Normal spatial attention but impaired saccades and visual motion perception after lesions of the monkey cerebellum

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Number of figures: 8
Number of supplemental figures: 2
Number of tables: 1
Number of pages: 29
Number of words in Abstract: 148; in Introduction: 384; in Discussion: 1144

Key words: vermis, perception, luminance detection, fastigial nucleus, cognition, rhesus monkey

Acknowledgements: we are grateful to Hendrik Dietrich for practical contributions in an early phase of the study and to Ute Grosshennig for help with the histology. This work was supported by grants SFB 550-A2 and A7 from the Deutsche Forschungsgemeinschaft

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Abstract:

Lesions of the cerebellum produce deficits in movement and motor learning. Saccadic dysmetria, for example, is caused by lesions of the posterior cerebellar vermis. Monkeys and patients with such lesions are unable to modify the amplitude of saccades. Some have suggested that the effects on eye movements might reflect a more global cognitive deficit caused by the cerebellar lesion. We tested that idea by studying the effects of vermis lesions on attention as well as saccadic eye movement, visual motion perception and luminance change detection. Lesions in posterior vermis of four monkeys caused the known deficits in saccadic control. Attention tested by examination of acuity threshold changes induced by prior cueing of the location of the targets remained normal after vermis lesions. Luminance change detection was also unaffected by the lesions. In one case, after a lesion restricted to lobulus VIII, the animal had impaired visual motion perception.

Introduction:

In addition to its known role in motor control, some have suggested that the human cerebellum may also play a role in non-motor functions, such as attention and visual motion perception (Ivry and Diener, 1991; Nawrot and Rizzo, 1995; Thier et al., 1999; Jokisch et al., 2005.) The relevant locus appears to be the midline cerebellum, but the nature of the deficit remains incompletely understood (Thier et al., 1999). Townsend and coworkers (1999) found spatial attention deficits in adult cerebellar patients, which they interpreted as an attentional dysmetria, similar to the dysmetria of saccades caused by posterior vermal lesions (Akshoomoff and Courchesne, 1992; Akshoomoff et al., 1992; Courchesne et al., 1994; Allen et al., 1997). However, Golla and coworkers (2005) and
earlier studies (Schoch et al., 2004; Helmuth et al., 1997) did not find an impairment of spatial and non-spatial shifts of attention in cerebellar patients. Previous attempts to clarify the role of the cerebellum in non-motor functions in humans have been based on patient studies and non-invasive imaging of the cerebellum of healthy subjects. However, patient studies may lead to wrong conclusions because of the possibility of extra-cerebellar pathology too subtle to be detected by routine tests. Conclusions based on imaging may be contaminated by artefacts of uncontrolled inadvertent motor behaviour (Haarmeier and Thier, 2007). Nixon and Passingham (1999) assessed the effect of lesions on working memory and visual associative learning. The monkeys showed no deficit on tasks of delayed spatial alternation or visual associative learning after lesions of the dentate nucleus.

In the present paper we describe tests of spatial attention shifting and visual motion perception in monkeys. The lesions were confined to posterior vermis since previous studies in patients (Nawrot and Rizzo, 1995; Townsend et al., 1999) had suggested a role of this part of the cerebellum in both spatial attention and in visual motion perception. In addition to these two functions we tested the accuracy and modifiability of saccades, known to depend on the integrity of the posterior vermis (Takagi et al., 1998; Barash et al., 1999) and a non-spatial visual control task, luminance change detection. The ability to extract coherent motion is clearly impaired if the posterior vermal lesions include lobule VIII. However, none of the animals showed a deficit in spatial attention, despite the presence of saccadic dysmetria.
Methods:

General procedure

Four male rhesus monkeys (*Macaca mulatta*) (referred to as B, R, E and S) were implanted with a scleral search coil and a head post for painless head restraint using standard protocols (Thier and Erickson, 1992). Surgery was carried out under intubation anesthesia with isoflurane supplemented by continuous infusions of remifentanyl (1-2.5µg/kg/h) and monitoring of body temperature, heart rate, blood pressure, pCO2, and pO2. Buprenorphine was given postoperatively to minimize pain. All procedures complied with the NIH Guide for Care and Use of Laboratory Animals and were approved by the local animal care committee (RP Tübingen, FG Tierschutz). Monkeys were trained to enter a primate chair, where they sat in darkness, the head restrained. Their head was positioned 22 cm away from the computer monitor for testing visually-guided saccades, shifts of attention and motion direction discrimination and 60 cm away for luminance change detection (21-inch monitor, Flexscan F760i-W, frame rate 72 Hz, 1280*1024 pixels). Eye movements were monitored during all the tasks using the search coil technique (spatial resolution <0.1 deg of visual angle, temporal resolution 1 kHz). Background luminance of the display was 0.1cd/m². Eye movements were analyzed online by the computer which also controlled the presentation of stimuli. Deviations of eye position from the fixation point exceeding certain limits - a square centred on the fixation point with 2-2.5 deg side length during pre-operative testing were considered as errors and excluded from further analysis. Because fixation became more variable after the lesion a larger window size of 4 to 8 degrees was used in the first experiments immediately after the lesion.
Stimuli and experimental design

Visually-guided saccades

Animals were trained to make a visually guided saccade to targets (white spots with a diameter of 20 arcmin, luminance 12 cd/m²) presented at an eccentricity of 10 or 15 deg in 8 different directions (0 deg to 270 deg, Figure 1 A). A fixation point (white spot of 20 arcmin, luminance 12 cd/m²) appeared in the centre of the screen for 500ms followed by the disappearance of the fixation point and the simultaneous appearance of a saccade target which was shown for 700ms. Monkeys were trained to make precise saccades to the target for a fluid reward (water or juice, depending on the monkey’s preference) which they received if they moved their eyes to the target within 400ms after its appearance.

