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Patients with Cerebellar Ataxia Do Not Benefit from Limb Weights

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Abstract

Patients with cerebellar ataxia are sometimes treated by the addition of mass to the limbs, though this practice has received limited study. Recent work suggests that adding mass to the limbs might have predictable effects on the pattern of cerebellar dysmetria (i.e., over or undershooting) that depends on a hypothesized mismatch between the actual limb inertia and the brain's estimate of limb inertia. Based on this model, we predicted that addition of mass would only be effective in reducing dysmetria in hypometric patients. Cerebellar patients were challenged with making a single-joint, single degree of freedom reaching movement while various limb masses were tested. In this task, some single-jointed reaches were improved by adding masses that were optimized in a patient-specific manner. However, this improvement did not translate to multi-joint movements. In multi-joint movements, the "best" patient-specific masses (as determined in a single-joint task) generally exacerbated subjects' reaching errors. This finding raises questions as to the merits of adding limb weights as a therapy to mitigate the effects of dysmetria.

Keywords Cerebellar Ataxia · Humans · Physical therapy modalities · Robotics

Introduction

The addition of mass to the limbs of patients with ataxia has become a common, though debated, therapeutic practice. In patients with cerebellar ataxia, limited evidence has been published attesting to its efficacy. For example, M. H. Morgan's 1975 paper "Ataxia and Weights" reported that three out of six patients with degenerative disorders of the cerebellum experienced improvement with the addition of weight in a simple point to point reaching task [1]. While this was an interesting observation, the hypothesis was unclear as to why three patients improved and the other three did not. Indeed, a study from Manto et al. concluded that hypermetria was exacerbated by the addition of mass to the limb [2]. Torso weighting has also been tested in this patient population with the aim of improving gait, but no systematic improvement has been demonstrated [3].

Bhanpuri et al. recently found that cerebellar damage might cause an inertial mismatch between an internal representation of body dynamics and the actual body dynamics [4]. Due to cerebellar patients' impairments in motor learning, this mismatch does not improve over time. This work showed that patients could be categorized into two broad phenotypes: overshooters (hypermetric) and undershooters (hypometric) in a single-joint reaching task. According to these results, the hypometric patients underestimated their limb's inertia and hypermetric patients overestimated it. This work also showed that altering the apparent inertia of the limb to correct the mismatch via a robot could improve simple single-jointed elbow movements for both types of patients.

Based on this work, it follows that for single-joint movements, hypometric patients should theoretically improve with the addition of mass to the limb because it would reduce the discrepancy between the internal model and the actual limb

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dynamics. Conversely, hypermetric patients should theoretically worsen (i.e., overshoot more) with the addition of mass. This would provide a possible explanation for the disparity in outcomes seen in the literature [1, 2]. Here, we set out to replicate the effect of adding inertia using actual masses rather than robot-rendered inertia and then investigate the effectiveness of this intervention in multi-joint movements.

Patients and Methods

Patient Selection

The cerebellar patient population tested is detailed in Table 1. Each subject used his or her dominant arm for the task, with one exception. Subject 10 had unilateral cerebellar damage, so she completed all tasks with her affected, non-dominant hand. All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study. Patients were excluded if they had any clinical or MRI evidence of damage to extra-cerebellar brain structures, dementia, aphasia, or peripheral vestibular loss. We performed a clinical examination of each individual's arms for sensory loss (Semmes Weinstein monofilaments), proprioception, hyperreflexia, and abnormal muscle tone and only tested the individuals who had none of these sensorimotor abnormalities in their arms.

Experimental Apparatus

All experiments were performed using the Kinarm Exoskeleton robot (BKIN Technologies Ltd.), shown in Fig. 1a, which provided gravitational arm support while restricting arm movement to a horizontal plane. A black horizontal screen occluded the subject's view of their arm. On the screen, a white, 1-cm-diameter circle (cursor) was displayed, representing the veridical position of the subject's fingertip (Fig. 1b–d). The display was calibrated so that the cursor would appear as if it were on top of the fingertip, as viewed by the subject. A black drape occluded the subject's view of the upper arm and of mass bars added to the robot.

Mass bars were made from flat rectangular metal bars (30.5-cm long, in increments of 50 g) and were attached to the bottom of robot arm support using brackets. Interlocking plastic strips, attached to the mass bars and brackets, were used to securely mount the mass bars to the brackets or additional bars without slipping. We chose to use physical masses in this experiment because they are used clinically in an effort to reduce ataxia. Physical masses are also advantageous relative to robot-mediated torque because they eliminate any possible effect of processing delay or unwanted motor dynamics present within the robot.

Mass bars were attached to the robot so that the center of mass (COM) of the bar approximated the COM of the limb segment. The COM of the limb segment was calculated based on anthropometric tables, using the subject's forearm, hand, and upper arm lengths as well as the subject's weight [5].

