

**Sensory prediction errors drive
cerebellum-dependent adaptation of reaching**

Ya-weng Tseng^{1,2}, Jörn Diedrichsen⁴, John W. Krakauer⁵,

Reza Shadmehr³, and Amy J. Bastian^{1,2}

Authors' addresses: Kennedy Krieger Institute¹, Departments of Neurology²
and Biomedical Engineering³
The Johns Hopkins University School of Medicine,
Baltimore, Maryland
21205

⁴School of Psychology
University of Wales, Bangor
Bangor, Gwynedd, LL57 2AS
United Kingdom

⁵The Neurological Institute
Columbia University College of Physicians and Surgeons
New York NY 10032

Corresponding author: Amy J. Bastian
Dept of Neurology
The Johns Hopkins School of Medicine
Kennedy Krieger Institute
707 North Broadway- G04
Baltimore, Maryland 21205
PH: 443-923-2716
FAX: 443-923-2715
Email: bastian@kennedykrieger.org

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Abstract

The cerebellum is an essential part of the neural network involved in adapting goal-directed arm movements. This adaptation might rely on two distinct signals: a sensory prediction error, or a motor correction. Sensory prediction errors occur when an initial motor command is generated but the predicted sensory consequences do not match the observed values. In some tasks, these sensory errors are monitored and result in online corrective motor output as the movement progresses. Here we asked whether cerebellum-dependent adaptation of reaching relies on sensory or online motor corrections. Healthy controls and people with hereditary cerebellar ataxia reached during a visuomotor perturbation in two conditions: “shooting” movements without online corrections, and “pointing” movements that allowed for online corrections. Sensory (i.e. visual) errors were available in both conditions. Results showed that the addition of motor corrections did not influence adaptation in control subjects, suggesting that only sensory errors were needed for learning. Cerebellar subjects were comparably impaired in both adaptation conditions relative to controls, despite abnormal and inconsistent online motor correction. Specifically, poor online motor corrections were unrelated to cerebellar subjects’ adaptation deficit (i.e. adaptation did not worsen), further suggesting that only sensory prediction errors influence this process. Therefore, adaptation to visuomotor perturbations depends on the cerebellum, and is driven by the mismatch between predicted and actual sensory outcome of motor commands.

Introduction

Adaptation may be of fundamental importance to our ability to perform accurate movements because both our body and the environment that we interact with undergo changes. A critical feature of adaptation is that it allows individuals to alter their motor commands based on errors from prior movements. Adaptation has been demonstrated across many different tasks (Krakauer et al. 2000; Martin et al. 1996; Morton and Bastian 2004; Reisman et al. 2005; Shadmehr and Mussa-Ivaldi 1994) and the cerebellum appears to be necessary for this form of learning (Chen et al. 2006; Diedrichsen et al. 2005; Martin et al. 1996; Maschke et al. 2004; Morton and Bastian 2006; Smith and Shadmehr 2005). However, there are multiple potential teaching signals that could drive adaptation.

Here we distinguish between two possible sources of information that could be used to drive reach adaptation: sensory prediction errors versus motor corrections. Sensory prediction errors are the difference between the actual sensory feedback and the expected sensory feedback for a given motor command (Miall and Wolpert 1996). For example, visuomotor adaptation occurs when visual information is shifted or rotated (e.g. prism glasses, cursor rotation), causing discrepancies in gaze versus reach directions (Held and Hein 1958; Krakauer et al. 2000). This results in a difference between where the arm is seen and where the brain expects to see it based on the motor command (Figure 1A). The idea that sensory prediction errors are the dominant influence driving cerebellar adaptation is supported by theoretical, neurophysiological and behavioral studies (Ito 1982, 1972; Martin et al. 1996; Mazzoni and Krakauer 2006; Wallman and Fuchs 1998; Wolpert et al. 1998).

Alternatively or in addition, the motor correction of the error (for example, via reflexive pathways) may be a training signal for adaptation (Kawato 1996). These motor corrections may act as a teaching signal for the brain (Miles and Lisberger 1981; Thoroughman and Shadmehr 1999). For example, when arm movements are perturbed with unexpected forces, reflex pathways respond to partially compensate for the sensory prediction errors (Thoroughman and Shadmehr 1999). The response is a motor command reflecting error that can be added, with a slight time advance, to the motor commands that initiate the next movement to prevent the same error from occurring again (Figure 1B). The error feedback learning theory of the cerebellum relies on this motor correction (Kawato 1996). Indeed, during saccade adaptation, motor corrections are unnecessary for adaptation, but their presence helps increase the rate of adaptation (Wallman and Fuchs 1998). Therefore, an open question is whether cerebellum-dependent adaptation relies on sensory prediction errors, motor corrections, or both.

Here, we studied adaptation to visuomotor rotation in control subjects and individuals with cerebellar damage during two reaching tasks. In one task subjects made fast reaches (“shooting”) with no online corrections, and thus had to rely primarily on sensory prediction errors for adaptation. In the second task subjects were allowed to reach and correct the reach errors in a continuous movement. If motor corrections were used as an additional training signal, then healthy subjects might learn faster when they were allowed online corrections. In comparison to shooting movements, people with cerebellar disease might show further deterioration of adaptive ability because their abnormal online corrections (Holmes 1939; Vilis and Hore 1980) would serve as a poor teaching signal.

Methods

Subjects

Seven individuals with hereditary cerebellar ataxia (55 ± 11 years old) and seven gender, age, and handedness matched healthy controls (53 ± 9 years old) participated in this study (Table 1). Subjects performed a reaching task using their dominant arm. Five individuals had a genetically defined spinocerebellar ataxia (SCA), type 6 or type 8. These are slow, progressive and predominantly cerebellar ataxias (Day et al. 2000; Gomez et al. 1997). Two subjects were from a family with an undiagnosed genetic ataxia. These individuals had only cerebellar signs on neurological examination, and thus fell into the classification of autosomal dominant cerebellar ataxia type III (ADCA III, Harding 1993). Some subjects showed evidence of mild pontine atrophy on MRI, but no subject had sensory deficits, weakness, or spasticity of the arm. Severity of ataxia was rated using the International Cooperative Ataxia Rating Scale (Trouillas et al. 1997). All subjects gave their written consent (Institutional Review Board, The Johns Hopkins University School of Medicine) prior to the study.

Task

Subjects held the handle of a two-joint manipulandum mounted in the horizontal plane. Sensors on the manipulandum recorded the position of the handle sampled at 100 Hz. A computer monitor mounted above the manipulandum was used to display the reach targets and the cursor. The handle position was represented by a 5 mm cursor on the computer monitor and visual feedback of the cursor was provided before and during the

movement, but not during the return to the starting location. Subjects were instructed to move the cursor from a 1 cm square located at the bottom of the workspace (starting location) toward one of the three targets represented by a 1 cm square. The target was located 5 cm above the starting location, at an angle of 0, 45° or -45°.

