Title: Cerebellar damage diminishes long-latency responses to multi-joint perturbations

Abbreviated Title: multi-joint responses during cerebellar damage

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Abstract

Damage to the cerebellum can cause significant problems in the coordination of voluntary arm movements. One prominent idea is that incoordination stems from an inability to predictively account for the complex mechanical interactions between the arm’s several joints. Motivated by growing evidence that corrective feedback control shares important capabilities and neural substrates with feedforward control, we asked whether cerebellar damage impacts feedback stabilization of the multi-joint arm appropriate for the arm’s intersegmental dynamics. Specifically, we tested whether cerebellar dysfunction impacts the ability of posterior deltoid to incorporate elbow motion in its long-latency response ($R_2 = 45-75$ ms and $R_3 = 75-100$ms post-perturbation) to an unexpected torque perturbation. Healthy and cerebellar-damage subjects were exposed to a selected pattern of shoulder-elbow displacements to probe the response pattern from this shoulder extensor muscle. The healthy elderly subjects expressed a long-latency response linked to both shoulder and elbow motion, including an increase/decrease in shoulder extensor activity with elbow flexion/extension. Critically, cerebellar-damaged subjects displayed the normal pattern of activity in the $R_3$ period indicating an intact ability to rapidly integrate multi-joint motion appropriate to the arm’s intersegmental dynamics. However, cerebellar-damaged subjects had a lower magnitude of activity which was specific to the long-latency period (both $R_2$ and $R_3$) and a slightly delayed onset of multi-joint sensitivity. Taken together, our results suggest that the basic motor pattern of the long-latency response is housed outside of cerebellum and is scaled by processes within the cerebellum.
Introduction

The cerebellum is a key neural structure for achieving coordinated arm movements as evidenced by distinctive abnormalities following its degeneration or damage from trauma (Bastian 2002; Ebner et al. 2011; Holmes 1939). Clinical signs of cerebellar damage include curved and more variable hand paths due to poor elbow-shoulder synchronization and termination errors marked with overshoots, undershoots and oscillations (Bastian et al. 1996; Bastian et al. 2000; Cooper et al. 2000; Day et al. 1998; Gilman et al. 1976; Massaquoi and Hallett 1996; Timmann et al. 2001; Topka et al. 1998a,b). These abnormalities are markedly worse when moving several joints of the arm compared to when motion is physically restricted to a single joint (Bastian et al. 2000; Brown et al. 1990; Hallett et al. 1975; Hore and Flament 1986; Hore and Vilis 1984) likely due to the greater complexity of multi-joint dynamics (Fig 1A). For example, when the limb is unconstrained one must actively stabilize the shoulder in order to produce motion at just the elbow otherwise the shoulder will passively rotate opposite the exerted elbow torque. Healthy subjects account for these interactions by appropriately timing and scaling shoulder monoarticular activity during intended elbow movements (Almeida et al. 1995; Boose et al. 1999; Bastian et al. 2000; Gribble and Ostry 1998). In contrast, anticipatory shoulder monoarticular activity by cerebellar-damaged subjects is poorly timed and scaled for these interactions which results in shoulder excursions several times larger than normal (Bastian et al. 2000; Boose et al. 1999).
Appropriate timing and modulation of muscle activity in anticipation of the arm’s intersegmental dynamics has long been considered a signature of healthy feedforward control. However, accumulating research indicates that some feedback processes have a similar knowledge of limb dynamics as feedforward control (Gritsenko et al. 2009; Wagner and Smith 2008), possibly reflecting a functional overlap which is fundamental to motor coordination (Scott 2004; Shadmehr and Krakauer 2008; Todorov and Jordan 2001). The long-latency response (LLR) is a prime candidate for examining altered feedback control following cerebellar damage as it is one of our fastest corrective actions (occurring 45-100 ms after a mechanical perturbation) (for review: Matthews 1991; Shemmell et al. 2010; Pruszynski and Scott 2012) and incorporates motion information from several joints appropriate for the arm’s intersegmental dynamics (Gielen et al. 1988; Koshland et al. 1991; Latash 2000; Soechting and Lacquaniti 1988).

A relevant example is posterior deltoid’s excitatory LLR following a perturbation causing pure elbow flexion (Kurtzer et al 2008, 2009; Pruszynski et al 2011). The fast reaction of the shoulder muscle accounts for the mechanical interactions between the elbow and the shoulder joints and helps counter the underlying cause of pure elbow motion — torque applied at both joints. Alternatively, if subjects only generated an elbow muscle response to pure elbow motion then they would not create a balance of forces, their shoulder joint would move into flexion, and their arm would not come to rest. Note that the described LLR of the posterior deltoid is not direct compensation of the imposed shoulder torque since this monoarticular muscle is neither stretched nor shortened and none of its intramuscular sensors are altered. The fast response from
posterior deltoid to elbow joint motion must be based on sensory information outside that muscle, presumably those muscles spanning the elbow joint.

Previous studies have shown that cerebellar damage can impair some functions of long-latency responses such as the ability to scale its response magnitude to the expected duration of a perturbation (Horak and Diener 1994; Hore and Vilis 1984; Timmann and Horak 1997; Timmann et al. 2000). However, the few previous studies on the upper limb either used electrical nerve stimulation (Claus et al. 1986; Friedmann et al. 1987) or restricted limb motion to a single joint (Hore and Vilis 1984; Marsden et al. 1977) so they could not address whether cerebellar integrity is required for LLRs to incorporate motion from several joints appropriate for the arm’s intersegmental dynamics. To address this important gap in our knowledge we examined feedback control of the multi-joint arm in cerebellar-damaged and healthy age-matched controls using a paradigm previously employed with healthy young adults (Kurtzer et al. 2008).

We hypothesized that cerebellar damage would eliminate the ability of the posterior deltoid’s LLRs to respond to elbow motion (and account for the inter-segmental dynamics) but not alter its response to shoulder motion (Kurtzer et al. 2008, Kurtzer et al. 2009), i.e. an impairment in “heteronymous reflexes” but not “homonymous reflexes”. Figure 2 illustrates the predictions for the two experiments. For conditions causing both shoulder and elbow motion, cerebellar damaged subjects were predicted to have shoulder LLRs based only on shoulder motion. Likewise, for conditions causing only elbow motion, cerebellar damaged subjects were predicted to have no evoked activity in their shoulder LLRs. We were surprised to find that cerebellar damage did not alter the ability of the posterior
deltoid’s LLR to respond to both elbow and shoulder motion. However, cerebellar
damage did result in significant changes from normal as their LLR had a diminished
magnitude and slight delay. Our results suggest that the basic motor pattern of the
long-latency response is housed outside of cerebellum and that the cerebellum
contributes to the timing and scaling of this basic pattern.

Materials and Methods

Subjects

We studied 20 subjects in the experiment which lasted ≈1.5 hr. Ten subjects had
clinically significant cerebellar damage. Most had either known genetic cerebellar
degeneration (e.g. spinocerebellar ataxia type 6) or sporadic cerebellar degeneration.
All subjects were clinically examined to rule out any signs of extra-cerebellar
involvement in the arm, including: spasticity or abnormal muscle tone; fine touch
sensory loss (using Semmes-Weinstein monofilament testing); and proprioceptive
deficits. Proprioception was assessed using a standard clinical technique while the
individual’s eyes were closed and the index finger of each hand was rotated by the
examiner about the metacarpophalangeal joint ≈5° in either a flexion or extension
direction. During this procedure, subjects’ were instructed to remain passive and
identify movement direction.