Spatial attention

In two monkeys (B and S) we tested the possible beneficial effect of prior cueing of the location at which an acuity target was presented. In order to receive a fluid reward the monkeys had to correctly identify the orientation of a Landolt “C” (6.2 cd/m²) while keeping their gaze centred. They were trained to indicate the orientation of the Landolt “C”-gap, which was one fifth of the size of the C, by making a saccadic eye movement toward one of two possible targets which were presented 9 deg above and below the fixation point. A gap at the top of the Landolt ring required an upward saccade and a gap at the bottom of the Landolt “C” a downward saccade. We scored the response as correct if the saccade was executed within the first 1000ms after the Landolt “C” had disappeared, and the eye landed within a square of 4 deg (side length) centred on the saccade target.

“Cue” and “non-cue” trials were presented randomly interleaved in a typical experimental session. In non-cued trials, a central red fixation point (10 min of arc, 2cd/m²) appeared
on the screen for 500ms, followed by the Landolt “C” at one of two possible locations along the horizontal axis at 9 deg eccentricity. In cue trials, the cue, a white dot (20 min of arc, 6.2 cd/m²), was presented for 100ms after a 500ms fixation at one of two possible locations along the horizontal axis at 9 deg eccentricity. After an interval of 150 ms the Landolt “C” appeared at the location of the prior cue for 150 ms. In order to minimize afterimages, the “C” was not removed but converted into an “O” by closing the gap before disappearing 200 ms later.

The size of the gap in the Landolt “C” was varied according to an adaptive staircase procedure (PEST= parameter estimation by sequential testing) (Lieberman and Pentland, 1982). Since there were two possible target positions and two different cueing conditions, four independent PEST strategies were implemented in one experiment, all starting with the same Landolt “C” size (with gap sizes ranging from 20 to 28 min of arc for different monkeys). The orientation decisions (correct/incorrect) were plotted as a function of gap size and fitted by probit functions (McKee et al., 1985). Acuity thresholds were defined as the size of the “C”-gap, for which the probit function predicted 75% correct orientation decisions (chance level in two-alternative forced choice =50%). In order to prompt the monkeys to work close to their acuity threshold, an “extra-reward” procedure was applied (Golla et al., 2004): Animals received “extra-rewards” twice as large as standard rewards after every third correct trial until making the first incorrect trial. In order to motivate the monkeys to work reliably near threshold, they received a “mega reward” of three times the amount of a standard reward for each correct answer given in response to Landolt “C” gaps smaller than 120% of the expected threshold.
Two monkeys (E and S) were trained to detect the dimming of a peripheral visual target and report it by releasing a touch bar (Moore and Fallah, 2001). In a typical trial the central fixation point appeared as soon as the animal pressed the touch bar which was positioned in front of him. Following 400ms of fixation, a peripheral target appeared (red dot; diameter 0.5 deg, initial luminance 4.3 cd/m²d) randomly in one out of 4 locations (up, down, right and left of central fixation point) at 8.5 deg eccentricity. While keeping their gaze on the central fixation point and holding the touch bar, the monkeys were required to detect the change in luminance of the peripheral target which occurred randomly between 200ms and 1200 ms after the target first appeared. Monkeys were given a time window of 200-700 ms to release the touch bar to indicate the detection of a change in target luminance. Upon correct detection, the monkeys were rewarded with a unit of fluid. The individual luminance change threshold, i.e., the lowest target luminance change that a monkey could detect was determined by varying the changes in target luminance, based on the method of constant stimuli (MCS) (Snodgrass, 1975). In principle, the monkeys might simply release the touch bar after a safe time period, thereby getting reward in 50% of trials without relevant effort. To increase the incentive to pay attention to the luminance changes, we introduced 40% of trials with percentage luminance changes well below the monkey’s detection threshold in which they were required to keep the touch bar pressed throughout the trial for a reward. The other 60% of the trials were rewarded for correctly releasing the touch bar within the specified period (Figure 1 C). Monkeys’ responses (detected/non detected changes) were plotted as a function of percent luminance change and fitted by probit functions. The luminance change threshold level was defined as the percent luminance change for which the change was detected in 62.5% of cases (chance level to detect the change within required time-window =25%).
Motion direction discrimination

Motion detection thresholds were tested in four monkeys (B, R, E and S). Random dot cinematograms (RDC) were presented within apertures that were located at eccentricities of 16 deg in the central or peripheral parts of the visual field. The RDCs were constructed so that neither the spatial or temporal frequency of dots, nor the mean luminance, or contrast or position cues could be used to infer the direction of motion. Dots first appeared in randomly chosen locations, where they moved at a speed of 10 deg/sec. When a dot moved outside the aperture, a “wrap-around” procedure reintroduced it at the opposite side of the aperture from where it continued to move in the same or a new direction. Each dot had a lifetime of 200 ms (for monkeys B. and R.) or 400 ms for monkeys E. and S. and was born at random times relative to the start of the trial. It was reborn at a new, randomly chosen position where it continued the movement. The RDCs consisted of two groups of black dots, “signal” and “noise” dots respectively (overall number 200, size 5 arcmin, luminance 0.1 cd/m2), moving on a bright circular background (aperture diameter 16 deg, luminance 30.0 cd/m2). Signal dots moved coherently in one of four cardinal directions. They were presented mingled with “noise” dots which moved in random directions. The RDCs were presented in one of five positions, centrally or at 16 degrees eccentrically. The amount of dot displacement was always constant from frame to frame. Dots had a probability of 50% to change groups with each new frame (Figure 1 D). For this reason, it was not possible to infer the signal direction by just tracking a single dot.