We studied a visuomotor rotation paradigm that included a baseline phase where there was no perturbation, an adaptation phase with a 20° visuomotor perturbation, and a post-adaptation phase with no perturbation. During the perturbation, the displayed cursor path was rotated by 20° around the starting location from the actual reaching path, either clockwise or counter-clockwise. We used two types of reaching tasks: 1) “pointing” which allowed for online corrections during the movement. If the cursor path deviated away from the target direction, subjects had to “correct” for that error and stop inside the target square. This way, they had visual prediction error and a motor correction. 2) During the “shooting” task the participants were instructed to move through the target without stopping. A soft wall (spring constant 150 N/m) directly behind the target assisted the termination of the movement. We designed this “soft-wall”, rather than a rigid wall that would stop the motion abruptly, because it made the movement feel more natural and it encouraged the subjects to move rapidly. Secondly, the participants likely learned to rely on the wall for stopping their movement and therefore did not to break the movement by themselves. In the shooting movements, subjects experienced errors in their movements without an opportunity to issue motor commands that corrected those movements. After the movement stopped in either condition, the handle of the manipulandum moved back to the starting location by the robot motor. No visual feedback was provided during this phase.

Four experimental sets were performed sequentially: pointing movements with clockwise or counter-clockwise rotational perturbation and shooting movements with clockwise or counter-clockwise rotational perturbation. We counter-balanced the order of rotational directions and reaching types across subjects. Each set included the above-mentioned baseline, adaptation and post-adaptation phases. A set was further divided into blocks of thirty-six reaches. Within each block, the target sequence was randomized. For the first pointing or shooting condition, the set started with two to four blocks of baseline trials to help subjects become familiar with the task and the inertia of the robot. Once subjects had completed one set of each reaching condition, the set started with just one block of baseline trials. The baseline phase was always followed by three blocks of adaptation trials and one block of post-adaptation trials. During adaptation, 1/6 of the trials had no visual rotation imposed (catch trials). We inserted these catch trials randomly, such that we could compare these trajectories to trajectories during perturbed trials and determine whether and when online corrections occurred during the movement. We also included catch trials when estimating the rate of adaptation (see below: State-space model of trial-to-trial learning). The entire experiment took one and half to two hours to finish.

We instructed the subjects to move the cursor from the starting location toward the target smoothly without pausing. We emphasized that they can take as much time as they needed before initiating the reach. They had no knowledge of whether the cursor path would be perturbed or not. Individuals with cerebellar damage were encouraged to move as fast as they could. Trials that were completed within a time limit were rewarded by a visual “explosion” of the target. Based on the severity of the cerebellar symptoms,

there were significant variations among individuals in the average peak speed; it ranged between 15 and 45 cm/sec and between 30 and 70 cm/sec for pointing and shooting movements, respectively. We therefore adjusted the time limit adaptively for each participant, such that 50% of the trials were rewarded. Control participants were instructed as to how fast to move, such that each cerebellar-control pair was matched in peak movement speed.

Data Analysis

Movement duration. Movement onset was defined as the first time that the velocity of the hand movement exceeded a threshold of 3 cm/sec for at least 180 ms consecutively in the forward movement direction. Note that small adjustments of these criteria were made for some cerebellar subjects because they showed oscillations at the start position, which was not considered as movement onset. Shooting movements were considered terminated when the cursor passed the circle on which the targets were displayed (5 cm movement length). This portion of the shooting movement is shown in Figure 2 (hand path). For the pointing condition in which online corrections were allowed, movement termination was based on the end of corrective movements, i.e., when the cursor reached the target and when cursor velocity dropped below 3cm/s continuously for 100 ms. Movement time was defined as the duration elapsed between movement onset and termination.

Aiming error. We were interested in the predictive, feedforward part of the movement given that the cerebellar adaptive mechanism is particularly important for this process (Lang and Bastian 1999). We defined aiming error as the angle between the

position of the cursor at 180 ms after movement onset and the target relative to the starting location of the movement. This time window represented the initial, predictive part of the reaching movement; further analyses demonstrated that no online corrections were present prior to 180 ms after movement onset. Counter-clockwise aiming errors were defined as positive. The averaged aiming error for each movement direction during the baseline phase was computed and subtracted from the corresponding direction for all trials, removing any constant error caused by the passive dynamics of the robot (Smith and Shadmehr 2005).

Adaptation measures. Three measures were used to quantify the extent of adaptation. First, the residual error was calculated as the averaged aiming error of the last twenty-five trials during the adaptation phase for each condition (no catch trials were included in this calculation). Second, the after-effects of adaptation were measured as the difference between aiming error averaged over the first three trials in the post-adaptation phase and the averaged baseline. Third, we used a state-space model to estimate sensitivity to error.

State-space model of trial-to-trial learning. The third measure was derived from a recently developed state-space model of reach adaptation and generalization (Donchin et al. 2003; Thoroughman and Shadmehr 2000). The output equation of this model states that the predicted aiming error during the current trial (\hat{y}_n) is determined by the difference between the perturbation u_n and the intended movement direction.

$$\hat{y}_n = u_n - \mathbf{k}^T \mathbf{z}_n \quad (1)$$

In Eq. (1), \hat{y}_n is a scalar and \mathbf{z}_n is a vector with three components representing the state for each movement direction. \mathbf{k} is a column vector with two 0s and one 1 at the place for

the current movement direction, such that it selects one element of the state vector \mathbf{z} , depending on the target sequence used in the experiment. The second equation characterizes how intended movement directions of the next trial are determined by the current state, the rate of generalization B and error experienced in the current trial.

$$\mathbf{z}_{n+1} = \mathbf{z}_n + B\mathbf{k}\hat{y}_n \quad (2)$$

B is a symmetric 3x3 matrix with three components that represent error generalization for three movement directions (0° & $\pm 45^\circ$). Because the individual components of B cannot be estimated independently due to limited movement directions, we constrained the individual values to a linear relationship based on a generalization function, C , obtained from normal control participants using the same paradigm with eight movement directions (Hemminger et al. 2006), $B = \beta * C$. Therefore, the three components of B were reduced to one free parameter, β . This free parameter represents the amount that movement direction changed in response to an error experienced during the prior trial in that direction. Higher β -rates indicate that more was learned from one trial's error to the next. In order to estimate the actual value of β for each subject, we used a numerical optimization method to find β so that it minimized the difference between the sequence of aiming error predicted by the model and the actual aiming error that was experimentally observed. This procedure allowed us to estimate both mean and inter-subject variability of β for each group. We will refer to β as trial-to-trial adaptation rate, since higher values represent larger corrections of prior errors, and thus faster adaptation rates.