Table 1 Patient demographics

Subject no.	Patient age	Sex	Pathology	ICARS	Best forearm mass (g)	Best upper arm mass (g)	Percent hypometric reaches (%)	Percent on-target reaches (%)	Percent hypermetric reaches (%)
1	44	M	SCA8	60	100	0	78	11	11
2	52	M	ADCAIII	28	1200	0	90	10	0
3	54	M	Sporadic	59	600	0	100	0	0
4	55	F	SCA8	41	0	600	40	50	10
5	60	M	MSA-C	54	300	500	0	29	71
6	62	M	SCA6/8	60	600	200	0	25	75
7	63	M	SCA6	41	500	600	43	43	14
8	65	M	Idiopathic	34	600	200	90	10	0
9	65	M	ADCAIII	12	500	0	50	50	0
10	67	F	L Stroke	32	800	0	78	22	0
11	69	F	ADCAIII	52	600	0	100	0	0
12	72	F	SCA6	49	700	500	100	0	0
13	73	M	SCA6	50	700	0	38	46	15

The demographics of the patients who were tested, the masses that were determined experimentally to provide the greatest improvement in dysmetria, and the percentages of dysmetric reaches

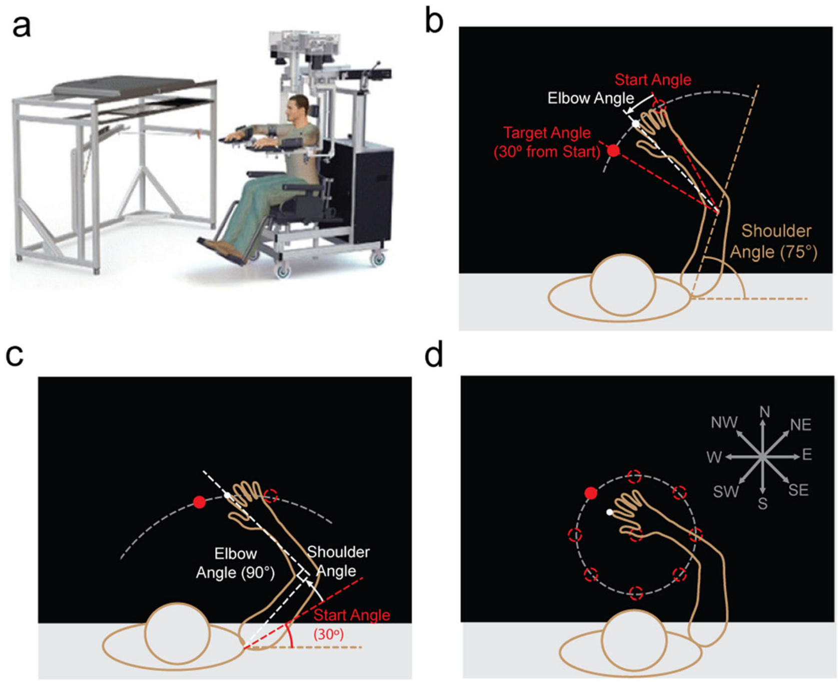

Fig. 1 Experimental setup. Dashed lines and the arm position are not visible to subjects. **a** The Kinarm Exoskeleton robot (BKIN Technologies Ltd.) where all experiments took place. **b** The elbow-only task. **c** The shoulder-only task. **d** The eight-target multi-joint task. The compass rose is not visible to the subjects. The compass rose indicates the naming convention for the eight targets

Experiment 1: Adding Mass to Planar, Single-Joint Movements

In this experiment, subjects completed single-joint 30° flexion and extension movements with various masses added to their limb in order to determine the masses which would most greatly reduce each subject's dysmetria.

For the first portion of this experiment, the elbow was the only freely mobile joint; the shoulder was locked at a 75° angle and the wrist was immobile as shown in Fig. 1b. A red target dot appeared at an elbow angle of 55°. Subjects were instructed to move the white dot (finger cursor) to the red dot (the target, 1.5-cm diameter) as smoothly and accurately as possible without over or undershooting. After the subject kept his or her cursor within the red dot for 2 s, the red dot disappeared and another red dot appeared at an elbow angle of 85° (+ 30°). After the subject made a 30° flexion movement to this second target and remained within the second target for 2 s, the original target reappeared and the subject made a 30° extension movement back to the original target. Ten repetitions of this cycle comprised a block of trials. If subjects did not enter a 1.75-cm radius of the destination target within 1 s of leaving the start target, the target changed from red to blue, indicating the subject should try to move faster during the next trial. The reach was timed from when the subject left one target to when they entered the destination target.

The angle of the subject's angle of first correction (a measure of initial reach magnitude) was computed for each individual reach. The angle of first correction was defined as the angular position of the subject's arm when the acceleration crossed two degrees per second squared for a second time or when the velocity crossed two degrees per second after the initiation of movement—whichever came first. From this angle, we could categorize each reach as hypermetric (overshooting), hypometric (undershooting), or on-target. We classified angles of first correction less than 29.1° as hypometric and those greater than 30.9° as hypermetric. These thresholds for an on-target reach were computed as being within ± 3% of 30°.