RDCs appeared only in a particular location in a given block of trials. Each experimental block comprised of 80-120 trials in which the percentage of dots moving coherently was varied according to the method of constant stimuli (Snodgrass JG. 1975). A trial commenced with the appearance of a central fixation point whose successful fixation for 500ms triggered the appearance of the RDC for one second. Following the termination of
the RDC two response targets (dots 40 arc min size) appeared at 12 deg on an axis orthogonal to the axis on which the signal dots had been presented. Monkeys had 1000 ms to indicate their directional decision by making a saccade to the corresponding response target (a target up on the vertical axis corresponded to rightward motion, down to leftward motion, a target on the right of the horizontal axis to upward motion and finally on the left to downward motion. We adopted the “extra-reward” strategy for responses near threshold. The percentage of correct responses was plotted as a function of the percentage of coherently moving dots and fitted by a probit function. The perceptual threshold was defined as the motion coherence level at which 75% (chance level in the two-alternative forced choice =50%) of the trials yielded correct responses.

To quantify the quality of fixation during the presentation of discriminanda, we applied a principal component analysis (PCA) to measured horizontal and vertical positions of the eyes during the presentation of the Landolt Cs and the RDC respectively. The PCA determined the 2 orthogonal directions of maximal variance in the X-Y plane defining “fixation ellipses“, representing fixation quality at various times before and after the lesion. In order to assess the influence of the lesion, we compared the areas of the ellipses by repeated measures 1-way ANOVA with the factor “time relative to lesion” (in short “time”).

Vermal lesions

A vermis lesion was carried out as described in Barash et al. (1999) when a monkey was proficient on the tasks and his pre-lesion performance well-documented. Surgery and post-surgical care followed the procedures described earlier, except that the anesthesia with isoflurane was replaced by propofol (0.1 mg/kg/min). Antibiotic and analgesic medication was administered for a week after the surgery. The lesions were centred on somewhat different parts of the posterior vermis, but all four initially showed the expected
Monkey S demonstrated an unexpectedly quick recovery on the fifth day post lesion from the initial saccadic hypometria and he was able to adapt saccade amplitude. In order to assess the lesion location in this surprising case in-vivo, we used high-resolution MRI. Figure 3 A demonstrates the location and extent of the lesion, which included lobule VIII and the caudal part of lobule VII. Importantly, rostral lobule VII and caudal lobule VI had been spared in the first operation. When post-operative performance was stable, 36 days after the first lesion, we did a second ablation (L2) aiming to destroy lobuli VI and remaining lobule VII. High resolution MRI following the second operation showed that the lesion now included lobuli V, VI and VII, in addition to lobuli VIII as well as the caudal parts of lobulus VII that had been removed earlier L1) (Figure 3 B).

At the completion of the experiments (3 months for monkey R, 6.5 months for monkey B, 3.5 months monkey for E and 4.5 months (after the first ablation) for monkey S, the monkeys were deeply anesthetized by a lethal dose of pentobarbital and perfused intracardially with saline followed by fixative (4% paraformaldehyde). The cerebellum was sectioned parasagittally in 60 μm sections and Nissl stained. Figure 2 A-D and Table 1 summarize the location and extent of the lesion.

Results:

Saccadic hypometria after posterior vermal lesions

All four monkeys initially demonstrated hypometric saccades following lesions of the midline cerebellum. This is exemplified in Fig. 4A, which shows eye-traces recorded from monkey R making visually-guided saccades to a 15 deg target presented to the right prior to the lesion, 3 days, and 60 days after the lesion. Prelesion saccades were normometric and accurate with little variability of saccade endpoints. Shortly after the lesion, the saccades became significantly more variable and in general too short (=hypometric) to
reach the target, which is why the monkey had to add a second corrective saccade following the initial one. Two months after the lesion the average saccadic amplitude had recovered (=normometric). However the variability remained increased. In order to demonstrate that the early postlesion hypometria was observed in all monkeys and for all 8 directions tested, we plotted the distribution of the saccade end-points made by 3 monkeys (R, B and E) to targets presented at 15 deg eccentricity 3-6 days after the lesions and compared them to prelesion saccades (Figure 4 B-D). Also in monkey S, 2 days after a first lesion centred on lobule VIII, we observed increased variability of saccadic end-points and hypometria (Figure 4E). However, the hypometria quickly subsided and the recovery is illustrated in Figure 4 F which compares the performance of monkey S in the same task 20 days after the first lesion and initially after the second lesion that ablated lobules V, VI as well as the remainder of VII. The second lesion reinstituted the hypometria that had completely disappeared within 7 days after the first lesion.