Onset of online corrections. To determine if and when online corrections occurred during the pointing and shooting conditions, we compared the perturbed and catch

(rotational perturbation was turned off unexpectedly) trials. For each block, we calculated the average aiming direction of the hand. We then calculated the velocity of the hand in the direction perpendicular to that direction. This represents the earliest deviation of the hand from the aiming direction, and represents a sensitive measure of onset of corrective movements (Diedrichsen et al. 2004). For shooting movements, the perpendicular velocity of the hand should not differ systematically between perturbed and catch trials, as the movements were too fast for online corrections. For pointing movements, the first time point when the perpendicular velocity was significantly different between perturbed and catch trials, and remained so for at least 100 ms, signified the beginning of the online correction. This was determined using individual t-test at each time point. The time spent on correction was from this onset until movement end.

Efficiency of online corrections. We determined the efficiency of online corrections by comparing the path distance traveled from the onset of path correction to movement termination to the shortest (straight) path to target acquisition. If this ratio equaled 1, the corrective movements would be perfectly straight and efficient. Any value greater than one is indicative of more curved and less direct path to achieve the target.

Statistical analysis. We used a 2 x 2 repeated measure ANOVA design to compare the effect of group (control and cerebellar individuals) and with-in subject factors (reaching condition and rotation direction) on adaptation- (residual error, after-effect and β) and correction-related (onset and efficiency of online correction) variables. For kinematic related variables (such as movement time, peak velocity and variability of aiming angle), we used a 2 x 2 x 5 ANOVA to compare the effect of group and with-in subject factors of reaching condition, rotation direction and block (average of the last 5

trials in the baseline phase; average of the first, middle and last 5 trials in the first, second and third blocks in the adaptation phase, respectively; average of the first 5 trials in the post-adaptation phase) in order to further assess the effect of time on these variables. An additional ANOVA was used for each group separately, to test whether there was an order effect (first versus second exposure) of different rotation directions (clockwise versus counter-clockwise) for the two movement conditions (pointing versus shooting). The Tukey post-hoc test was used to further examine significant interaction effects. Significance level was set at $p < 0.05$.

Results

Cerebellar deficits in shooting versus online correction performance

Example traces of hand paths and hand velocity for the two groups of subjects are shown in Figure 2 (A&B). In order to ensure that control and cerebellar movements were as similar as possible, we matched movement peak speed between groups. Figure 3A shows that peak speed was statistically equivalent between groups ($p = 0.4$). As expected, both groups made shooting movements faster than pointing movements (main effect of condition: $F_{1,12} = 70.7$, $p < 0.001$). There was no significant effect related to block for peak speed.

During the shooting task, we first determined whether subjects made any corrective movements by comparing the velocity of the hand perpendicular to the direction of movement for perturbed versus catch trials (see **Methods**). Controls demonstrated no evidence of path corrections during shooting movements as well as most

of the cerebellar subjects (Figure 2C). Three cerebellar subjects showed slight path deviations: two cerebellar subjects deviated when reaching to one target only, and the other subject deviated when reaching to two targets. For these four instances, the path deviation analyses showed separation of catch vs. non-catch trials, though the time of separation could not be determined based on $p < 0.05$ because paths were quite variable (i.e. no significance). Further, these corrections were not obvious by visual examination of individual trials, and removing these trials did not affect subsequent analyses. Given this, we included these trials in the shooting condition.

Movement trajectories were comparable for cerebellar subjects and controls in the shooting condition. However, cerebellar subjects were more variable than controls (Figure 2A). During baseline trials (i.e. no rotation), the standard deviation of targeting angle in the shooting condition was $4.5^\circ \pm 0.3$ for controls versus $7.9^\circ \pm 0.8$ for cerebellar subjects. A similar difference was also present in the pointing condition ($4.8^\circ \pm 0.3$ versus $8.1^\circ \pm 0.8$, Figure 2B). This resulted in an overall group effect ($F_{1,12}=16.3$, $p < 0.01$), with cerebellar subjects showing more variability in path direction than controls. There was also a main effect of block ($F_{4,48}=77.7$, $p < 0.001$), indicating that the targeting angle was more variable during the adaptation phase ($10.3^\circ \pm 0.9$) than the baseline ($5.7^\circ \pm 1.1$) or the post-adaptation ($6.9^\circ \pm 1.2$) phase. There were no other interpretable effects related to block.

Cerebellar subjects were more severely impaired in the production of the pointing movements; they had longer movement times, with increased path lengths and curvature, especially towards the end of the movement (Figures 2B). In order to quantify these observations, we first examined movement duration (Figure 3B). As expected, the main

effect of condition was significant ($F_{1,12}=152.2$, $p<0.001$). More importantly, there was also a significant group by condition interaction ($F_{1,12}=13.8$, $p<0.01$). This indicates that movement duration for the cerebellar group was especially prolonged when online corrections were required ($F_{1,12}=14.6$, $p<0.01$). In contrast, there was no difference in movement duration between the two groups in the shooting task ($p=0.96$). Movement time was not significantly affected by block.

To determine whether the prolonged movement duration was caused by delays in feedback-driven corrections, we calculated the onset time of the online correction (Figure 3C). During pointing movements, all subjects made path corrections and the time of correction occurred after 180 ms (where the feedforward component of aiming error was determined). Healthy subjects (open bars) made path corrections earlier in time (median: 300 ms) compared to the cerebellar subjects (median: 385 ms; filled bars). Furthermore, this timing was more consistent among the control subjects (range: 240-350 ms) as compared to the cerebellar group (range: 230-1020 ms).

Finally, we asked about the efficiency of the online correction during pointing movements. We used the length of path traveled after the onset of the online correction divided by the shortest path length from that location to the target. A clear difference between the groups was present ($F_{1,12}=11.7$, $p<0.01$), with the cerebellar group showing less efficient corrections (2.62, $SD = 0.63$) than the normal controls (1.78, $SD=0.18$).

In summary, participants with cerebellar degeneration were impaired in the online correction phase of the pointing movement. Despite matching of peak speed, the movement time was significantly longer when online corrections were involved; the corrections occurred later and were less efficient. When no online corrections were

required, movement trajectories of the patients were comparable to our control group, though more variable in direction.

Online corrections did not aid adaptation in healthy controls

To measure the time course of the adaptation, we measured the trial-to-trial change of aiming error. As can be seen for pointing (Figure 4A) and shooting (Figure 4B) movements, the aiming error was close to zero during the baseline phase and increased significantly when the 20° rotational perturbation was applied. During the adaptation phase (shaded area), healthy subjects showed an exponential reduction of the error, and exhibited after-effects during post-adaptation. Visual comparison suggests that the rate and amount of adaptation were similar for the two tasks.