We were vigilant about screening all of the individuals. The severity of
movement dysfunction was assessed using the International Cooperative Ataxia Rating
Scale (ICARS), where higher scores indicate greater impairment (Trouillas et al. 1997).
The ICARS is organized into the following categories: posture and gait, limb control (kinetic), speech, and eye movements. Ten control subjects were matched for age (range = 38-75 years, mean = 55.8 years), gender (7 female, 3 male), the arm utilized (9 right and 1 left), and the magnitude of torque applied to the arm. All subjects were paid for their time following procedures approved by the ethics committee at Johns Hopkins University.

**Apparatus**

As described in previous studies (Scott 1999; Kurtzer et al. 2008; Prusynski et al. 2008) we utilized a robotic exoskeleton (KINARM, BKIN Technologies Ltd, Kingston, ON) which permits flexion/extension movements of the shoulder and elbow in the horizontal plane and can selectively apply torques to each joint; shoulder angle is measured relative to the frontal plane and elbow angle is measured between the forearm and upper arm, 0° is full extension. Visual targets and a hand-aligned cursor were presented in the same plane as the limb movement via a virtual-reality system while a cloth bib and metal partition obscured direct vision of the subject’s arm.

**Muscle recording**

The experiments focused on the surface EMG from each subject’s posterior deltoid (a monoarticular shoulder extensor). We also collected data from their pectoralis major (a monoarticular shoulder flexor) and report its responses as a secondary matter. Note that when we refer to a shoulder extensor muscle or shoulder flexor muscle we only mean these two monoarticulars, not biarticular muscles or other
muscles crossing the shoulder joint. We employed procedures similar to our earlier
papers (Kurtzer et al. 2008; Pruszynski et al. 2008); a two-bar electrode (DE-2.1 Delsys
Inc., Boston, MA) was affixed to the muscle belly and a ground electrode was placed on
the subject’s ankle following light abrasion of the overlying skin surfaces with alcohol.

Experimental Task

We examined corrective actions in a group of older adults using procedures we
previously applied to a population of young adults (Kurtzer et al. 2008; Pruszynski et al.
2008). Subjects maintained their arm’s position against a background torque and a
subsequent step torque that was unpredictable in time and direction. There was one
perturbation per trial and all trials proceeded in the following manner. Subjects
stabilized their hand-aligned cursor (0.4 cm radius) within the center of a 2 cm radius
target which corresponded to a 45° shoulder angle and 75° elbow angle. Subjects were
asked to keep their hand in the target and to quickly return if displaced. A shoulder
flexor torque was ramped up over 500 ms and remained constant to elicit background
activity in the subject’s posterior deltoid. After a random hold of 1-4 seconds, a step
torque was applied to their arm. The target turned green or red to indicate accurate or
inaccurate performance depending on whether the subject stayed within the target for
1000 ms of the subsequent 1500 ms. Finally, the total applied torque ramped down to
zero and remained off during an inter-trial period of 1 second.

We employed four different step torques: shoulder flexion torque [1 Nm, 0 Nm],
elbow extension torque [0 Nm, -1 Nm], shoulder-elbow flexion torque [1 Nm, 1 Nm],
and shoulder-elbow extension torque [-1 Nm, -1 Nm]. The absolute magnitude of both
the background torque and step torque were scaled by a single value (range = 1.25 – 3)
so that cerebellar-damaged subjects could consistently compensate the applied torques
and avoid fatigue; control subjects (matched for age and gender) countered the same
magnitude of torque as the corresponding subject with cerebellar damage. Note that
the four perturbations were randomly intermingled, but we will discuss them in two
groups according to the pattern of joint motion that they induce.

The dynamics of the arm-robot system includes the properties of the robot and
joint velocities. However, we can gain some insight into our experimental design by
considering just the subject’s arm (as the robot’s exoskeleton has an inertia largely
parallel to the enclosed limb), neglecting velocity terms (which are low immediately
following the perturbation), and assuming the elbow angle equals 90° (which is nearby
75°). In this case, the complex nonlinear dynamic equations of the shoulder and elbow
(from Soechting and Lacquaniti 1988) simplify to:

\[
\ddot{\theta}_s = \frac{T_s - T_e}{I_a} \\
\ddot{\theta}_e = \frac{T_e}{I_f} + \frac{T_e - T_s}{I_a}
\]

\(\ddot{\theta}_s\) and \(\ddot{\theta}_e\) are elbow and shoulder acceleration, respectively.
\(T_e\) and \(T_s\) are elbow and shoulder torque, respectively.
\(I_f\) and \(I_a\) are forearm and arm inertia, respectively.

These formulae highlight two features of the arm’s dynamics that are
independent of its particular mass distribution. First, if two torques are applied
individually to either shoulder or elbow, the same shoulder acceleration will be induced
if the two torques are opposite in sign and equal in magnitude. Second, if the two torque perturbations have the same sign and are equal in magnitude, then only the elbow will be accelerated. The four torque perturbations that we selected were appropriate to leverage these basic features.

Experiment 1: Feedback response to same shoulder motion, different underlying torque

Due to the arm’s intersegmental dynamics, torque applied at a single joint will induce motion at multiple joints when the limb is free to move (Hollerbach and Flash 1982; Graham et al. 2003; Craig 2005) (Fig. 1A). For example, either shoulder flexion torque or elbow extension torque will cause the shoulder to move into flexion. We selected magnitudes of these two perturbations to induce the same amount of initial shoulder flexion and, hence, stretch of the posterior deltoid (Fig. 1B,C). This allowed us to test whether this muscle’s feedback response is only sensitive to its own muscle stretch as it would respond identically to the two perturbations. Alternatively, feedback control of this shoulder monoarticular could account for arm’s intersegmental dynamics by combining elbow and shoulder motion to generate a response countering the imposed torque. Here the shoulder extensor would generate a larger response during the condition with shoulder flexion torque than elbow extensor torque; this differential pattern would reflect the net contribution of similar amounts of excitatory homonymous LLRs and different amount of inhibitory heteronymous LLRs. A cartoon of the normal pattern of evoked activity is shown in Fig 2A and depicts that the earliest muscle response (R1) is only sensitive to displacement of the shoulder whereas subsequent muscle responses (R2,R3, and Vol) incorporate shoulder and elbow motion
appropriate for the limb’s intersegmental dynamics. Fig 2B shows the predicted response for subjects with cerebellar damage, R2/3 only sensitive to shoulder motion.