In all the four monkeys the hypometria was most pronounced for horizontal saccades compared to those directed to other target locations (Fig 4B-D). In monkey S, hypometria was characterized by a general downward shift of saccade end-points immediately after the first lesion, most obvious for up- and downward saccades (Figure 4 E). This shift was compensated in the late period after the first lesion, but then was reinstated by the second lesion (Figure 4 F). Figure 4 G compares the saccade gains (i.e. the ratio of saccade and target amplitude) of 10 deg horizontal saccades (left and right pooled) for monkeys B, R and E before the lesion, within the first week after the lesion, late after the lesion (1-2 months) and in the case of monkey B 5-6 months after the lesion. In all three animals, the lesion caused a reduction of saccade gain of between 16 and 22%. The gain loss recovered somewhat in the post-lesion period but had not completely disappeared in monkeys R and E at the end of the observation period at 1-2 months after the lesion.
However, in monkey B, saccades were followed until day 190 after the lesion, a time at which the average gain showed complete recovery. In addition to the gain reduction following the vermal lesions, there was also increased variability in post-lesion saccades amplitudes. While variability remained increased in monkeys B and R until the end of the observation period, it had disappeared in monkey E by the end of the observation period (STD of prelesion saccades in: monkey B= 0.32±0.01 deg, monkey R= 0.35±0.01 deg, monkey E= 1.03±0.11 deg vs. STD of late postlesion saccades in: monkey B= 1.16±0.07 deg, monkey R= 0.46±0.02 deg, monkey E= 0.69±0.11 deg).

In monkey S, who was subjected to two successive lesions, we compared saccade gains for 10 deg horizontal saccades before the first lesion, 2-4 days after the first lesion, 20-30 days after the first lesion, 2-5 days after the second lesion and 15-30 after the second lesion (Figure 4 H). After the first lesion, saccade gain was reduced by 20% and saccade amplitudes were more variable. Late after the first lesion the monkey recovered completely from hypometria and showed a post-lesion saccade amplitude equivalent to pre-lesion performance. The second lesion reinstated a substantial gain loss of 28% compared to the prelesion baseline. Three weeks later this hypometria had again disappeared, but the increase in saccade amplitude variability remained (STD of prelesion saccades in monkey S= 0.29±0.03 deg, STD of saccades late after L1= 0.45±0.03 deg, and STD of saccades late after L2= 1.16±0.10 deg).

Spatial attention remains unimpaired after posterior vermal lesions

In monkeys S and B we studied the effects of posterior vermal lesions on spatial attention. After a training period of 3 and 4 months respectively, both monkeys showed clear improvements of visual acuity at 9 deg eccentricity on the order of 9.3% in monkey B and 16.1% in monkey S when the future location of the Landolt C ring had been cued (see Figure 5 for details).
Monkey S had two successive lesions, 36 days apart. The first lesion involved lobule VIII and the caudal end of VII. The second lesion included lobules V, VI, and the remainder of VII. Acuity with and without cueing was tested shortly after the first lesion (days 3-9) and shortly after the second lesion (days 3-13), during the time in which saccadic eye-movements were still hypometric. Measurements were also made in the late post-lesion period, when the saccadic eye movements were no longer hypometric (days 11-30 after the first lesion and between days 14-48 after the second one). Spatial cueing improved performance under all conditions. (2-way ANOVA with the factors “time” and “cue”, main effect of “cue” \( p<0.05 \), main effect of “time” \( p<0.05 \), interaction “cue”\{"time\\}, \( p=0.63 \)).

Since fixation performance during the presentation of the Landolt C showed no significant change (1-way ANOVA with the factor “time”, \( p>0.05 \)), the transient acuity gain after the first lesion cannot be explained by fixation instability.

Monkey B could be studied only in the late post-lesion period (days 60-69) as his performance on the task in the early post-lesion period was poor. Figure 5 B compares mean visual acuity thresholds with and without cueing before and after the lesion. Absolute acuity was better in the post-lesion period whereas the improvement of acuity by spatial cueing was unaltered (2-way ANOVA with the factors “cue” and “time”; main effect of “cue” \( p<0.05 \); main effect of “time” \( p<0.05 \); factor interaction \( p=0.54 \)).

Motion perception after posterior vermal lesion.

The ability to extract the direction of coherent motion from RDCs was measured in all four monkeys before the lesion (measured every day two weeks prior to the lesion, one data set per day per aperture location) and at different time periods after the lesion (measured daily within first two weeks after the lesion and every 3-4 days starting from the third week after the lesion) (Figure 6). In monkey R we tested motion discrimination for 3 RDCs locations (central, up and right) (Figure 6 A). There was no deficit in motion
perception after the vermal lesion. Monkey B was impaired in the early postlesion period at all the locations tested (central, right and left) (1-way ANOVA with the factor “time”, p<0.05), but recovered when tested on days 33-60 after the lesion (1-way ANOVA with the factor “time”, p>0.05) (Figure 6 B).

In order to test whether the motion perception deficits observed early after the lesion in monkey B were secondary to a deterioration of fixation, we compared the animal’s fixation during the 1000 ms of RDCs presentations before, early and late after the lesion (Figure 6 B). Following the lesion, fixation performance was impaired, there was about a two fold increase in the area of the fixation dispersion after the lesion (1-way ANOVA with the factor “time”, p<0.05). Fixation was less precise in the early and late post-lesion periods. However, the motion perception deficit had recovered completely at the time of the late post-lesion period, although the fixation disturbance persisted. In other words, there does not seem to be a link between the occurrence of fixation variability after the lesion and the development of a motion perception deficit.

