Cerebellar ataxia impairs modulation of arm stiffness during postural maintenance

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1Department of Mechanical Engineering, Johns Hopkins University, Baltimore, Maryland; 2Department of Mechanical Engineering, Stanford University, Stanford, California; 3Kennedy Krieger Institute, Baltimore, Maryland; and 4Department of Neuroscience, Johns Hopkins School of Medicine, Baltimore, Maryland

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Gibo TL, Bastian AJ, Okamura AM. Cerebellar ataxia impairs modulation of arm stiffness during postural maintenance. J Neurophysiol 110: 1611–1620, 2013. First published July 10, 2013; doi:10.1152/jn.00294.2013.—Impedance control enables humans to effectively interact with their environment during postural and movement tasks, adjusting the mechanical behavior of their limbs to account for instability. Previous work has shown that people are able to selectively modulate the end-point stiffness of their arms, adjusting for varying directions of environmental disturbances. Behavioral studies also suggest that separate controllers are used for impedance modulation versus joint torque coordination. Here we tested whether people with cerebellar damage have deficits in impedance control. It is known that these individuals have poor motor coordination, which has typically been attributed to deficits in joint torque control. Subjects performed a static postural maintenance task with two different types of directional force perturbations. On average, patients with cerebellar ataxia modified stiffness differentially for the two perturbation conditions, although significantly less than age-matched control subjects. Thus cerebellar damage may impair the ability to modulate arm impedance. Surprisingly, the patients’ intact ability to generally alter their limb stiffness during the postural task (albeit less than age-matched control subjects) improved their movement performance in a subsequent tracing task. The transfer of stiffness control from the static to the movement task may be a strategy that can be used by patients to compensate for their motor deficits.

cerebellar ataxia; impedance control; arm stiffness

THE ABILITY TO MODULATE the mechanical impedance of our limbs is essential, given the variety of motor control tasks that we perform and the objects and environments with which we interact. By altering our impedance, we can change the way in which our body movement is affected by forces. Thus impedance control is believed to be especially important in maintaining stability during both postural control and movement. Changes in limb impedance can be used to reduce instability that results from environment disturbances (De Serres and Milner 1991; Milner 2002) or signal-dependent motor noise (Selen et al. 2009). Limb impedance can also be modulated according to different task requirements, conditions, and constraints (Damm and McIntyre 2008; Gribble et al. 2003).

Impedance is commonly modeled as a combination of mass, damping, and stiffness components, which relate force and torque to acceleration, velocity, and position, respectively. While the mass is primarily affected by joint configuration, the viscoelastic properties of damping and stiffness are affected by joint configuration, muscle activity, cocontraction of agonist-antagonist muscles, and changes in reflex and feedback gains (Hogan 1985). However, increased impedance due to cocontraction has a high energy cost, leading people to find a balance between metabolic efficiency, stability, and task performance.

Previous work has shown that not only are people able to control global increases in end-point stiffness (at the hand) via cocontraction but they can also modify the geometry of their end-point stiffness by tuning cocontraction of different muscle pairs. This selective modulation of cocontraction can help balance stability with metabolic cost. People have been shown to specifically tune the end-point stiffness of their arm in the direction of destabilizing forces during reaching movements (Burdet et al. 2001; Franklin et al. 2007) and static postural maintenance tasks (Darainy et al. 2004, 2006; Krutky et al. 2009, 2013). However, the extent to which people modulate the geometry of their hand stiffness is substantially lower in a postural task compared with movement, even after multiple days of training in a static condition.

Behavioral work has suggested that control of impedance is separate from dynamics control. The latter would allow coordination of joint torques based on a neural representation of the body’s movement dynamics (Wolpert et al. 1998). The former method of control produces cocontraction, whereas the latter produces reciprocal activation of agonist-antagonist muscles. Both impedance and dynamics control may constitute a feedforward internal model (Osu et al. 2003). The interaction and specialization of these two controllers have been studied with regard to different phases of movement (Scheidt and Ghez 2007), stability of environment dynamics (Franklin et al. 2003; Osu et al. 2003), stages of adaptation (Osu et al. 2002), and handedness (Wang and Sainburg 2007).