This observation was confirmed by ANOVA. First, the adaptation rate (β), estimated in the trial-to-trial analysis was ~ 0.2 for both tasks (Figure 5A). This means that in the control group, the error on any given trial produced a 20% adaptation as measured in the movement of the subsequent trial. The main effect of reaching condition was not significant ($p=0.4$), indicating that this adaptation rate was comparable across tasks. There were no other significant interaction effects. We also quantified the extent of adaptation by calculating the residual error at the end of the adaptation phase (Figure 5B). Note that complete compensation for the rotation would be 83% of the perturbation magnitude (i.e., 83% of 20°=16.6°) because 83% (5/6 ratio) of the trials being non-catch trials. On average, the control group achieved $\sim 70\%$ of complete compensation, again with no differences between the tasks ($p=1$). Lastly, the size of the after-effects (Figure 5C) was statistically equivalent for the shooting and pointing tasks, as indicated by a non-

significant main effect of condition ($p=0.86$). Thus, in healthy individuals, presence or absence of online corrections did not influence the adaptation rate, asymptote of adaptation, or size of after-effects.

We did not find any significant effects related to the order of exposure for residual error among healthy individuals. A main effect of order was found for after-effects ($F_{1,6}=5.3$, $p<0.05$). However, controls showed a slightly larger after-effect during the second exposure ($-10.5^\circ \pm 0.9$) to the perturbation compared to the first exposure ($-7.7^\circ \pm 0.9$). This result argues against the possibility that the first adaptation interfered with the second.

Cerebellar patients showed the same adaptation deficit with and without online corrections

The aiming errors in the baseline, adaptation, and post-adaptation phases for the cerebellar subjects are shown in Figure 4 (C&D). Analyses showed that the adaptation rate of the cerebellar group was significantly lower ($\beta \approx 0.04$) than the rate of healthy controls, as shown by a significant main effect of group ($F_{1,12}=17.1$, $p<0.01$; Figure 5A). People with cerebellar disease also showed a smaller amount of adaptation (~50% of complete adaptation) compared to controls (main effect of group: $F_{1,12}=5.5$, $p<0.05$; Figure 5B), with significantly reduced after-effects (main effect of group: $F_{1,12}=11.1$, $p<0.01$; Figure 5C) compared to healthy subjects. Most importantly, the cerebellar adaptation deficit was the same size in the pointing and shooting tasks. All group by condition interactions were not significant (all $p>0.3$). Furthermore, we did not find that

adaptation was significantly related to the order of exposure to different perturbation directions for the cerebellar group ($p > 0.5$).

We also examined the subject-by-subject relationship between pointing and shooting adaptation rates (Figure 6). This was done to further assess whether corrective movements in pointing might have an effect on adaptation rate. For example, if the corrective movements produce useful signals that aid adaptation, then controls with smaller values of β in the shooting task might improve their rates in the pointing task. However, we found that controls (open circles) who had lower adaptation rates in shooting demonstrated similarly low adaptation rates in pointing. It is also possible that some cerebellar subjects may have shown some preservation of adaptation in the shooting task that was then reduced in the pointing task due to inefficient corrective movements. This, however, was not the case, as the cerebellar subjects (filled markers) who had a higher adaptation rate in shooting also tended to show a higher rate in pointing.

Cerebellar subjects' adaptive ability correlated with the clinical severity of their cerebellar symptoms. The ICARS scores measuring the upper and lower limb ataxia (i.e. kinetic function subscore) were negatively correlated with adaptation rates (pointing $r = -0.82$, $p = 0.005$; shooting $r = -0.83$, $p < 0.05$) and positively correlated with residual error (pointing: $r = 0.89$, $p < 0.01$; shooting: $r = 0.84$, $p < 0.05$). This demonstrates that people with more severe symptoms (i.e. higher ICARS scores) learned at a lower rate and had greater residual errors. These correlations were also significant when performed with only the upper limb ataxia score, removing the lower limb scores.

In the pointing condition, the ICARS kinetic score was weakly correlated with the amount of time spent making online corrections ($r = 0.66$, $p = 0.11$) and movement time

($r=0.67$ $p=0.10$). That is, people with more severe symptoms took longer to correct and made slower movements overall. There were no significant correlations between measures of the online corrections (i.e. time, efficiency) and measures of adaptation (i.e. rate, residual error, after-effects). However, weak correlations existed between online correction time during pointing and adaptation rates for both pointing ($r=-0.62$, $p=0.13$) and shooting ($r=-0.72$, $p=0.06$). People who spent a longer amount of time correcting during pointing also tended to adapt slower during either pointing or shooting. This suggests that the overall level of impairment for feedback and feedforward control were somewhat related. However, the impaired corrective movements were *not* the teaching signal driving faulty adaptation rates since the same rates occurred with and without motor corrections.

In summary, the cerebellar group exhibited a significant deficit in visuomotor adaptation compared to a control group, matched for age, demographic variables and movement speed. The deficit was the same whether or not online corrections were allowed, suggesting that the presence or absence of motor corrections did not affect adaptation. Clinically more affected subjects tended to have larger adaptation deficits in both tasks, and they were also more impaired in their ability to correct their movements online.

Discussion

Sensory prediction errors, not motor corrections, drive visuomotor adaptation

In this study, we explored whether sensory prediction errors and/or motor corrections drive reaching adaptation during a visuomotor task. Healthy controls showed no differences in adaptation rate, amount of adaptation, or after-effect magnitude when they had access to sensory prediction errors alone, versus with on-line motor corrections. This finding is largely consistent with previous work on adaptive control of eye movements (Wallman and Fuchs 1998), though we acknowledge that the adaptive mechanisms regarding to eye and arm movements may be quite different (Bock 1992; Deubel 1987). During saccade gain adaptations, the occurrence of corrective saccades, in addition to a visual error signal, could increase the adaptation rate, but was not necessary for adaptation. In our study of arm movements, adaptation rates, extent of adaptation and after-effects were similar with or without corrections, suggesting that online corrective movements do not contribute to visuomotor adaptation.

We also assessed cerebellar subjects' adaptive abilities using sensory prediction errors alone or with motor correction. We found that while cerebellar subjects had clear abnormalities in timing and efficiency of corrective movements, the presence or absence of the motor corrections did not affect adaptation. This suggests that sensory prediction errors drive cerebellum-dependent visuomotor adaptation of arm movements, and is congruent with work showing cerebellar subject deficits in prism adaptation during ball throwing, where corrective movements are not possible (Martin et al. 1996).

An interesting side observation relates to the time course of the cerebellar group's adaptation compared to the controls (e.g. Figure 4). The cerebellar group qualitatively appears to have lost an initial fast-adaptive component, with a more preserved slow-adaptive component. This is present in both the adaptation and the de-adaptation phases

of the task. Recent work has shown evidence for two processes with different timescales contributing to force-field reaching and saccade adaptation paradigms (Smith et al. 2006). It is possible that the cerebellar pattern is indicative of a specific deficit in a faster process, though the data presented here cannot adequately address this. Further work should be done to explore this possibility.