In monkey S measurements were obtained for the RDC aperture presented in the central visual field, and at 16 degrees eccentricity in all four cardinal directions. We observed a transient deficit in motion direction discrimination, characterized by a significant increase of the motion direction discrimination threshold by a factor of about 1.6 compared to the average prelesion threshold after the first lesion for all the visual fields locations except for the upper field (1-way ANOVA with the factor “time”, p<0.05) (Figure 6 C). After one week the monkey’s thresholds returned to normal for all visual fields locations, except for the right visual field location, where it stayed impaired for the first 12 days after the first lesion. The fixation performance for the right visual field location was not significantly different from prelesion performance (1-way ANOVA with the factor “time”, p>0.05) (Figure 6 C.). After the second lesion, the motion direction discrimination thresholds remained unaffected for all the visual field locations tested. Figure S1 plots the motion
direction discrimination thresholds for monkey S as a function of time after the lesions. We also measured motion direction discrimination thresholds for monkey E. RDCs were presented only in three spatial locations: central, down and up. As in monkey S, we observed a transient deficit at the central and the down location immediately after the lesion, whereas performance at the up location was unchanged. Although there was some improvement, thresholds remained increased for the rest of the monkey’s life (Figure 6 D). The motion perception deficits could not be explained by disturbances of fixation, although there was a transient deterioration of fixation stability and a somewhat lesser deficit at the lower visual field location. Moreover, fixation stability normalized within one week while the motion discrimination deficit remained (Figure 6 D). Motion discrimination thresholds of monkey E plotted as a function of time are shown in Figure S2.

We calculated average thresholds as a function of time for the 3 monkeys B, E and S that had shown effects of the lesions. Data were pooled for central apertures, and for affected and non-affected peripheral apertures. The thresholds were normalized to the average motion direction discrimination threshold for the given spatial location before the lesion and are summarized in Figure 7. The lesions led to almost 2 fold increases in the thresholds with complete recovery for the central aperture but incomplete recovery for the affected peripheral visual field locations.

Luminance change detection is unimpaired after posterior vermal lesion

In order to assess the specificity of the motion perception deficit, we tested luminance detection in monkeys E and S. Detection thresholds were measured for foveal as well for peripheral presentations (8.5° eccentricity throughout). Since the thresholds for the peripheral eccentricity were similar, independent of whether the target was presented 8.5 deg up, down, left or right, they were pooled. The monkeys exhibited lower thresholds for
the central visual field as compared to the peripheral field (35.8± 3.3% vs. 46.2±9.5% in monkey E and 55.1±10.5% vs. 62.7±14.2% in monkey S, both before lesion).

Figure 8 A compares the luminance change detection thresholds in monkey S for the central and the peripheral visual field presentations before the lesion, on days 8-29 after the first lesion and on days 16-76 after L2. Figure 8 B demonstrates luminance change detection thresholds for monkey E before the lesion and on days 19-98 after the lesion. The effect of the lesion on the luminance change detection thresholds were tested by repeated one-way ANOVAs with the factor “time”. They demonstrated that neither monkey E nor monkey S experienced significant impairments in luminance change detection as a consequence of the lesions.

Table 1 gives a summary of the locus of the lesions and their functional consequences in the four monkeys.

**Discussion:**

Previous work on cerebellar patients had suggested that visual attention and motion sensitivity are impaired after lesions of the posterior vermis. This study was designed to assess the role of the posterior cerebellar vermis on covert shifts of attention and visual motion perception in monkeys. We studied circumscribed surgical lesions of distinct parts of the posterior vermis of the rhesus monkey. As a control for possible visual deficits, we also tested detection of luminance change. Finally, visually guided saccades, well-known to depend on the integrity of vermal lobules VI and VII allowed us to observe another functional impact of the lesions.

Lesions involving lobuli VI and VII of the vermis caused the expected early saccadic dysmetria in all four animals. The dysmetria persisted in three of the four animals. In the one monkey in which the first lesion spared lobule VI and most of VII, there was only a very brief saccadic dysmetria. A second lesion was made that included lobules V, VI and
the remainder of VII produced the expected dysmetria (Table 1). The findings are entirely
consistent with earlier work (Takagi et al., 1998; Barash et al., 1999; Golla et al., 2008).
The two monkeys B and S with extensive lesions, encompassing lobuli V to VIII and
presenting clear deficits of saccades, were unimpaired in tests of visual attention which
was assessed by measuring visual acuity with or without prior spatial cueing (Table 1).
The observation that monkeys with vermal pathology are able to use spatial attention to
improve visual acuity, while suffering from disturbances of visually guided saccades is in
complete agreement with a previous study by Golla et al. (2005) who reported the same
dissociation for human cerebellar patients. Unlike the monkeys, who actually showed a
transient improvement of their absolute visual acuity after the lesion, the cerebellar
patients studied by Golla et al. exhibited an impairment in acuity that was unrelated to
spatial attention. The authors speculated that the impaired acuity in the patients might
actually have reflected an inadvertent involvement of extra-cerebellar parts of the brain or
the retina. The fact, puzzling at first glance, that both monkeys B and S showed improved
visual acuity after the lesion most probably reflects increased familiarity with the task. The
improvement of the visual acuity after the lesions in monkeys B and S remains
unexplained. The lesions were carried out only after the performance had fully saturated,
which is why an artifact of continued perceptual learning can be ruled out. Normal spatial
attention after vermal lesions reported here and earlier by Golla et al. (2005) is at odds
with a previous report by Townsend et al. (1999) in which subjects used a joystick lever
to indicate four possible target orientations of the letter E. Normal subjects could shift
attention to the relevant location within 100 ms after cue onset. Patients with acquired
cerebellar pathology (stroke or tumour) performed worse and needed 800-1200ms of cue
to target delay in order to reach the performance level of normal subjects. In that study,
subjects had to operate a joystick to report their decisions, arguably more demanding
than making an indicative saccade (this study) or pressing a simple response button.
(Golla et al., 2005). However, while hand motor disturbances may explain the slower reaction times observed in the cerebellar patients, they do not explain, why accurate perceptual decisions might have required more time in the patients studied by Townsend and colleagues. One possibility may be the lack of fixation control in the study by Townsend et al. in contrast to the study by Golla et al. and the present one, since cerebellar lesions may jeopardize fixation. In summary, our results strengthen the notion that the posterior cerebellar vermis plays a role in the control of saccades, rather than being part of a common network for both overt and covert spatial shifts of attention.