A few studies have provided evidence for distinct neural mechanisms in the control of impedance and joint torque. Activities in the primary motor cortex, dorsal premotor cortex, ventral premotor cortex, cerebellum, supplementary motor area, and putamen were shown to be differentially related to voluntary cocontraction and reciprocal activation (Haruno et al. 2012; Humphrey and Reed 1983). While some studies have highlighted the role of the cerebellum in controlling and adapting movement via dynamics models (Wolpert et al. 1998), less work has focused on the structures involved in impedance control. On the basis of neural recordings and lesion studies, Smith (1996) hypothesized that the cerebellum also functions to control joint stiffness, but this theory has yet to be thoroughly tested.
Ataxia (i.e., uncoordinated movement), the neurological symptom caused by damage to the cerebellum, has been hypothesized to result from abnormal control of joint torques and improper compensation for movement dynamics in a feedback manner (Bastian et al. 1996, 2000; Schweighofer et al. 1998). Movement dynamics are largely affected by the mass component of impedance, which people have limited control over modifying. This led us to the question: Although people with cerebellar ataxia are impaired at counteracting their movement dynamics, are they capable of voluntarily modifying other components of their impedance? Particularly, can they optimally modulate arm stiffness relative to environment instabilities, or do they adopt a strategy of generally increasing stiffness of all muscles? We tested an arm posture maintenance task with cerebellar patients and age-matched control subjects to determine whether impedance control is dependent on the cerebellum. A tracing task was also performed after the posture task to see whether modified stiffness from the static condition was retained during ensuing motion, perhaps improving patients’ impaired movement.

MATERIALS AND METHODS

Stiffness representation. Movement of the human arm in the horizontal plane can be modeled by the equation

\[ f = M \ddot{x} + B \dot{x} + K(x - x_0) \]  

(1)

where \( f \) is the Cartesian force vector at the hand, \( x, \dot{x}, \text{ and } \ddot{x} \) are the position displacement, velocity, and acceleration vectors, and \( M, B, \text{ and } K \) are the mass, damping, and stiffness matrices at the equilibrium position \( x_0 \) in hand space (Dolan et al. 1993). These three terms constitute the basic components of mechanical impedance.

The hand stiffness matrix

\[ K = \begin{bmatrix} K_{xx} & K_{xy} \\ K_{yx} & K_{yy} \end{bmatrix} \]  

(2)

contains four parameters characterizing the elastic behavior of the hand, where \( K_{xx} \) relates force and displacement in the \( x \)-direction, \( K_{xy} \) relates force in the \( x \)-direction and displacement in the \( y \)-direction, \( K_{yx} \) relates force in the \( y \)-direction and displacement in the \( x \)-direction, and \( K_{yy} \) relates force and displacement in the \( y \)-direction. This matrix can be visually represented as an ellipse (Mussa-Ivaldi et al. 1985), where the major axis signifies the direction of the largest restoring forces to a displacement. The mass \( M \) and damping \( B \) matrices can similarly be represented as ellipses.

The corresponding joint stiffness matrix \( R \), the stiffness transformed in joint space, can be calculated by

\[ R = J^T K J \]  

(3)

\[ J = \begin{bmatrix} L_1 \sin \theta_1 + L_2 \sin(\theta_1 + \theta_2) & -L_2 \sin(\theta_1 + \theta_2) \\ L_1 \cos \theta_1 + L_2 \cos(\theta_1 + \theta_2) & L_2 \cos(\theta_1 + \theta_2) \end{bmatrix} \]  

(4)

where \( J \) is the Jacobian matrix at the equilibrium arm configuration. The Jacobian, which relates hand velocity to joint angular velocity, depends on the length of the upper arm \( L_1 \), the length of the forearm \( L_2 \), the shoulder angle \( \theta_1 \) and the elbow angle \( \theta_2 \). Analogous to the hand stiffness matrix, the joint stiffness matrix relates joint torques to joint displacements

\[ R = \begin{bmatrix} R_{ss} & R_{se} \\ R_{es} & R_{ee} \end{bmatrix} \]  

(5)

where \( R_{ss} \) relates shoulder torque and shoulder displacement, \( R_{se} \) relates shoulder torque and elbow displacement, \( R_{es} \) relates elbow torque and shoulder displacement, and \( R_{ee} \) relates elbow torque and elbow displacement.

Subjects. Eleven patients with cerebellar ataxia (Table 1) and eleven healthy subjects matched for age, handedness, and sex participated in the study. The mean and standard deviation of the ages of the patients and age-matched control subjects were 62 ± 13 yr and 60 ± 12 yr, respectively. We rated the severity of the patients’ ataxia with the International Cooperative Ataxia Rating Scale (ICARS) (Trouillas et al. 1997). To ensure that patients’ symptoms were primarily cerebellar, we did an additional neurological exam to test reflexes, proprioception, and fine touch via monofilaments. The experiment protocol was approved by the Johns Hopkins University School of Medicine Institutional Review Board, and all subjects signed a consent form prior to participating.

For the majority of subjects, the dominant arm was used in the experiment. Patient 4 had a left-sided cerebellar stroke; thus the left hand (ipsilateral to the cerebellar damage) was used although the patient was right-handed. The left hand of a right-handed age-matched control subject was similarly tested. Patient 5 had a craniectomy to repair a right-sided cerebellar arteriovenous malformation (AVM). The arm ipsilateral to the cerebellar damage was also the patient’s dominant arm.