Computational models and cerebellar adaptive control

Recent computational work has proposed that adaptation is achieved by changes in internal models within the nervous system, and perhaps specifically within the cerebellum (Kawato et al. 1987; Kawato and Gomi 1992; Shadmehr and Mussa-Ivaldi 1994; Wolpert et al. 1995). Within this computational framework, one can distinguish between forward and inverse models, both of which are used to control the movement. The inverse model transforms the desired sensory states into a motor command. The forward model predicts the sensory outcome based on an efference copy of a motor command.

Adaptation could theoretically occur in either forward or inverse model, or in both. It is very difficult to discern the two using behavior of only a single limb, since adaptation of either model could lead to changes early in the limb's movement (Bhushan and Shadmehr 1999). However, there is a clear affinity between the source of the teaching signals and the type of model that needs to be adapted. Sensory prediction errors are in the same space (i.e. sensory states) as the output of the forward model, making them a natural teaching signal for adaptation of forward models. Conversely, online

motor corrections are coded in the same space (i.e. muscle commands) as the output of the inverse model and thus can naturally serve as a teaching signal for inverse models.

Here we found that presence of corrective movements did not aid adaptation of healthy or cerebellar subjects. Rather, the presence of sensory prediction errors was sufficient for adaptation in both subject groups. This would suggest that adaptation to visuomotor perturbations during reaching is primarily dependent on sensory prediction errors, i.e., errors that train forward models, and the cerebellum is a crucial node in adapting the forward models.

A recent neurophysiology study provides evidence that in over-trained monkeys, Purkinje cells in the cerebellar cortex code for kinematic (i.e. sensory state) and not dynamic information (i.e. muscle commands, Pasalar et al. 2006). These results are consistent with the idea that cerebellar cortical output represents the output of a forward model, rather than of an inverse dynamics model. In contrast, cells in the motor cortex and other frontal motor areas show strong sensitivity to task dynamics in a similar task (Li et al. 2001; Padoa-Schioppa et al. 2004; Richardson et al. 2006). Together, one might postulate the role of computing a forward model for the cerebellum and an inverse model for the motor cortex.

In contrast, a recent computation model on cerebellar saccade adaptation (Fujita 2005) uses motor correction errors to let the cerebellum learn to generate these corrections in anticipatory fashion. This model can learn from sensory prediction errors only when one postulates that the brain always issues a covert corrective motor command, even in the absence of online corrections. Even if this was the case, it seems rather

unlikely that a covertly generated motor commands would lead to the same amount of learning as motor corrections that were really executed.

Cerebellar contributions to feedback versus feedforward control

The cerebellar subjects' similar adaptation rates during pointing and shooting conditions suggest that corrective movements were not the operational training signal. Cerebellar subjects showed deficits in making corrections during the pointing task as well as trial-to-trial adaptation, which were both related to the severity of their ataxia. Impaired computation of forward models and impaired adaptation of these models can explain both deficits. Adaptation would be slow or absent, because the forward model could not provide accurate sensory predictions, precluding computation of sensory prediction errors. Aiming direction would be variable due to reliance on miscalibrated predictive models for movement planning. Online corrections would be inefficient because they would have to rely more on time-delayed rather than predicted sensory and visual feedback. Excessive reliance on delayed feedback means that movement corrections would never be optimal since they are always computed for a portion of the trajectory that occurred in the past.

Summary

We suggest that the most parsimonious explanation of our findings is that the cerebellum's role in adaptation to novel visuomotor transformation is to use sensory prediction errors to change a forward model (Miall et al. 1993; Wolpert et al. 1998). The output of this forward model can then also be used in the online control of movement by anticipating the errors.

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Figure Captions

Figure 1. Illustration of two different types of error. A: sensory prediction error (S_e). Based on an initial motor command (u), the forward model makes prediction about the sensory outcome of the movement (\hat{S}). The difference between the actual hand position (S) and the predicted hand position (\hat{S}) based on visual feedback represents sensory prediction error (S_e). B: sensory prediction error can be monitored and transformed into motor commands (m) that produce motor corrections to compensate for this error. In all plots, the square represents target position.

Figure 2. Representative hand paths, tangential velocities (solid) and accelerations (dashed). A: shooting task. B: pointing task. In the shooting task, the robot acts to damp the movement after the hand crosses the target zone. The braking portion is indicated by the gray shaded area. The hand path is shown up to the point of designated movement termination, which is indicated by the black vertical bar on the velocity trace. Cerebellar subjects had relatively straight hand path for shooting movements but movement direction was more variable compared to healthy controls. They also had increased path curvatures for pointing movements. C: hand paths for catch (dashed line) and perturbed (solid line) trials averaged over one adaptation phase during the shooting task. This is to demonstrate that no sign of online correction is found by visual inspection. We confirmed this by conducting a statistical analysis (see Onset of online corrections in **Methods**). The square represents target position. Position traces in B&C are drawn to the same scale as in A.

Figure 3. Movement characteristics of the cerebellar (filled bars) and healthy individuals (open bars). A: mean peak speed with SEM (standard error of the mean) for pointing and shooting tasks; B: mean movement time with SEM. *: $p < 0.01$; C: histogram of the onset time of path correction for the cerebellar and healthy individuals.

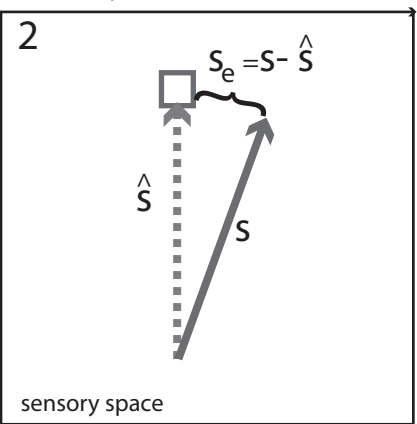
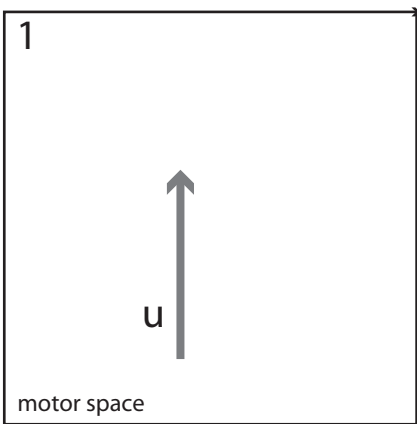
Figure 4. Aiming error during the course of adaptation averaged over subjects for each group. A, B: pointing and shooting conditions for healthy individuals; C, D: pointing and shooting conditions for cerebellar individuals. The abscissa indicates trial number and it starts from baseline, adaptation (shaded area), and post-adaptation.

Figure 5. A: adaptation rate; B: residual error; C: after-effect; significant group effect is indicated by the corresponding brackets. *: $p < 0.05$; **: $p < 0.01$. Error bars are SEM.