A number of studies have consistently found visual motion deficits in cerebellar patients (Ivry and Diener, 1991; Nawrot and Rizzo, 1995; Thier et al., 1999; Jokisch et al., 2005). In agreement with those studies, the present work demonstrates increased perceptual thresholds for the discrimination of coherent motion in 3 out of the 4 monkeys with posterior vermal lesions (Table 1). The deficits were restricted to particular subsets of the visual field locations tested, not obviously related to the details of the lesions, although the severity of the deficits and their duration was clearly associated with the size and the location of the lesions. Although, the oculomotor part of the vermis (lobuli VIb, VIc and VII) was our main target, some of the lesions extended to include lobuli V, lobuli VIII, lobuli VIa, crus II and the fastigial nuclei to various amounts in the four monkeys studied. Lobule VIII, rather than the oculomotor vermis proper (lobuli VI and VIIA) is most closely associated with severity and lasting of the deficit. Monkey E, in which the lesion had disrupted the whole of lobulus VIII continued to exhibit persistent motion perception deficits in the lower visual field even 8 weeks after the lesion. In the other animals, the deficits were transient, lasting only a few weeks at most. Vermal lesion centred on more anterior lobuli of the vermis did not impair motion perception. Fixation behaviour was unrelated to the degree of motion perception deficit (Table 1). A motion perception deficit after lesions emphasizing lobulus VIII is in accordance with the observations of motion
perception deficits in cerebellar patients with chronic lesions of the midline cerebellum which most probably involved lobulus VIII (Nawrot and Rizzo, 1995, 1998). Our findings in monkeys clearly rule out that such deficits in patients were secondary to extra-cerebellar disease. The recovery of the deficit in all cases except monkey E when compared to the persistence of the deficits in patients most probably reflects differences in the size of the lesion and suggests a role of para-vermal tissue or more posterior lobuli.

We do not know why lesions of lobulus VIII should lead to motion perception deficits. The little we know about lobulus VIII is based on single-unit recording studies which demonstrated the existence of neurons responding to optokinetic stimulation, only rarely encountered in lobuli VI and VIIA (Sato and Noda, 1992). However, it remains unclear what the role of that sensitivity could be in motion perception.

The independence of the motion perception deficit is not only indicated by normal visual acuity and normal spatial attention following lobulus VIII lesions, but, also by a completely normal ability to detect luminance changes (Table 1). These negative findings extend the growing list of observations on patients, speaking against non-spatial visuo-perceptual functions of the cerebellum, usually associated with the “what” pathway of visual processing. More generally, they clearly propose to use a more careful and differentiated approach when considering role of cerebellum in functions beyond its well-established ones in motor control (Glickstein, 2006; Glickstein, 2007).
References:


**Figure legends:**

**Fig. 1** Explanation of oculomotor and perceptual paradigms.

**(A)** *Visually-guided saccades paradigm.* Monkeys fixated on the central fixation point and executed saccades in 8 directions.

**(B)** *Covert spatial attention paradigm.* Cued and non-cued trials were randomly interleaved. Monkeys indicated the orientation of the Landolt C by corresponding saccadic eye movements.

**(C)** *Luminance change detection paradigm.* The monkey indicated the detection of luminance change of central or periphery target while fixating by releasing the touch bar.

**(D)** *Motion perception paradigm.* Monkeys viewed random dot cinematograms (RDCs) consisting of two groups of dots, the first group moving in random directions, the second group moving coherently in one out of two possible directions. During the presentation of the RDC, monkeys had to maintain fixation. Monkeys indicated the direction of perceived motion by making indicative saccades to one out of two saccade targets corresponding to the directions of coherent motion which appeared after the RDC had been extinguished.

**Fig. 2 (A-D)** Dorsal view of posterior vermal lesions in monkeys B, R, E and S respectively. Para-sagittal sections are taken at positions (numbers 1 to 7) superimposed on the dorsal view. FN=fastigial nucleus.

**Fig. 3 (A)** Anatomic in-vivo MRI sections obtained 32 days after the first lesion (T2 sagittal section taken at the level of the midline, in monkey S). Right: orthogonal view (40° tilted towards the frontoparallel plane) at the position of the lesion, indicated by the
white dashed vertical line. The images represent the extent of the first lesion, which was
confined to the caudal part of lobule VII and lobule VIII and had no lateral extension.