Impedance estimation. Experiments were done with the KINARM Exoskeleton Lab (BKin Technologies, Kingston, ON, Canada), an exoskeleton robotic device that allows for movement of the shoulder and elbow joints in the horizontal plane while supporting the arm against gravity. A subject’s arm is placed in the upper arm and forearm trays, which can be adjusted appropriately to match his or her arm parameters, thus coupling the limb to the robot linkages. Because of factors such as belt elasticity, the intrinsic compliance of the cable-driven KINARM (Ball et al. 2007) was greater than some devices used in prior stiffness measurement studies (e.g., Gomi and Kawato 1997). This compliance limited our ability to produce quick, accurate position displacements that are necessary for the direct stiffness measurements of some methods (Flash and Mussa-Ivaldi 1990). Thus a modified version of the impedance measurement method proposed by Dolan et al. (1993), which estimates \( M, B, \text{ and } K \) simultaneously (Eq. 1), was used.

Trapezoidal position displacements of 7 mm were randomly presented in eight different directions (0°, ±45°, ±90°, ±135°, 180°) (Fig. 1). The position displacements consisted of 100-ms ramp-up phase, 200-ms hold phase, and 100-ms ramp-down phase (using a PD controller with stiffness of 3,000 N/m and damping of 40 Ns/m). The average position, velocity, acceleration, and force trajectories for a given direction were used to estimate the mass, damping, and stiffness with Eq. 1 and linear regression. To minimize the inclusion of any voluntary responses to the displacements, while still using a sufficient amount of data, the first 300 ms of kinematic and force data was used.

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ICARS, International Cooperative Ataxia Rating Scale; SCA, spinocerebellar ataxia; ADCA, autosomal dominant cerebellar ataxia; AVM, arteriovenous malformation. *Subject right-handed but used left hand in experiment.
Because the arm mass only varies with joint positions and a single arm configuration was used throughout the experiment, the \( M \) matrix was constant for each subject (as determined from the baseline arm impedance measurement). The accuracy was validated by implementing virtual springs in both Cartesian and joint space and measuring the resulting changes in stiffness.

**Experimental protocol.** Subjects were seated in the robot with their arm positioned in the arm trays. The visual display system showed a virtual target (radius 1.25 cm) and hand position (radius 0.75 cm) overlaid on a plane above the arm, while view of the actual arm was hidden.

Subjects first completed a Familiarization session (Fig. 1) to practice the tracing task. A target appeared at the beginning of every trial, located at the position where the shoulder and elbow joints were 45° and 90°, respectively. The target turned green when the hand cursor was completely within the target and was red otherwise. Once subjects placed their hand cursor within the target, a light blue parallelogram was completely within the target and was red otherwise. Once subjects located at the position where the shoulder and elbow joints were 45° and 90°, respectively. The target turned green when the hand cursor overlaid on a plane above the arm, while view of the actual arm was hidden.

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Subjects were instructed to trace the template in one smooth motion without stopping. They were also told to move in one direction along the template and not backtrack, even if they were ahead of pace (indicated by the change in template line color).

The parallelogram shape was chosen in an attempt to isolate shoulder and elbow movement. The top and bottom sides require mainly shoulder extension and flexion, whereas the left and right sides require mainly elbow extension and flexion, respectively. The motivation was that stiffness changes at individual joints may influence tracing performance along particular sides of the template.

Next, subjects completed six blocks of the Baseline Pre session, from which an initial measurement of their baseline arm impedance was determined. Subjects were instructed to bring their hand to the target and then keep their arm as relaxed as possible. They were instructed to avoid reacting to the forces used to generate the position displacements. Each block consisted of eight impedance measurements (position displacements described in *Impedance estimation*), followed by one trial of the tracing task. The tracing task was used as baseline performance, when subjects were relaxing their arm prior to movement.