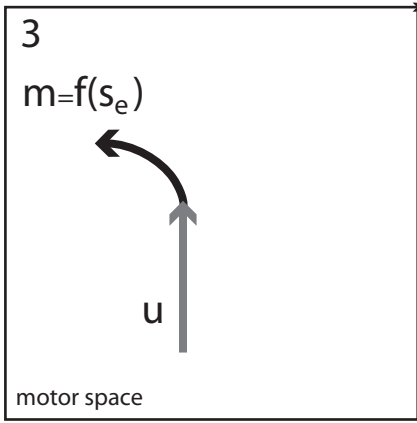
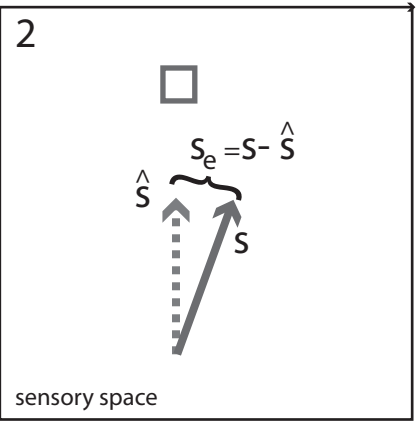
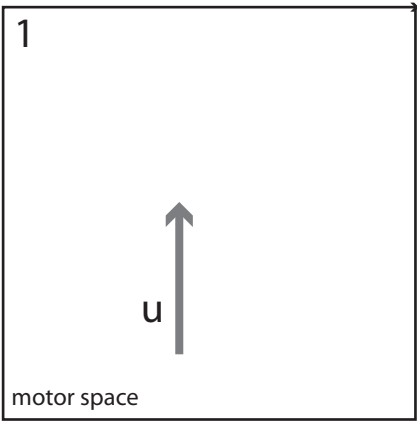
Figure 6. Pointing versus shooting adaptation rates for each individual subject in cerebellar (filled symbols) and control (open symbols) groups. The solid line indicates $x=y$.

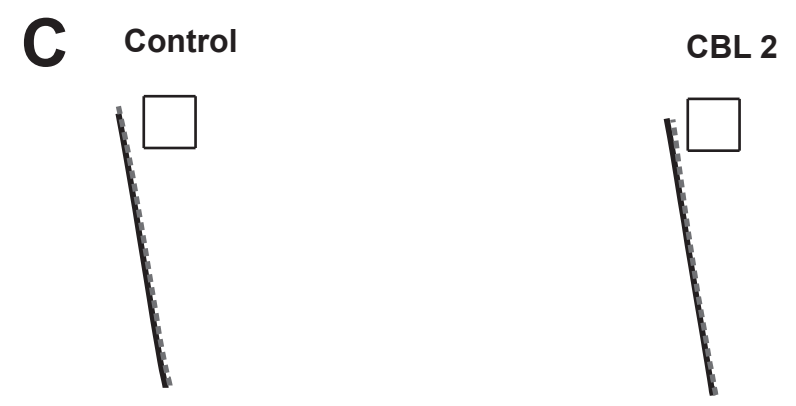
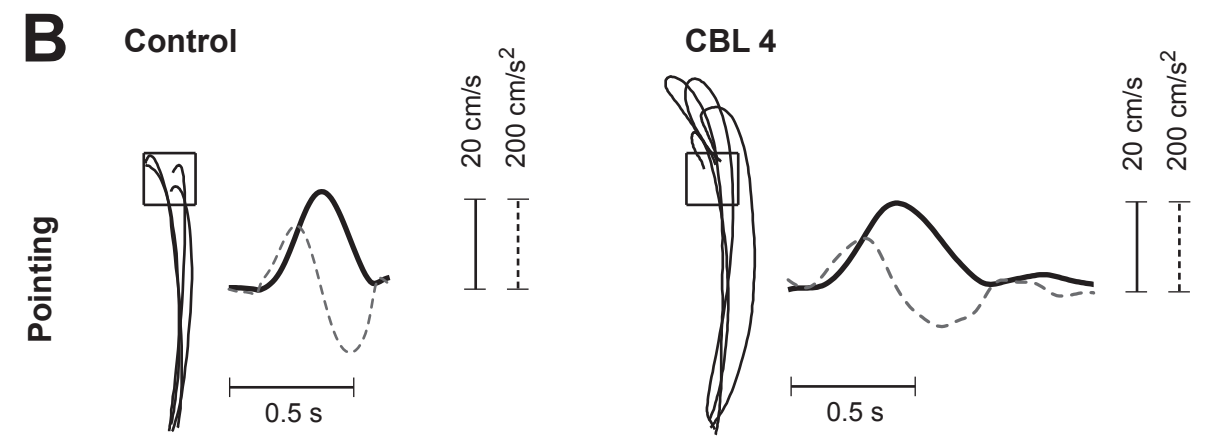
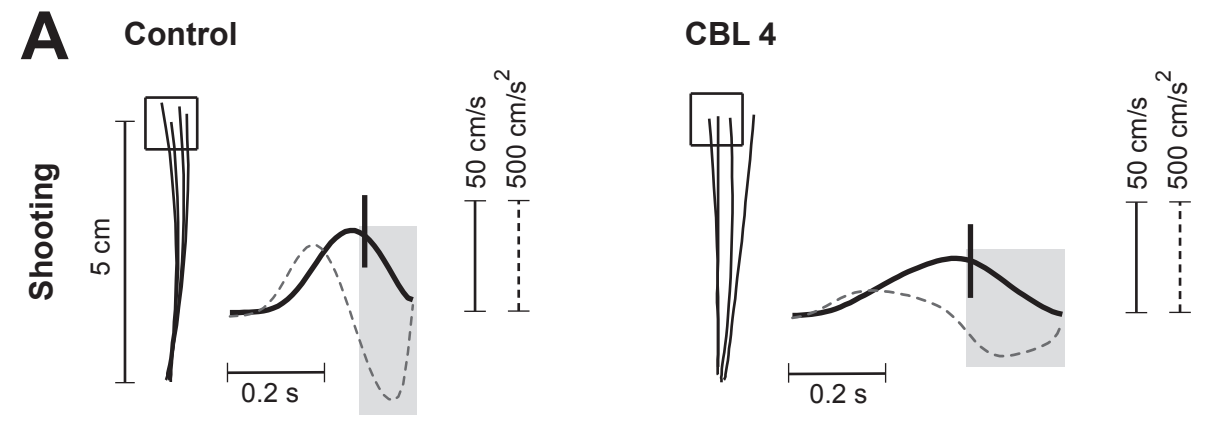
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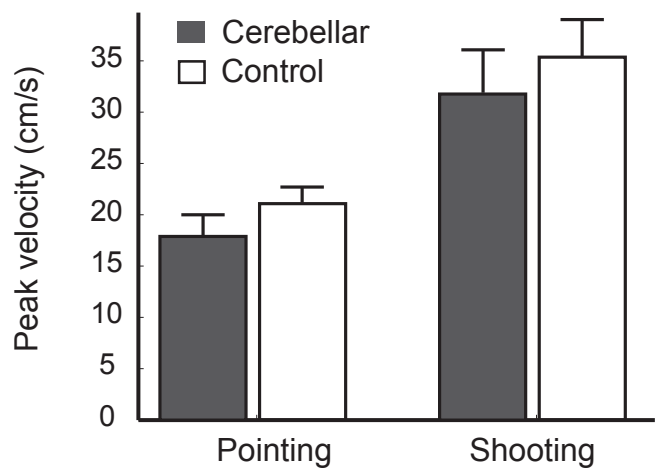