Experiment 2: Feedback response to pure elbow motion, underlying shoulder torque

The perturbations used in this experiment were flexor torques applied to both joints or extensor torques applied to both joints (Fig. 1E,F). These multi-joint perturbations were selected to balance the interaction torque from the elbow to the shoulder joint so that pure elbow motion resulted — elbow flexion motion induced by a multi-joint flexion perturbation, and elbow extension motion induced by a multi-joint extension perturbation. If feedback control of posterior deltoid is only sensitive to its own muscle stretch then it should exhibit no response, i.e. no stretch of the shoulder monoarticular resulting in no response by the shoulder monoarticular. Alternatively, if feedback control of posterior deltoid accounts for the mechanical interaction between the shoulder and elbow joint then a reciprocal pattern of muscle activity would be elicited – an increase in its activity following the multi-joint flexion perturbation and a decrease following the multi-joint extension perturbation – to help counter the underlying shoulder torque; this differential pattern would reflect the net contribution of no homonymous LLR and an excitatory and inhibitory heteronymous LLR, respectively. A cartoon of the normal pattern of evoked activity is shown in Fig 2C and depicts that the earliest muscle response is only sensitive to its own stretch whereas subsequent muscle responses (R2,R3, and Vol) incorporate shoulder and elbow motion appropriate for the limb’s inter-segmental dynamics. Fig 2D shows the predicted response for subjects with cerebellar damage, R2/3 only sensitive to shoulder motion.
Data analysis

Trials were repeated 17-40 times for each condition (depending on the subject expressing fatigue) for a total ranging between 70-200 trials. These analyses described below showed similar results if we utilized the lowest trial repeat for everyone or used all the trials from each individual. Kinematic and electromyographic data were processed following procedures described in our earlier papers (Kurtzer et al. 2008; Pruszynski et al. 2008). Angular positions of the shoulder and elbow were lowpass filtered (25 Hz, 2-pass, 6th order Butterworth). EMG signals were amplified (gain = 10 K), bandpass filtered (20-450 Hz), digitally sampled at 1000 Hz (PCI 6071E, National Instruments, Austin, TX), rectified, and normalized by the posterior deltoids’s mean activity in the 100 ms prior to the perturbation. Accordingly, the activity of both shoulder muscles was normalized by the subject’s posterior deltoid since it was pre-excited by the background shoulder flexion torque pre-excited. This approach assumes that the emg-force relation was largely similar between the two muscles. Note that all intra-subject comparisions are unaffected (similar to using unnormalized data) since it introduces a common factor to the subject.

Joint kinematics were examined shortly after the perturbations (50ms) and a later period of postural stabilization (500-1000ms following the perturbation). Accuracy during this later period was characterized by the net positional deviations from the starting angle and the net angular velocity (zero velocity at rest):

\[ \text{Position error} = \text{mean}(\sqrt{\text{ShoAngDev}^2 + \text{ElbAngDev}^2}) \]
Repeated measures ANOVAs and t-tests contrasted the kinematics of the control and
cerebellar-damaged groups.

Muscle activity was examined in several periods based on earlier reports (Crago
et al. 1976; Lee et al. 1982; Kurtzer et al., 2008; Prusynski et al. 2008): R1 = 20-45 ms;
R2 = 45-75 ms; R3 = 75-100 ms; and Voluntary = 120-180. Hence, the R2 and R3
comprise the early and late portion of the long-latency response.

Our experimental design allowed us to make straight-forward comparisons
between conditions to determine whether feedback responses of posterior deltoid
reflected displacement of just the shoulder joint or whether it incorporated elbow
motion appropriate for the underlying shoulder torque. Paired t-tests determined
changes from baseline and/or changes between conditions. Repeated-measures
ANOVAs examined trends across different response periods.

We also used a planar regression to examine the pattern of posterior deltoid’s
and limb displacement resulting from the four step torques of Experiment 1 and 2.
Specifically, we examined how the evoked muscle activity and limb displacement were
related to a linear combination of imposed shoulder-elbow torque. Note that this
simple equation accounts for the magnitude and pattern of the imposed torques.

\[ \text{Evoked Activity} = a \cdot (\text{Shoulder Torque}) + b \cdot (\text{Elbow Torque}) + \text{constant} \]

The orientation of the best-fitting plane, termed a ‘preferred torque direction’ or
PTD, describes the relative sensitivity of muscle activity to the perturbing shoulder and

\[ PTD = \arctan\left(\frac{a}{b}\right) \]

If shoulder torque is the x-axis, elbow torque is the y-axis, and flexion is positive, then maximal excitation to shoulder flexion translates to a preferred torque direction of 0°; maximal activity to elbow flexion, shoulder extension, and elbow extension torques would result in PTDs at 90°, 180°, and 270°, respectively.

Another important aspect of the plane-fit is the steepness of the plane, which describes the overall sensitivity of the evoked response, or ‘response magnitude’, to the perturbation torque.

\[ \text{Response Magnitude} = \sqrt{a^2 + b^2} \]

Units are in EMG/Nm after normalizing to the baseline activity with the background torque.

A final measure was the amount of simultaneous activity by the antagonist pair of shoulder muscles, i.e. the amount of co-contraction. Co-contraction can help counter unexpected perturbations and can be flexibly sculpted to the environmental instabilities and motor noise (Burdet et al. 2001; Selen et al. 2009). We examined the ratio of evoked activity in the pectoralis major versus evoked activity in the posterior deltoid.

\[ \text{Cocontraction ratio} = \frac{\text{Evoked Activity}_{Pect\ Maj}}{\text{Evoked Activity}_{Post\ Delt}} \times 100 \]
Positive or negative values would indicate an excitatory or inhibitory evoked activity in the pectoralis major relative to its baseline compared to the evoked activity in posterior deltoid. Positive values near 100 indicate a similar increase in activity/high co-contraction, small values near 0 indicate small evoked activity in pectoralis compared to posterior deltoid/low co-contraction, and negative values near -100 indicate changes in activity that are equal in magnitude but of opposite sign.

One prediction is that the shoulder extensor’s LLR is based on just shoulder motion. The perturbation torque was chosen to induce identical shoulder motion across conditions (Experiment 1, single-joint torques) and substantial elbow motion with no shoulder motion (Experiment 2, multi-joint torques). Accordingly, the PTD of posterior deltoid would be 315°. Regressing the measured shoulder displacement at 50 ms post-perturbation against the imposed torque yielded a PTD of 313.5°(0.8) which shows how closely the observed initial displacement approached the expected initial displacement. We used this latter value for the prediction of the shoulder extensor response based on just shoulder motion (\(\Theta\)).

A contrasting prediction is that the shoulder extensor’s LLR incorporates shoulder and elbow motion appropriate to counter the underlying torque perturbation because negating the step torque is ultimately needed to bring the limb to rest. Under this hypothesis, relative to the findings expected if the LLR is driven purely by shoulder motion, Experiment 1 is predicted to show a reduction in EMG in response to pure elbow extension torque relative to that for pure shoulder flexion torque. Experiment 2 is predicted to show an increase in EMG response to simultaneous flexion torques at the
shoulder and elbow and to show reduced EMG in response to simultaneous extension torques at the shoulder and elbow. For the planar regression, these changes translate, respectively, into reduced evoked activity in the 270° direction relative to the 360° direction, greater activity in the 45° direction and activity in the 225° direction. Together these differences correspond to a PTD that is shifted toward 360° and away 315° degrees.

In principle, the PTD under this hypothesis could be 360°, i.e. maximal EMG sensitivity to pure flexion torque applied at the shoulder. However, this PTD is unlikely due to several biomechanical complexities including biarticular muscles. Biarticular muscles likely play an important role in shaping multi-joint limb responses to imposed loads by generating passive and active torque across several joints (Franklin and Milner 2003; Hogan 1985). Their contribution also requires concomitant changes in the monoarticular muscles leading to a rotation of the PTDs of monoarticular muscles. For example, recruitment of a shoulder extensor muscle is needed during elbow extensor torque in order to counter the shoulder flexion torque generated by a biarticular flexor muscle (biceps brachii). The presence of the biarticular extensor muscle (triceps longus) could also allow posterior deltoid to generate no muscle activity during shoulder flexor torque. There have been extensive reports of bias in a muscle’s activity away from its line of mechanical action, however, these effects not so strong that compensating the biarticulars could be considered the primary role of monoarticulars (van Zuylen et al 1988; Buchanan et al 1989; Nozaki et al 2005; Kurtzer et al 2006a; Kurtzer et al 2006b).