The Clockwise (CW) Perturbation session consisted of six blocks, during which subjects were instructed to actively resist the larger force perturbations that would push their hand outside of the target. Subjects were told to try and maintain a constant (tonic) level of moderate muscle activity in their arm, while avoiding excessive muscle contraction to avoid fatigue. The static postural maintenance task was selected so as not to confound the results with patients’ movement deficits. Each block consisted of 40 force perturbations and 8 impedance measurements (pseudorandomly presented), followed by 1 trial of the tracing task. Only once the subject’s hand cursor was stationary within the target did the robot begin to apply any forces. The perturbations were applied in two directions along an axis 45° clockwise of the major axis of each subject’s baseline stiffness ellipse. The sinusoidal force perturbations had a magnitude of 2 N and lasted for 300 ms. A force channel (with a wall stiffness of 2,000 N/m and damping of 10 Ns/m) was used to constrain hand movement to the axis along which the perturbations were applied. After each perturbation, subjects saw a numerical score that reflected the amount of time their hand was outside the target, ranging from 100 (hand never left the target) to 0 (more than 800 ms). The timer started upon onset of the perturbation and stopped once the hand returned to the target.
and remained there for 1 s (the incrementing timer was not shown). The cumulative score was also displayed to the subjects at the end of each block. Short breaks (~1 min) were given between each block, to reduce the effect of muscle fatigue, and a longer break (~5 min) was given between blocks 3 and 4. The purpose of the tracing task in this session was to test whether subjects’ movement performance was affected by the postural maintenance task immediately prior.

Subjects then received the same instructions for the six blocks of the Isotropic Perturbation session. However, the perturbations were now applied in eight different directions, along the 0°, 45°, 90°, and 135° axes. As in the CW session, hand movement was constrained to these axes via a force channel. The magnitude of the perturbations differed by direction (2.5, 1.5, 3, and 5 N, respectively), as determined from pilot studies, to ensure approximately equivalent displacement in all directions (due to the anisotropy of arm impedance). Once again, the tracing task was evaluated at the end of every block.

Finally, a Baseline Post session was performed to reevaluate the baseline arm impedance and baseline performance in the tracing task. Each of the three blocks consisted of eight impedance measurements, followed by one trace trial.

Data analysis. All of the impedance measurements in each of the Baseline Pre, CW, Isotropic, and Baseline Post sessions were used to compute a single impedance estimate for each condition. To assess stiffness modulation during the postural maintenance task, stiffness estimates from the CW and Isotropic Perturbation sessions were compared for each subject. As mentioned in Stiffness representation, hand stiffness can be visualized as an ellipse. An ellipse is defined by three parameters: orientation, aspect ratio, and size. The orientation is the angle of the major axis (principal eigenvector) relative to the positive x-axis, determined by singular value decomposition of the hand stiffness matrix K. The aspect ratio is computed as the ratio of the lengths of the major axis to the minor axis, where a value of 1 indicates a circle and 0 indicates a line. The size corresponds to the area of the ellipse. Performance in the tracing task was quantified by the total area between the template and a subject’s hand path. Regardless of whether the subject’s hand path was inside or outside the template, the enclosed area was given a positive value.

Statistical analysis by ANOVA tested for differences in the between-subjects factor of diagnosis (control subjects and patients) and the within-subject factor of condition (Baseline, CW, and Isotropic). Paired t-tests were also used to compare repeated measures (CW and Isotropic perturbations) within a group.

RESULTS

Impedance measurements. An estimate of impedance was obtained for each subject during the Baseline Pre, CW, Isotropic, and Baseline Post sessions. The estimated M, B, and K, in addition to the measured kinematics, were used to reconstruct the forces applied at the hand, which were then correlated with the actual force trajectories. For the impedance measurements in all conditions, correlation coefficients for the control subjects and patients were 0.83 ± 0.07 and 0.81 ± 0.06, respectively.

Similar to previously reported impedance estimates, the mass ellipse was roughly aligned with the forearm, whereas the baseline stiffness ellipse generally pointed along the axis connecting the hand and the shoulder (Tsuji et al. 1995). A large range of stiffness values has been reported, as the magnitude of estimated baseline stiffness values depends on the perturbation amplitude (Gomi and Kawato 1996). Our stiffness estimates were of the same order of magnitude as those reported by Tsuji et al. (1995).

Postural maintenance performance. Performance in the postural maintenance task was measured by the amount of time the hand cursor was outside the target after a force perturbation.

The timer stopped once the hand was completely within the target and remained there for 1 s, thus penalizing any overshooting or oscillatory movements around the target.

Figure 2 shows group performance during the postural maintenance tasks, with the time-out metric averaged over the last 20 perturbations in each block (data collapsed across perturbation direction). All subjects were able to maintain a static arm posture better during the CW perturbations compared with the Isotropic perturbations. This is not surprising since the Isotropic perturbations were less predictable, occurring in eight different directions instead of two. Averaging the time-out metric across all six blocks for each subject, a two-way ANOVA verified a main effect of condition (CW/Isotropic, P < 0.0001), with subjects spending more time outside the target in the Isotropic condition, and a main effect of diagnosis (control subjects/patients, P = 0.0096), with patients taking a longer time to recover from the perturbation. There was no interaction effect (P = 0.11).