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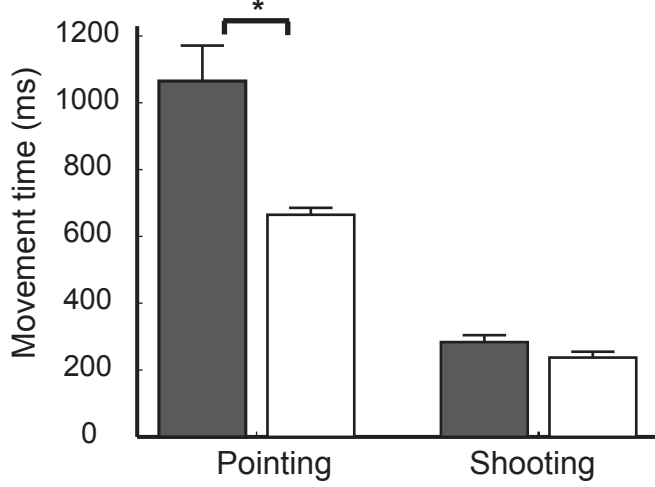




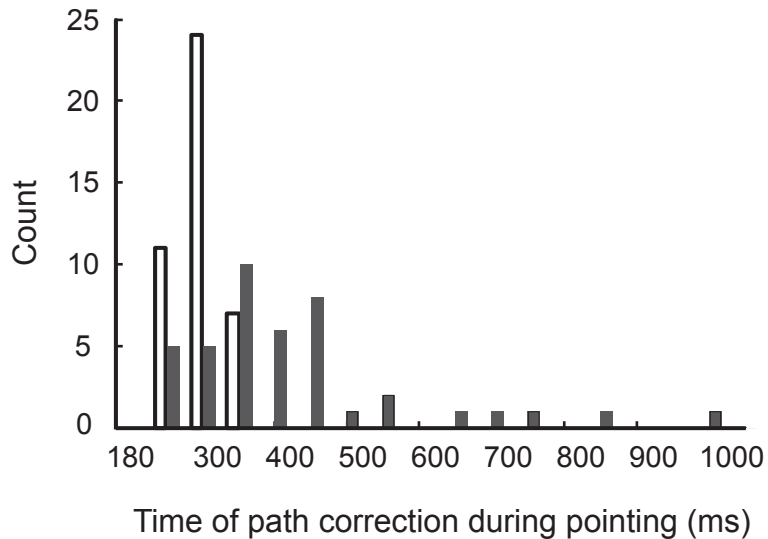
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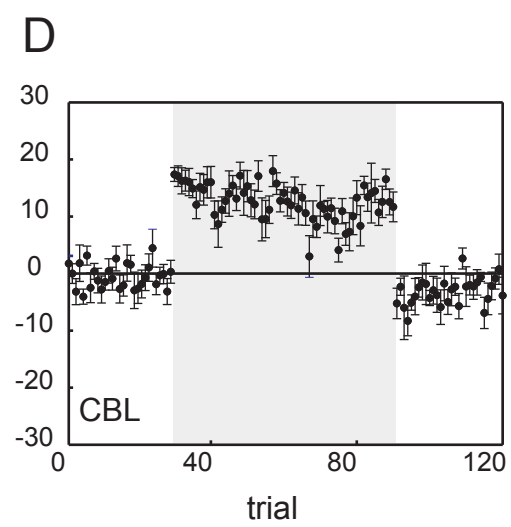
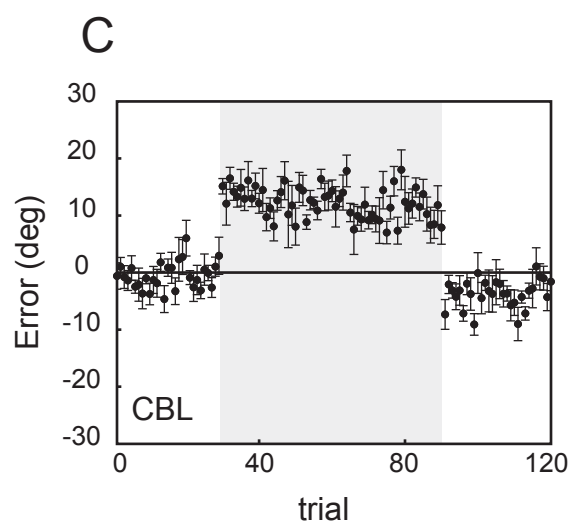
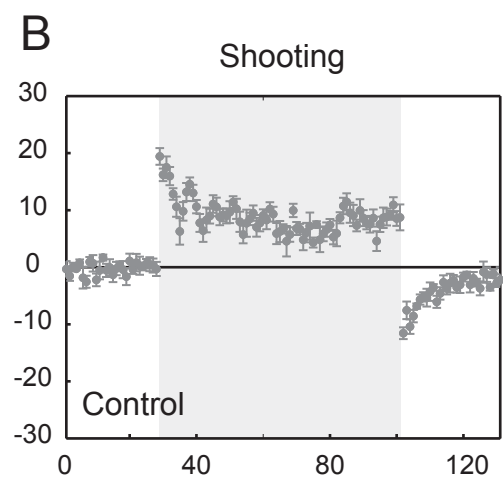
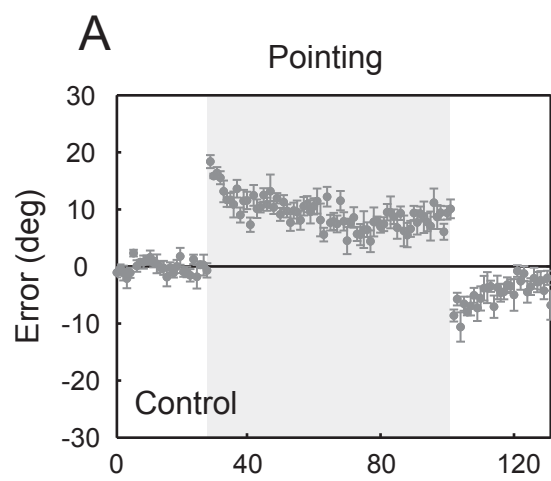