(B) Upper panel: post-mortem photograph of monkey S’s cerebellum, showing the
combined extent of lesions 1 and 2. Lower panel: The anatomic MRI sections (T2-
weighted sagittal section taken at the level of the midline. Right, orthogonal section
indicated by the position of the white dashed vertical line (20° tilted towards the
frontoparallel plane) shown on the left and in the middle respectively were obtained at
day 17 after the second lesion. The orientation and location of the sagittal MRI section on
the left corresponds approximately to those of the histological Nissl-stained section on
the right.

Fig. 4 (A) Examplary records of horizontal saccades to a target at 15 deg before the
lesion, 3 days and 60 days after the vermal lesion in monkey R.

(B-D) Comparison of saccade end points for targets presented at 15 deg eccentricity in
eight different directions in the frontal plane before the vermal lesion (light grey) and early
after (black) vermal lesions. (B) Monkey B (postlesion data for day 6), (C) Monkey R
(post-lesion data for day 4), and (D) Monkey E monkey E (post-lesion data for day 3).
The central squares mark the fixation point. The peripheral eight squares indicate the
saccade target positions.

(E-F) Plots of saccade end points for targets presented at 10 deg eccentricity in eight
different directions in the frontal plane before and after vermal lesions in monkey S. The
peripheral eight squares indicate the saccade target positions. (E) Comparison of pre-
lesion saccades (light grey) and saccades obtained on day 3 (black) after the first lesion.
(F) Comparison of saccades collected one month after the first lesion (dark grey) and on
day 2 after the second lesion (black).
(G) Average saccadic gains ± standard deviations (STD) (saccadic gain = saccade amplitude/target eccentricity) of monkeys B, R and E before (light grey), early after (black) and late after (dark grey) the vermal lesions. In monkey B, a very late measurement was obtained 4-6 months after the lesion, represented by the white bar. The asterisks indicate significant differences between gains as revealed by t-test, *p<0.05, **p<0.01, ***p<0.001, corrected for multiple comparisons; n.s. denotes no statistical difference. To assess changes of saccade variability we compared the STDs by 1-way ANOVA (factor “time”) with subsequent Scheffe tests before and after lesions. This analysis demonstrated that in monkeys B and R saccades were significantly more variable after the lesion, p<0.01. On the other hand, the variability of post-lesion saccades in Monkey E was not different from pre-lesion saccades, p>0.05.

(H) Average saccadic gain ± STD of monkey S before (light grey), early after L1 (days 2-4 – black), late after L1 (days 20-30 – dark grey), early after L2 (days 2-5 – black) and late after L2 (days 15-50 – white). Tests and conventions are the same as in G. In monkey S saccade gain dropped significantly after each lesion and each time fully recovered. After the first lesion saccades were more variable than before the lesion (p<0.001). Late after the first lesion, at a time, the monkey had completely recovered from hypometria, surprisingly this was accompanied by a normalization of saccade amplitude variability (no difference compared to prelesion variability; significant improvement compared to variability early after the first lesion, p<0.001). The second lesion reinstituted the increased saccade variability (p<0.001) which remained until the end of the observation period.

Fig. 5 (A) Acuity thresholds obtained in monkey S in cued (grey squares ± STD) and non-cued (black diamonds ± STD) trials before the lesion, between days 3-9 and 11-30 after the first lesion and between days 3-13 and 14-48 days after the second lesion.
Acuity thresholds are compared by 2-way ANOVA with the factors “time” and “cue”, main effect of "cue" p<0.05, main effect of “time” p<0.05, interaction “cue”*“time”, p=0.63.

(B) Acuity thresholds obtained in monkey B in cued and non-cued trials before and between days 60-69 after the vermal lesion in monkey B. Acuity thresholds are compared by 2-way ANOVA with the factors “cue” and “time”; main effect of „cue“ p<0.05; main effect of „time“ p<0.05; factor interaction p=0.54

Fig. 6 Motion direction discrimination thresholds before and after lesions in monkeys R, B, S and E. For monkeys B, S and E, which exhibited early post-lesion motion direction discrimination deficits, the corresponding panels in addition show box and whisker plots of a measure of fixation stability, corresponding to the area of the “fixation ellipses” (see Methods). The boxes represent the standard error, the whiskers the standard deviation of this measure. Motion direction discrimination thresholds are represented by average bars plus standard deviations. The asterisks indicate significant differences between means of fixation stability and motion perception thresholds respectively as revealed by one-way ANOVA with the factor “time”, *p<0.05, **p<0.01, ***p<0.001; n.s. denotes no statistical difference.

(A) Monkey R: RDCs were presented in the centre of the visual field, at 16 deg up and at 16 deg right (as shown in the insets). The motion direction discrimination thresholds and the fixation variability were measured before the lesion (white), between days 6-11 (grey) and between days 33-60 after the lesion (light grey).

(B) Monkey B: RDCs were presented in the centre of the visual field, at 16 deg right and at at 16 deg left (as shown in the insets). The motion direction discrimination thresholds and the fixation variability were measured before the lesion (white), between days 6-11 (grey) and between days 33-60 (light grey) after the lesion.
**Monkey S**: RDCs were presented 16 deg right from the centre of the visual field, in
the centre of the visual field, at 16 deg left, at 16 deg down and at 16 deg up (as shown
in the insets). The motion direction discrimination thresholds and the fixation variability
(during RDCs presentations on the right) were measured before the lesions (white),
between days 2-5 (dark grey), days 6-12 (grey), days 33-60 (light grey) after the first
lesion and between days 6-12 (black) after the second lesion.