Fig. 2. Kinematics of postural maintenance task. A: representative perturbation kinematics (mean ± SD) of a control subject and a patient in response to CW (top) and Isotropic (bottom) perturbations. Position trajectories were collapsed over all directions, where a positive value represents displacement in the direction of the force perturbation. The perturbation was applied between the dotted lines. The shaded gray region represents the area in which the hand cursor was completely within the target. B: group data for the time spent outside the target (mean ± SE). The timer started upon initiation of the force perturbation and ended when the subject’s hand was inside the target and held there for 1 s. C: overshoot of the target (mean ± SE), after the force perturbation, in control subjects (C) and patients (P). Overshoot was measured as the maximum negative displacement (in the direction opposite the applied perturbation). Data were averaged over the last 20 trials of each block, over all 6 blocks. *P < 0.05.
The control subjects showed improved performance over time, whereas the performance of the patients appeared more variable. A paired \( t \)-test comparing performance in the first and last blocks showed a significant improvement in the control subjects for both the CW (\( P = 0.004 \)) and Isotropic (\( P = 0.04 \)) perturbations but no difference in the patients (\( P = 0.83 \); Isotropic, \( P = 0.93 \)).

In addition, we observed that subjects tended to overshoot the target when restoring their hand position after the perturbations. A two-way ANOVA revealed a main effect of condition (\( P = 0.005 \)), with subjects overshooting the target more after Isotropic perturbations, but no main effect of diagnosis (\( P = 0.29 \)). There was also an interaction effect (\( P = 0.02 \)), indicating that patients exhibited larger overshoot than control subjects, but only in the Isotropic condition.

**Stiffness modulation.** The design of the CW and Isotropic Perturbation sessions was intended to cause different modulation of arm stiffness, as previously shown in Darainy et al. (2004). For the CW session, the axis along which perturbations were applied was \( 70 \pm 7^\circ \) and \( 77 \pm 9^\circ \) for the control subjects and patients, respectively. An ANOVA showed that there was no significant difference between the perturbation directions for the two groups.

On average, both groups showed counterclockwise rotation (increased angle of orientation) of their hand stiffness ellipse from the CW to the Isotropic condition (Fig. 3A). As previously described, the orientation of the ellipse can be determined by singular value decomposition of the representative matrix. Significant rotation of the stiffness ellipse was confirmed by one-sided pairwise \( t \)-tests for control subjects (\( P < 0.0001 \)) and patients (\( P = 0.012 \)). A one-way ANOVA showed a main effect of diagnosis (\( P = 0.05 \)). Although the stiffness ellipse of the CW condition was rotated clockwise to that of the Isotropic condition, it was still far from aligning with the axis along which CW perturbations were applied. The orientation of the hand stiffness ellipse was offset from the axis of instability by \( 44 \pm 8^\circ \) for control subjects and \( 38 \pm 10^\circ \) for patients. A one-way ANOVA showed no main effect of diagnosis (\( P = 0.12 \)). This agrees with previous work that found smaller orientation changes for static tasks compared with movement tasks (Burdet et al. 2001; Darainy et al. 2004).

The two other properties characterizing an ellipse are its aspect ratio and size. For the control subjects the aspect ratio of their hand stiffness ellipse decreased from the CW to the Isotropic condition (1-sided pairwise \( t \)-test, \( P = 0.008 \)), whereas no significant difference was seen in the patients (\( P = 0.12 \)) (Fig. 3A). This indicates that the stiffness ellipse of the control subjects was more circular in the Isotropic than the CW condition. This intuitively makes sense, as the Isotropic session required subjects to resist perturbations in many different directions.

The control subjects were also better at modifying the size of their hand stiffness ellipse between the two perturbation conditions (Fig. 3A). Their stiffness ellipse was larger in the Isotropic than the CW condition (1-sided pairwise \( t \)-test, \( P = 0.02 \)), whereas the patients (\( P = 0.31 \)) failed to show a consistent change in ellipse size. The greater overall stiffness of the control subjects in the Isotropic condition was also shown in the Darainy et al. (2004) study.
Figure 3B shows the average hand stiffness ellipse size for the Baseline Pre and Post sessions (data combined) and the CW and Isotropic sessions. A two-way ANOVA showed a main effect of session \( (P < 0.0001) \), and a post hoc Tukey’s test confirmed that all subjects were stiffer in the CW and Isotropic conditions compared with the Baseline sessions. There was no main effect of group \( (P = 0.9) \); the stiffness magnitude of the control subjects and patients was not significantly different for any of the three conditions.

