptation to reflect the ever-changing (sensory) environment (Roth et al. 2013). In this study, participants had to form predictions about the spatiotemporal behavior of a partly occluded visual target. Cerebellar patients showed a clear deficit in updating their spatiotemporal predictions in response to changed stimulus statistics compared to healthy controls, while this difference was not due to eye movement differences (Fig. 10.2c). A recent similar study seems to support these findings (Deluca et al. 2014). Additionally, the cerebellar output seems to be functionally coupled to many areas that are also involved in motion processing (Sultan et al. 2012).

In general, predicting upcoming visual events is a very crucial ability of our central nervous system. It allows us, for example, to direct attention, to react faster to predictable stimuli and to attenuate or even cancel out self-induced sensory afference. And it seems likely that at least some parts of the already existing machinery used predominantly for action could additionally be employed in predicting – and especially recalibrating predictions about – upcoming (visual) sensory events because these predictions are highly informative and in fact used by the motor system to perform appropriate actions.

10.4 Conclusion

The cerebellum receives massive input from visual and oculomotor regions in cerebral cortex and also from subcortical regions. Projections from these areas thereby mainly take the route through the pontine nuclei (PN). From there, neurons project through the middle cerebellar peduncle to the granular layer of cerebellar cortex and make up the mossy fibers. The most important oculomotor and visual regions of cerebellar cortex that have been identified so far are lobuli VII and VIc of the posterior vermis and the dorsal paraflocculus. Damage to these areas lead to imprecise saccadic and smooth pursuit eye movements and absent adaptation of these movements. Such adaptation is believed to depend on updating of forward models of movement commands. Also for perceptual purposes such forward models are important in order to cancel or attenuate self-induced retinal image slip and therefore contribute to the perception of a stable world despite eye movements. Compatible with this idea, cerebellar patients show deficits in coherent motion perception, supporting the importance of the cerebellum also for such perceptual tasks. Furthermore, recent evidence suggests that the cerebellum is involved in optimizing perceptual predictions about visual motion also in non-motor tasks. It therefore seems that the existing machinery of the cerebellum mostly involved in visual information processing for the sake of eye movements can in addition be used for optimizing (visual) perception. The pattern of cerebellar projections to cerebral cortex strengthens this notion.

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