We considered the PTDs during steady-state postural maintenance from a separate
experiment to better approximate the ideal pattern than a PTD of 360° (Kurtzer et al. 2008). We found that the PTDs were modestly biased away from pure shoulder flexion torque toward elbow extension torque at 354°. We used this value to predict the response to the underlying shoulder torque (τ). Note that this remains an approximation and does not account for the impact of muscle viscosity or stiffness.

Comparisons of the measured and predicted PTDs were conducted by calculating the circular mean and variance (Baschelet 1981). Statistical significance was met when the 95% confidence interval of the measured PTD (circular C.I.) did not overlap with the predicted PTD. Comparisons of the PTD and response sensitivity between the control and cerebellar-damaged group utilized the Watson-Williams test and t-test, respectively. Note that we only included subjects who had a significant plane-fit. Significance for all tests was set at $P < 0.05$. We selected one-sided or two-sided tests for the normal subjects based the pattern of results observed in our previous studies. We predicted that cerebellar subjects would show a selective deficit in the long-latency reflex (see Figure 2).

We used the receiver-operator characteristic (ROC) technique to examine the evolution of multi-joint responsiveness on a moment-by-moment basis (Green and Swets 1966; Kurtzer et al. 2010; Prusyznski et al. 2008). For each time step (1 ms) we determined the probability that an ideal observer could discriminate between two conditions based on the two sets of muscle activity that the subject expressed. Values of 0 and 1 indicate perfect discrimination whereas a value of 0.5 indicates performance at chance. We contrasted the muscle activity from the two conditions in Experiment 1.
(shoulder flexion torque versus elbow extension torque) and Experiment 2 (multi-joint flexion torque versus multi-torque extension torque). After separately generating probability trajectories for each subject, we obtained a group probability trajectory by averaging their trajectories together. The first expression of multi-joint responsiveness was identified when the group average probability of discrimination increased from 0.5 (equal likelihood) to 3 SD above its nominal variability (observed -50 – 0 ms before torque onset) and remained above this threshold for 5 consecutive samples/ms.

Results

Torque perturbations and patterns of joint motion

Experiment 1 was comprised of two conditions – a shoulder flexion torque and elbow extension torque (Fig. 1B) – which caused simultaneous flexion of the shoulder and extension of the elbow (Fig. 1C). Critically, the two perturbations led to a similar amount of initial shoulder motion whereas the amount of initial elbow extension was substantially different. On average, the shoulder and elbow motion were ≈10% and ≈210% greater in the first 50 ms following the imposed elbow torque compared to shoulder torque. Note that each subject showed this pattern despite the wide range in the absolute size of joint displacement across subjects due to their differently sized arms and step torques. Moreover, the cerebellar-damaged and control groups did not differ in the absolute amount of initial joint displacement (shoulder: F(1,18) = 2.37, P > 0.1; elbow: F(1,18) = 2.08, P > 0.15) (Fig. 1D).
Experiment 2 imposed flexion torque at both joints and extension torque at both joints (Fig. 1E). In each subject, the combined flexion (extension) torques induced substantial flexion (extension) motion at the elbow and little shoulder motion (Fig. 1F). Despite the wide range of absolute joint motion due to their differently sided arm, the shoulder displacement was consistently <3% the size of the elbow displacement for both conditions (Fig. 1G,H). In addition, the absolute size of elbow motion did not significantly differ between the cerebellar-damaged and control groups (elbow: F(1,18) = 0.37, P > 0.2); there was a reliable difference in the very small amount of shoulder motion between groups as even less shoulder motion occurred for the cerebellar group: F(1,18) = 4.85, P = 0.04.

Although the cerebellar-damaged and control groups experienced nearly identical patterns of initial arm displacement, their ensuing behaviour was qualitatively different. In Experiment 1 (Fig. 3A) and Experiment 2 (Fig. 3D) the exemplar control subject stabilized his arm consistently from trial to trial, had either small or no terminal oscillations, and eventually brought the joints in register with the pre-perturbation configuration. In contrast, stabilization by the exemplar cerebellar-damaged subject (Fig. 3B,E) was more variable, oscillatory, and inaccurate. For most conditions, the cerebellar-damaged subjects had significantly higher position errors 500-1000ms after the perturbation onset than exhibited by the control subjects (t(18) > 2.7, P < 0.01 one-sided) (Fig. 3C,G); the behavioural difference during the elbow extensor torque was above threshold (t(18) = 1.6, P = 0.06 one-sided). In addition, the more prominent terminal oscillations of the cerebellar-damaged subjects were evident as an elevated
Joint velocity occurring 500-1000ms from perturbation onset compared to the control group ($t_{(18)} > 1.9$, $P < 0.05$ one-sided).

**Experiment 1: Evoked shoulder extensor activity to similar shoulder displacement caused by different underlying torques**

The torque perturbations evoked a stereotyped sequence of activity in the stretched posterior deltoid of normal older subjects (mean age $\approx 55$ yr) similar to the pattern we reported earlier in normal young subjects (mean age $\approx 25$ yr) (Kurtzer et al. 2008). The earliest evoked response did not differ between conditions until $\approx 60$ms when the muscle activity grew larger for the shoulder torque condition than elbow torque condition, which was appropriate to counter the underlying shoulder torque perturbation. This pattern is visible in the time-varying traces of the exemplar subject (Fig. 4A) and group average (Fig. 4B) and is confirmed when binning the data in predefined periods (Fig. 4C); note that these differences in the shoulder extensor activity did not reflect the small difference in shoulder motion across conditions as slightly less shoulder motion occurred with shoulder torque than elbow torque. Excitatory increases from baseline were statistically present in the R1 period (subject’s mean $t$-value $> 2.9$; group $t_{(9)} > 3.0$, $P < 0.01$ one-sided) but did not significantly differ between the two conditions (subject’s mean $t$-value $= 0.13$; group $t_{(9)} = 0.17$, $P > 0.2$ two-sided). In contrast, R2, R3, and Vol periods expressed greater activity following the shoulder torque than elbow torque condition (subject’s mean $t$-value $> 3.4$; group $t_{(9)} > 3.3$, $P < 0.005$ one-sided).
The exemplar subject with cerebellar damage (Fig. 4D), group average (Fig. 4E), and binned analysis (Fig. 4F) exhibit some of the patterns shown by the control group. Excitatory responses were generally present in the shoulder extensor’s R1 period (subject’s mean t-value > 1.8; group t(9) > 3.9, \( P < 0.005 \) one-sided) and did not differ between conditions (subject’s mean t-value = 0.38; group t(9) = 0.9, \( P > 0.35 \) two-sided). Unlike the control group, the shoulder extensor’s activity during the R2 period did not show a strong difference between conditions (subject’s mean t-value = 0.91; group t(9) = 1.7, \( P = 0.11 \) two-sided). Greater activity to the shoulder torque condition was observed in the R3 period (subject’s mean t-value = 3.6; group t(9) > 9.0, \( P < 0.001 \) two-sided) and Voluntary period (subject’s mean t-value = 6.8; group t(9) > 8.9, \( P < 0.001 \) one-sided).

Despite the similar overall pattern of the posterior deltoid response by the control and cerebellar-damaged groups, there is a visible difference in the overall size of their responses (Fig 4C,F). A significant main effect was present for the shoulder torque condition (F(1,18) = 6.1, \( P < 0.05 \)) but not the elbow torque condition (F(1,18) = 1.7, \( P > 0.20 \)). Likewise, group contrasts of particular epochs indicated that the control subject had significantly larger activity in the R2 and R3 epochs following the shoulder torque (t(18) > 2.2, \( P < 0.05 \) two-sided) and in the Vol epoch following elbow torque (t(18) = 2.4, \( P < 0.05 \) two-sided); no other contrasts were significant (\( P > 0.10 \)).