Individual hand stiffness ellipses, estimated from the CW and Isotropic sessions, of each control subject and patient are shown in Fig. 4. The variance of the estimated orientation due to trial fluctuations was computed with a bootstrap method (Gomi and Osu 1998). During both the CW and Isotropic conditions, impedance measurements (position displacements) were applied six times in each of the eight directions. For a particular direction, six measurements were randomly chosen, with repeated measurements allowed, and the average trajectories \( (x, \dot{x}, \ddot{x}, f) \) were computed (462 possible combinations). This was done for each of the eight directions, thus forming one data set (462^8 possible data set combinations). We repeated this process 300 times, computing the stiffness matrix and ellipse orientation from each data set. Figure 4 shows the probability density function of the estimated stiffness ellipse orientation for each subject. Estimates from the CW and Isotropic data sets (each containing 300 values) were randomly paired, and the difference in orientation was computed. The percentage of pairs that showed a positive change in orientation was then determined. For all but 3 of the 11 control subjects, their hand stiffness ellipse in the Isotropic condition was rotated counterclockwise from that of the CW condition for at least 95% of the data sets. Only 5 of the 11 patients showed such counterclockwise rotation of their stiffness ellipse.

Changes in the hand stiffness ellipse can also be related to changes in shoulder and elbow joint stiffness (Eq. 3). For each subject, hand stiffness matrices \( K \) for the CW and Isotropic conditions were transformed into joint stiffness matrices \( R \). A ratio of the \( R_{\theta\theta} \) to \( R_{\theta e} \) terms (Eq. 5) can provide insight into the relative shoulder and elbow stiffness. Both groups experienced an increase in this ratio from the CW to the Isotropic condition (control subjects: \( P < 0.0001 \); patients: \( P = 0.001 \)).

Differences in the nature of the CW and Isotropic perturbations can explain the increase in shoulder stiffness. Given the direction of perturbations, the CW session resulted in more displacement at the elbow joint. Alternatively, the Isotropic perturbations produced movement at both joints, because of the forces in different directions, causing subjects to increase stiffness of the shoulder joint in order to maintain their arm posture.

The change in joint stiffness can help to explain the rotation of the hand stiffness ellipse. Gomi and Osu (1998) made measurements of the arm stiffness ellipse while subjects voluntarily controlled cocontraction of different agonist-antagonist muscle pairs, using EMG biofeedback. In all five arm
configurations tested, cocontraction of the shoulder muscles resulted in counterclockwise rotation of the stiffness ellipse, and the joint stiffness $K_{ss}$ value was larger than the $K_{se}$ value. Their results are consistent with the changes in hand and joint stiffness reported in our experiment. Furthermore, we can infer that our subjects increased cocontraction of muscles crossing the shoulder joint during the Isotropic condition compared with the CW condition.

**Tracing performance.** Performance in the tracing task was evaluated throughout the Baseline Pre, CW, Isotropic, and Baseline Post sessions. Figure 5A shows example hand trajectories of a representative patient. During the Baseline Pre session, the patient’s hand deviated considerably from the parallelogram template. Tracing performance improved during both the CW and Isotropic sessions, with the subject’s hand following the template more closely. During the Baseline Post session, however, the patient’s performance declined, resembling the hand trace in the Baseline Pre session.

As explained in Experimental protocol, the parallelogram shape was chosen to separate the effects of increased shoulder and elbow stiffness on movement. However, the differences in joint stiffness between the CW and Isotropic sessions did not elicit any detectable changes in tracing performance. General increases in stiffness, as determined by the size of the hand stiffness ellipse, appeared to have a much larger effect on tracing performance for the patients (Fig. 5B). During the Baseline Pre and Post sessions, when subjects were instructed to keep their arm relaxed, the measured stiffness was low. Thus data from these two sessions were combined. Alternatively, hand stiffness was high during the CW and Isotropic Perturbation sessions, during which subjects attempted to maintain an arm posture while resisting perturbations. Data from the CW and Isotropic sessions were thus combined. One-way paired $t$-tests confirmed that stiffness during the perturbation sessions was significantly higher than stiffness during the baseline sessions for both control subjects ($P = 0.0001$) and patients ($P = 0.01$).

This difference in overall stiffness, however, only had an effect on the tracing performance of patients, as determined by the total area between the template and a subject’s hand trajectory. One-way paired $t$-tests were used to assess changes in tracing performance. While patients showed a decrease in the trace area error ($P = 0.03$), control subjects showed no such improvement in their trace performance ($P = 0.99$). An additional paired $t$-test showed no difference between the patients’ trace area error during the Baseline Pre and Post sessions ($P = 0.29$), suggesting that their improved performance during the CW and Isotropic sessions was not simply due to more practice with the tracing task.

All subjects completed the tracing task within a comparable amount of time (Fig. 5C). A two-way ANOVA showed no main effects of diagnosis or condition and no interaction effect (all $P > 0.27$). The average hand speed for all subjects was 7 cm/s, and there were no significant main effects or interaction effect (all $P > 0.24$). Thus the improved tracing performance cannot be explained by slower movement.