**Monkey E**: RDCs were presented in the centre of the visual field, at 16 deg down and
at 16 deg up (as shown in the insets). The motion direction discrimination thresholds and
the fixation variability (assessed only for RDCs presentations in the centre and down)
were measured before the lesion (white) and between days 2-3 (dark grey), between
days 6-11 (grey) and between days 33-60 (light grey) after the lesion.

**Fig. 7 (A-C)** Mean normalized motion direction discrimination threshold as function of time
based on data from monkeys B, E and S. For each monkey the data was normalized by
taking the average thresholds before the lesions as 1 (“Before”) and expressing average
thresholds for each time window (“Immediate” – days 2-5 after lesions for monkeys E
and S, “Early” – days 6-12 for monkeys B and E after lesions and monkey S after L1 and
L2, “Late” – days 20-60 after lesions in monkeys B and E and after both lesions in
monkey S) relative to this prelesion baseline value of 1 (i.e. a normalized value of 2
would indicate a doubling of the postlesion threshold). Normalized thresholds plus
standard deviations based on pooled data from the three animals are shown for
stimulation in the center of the visual field in (A). B depicts normalized thresholds based
on pooling data from the three monkeys from the “affected” peripheral visual field
locations. Data was included for those peripheral visual field location, for which the lesion
had a significant effect at least in the immediate and early periods after the lesion.
Finally, C shows the complement, i.e. pooled data for peripheral visual field locations, for which there was no significant effect of the lesion in the early post-lesion period.

**Fig. 8 (A)** Luminance change detection thresholds in monkey S before the lesions (white bars ± STD), between days 8-29 after the first lesion (L1; grey bars ± STD) and between days 16-76 after the second lesion (L2; black bars ± STD) for central and peripheral targets.

**(B)** Luminance change detection thresholds in monkey E before the lesion (white bars ± STD) and between days 19-98 after the lesion (grey bars ± STD) for central and peripheral targets.

**Table 1** Summary of results. The boxes describe the extent of the various lesions. Black cells indicate a complete ablation of the anatomic structure, grey cells partial ablations and white cells intact structures. The table summarizes the consequences of lesions on overt and covert shifts of attention, visual motion perception, fixation stability and luminance change detection. Additionally, following pertinent clinical observations were made after the different lesions: slight trunk ataxia in monkeys B and S after L2, which showed improvement over time but persisted even after 3 months; quick-phase rightward nystagmus in monkeys B and S (after L2), which disappeared within 7 days, quick-phase leftward nystagmus in monkey E which disappeared within 3 days of the lesion; dysmetric hand movements towards food targets (were slow and inaccurate), which recovered after 7 days.
A  Visually guided saccades

Fixation spot 500 ms
Target 700 ms
Eye position

B  Covert shifts of attention

Time

Fixation, 500 ms
Spatial cue, 100 ms
Fixation, 150 ms
Landolt C, 150 ms
Mask, 200 ms
Response

Gap up or down?

C  Luminance change detection

Time

Trial initiation, fixation, 400 ms
Target appearance
Target luminance changes, 200-1200 ms variable,
Change is not detected, keep holding touchbar, 800 ms
Change is detected, release touchbar, 200-700 ms after change

D  Motion perception

Movement to the right or to the left?
Before lesion

Before 3-9 11-30

A

Monkey S

Size of the C-gap (arcmin)

Before lesion 3-9 11-30 3-13 14-48
days after L1 days after L2

B

Monkey B

Size of the C-gap (arcmin)

Before lesion 60-69
days after lesion

*non-cued

+cued
### Central location

- Normalised motion perception thresholds
  - Before: 3.4
  - Immediate: 2.6
  - Early: 1.8
  - Late: 1

### Affected peripheral locations

- Normalised motion perception thresholds
  - Before: 3.4
  - Immediate: 2.6
  - Early: 1.8
  - Late: 1

### Unaffected peripheral locations

- Normalised motion perception thresholds
  - Before: 3.4
  - Immediate: 2.6
  - Early: 1.8
  - Late: 1
A

Monkey S

Central targets

Peripheral targets

Luminance change detection threshold (%)

Before lesions
8-29 days after L1
16-76 days after L2

Before lesions
8-29 days after L1
16-76 days after L2

B

Monkey E

Central targets

Peripheral targets

Luminance change detection threshold (%)

Before lesion
19-98 days after lesion

Before lesion
19-98 days after lesion
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<th>lesion sites, lobulus</th>
<th>monkey B</th>
<th>monkey R</th>
<th>monkey E</th>
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<th>Lateral extension of lesions</th>
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<th>Clinical observations first days after lesions</th>
<th>slight trunk ataxia, nystagmus</th>
<th>no signs of ataxia, tremor, nystagmus, dysmetria</th>
<th>nystagmus in darkness</th>
<th>no signs of ataxia, tremor, nystagmus, dysmetria</th>
<th>slight trunk ataxia, nystagmus</th>
<th>tremor of both hands, dysmetric hand movements</th>
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<th>hypometria of horizontal, downward and oblique saccades</th>
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