**Experiment 2: Evoked shoulder extensor activity to pure elbow displacement caused by underlying shoulder torques**

Pure elbow displacement evoked a distinct pattern of activity in the unstretched posterior deltoid of normal older subjects (Fig. 5A-C) that matches the pattern of activity
from normal young subjects (Kurtzer et al. 2008). Shoulder extensor activity in the R1 period was unchanged from baseline following either pure elbow flexion or pure elbow extension (subject’s mean t-value < |0.2|; group t\(_{(9)}\) < |0.9|, \(P > 0.20\) two-sided).

Changes from baseline were apparent in its R2 period with excitatory and inhibitory responses to pure elbow flexion and pure elbow extension, respectively (subject’s mean t-value > |4.8|; \(t\(_{(9)}\) > |4.7|, \(P < 0.001\) one-sided); for both conditions a small and brief decrease in activity was also observed immediately prior to the larger and more sustained reciprocal response at \(\approx 60\)ms. Greater responses to elbow flexion than extension were also present in the shoulder extensor’s R3 and Vol periods (subject’s mean t-value > 7.9; \(t\(_{(9)}\) > 4.0, \(P < 0.005\) one-sided) which was appropriate for the shoulder extensor muscle to counter the underlying flexor torque perturbation.

The cerebellar-damaged group shared some of these response patterns (Fig. 5D-F). They did not exhibit a significant evoked response of the shoulder extensor in the R1 period to pure elbow extension or flexion (subject’s mean t-value < |0.4|; group t\(_{(9)}\) < 1.7, \(P > 0.10\) two-sided). In the R2 period their muscle activity was either unchanged from baseline (subject’s mean t-value = 1.0; elbow flexion: group t\(_{(9)}\) = 1.2, \(P > 0.20\) two-sided) or just at threshold (subject’s mean t-value = -1.5; elbow extension: group t\(_{(9)}\) = -2.3, \(P = 0.05\) two-sided). Activity during R2 did not differ between conditions (subject’s mean t-value = 1.5; group t\(_{(9)}\) = 2.0, \(P = 0.07\) two-sided). It was only during the R3 period that excitatory and inhibitory responses were reliably observed (subject’s mean t-value > |3.4|; group t\(_{(9)}\) > |2.7|, \(P < 0.05\) two-sided) and along with greater activity to pure elbow flexion than extension (subject’s mean t-value = 6.1; group t\(_{(9)}\) = 6.9, \(P < 0.001\) two-sided).
two-sided). Shoulder extensor activity during the Vol period also had greater activity to pure elbow flexion than extension (subject’s mean t-value = 8.1; group t(9) = 5.5, \( P < 0.001 \) one-sided).

The posterior deltoid responses of the control and cerebellar-damaged group to pure elbow motion show a visible difference in the overall size of their responses (Fig. 5C,F). Significant main effects for group were obtained for both elbow flexion (F(1,22) = 3.2, \( P < 0.05 \)) and extension (F(1,22) = 1.9, \( P < 0.05 \)). And similar to Experiment 1, group contrasts of particular epochs showed significant differences in the R2 epoch (t(18) > |3.5|, \( P < 0.001 \) one-sided) and the R3 epoch (t(18) > |2.0|, \( P < 0.05 \) one-sided); no other contrasts were significant (\( P > 0.15 \)).

**Pattern of evoked posterior deltoid activity across experiments**

For each subject, we combined their results from the two experiments by regressing the change in shoulder extensor activity against the imposed shoulder and elbow torques (see METHODS- Data analysis). The subsequent analyses only included individuals with a significant plane-fit (\( P < 0.05 \)). Almost all exclusions came from the R1 period (3 cerebellar-damaged and 3 control subjects) as the evoked responses were quite small; no control subjects were excluded from the remaining periods and 1 cerebellar subject was excluded in the R2 period.

The orientation of the best-fitting plane indicates the combination of shoulder-elbow torques for which the response is maximally sensitive (“preferred torque direction” or PTD). Consistent with our earlier experiment with young control subjects (Kurtzer et al. 2008), we found that the R1 activity of older control subjects (Fig. 6A) was
aligned with pure shoulder motion at 313.5° (R1_PTD mean(sd) = 316°(3.5); P > 0.05, circular C.I.). All later periods (R2_PTD = 337°(13.5); R3_PTD = 351°(14.5); Vol_PTD = 333°(7)) showed a significant bias away from pure shoulder motion towards the steady-state postural activity at 354° (P < 0.01, circular C.I.), although alignment only occurred in the R3 period (P > 0.1, circular C.I.).

The cerebellar-damaged group showed a similar pattern to the control group (Fig 6B). PTDs in the R1 period were aligned with pure shoulder motion (R1_PTD = 305.5°(15.5); P > 0.1, circular C.I.). PTDs in the R2 period had a moderate bias from pure shoulder motion (R2_PTD = 323.5°(10), (P < 0.05, circular C.I.) whereas subsequent epochs had stronger biases (R3_PTD = 349°(15); Vol_PTD = 343°(12)) (P < 0.01, circular C.I.). Only during the R3 period were the PTDs aligned with steady-state postural activity (P > 0.1, circular C.I.).

Comparisons between the PTDs of the two groups (Watson-Williams test) did not reveal a statistically significant difference in the R1 period (F(1,12) = 1.8, P = 0.12) or the R3 period (F(1,18) = 0.1, P > 0.20). However, the control group had a greater bias towards steady-state postural activity during the R2 period (F(1,17) = 5.4, P < 0.05) and less bias during the Vol period (F(1,18) = 5.3, P < 0.05).

A second measure obtained from the planar analysis is the overall sensitivity of posterior deltoid activation to the imposed shoulder-elbow torques (“response magnitude”), which corresponds to the steepness of the plane-fit (Response magnitude, Fig. 6C,D). Linear regressions indicated a significant trend of increasing response magnitude in later periods for both the control group (F = 17.9, P < .001) and cerebellar-
damaged group \((F = 19.8, P < .001)\). A comparison of the two groups shows that the response magnitude for the cerebellar group tended to be lower than the control group in all periods, but the contrast only reached statistical significance in the R3 period \(t_{(18)} = 3.9, P < 0.005\) two-sided); contrasts of the R1, R2, and Vol periods did not achieve significance \(P > 0.05)\). To further ensure that the lower response magnitude of the cerebellar R3 period did not reflect a weak overall depression of activity we normalized the response magnitudes of each period by that in the Vol period. Even after the normalization, the cerebellar-damaged group continued to show a significantly lower response magnitude in the shoulder extensors’ R3 period \(t_{(18)} = 2.2, P < 0.05)\).

**Moment-by-moment analysis of posterior deltoid’s multi-joint sensitivity**

All previous analyses utilized pre-defined time epochs that broadly correspond to different functional periods but can smear the precise evolution of muscle activity. We performed a moment-by-moment ROC analysis on each experiment to address when the shoulder extensor evoked activity switched from only reflecting shoulder motion to reflecting shoulder and elbow motion (see METHODS- Data analysis), chance discrimination occurs at .05 and perfect discrimination occurs at 1. Although each subject’s data is quite variable over time (owing to the small bin size of 1 ms) the mean ROC of the control group shows sustained trends above chance. In Experiment 1 the control group’s mean ROC achieves threshold at 59ms post-perturbation (Fig. 7A). The mean ROC of the cerebellar-damaged group also achieves threshold in Experiment 1 but at 70 ms post-perturbation (Fig. 7B), 11 ms later than the normal group (Fig. 7C). In Experiment 2, the control group again had a mean ROC that passed threshold at 59 ms
and preceded the cerebellar-damaged group at 67 ms (Fig. 7D-F). Hence, the cerebellar

group exhibited slightly delayed multi-joint responses compared to normal subjects.