**DISCUSSION**

During a postural maintenance task, both patients and control subjects were able to increase their arm stiffness to resist the two different types of force perturbations presented. However, the control subjects were better than patients at selectively modulating their arm stiffness for the different types of perturbations. Interestingly, only the cerebellar patients showed transfer from the postural maintenance task to the tracing task, improving their movement performance after increased stiffness in a static posture. For the control subjects, performance in the tracing task was not influenced by the previous posture task.

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**Fig. 5.** Trace performance. A: traces from a representative patient during the Baseline Pre, CW, Isotropic, and Baseline Post sessions. Trace area error between the template (blue) and patient’s hand path (black) is shown in gray. B: the size of the hand stiffness ellipse (mean ± SE) was greater in the Perturbation sessions (CW and Isotropic measurements averaged) than in the Baseline sessions (Pre and Post measurements averaged) for both control subjects and patients. However, only the patients showed an improvement in trace area error between the Baseline and Perturbation sessions. Statistics represent the results of 1-way paired $t$-tests ($*P < 0.05$). C: time to perform the tracing task did not differ between groups or conditions.
Impaired stiffness modulation in cerebellar ataxia. All subjects were capable of generally increasing arm stiffness to maintain their initial arm posture under different force perturbations. While the majority of the age-matched control subjects were able to specifically modulate their arm impedance to resist the CW and Isotropic perturbations, this ability was impaired in the patients with cerebellar ataxia. On average, the control subjects modified all aspects of the hand stiffness ellipse—orientation, aspect ratio, and size—depending on the nature of the perturbations. Alternatively, the patient group only showed slight counterclockwise rotation of the stiffness ellipse when transitioning from the CW to the Isotropic session, with 6 of the 11 patients failing to show significant rotation in the proper direction at all. In addition, they did not appear to modulate the stiffness ellipse aspect ratio or size. For all subjects, the observed changes in the hand stiffness ellipse from the CW to the Isotropic session were primarily due to increases in shoulder joint stiffness.

In light of this result and previous studies, it may be that the cerebellum participates in fine-tuning of stiffness control. Hermansdorfer et al. (1994) reported normal increases in the overall magnitude of stiffness generated by cerebellar patients in a precision grip task; this may be akin to our finding of preserved ability to generally increase arm stiffness. They did not test the specificity of stiffness in its directional properties, which is where we found deficits. Thus, while the ability to generally increase stiffness appears intact despite cerebellar degeneration, the cerebellum may be involved in controlling muscle cocontraction to directionally tune limb stiffness to instabilities. Similar to other studies reporting abnormal perturbation responses due to cerebellar deficits (Hermansdorfer et al. 1994; Timmann et al. 2000), we found no correlation between ataxia severity (ICARS score) and the ability to modulate the hand stiffness ellipse.

The deficit in arm stiffness modulation of the patients suggests that the cerebellum may be contributing to impedance control. This type of cerebellar function was proposed by Smith and colleagues, who have shown cerebellar activity related to cocontraction in monkeys. Discharge frequency of task-related dentate and interposed nuclei increased with cocontraction of the forearm muscles (Wetts et al. 1985), whereas Purkinje cells decreased their firing (Frysinger et al. 1984). Monzee and Smith (2004) also trained monkeys to hold an object at a fixed position while resisting force perturbations. Activity in approximately one-third of the recorded interposed and dentate nuclei gradually increased as the monkeys learned to produce preparatory increases in grip force and wrist stiffness prior to the predictable perturbations. However, because of the limited number of studies regarding the cerebellum and impedance control, the exact role of the cerebellum in feedforward stiffness modulation via cocontraction is unknown.

How do these findings fit in with current thinking about cerebellar function? A prominent hypothesis is that the cerebellum is important for making predictions that can be used by other regions of the brain to optimize their respective functions (reviewed in Bastian 2011). For movement control, the cerebellum may act as a forward model to predict the consequences of motor output (Ebner and Pasalar 2008; Miall et al. 2007). This idea is often applied in the context of body movement. An efferent copy of the motor commands, in addition to knowledge of the dynamics of the environment and the musculoskeletal system, can be used to predict the state of the body—kinematics (position and derivatives) and/or somatosensory feedback. Impaired forward model prediction has been used to explain the abnormal motor behavior of cerebellar patients, including dynamics control during movement (Bastian 2006), motor adaptation (Tseng et al. 2007), and grip force (Rost et al. 2005). Extension of this concept to include dynamics parameters in the predicted state could suggest that the cerebellum also predicts the effect of muscle cocontraction on limb impedance. Faulty estimation of the effective limb impedance could explain why cerebellar patients were more impaired than control subjects at selectively controlling their arm stiffness. Alternatively, the cerebellar patients may have used a compensatory strategy of generalized cocontraction that masked their ability to effectively modulate arm stiffness. Other studies have shown that cerebellar patients increased cocontraction during slow voluntary arm movement (Beppu et al. 1984) and while maintaining full body postural equilibrium (Asaka and Wang 2011; Mummel et al. 1998). Increased cocontraction may help them minimize the instabilities that arise from their cerebellar deficits. It should also be noted that the patients’ impaired stiffness modulation cannot be attributed to an inability to increase arm stiffness, since their hand stiffness ellipses were no different in size from those of control subjects (Fig. 3B).