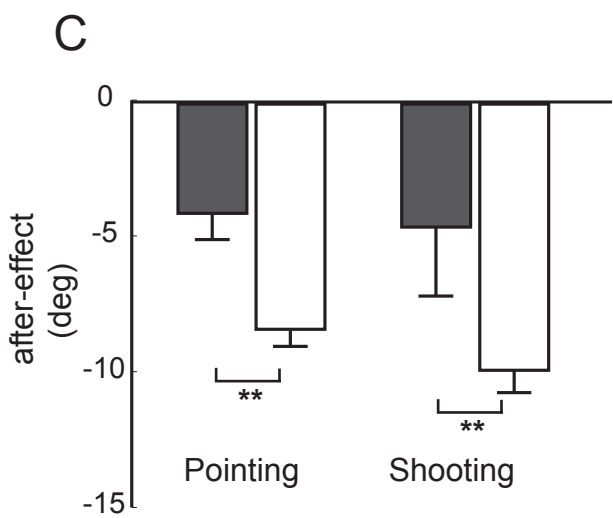
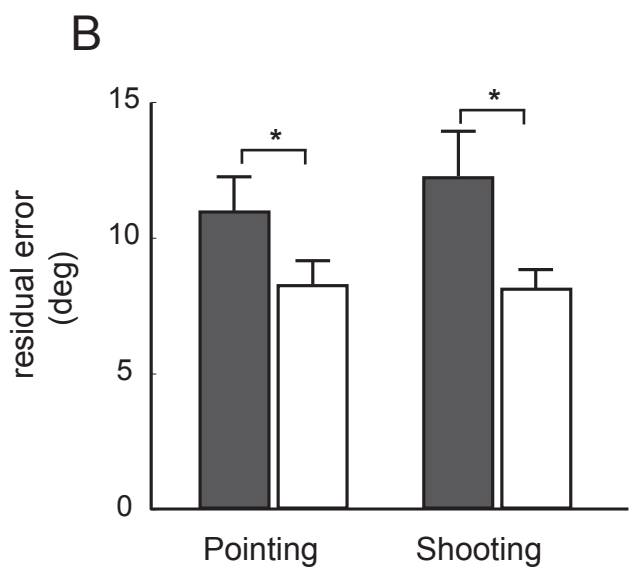
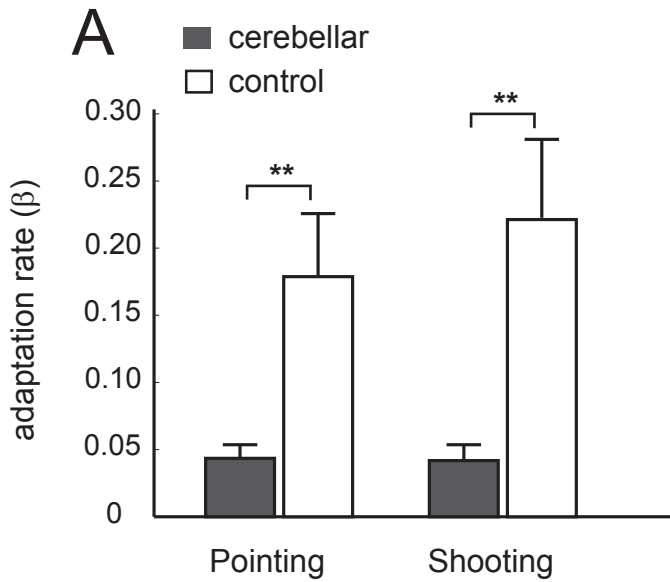
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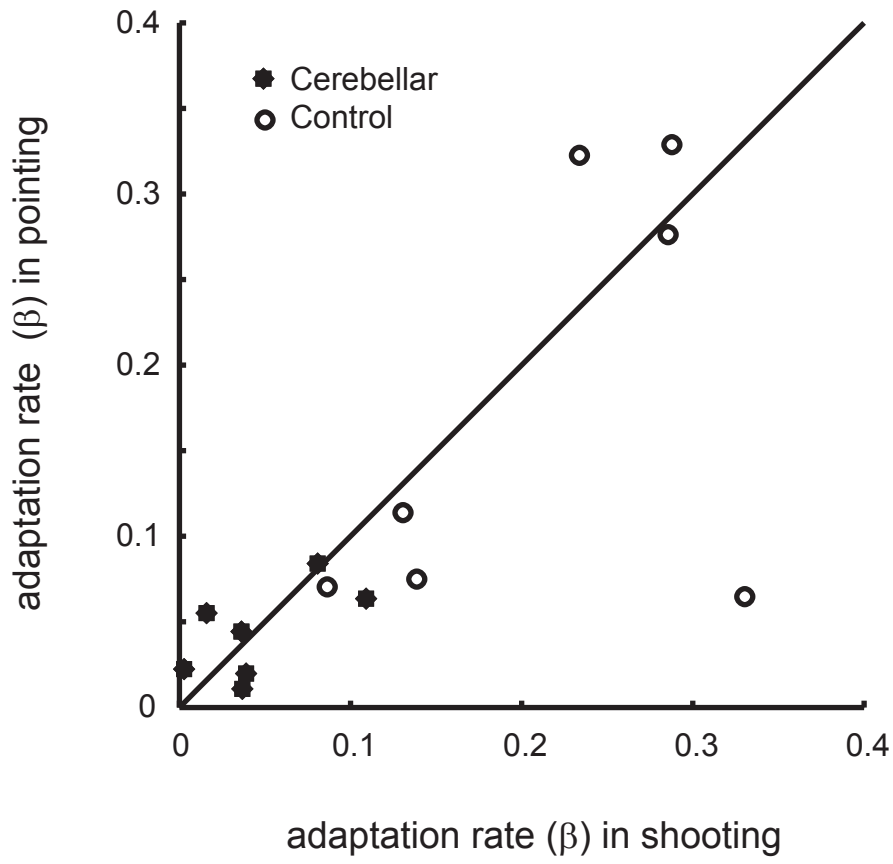


Table 1. Characteristics of cerebellar individuals

	Gender	Age	Handed-ness	Diagnosis	ICARS			
					Total	Posture & Gait	Limb Ataxia	Speech & Oculomotor Disorder
CBL 1	M	60	R	SCA 6	55/100	22/34	23/52	10/14
CBL 2	F	53	R	SCA 6	18/100	4/34	8/52	6/14
CBL 3	M	72	L	SCA 6	58/100	27/34	20/52	11/14
CBL 4	M	34	L	SCA 8	42/100	14/34	19/52	9/14
CBL 5	M	54	R	ADCA III	4/100	4/34	0/52	0/14
CBL 6	F	57	R	ADCA III	34/100	16/34	13/52	5/14
CBL 7	M	52	R	SCA 6 & 8	66/100	31/34	25/52	10/14

M: male; F: female; R: right-handed; L: left-handed; SCA: spinocerebellar ataxia; ADCA III: autosomal dominant cerebellar ataxia III which is a relatively pure cerebellar ataxia, though the genetics for these individuals is unknown (Harding 1993); ICARS: International Cooperative Ataxia Rating Scale (higher score means more severe ataxia).