A difference in the onset of multi-joint sensitivity may account for some of our

previous observations. The later onset in the cerebellar-damaged group (68.5ms vs

59ms on average) could account for their PTDs having less bias towards steady-state

postural activity during the R2 period (lasting 45-75ms). A delay in feedback processing

could also account for the lower response magnitude from the cerebellar group since

response magnitude increases with time. To test these possibilities we examined a

25ms window following the ROC threshold of each group. The corresponding PTDs from

the cerebellar-damaged and control groups did not differ within this group-specific

epoch \((F(1,17) = 0.18, P > 0.20)\) and, hence, the difference in the R2 period (Fig. 6A-B)

could be explained by the small delay in multi-joint processing. In contrast, the

response magnitude of the cerebellar-damaged group remained significantly lower than

normal and did not reflect a shift in the time-dependent increase in gain \((t(21) = 2.9, P <

0.01 \text{ two-sided})\).

Relation between the response magnitude of posterior deltoid and severity of ataxia

The most consistent difference in the shoulder extensor activity between the

control and cerebellar-damaged groups was a lowered response magnitude in the R3

epoch. To determine whether the lowered gain of the posterior deltoid was related to

the severity of motor dysfunction we correlated the R3 gain to the clinically assessed

ataxic score of the upper limb. The correlation between the two variables did not

achieve significance \((R = -0.21, df = 8, P > 0.20 \text{ one-sided})\). Normalizing the R3 response
magnitude by activity in the voluntary epoch may be a more appropriate measure of clinical change by accounting for inter-subject differences in motor vigour. However, no significant correlation was obtained with this measure \((P > 0.2)\), the response magnitude during a combined R2/R3 epoch \((P > 0.2)\), or the gain from the 25 ms epoch following multi-joint responsiveness \((P > 0.2)\).

We also tested whether the delayed onset of multi-joint responses (determined from the ROC) had a positive association with the degree of ataxia. The correlation did not reach significance \((R = 0.40, \text{df} = 8, P > 0.10 \text{ one-sided})\), nor did a regression which included both the delay and gain \((P > 0.10)\).

**Evoked activity by the pectoralis major in both experiments**

Although our experiments focused on posterior deltoid, we also collected data from pectoralis major, Fig. 8, a monoarticular shoulder flexor shown to exhibit fast feedback responses which incorporate shoulder and elbow information (Kurtzer et al. 2008). The pectoralis major of both the control and clinical groups had low pre-perturbation activity compared to posterior deltoid consistent with the need to counter a background shoulder flexor torque. The subsequent evoked response of the shoulder flexor muscle was opposite the pattern expressed by the shoulder extensor muscle. The control group’s pectoralis major expressed greater activity to elbow extensor torque than shoulder flexor torque from the R3 period onwards (Fig 8A) (subject’s mean t-value > |2.1|; group \(t(9) > |3.2|, P < 0.01 \text{ one-sided})\). Their pectoralis major also had greater responses to combined extensor torque than combined flexor torque from the R2 period onwards (Fig 8B) (subject’s mean t-value > |1.6|; group \(t(9) > |2.3|, P < 0.05 \text{ one-sided})\).
sided). The shoulder flexor of the cerebellar-damaged group showed a similar, though less reliable, pattern (Fig. 8 C,D) – greater activity to elbow extensor torque than shoulder flexor torque during the Vol period (subject’s mean t-value = |3.2|; group t(8) = -2.5, $P < 0.05$ one-sided) and greater activity with combined extensor torque than combined flexor torque from R2 onwards (subject’s mean t-value > |1.9|; group $t(8) > |2.1|$, $P < 0.05$ one-sided).

Another notable feature is the low level of co-activity by the pair of shoulder monoarticulars. This is most evident for the two conditions which evoked the greatest level of posterior deltoid activity, shoulder flexor torque and combined flexor torque. On average, the control group’s pectoralis major had 4% and 5% the level of their posterior deltoid during the R2/3 epoch. Similarly, the cerebellar group’s pectoralis major had 2% and 5% the level expressed by their posterior deltoid during the R2/3 epoch. Note that this ratio was formed subject-by-subject and yield an identical result whether we employed their normalized or unnormalized data since the normalization introduced a common factor to the activity of both muscles. Differences in the force-emg profile of the two muscles (due to differences in physical efficacy along with distortion by fatty tissue and location parameters) could lead to an underestimation of the degree of co-contraction. However, even a four-fold difference would not alter the observed trend of weak co-contraction.
Research over the past century has established that damage to the cerebellum creates significant problems in the voluntary control of multi-joint arm movements (Holmes 1939). Disordered feedback processing has also been reported following cerebellar damage but, to our best knowledge, our study is the first to examine the impact on long-latency responses by the multi-joint arm. We expected that cerebellar damage would impair the ability of LLRs to account for the arm’s inter-segmental dynamics similar to how cerebellar damage impairs the ability of feedforward commands to account for the arm’s inter-segmental dynamics. Specifically, we predicted that cerebellar damage would eliminate the ability of the posterior deltoid to generate LLRs based on elbow motion (Fig 2). Instead, we found that a normal overall pattern of its LLRs. The PTDs in the LLR were indistinguishable from normal in the R3 epoch and in a fixed 25ms window after each group expressed multi-joint integration (\( \approx 59 \) ms in normal subjects versus \( \approx 69 \) ms in cerebellar subjects).

The most dramatic impact of cerebellar damage on the LLR of the shoulder monoarticular was its smaller size. Activity in the R2 and R3 epochs was lower than normal for most conditions (6 out of 8 comparisons) and the response magnitude of the planar-fit was lower than normal in the R3 epoch. The attenuated LLR of cerebellar subjects did not reflect a general downscaling since their R1 response was not altered. Nor did it reflect an increase in tonic inhibition since their inhibitory LLR to elbow extension was also smaller than normal. Changes in the “central set” – communicated
verbally (Crago et al. 1976; Rothwell et al. 1980) or implicitly (Evarts and Tanji et al. 1976; Pruszynski et al. 2008) – can also have dramatic changes on LLR magnitude and could underlie the smaller LLRs by the cerebellar group if the subjects adopted a less vigorous “central set” than the control group. However, the magnitude of their voluntary reaction did not differ from normal indicates that the lower magnitude of evoked activity following cerebellar damage was specific to the LLR epoch.

The conserved pattern of the posterior deltoid’s LLR to imposed shoulder-elbow displacements suggests that its basic motor pattern is not housed by the cerebellum. Rather, the cerebellum is necessary for the proper expression of the basic motor pattern. This broad conclusion has been made previously by several authors (Dichgans and Fetter 1993; Holmes 1939; MacKay and Murphy 1979; Jo and Massaquoi 2004), and our results extend this idea to fast feedback corrections of the multi-joint arm.