Methodological considerations of stiffness modulation. While the control subjects in our experiment were better at modulating arm stiffness, their changes in hand stiffness ellipse orientation were much smaller than those reported on the first day of training in the Darainy et al. (2004) study. This could be due to methodological differences between the two studies. Each of the Darainy et al. (2004) subjects only practiced the postural maintenance task under one perturbation condition, so the range of orientation change was a between-subjects comparison. In contrast, the subjects in our repeated-measures study experienced both perturbation conditions. The first CW session may have interfered with our subjects’ ability to learn a new stiffness pattern in the subsequent Isotropic session (Darainy et al. 2006), thus resulting in a smaller orientation change. Our methodology differed from prior studies because of the practical considerations of testing cerebellar patients.

Postural maintenance task affects ensuing tracing performance in patients. The cerebellar patients generally showed worse performance than the control subjects in our tracing task, which was not surprising given that tracing ability is one of the assessments in the ICARS. However, it was interesting that increasing stiffness in the postural maintenance task had a positive effect on patients’ subsequent tracing. While it was expected that subjects increase their limb stiffness in response to perturbations in the static task, it was unclear as to whether their change in impedance would transfer to the subsequent tracing task. Although we did not estimate subjects’ impedance during the trace itself, we attribute patients’ improved performance at the end of the CW and Isotropic Perturbation blocks to increased stiffness. The decrease in trace error of patients cannot be explained as an effect of practice. Tracing performance during the final Baseline Post session (when stiffness was low) was worse than that of the previous CW and Isotropic sessions (when stiffness was high). As for the control subjects, their tracing performance was already good in the baseline session, so the lack of transfer may be attributed to a ceiling effect.
The effect of the postural maintenance task on the tracing task in patients was of particular interest, given that posture and movement are often considered to be distinctly controlled. A variety of experiments have suggested separate control processes based on task-dependent differences in neural activity and gains (Crammond and Kalaska 1996; Kurtzer et al. 2005), reflexes (Stein and Capaday 1988), and motor adaptation of midmovement and end point phases (Lackner and Dizio 1994). With regard to impedance modulation, the regulation of cocontraction patterns also appears to differ during posture and movement, as the coupling of monoarticular and biarticular arm muscle cocontraction is lower during movement than isometric conditions (Osu and Gomi 1999). Although postural maintenance is commonly associated with increased stiffness via cocontraction, and movement with dynamics control via reciprocal activation, such a distinct categorization may not exist, given that cocontraction can be used during both posture and movement (Humphrey and Reed 1983; Kurtzer et al. 2005).

In the primary motor cortex, some neurons have shown both posture- and movement-related activity with similar directional tuning but different gains (Crammond and Kalaska 1996; Kurtzer et al. 2005). If some of these neurons are also involved in cocontraction, the cerebellar patients in our study may have been able to take advantage of these intact networks to transition from the postural maintenance task to the tracing task. Additionally, the relatively slow pace of our tracing task, as opposed to a quick ballistic movement, may have also enhanced the transfer of stiffness between the two conditions.

Implications for patients with ataxia. People with cerebellar ataxia commonly rely on alternative strategies to help compensate for their movement deficits. In our experiment, patients’ tracing performance was affected by the state of their arm immediately prior to movement. Although a state of increased stiffness helped patients perform the tracing task, they did not voluntarily apply this strategy to improve performance during the Baseline Post session. One patient commented that he had an easier time following the template during the CW and Isotropic sessions compared with the Baseline Post session. A potential rehabilitation method could involve teaching patients to increase limb stiffness to help counteract their motor deficits. However, a more conscious strategy may be necessary for patients to strategically increase impedance during certain movements or phases of movement.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: T.L.G. conception and design of research; T.L.G. interpreted results of experiments; T.L.G. prepared figures; T.L.G., A.J.B., and A.M.O. edited and revised manuscript; T.L.G., A.J.B., and A.M.O. approved final version of manuscript.

REFERENCES