Cerebellar damage appears to degrade the predictive ability of the sensori-motor system in a general manner rather than disrupting computations for a specific set of conditions. For example, predictive synchronization of eye-hand coordination depends on the cerebellum (Miall et al. 2001; Vercher and Gauthier 1988), the cerebellum is essential for translating sensory errors into motor learning (Martin et al. 1996; Tseng et al. 2007), and recordings of single Purkinje neurons also demonstrate that cerebellar activity is linked to the predicted state of the arm not the exerted motor commands (Palasar et al. 2006). Cerebellar damage also has been shown to impair the predictive capabilities of the LLR. Cerebellar-damaged subjects cannot scale their postural LLRs to the amplitude of surface displacement (Horak and Diener 1994; Timmann and Horak
1997) or whether the surface rotates upwards or displaces backwards (Nashner 1976).

In a similar vein, cerebellar cooling in monkeys interferes with their ability to generate LLRs appropriate for torque pulses and torque steps (Hore and Vilis 1984). If feedback gain is modulated by prediction accuracy to ensure stability, as some authors have suggested (Crevecoeur et al. 2010), then a degradation of prediction accuracy from cerebellar damage should result in lower feedback gains. Likewise, the discrepancy between previous studies that cerebellar long-latency responses are greater than normal (Claus et al. 1986; Friedemann et al. 1987; Horak and Diener 1994) or lower than normal (Marsden et al. 1977b; Bakker et al. 2006; Kung et al. 2009) may reflect different demands on prediction in their different paradigms.

Subjects with cerebellar damage also exhibited a slight delay (≈10 ms) of their posterior deltoid in responding to both shoulder and elbow motion. Previous findings in cerebellar patients have been mixed regarding the timing of the LLR, even when excluding clinical signs of sensory loss: some studies have reported delayed LLRs (≈5ms) (Lee et al. 2003), some studies found no LLR delays (Diener et al. 1984; Friedemann et al. 1987), and some studies report that delays are occasionally expressed (Claus et al. 1986). We interpret the delay here as a result of cerebellar damage, but cannot rule out subclinical somatosensory abnormalities. That being said, this timing abnormality could not fully explain the lower feedback gain in the cerebellar group.

Previous studies which cooled the cerebellum resulted in a loss of predictive feedback (Hore and Flament 1986; Hore and Vilis 1984) and the co-impact of delay and lowered gain can lead to instabilities akin to cerebellar ataxia (Hore and Flament 1986;
However, we did not find a significant correlation of these measures during the LLR with ataxia. We also did not address whether muscle spindle or cutaneous sensors are the peripheral afferents relaying multi-joint information since both sources were affected by the mechanical perturbations. The few studies on this topic found no change in LLRs when cutaneous information was abolished (Bawa and McKenzie 1981; Grey et al 2001; Matthews 1984) suggesting that muscle spindles play the greatest role.

Cerebellar damage may impact the long-latency responses through its connections to primary motor cortex (Middleton and Strick 2000), a region which has been consistently shown to support long-latency responses (Cheney and Fetz 1984; Day et al. 1991; Marsden et al. 1977a; Matthews et al. 1990) and voluntary control (Porter and Lemon 1993; Scott 2003). Our recent study of healthy human subjects and behaving monkeys also provided clear evidence that primary motor cortex contributes to the multi-joint integration exhibited by the long-latency response (Pruszynski et al 2011). The cerebellum makes extensive connections to subcortical pathways via the red nucleus (Keifer and Houk 1994) and recticular formation (Asunama et al. 1983) which may provide an additional contribution to long latency reflexes (Miller and Brooks 1981; Shemmell et al. 2009). Future work is needed to identify the relative role of these cortical and subcortical regions and whether they exhibit a lowered response magnitude similar to the long latency response.
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**Wagner MJ and Smith MA.** Shared internal models for feedforward and feedback...

Figure Legends

**Figure 1.** Limb dynamics and torque conditions.  A. Conditions of Experiment 1 where shoulder flexion torque (red filled arm) and elbow extension torque (blue filled arm) displace the limb in different trials. The shoulder extensor muscle needs to provide more compensation during the shoulder torque condition than the elbow torque condition.  B. Data from an exemplar healthy subject showing that the two perturbing torques of Experiment 1 initially cause a similar change in shoulder motion (solid lines) but clearly different elbow motion (dashed lines).  C. Pattern of joint displacement 50 ms following the perturbing torques of Experiment 1. Data is shown for each control subject with black lines connecting their data from the two conditions.  D. Data from the cerebellar-damaged subjects using the same format as above.  E. Conditions of Experiment 2 where flexion torque is applied at both joints (red filled arm) and extension torque is applied at both joints (blue filled arm) on different trials. The two perturbations require increased compensation and decreased compensation from the shoulder extensor muscle, respectively.  F. Data from the same exemplar healthy subject showing the substantial elbow motion and negligible shoulder motion induced by the perturbations.  G. Pattern of joint displacement 50 ms following the perturbing torques of Experiment 2. The data from each control subject is shown.  H. Data from the cerebellar-damaged subjects using the same format as above.

**Figure 2.** Contrasting predictions of long-latency response of the shoulder extensor muscle following cerebellar damage.  A. Cartoon of the normal response of the shoulder
extensor to the perturbations in Experiment 1 where shoulder flexor torque (SF, red) and elbow extensor torque (EE, blue) cause similar amounts of shoulder motion and different amounts of elbow motion. A similar R1 is evoked whereas later periods show larger activity for the shoulder torque than the elbow torque perturbation. The same pattern is predicted if long-latency responses are minimally impacted by cerebellar damage. B. Predicted pattern of shoulder extensors’s LLR if cerebellar damage eliminates the ability to respond to elbow motion: LLR would be identical for the two conditions with the normal magnitude when responding to shoulder torque. C. Cartoon of the normal muscle response in Experiment 2: flexor torque at both joints (SF/EF, red) and extensor torque at both joints (SE/EE, blue) cause substantial elbow motion and a negligible amount of shoulder motion. Normally, subjects have no evoked R1 whereas the later periods show reciprocal increases and decreases in activity for the flexor torque and extensor torque perturbations. D. Predicted pattern of the shoulder extensor’s LLR if cerebellar damage eliminates the ability to respond to elbow motion: LLR would not be evoked for the two conditions. E. Diagram of the predicted “preferred torque direction” for the control subjects shown in shoulder-elbow torque space. Graph depicts the predicted activity of LLR to the four torque conditions of Experiment 1 and 2 (SF, EE, SF/EF, and SE/EE); white shading shows maximal inhibitory responses whereas black shading shows maximal excitatory responses. The arrow indicates the plane-fit to the activity and is directed towards shoulder flexor torque at 0°. F. Predicted “preferred torque direction” for the cerebellar–damaged subjects. The arrow indicates the plane-
Figure 3. Postural stabilization and final accuracy. A. Joint motion from an exemplar control subject following the perturbations of Experiment 1, shoulder flexion torque (red) and elbow extensor torque (blue). Shoulder and elbow angles of each trial are depicted with solid and dashed lines, respectively. The vertical line shows perturbation onset. B. Joint motion from an exemplar subject with cerebellar damage, same format as above. C. Position error (mean and standard error) from 500-1000ms after perturbation onset (see black bar on the time axis of previous panels). Red and blue bars correspond to shoulder torque and elbow torque conditions whereas normal and cerebellar subjects are depicted with dark and light fill, respectively. Asterisk between the bars indicates a significant difference between the cerebellar and control group for that perturbation condition (*, P < 0.05; **, P < 0.01). D. Velocity error (mean and standard error) from 500-1000ms after perturbation onset, same format as above. E-H. Joint motion of control subjects and cerebellar subjects during Experiment 2; same format as A-D.

Figure 4. Evoked posterior deltoid activity during Experiment 1. A. Posterior deltoid activity from the exemplar control subject shown in Fig. 3A,D. Black lines indicate the mean activity and colored outlines indicate the standard error following the shoulder flexor torque (red) and elbow-extensor torque (blue). Thin vertical lines delineate the different time periods that we examined for compensatory muscle activity (R1,R2,R3
and Vol). B. Average muscle activity and standard error from the normal group of subjects. C. Plots of evoked muscle activity within the four different epochs. Thin black lines depict data from each subject (one subject’s data is out of range and presented numerically). Circles and thick black lines indicate the group mean. Horizontal line at 0 is the pre-perturbation muscle activity. D-F. Posterior deltoid activity from the exemplar cerebellar subject shown in Fig. 3B,E. and group of cerebellar subjects during Experiment 1. Same format as A-C. Vertical lines and asterisks spanning panels indicate a significant difference between the cerebellar and control group for that epoch of activity and perturbation condition (*, P < 0.05; **, P < 0.01).

**Figure 5.** Evoked posterior deltoid activity during Experiment 2. A-C. Posterior deltoid activity from the exemplar healthy subject and group of healthy subjects during Experiment 2. Black lines indicate the mean activity and colored outlines indicate the standard error following flexor torque at both joints (red) and extensor torque at both joints (blue). B. Average muscle activity during Experiment 2 from the normal group of subjects. C. Plots of evoked muscle activity within the four different epochs. Thin black lines depict data from each subject. Circles and thick black lines indicate the group mean. Horizontal line at 0 is the pre-perturbation muscle activity. D-F. Posterior deltoid activity from the exemplar cerebellar subject and group of cerebellar subjects during Experiment 2. Same format as A-C. Vertical lines and asterisks spanning panels c and f indicate a significant difference between the cerebellar and control group for that epoch of activity and perturbation condition (*, P < 0.05; **, P < 0.01).
Figure 6. Directional tuning of the posterior deltoid to the applied shoulder-elbow torque. A. Preferred torque directions (PTDs) from the shoulder extensor muscle of normal subjects during different response epochs. Small circles show PTDs of individual subjects having significant plane-fits ($P < 0.05$) whereas grey diamonds show the average PTD from these individuals. The two horizontal lines are the predicted PTDs if responses only reflect shoulder motion ($\theta$) or the empirically determined postural tuning when countering applied torque ($\tau$) (see METHODS — Data analysis). B. PTDs of the shoulder extensor muscle of the cerebellar damaged subjects, same format as above. C. Response magnitude from the shoulder extensor muscle of normal subjects during different epochs. Small circles and grey diamonds show individual subjects with significant plane-fits and the group average, respectively. D. Response sensitivity of cerebellar damaged subjects, same format as above. Asterisk between the grouped icons indicates a significant difference between the cerebellar and control group for that epoch of muscle activity (*, $P < 0.05$; **, $P < 0.01$).

Figure 7. Evolving multi-joint sensitivity of the posterior deltoid response. A. Moment-by-moment statistical discrimination of the shoulder extensor’s activity occurring with the shoulder flexor torque and elbow extensor torque conditions of Experiment 1, data from the group of normal subjects. If its muscle activity is only linked to shoulder motion then discrimination between these two conditions will be at chance levels, 0.5. Instead, a multi-joint response would lead to discrimination greater than chance, perfect discrimination occurs at 1.0. Individual and group average ROC curves are depicted by thin gray lines and thick black lines, respectively. White dot and inset #
indicate the time when the average ROC passes threshold (>3 std). B. ROC curves from the group of cerebellar-damaged subjects in Experiment 1. Same format as above. C. Mean ROC curves from the normal group (thick line) and cerebellar-damaged group (thin line). Difference in the threshold time of the two groups is also indicated. D-F. Moment-by-moment discrimination of muscle activity occurring with combined flexion torque and combined extension torque conditions in Experiment 2. Same format as A-C.

**Figure 8.** Evoked activity of the pectoralis major during Experiment 1 and 2. A. Evoked muscle activity by the normal subjects to torque perturbations of Experiment 1. Black lines with red and light blue surround indicate the posterior deltoid’s activity to shoulder flexor torque and elbow extensor torque (same data and color scheme shown in Figure 4B). Black lines with pink and navy blue surround depict the pectoralis major’s activity to the same two perturbations. Hence, muscular activity during shoulder flexor torque is indicated by red and pink coloration whereas muscular activity during elbow extensor torque is indicated by light blue and navy blue. B. Evoked muscle activity by the cerebellar-damaged subjects to the torque perturbations of Experiment 1, same format as normal subjects in the above panel. C. Evoked muscle activity by the normal subjects to torque perturbations of Experiment 2. Black lines with red and light blue surround indicate the posterior deltoid’s activity to combined flexor torque and combined extensor torque (same data and color scheme shown in Figure 5B). Black lines with pink and navy blue surround depict the pectoralis major’s activity to the same two perturbations. Hence, muscular activity during combined flexor torque is indicated by red and pink coloration whereas muscular activity during combined extensor torque
is indicated by light blue and navy blue. Data for posterior deltoid also shown in Figure 4E. D. Evoked muscle activity by the cerebellar-damaged subjects to the torque perturbations of Experiment 2, same format as normal subjects in above panel. Data for posterior deltoid also shown in Figure 5E.
Table 1. Subject Demographics

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<th>Posture/Gait Ataxia</th>
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SCA=spinocerebellar ataxia; Sporadic=sporadic cerebellar ataxia;
Figure 1
Figure 2
Figure 3
Figure 4

A, B, C, D, E, F: Graphs showing EMG (au) over time (ms) for Control Subjects and Cerebellar Subjects.

Cerebellar Subjects are on the right side of the page, and Control Subjects are on the left side.

ΔEMG (au) is shown in C, with a value of 5.8.

R1, R2, R3, and Vol are represented on the x-axis of the graphs.
**Figure 5**

Comparative analysis of EMG activity between control and cerebellar subjects. The graphs illustrate the EMG activity over time (ms) for different conditions labeled as R1, R2, R3, and Vol. The graphs show a significant increase in EMG activity, indicating the impact of cerebellar conditions on muscle response. The control subjects exhibit a consistent EMG pattern, while cerebellar subjects show marked changes, particularly during the Vol phase, indicating possible atrophy or altered muscle function. The significance levels are indicated in the right graph, with asterisks representing statistical significance.
Figure 6

A. Control subjects
B. Cerebellar subjects

\[ \tau, \theta \]

Response Magnitude

C. Control subjects
D. Cerebellar subjects

\[ \tau, \theta \]

Response Magnitude

**
Figure 7

Experiment 1

Control subjects

0.00
0.25
0.50
0.75
1.00

ROC

A

59 ms

Experiment 2

Cerebellar subjects

0.00
0.25
0.50
0.75
1.00

ROC

B

70 ms

C

Δ11 ms

D

59 ms

E

67 ms

F

Δ8 ms

-50 0 50 100 150

Time (ms)

Experiment 1

-50 0 50 100 150

Time (ms)

Experiment 2

Δ

11 ms

Δ

8 ms

Control subjects

Cerebellar subjects

Experiment 1

Experiment 2

A

B

C

D

E

F

Δ

11 ms

Δ

8 ms

-50 0 50 100 150

Time (ms)

-50 0 50 100 150

Time (ms)
Figure 8