Subjects completed a block of reaches with each of the following masses added: 0, 200, 400, 600, 800, and 1000 g. Each reach was categorized as hypometric, hypermetric, or on-target. If a block of reaches had a mode of "on-target," that mass was categorized as the "best" mass for the subject. If multiple masses yielded a mode of "on-target," the mass which had the most on-target reaches was selected as the best mass. When the results were too similar to distinguish, the smaller mass was chosen.

If a satisfactory mass had not already been determined, more trials were conducted to try to find the best mass for that subject. Based on the mode of the flexion movement categories (hypometric, hypermetric, on-target) from a block of trials, the amount of mass added to the forearm was increased or decreased based on the PEST algorithm [6]. For hypometric reaches, the amount of mass was increased, and for hypermetric reaches, the amount of mass was decreased. The PEST algorithm stopped when [1] two blocks of reaches with zero added mass were hypermetric (i.e., we could remove no more mass as would be needed to correct hypermetria) [2], two blocks of reaches with the same applied mass were classified as on-target or [3] when the subject became fatigued. The starting mass was 0 g, the maximum mass was 1400 g, and the smallest mass increment was 50 g.

The second portion of this experiment was the same as the first portion except that the elbow was locked at a 90° angle and free motion of the shoulder joint was allowed (Fig. 1c). The start target angle for the shoulder was at 30°, and the second target was at 60°. Thus, all "flexion" and "extension" movements (here horizontal adduction and horizontal abduction of the shoulder joint) again had an amplitude of 30°. The best mass from the first portion of the experiment was placed on the distal limb. The standard masses were tested again, adding 0, 200, 400, 600, 800, and 1000 g to the proximal limb (upper arm). If 0 g on the proximal limb resulted in hypermetria, mass on the distal limb was reduced until the hypermetria was eliminated. The PEST algorithm was repeated, adjusting the amount of mass added to the upper arm. A single best mass value for the upper arm was obtained, leaving each subject with a best forearm mass and a best upper arm mass. A summary of the experimental procedure for experiments 1 and 2 is detailed in Table 2.

Subjects were not told that masses were being added to the robot (when questioned after all experiments had been concluded, most subjects were surprised to learn that masses had been added). The mass which most greatly reduced the subject's dysmetria remained on the forearm for the second portion of this experiment (even if that mass was 0 g).

Experiment 2: The Effect of Added Mass on Planar Multi-Joint Movements

In experiment 2, both the elbow and shoulder joints were free to move. A center "start" target was projected at the subject's midline. Eight "end" targets were placed at a 15-cm radius from the start target, as shown in Fig. 1d. The center target position was adjusted so that the subject was able to reach all eight "end" targets. All targets were 2 cm in diameter, and the cursor was 1 cm in diameter.

All subjects started the experiment at the central target. One of the radial targets was randomly displayed and the subject was instructed to move as smoothly and accurately to the target without over or undershooting. If a subject did not complete the reach within 1 s, the target changed from red to blue, indicating the subject should try to move faster during the next reach. When a subject's cursor was within a target, the border of the target would turn white. Once the subject remained within the end target for 2 s, the central target reappeared, and the subject moved back to the start position. The subject, again, had to remain within the start target for 2 s before the process repeated with another of the radial targets. Subjects completed five blocks. Each block consisted of reaches to all eight targets in a random order.

After the completion of experiments 1 and 2, we re-tested four subjects on the experiment 1 forearm task, but we randomized the order of the applied weight for each subject. This purpose of this test was to determine if changes in over or undershooting was an effect of ordering and not an effect of the progressively increasing mass.

Data Repository The data and code associated with this publication are made available through the Johns Hopkins University Data Archive. doi: https://doi.org/10.7281/T1/AYTUVI.

Results

Effect of Mass on Single-Joint Reaching

Figure 2 shows an example of a hypometric patient making elbow flexion and extension movements, with and without the optimal mass. This figure shows the time series of mean elbow angular position, velocity, and acceleration. Note that this patient showed the biggest beneficial response to the added mass, with a clear reduction of hypometria and reduced terminal oscillation (i.e., corrective movements).

The majority of our subjects tended to undershoot the target during most of their elbow movements without the mass (Table 1). We checked to see if, across subjects, there was a relationship between movement speed (i.e., mean peak

Table 2 Experimental procedure for experiments 1 and 2

Exp. no.	Experiment	Mobile joints	Participation
1	0, 200, 400, 600, 800, 1000 g added to distal limb	Elbow free, shoulder locked	All subjects
	PEST masses added to distal limb	Elbow free, shoulder locked	If best distal mass had not yet been determined
	0, 200, 400, 600, 800, 1000 g added to proximal limb (best distal mass remained on distal limb)	Shoulder free, elbow locked	All subjects
	PEST masses added to proximal limb (best distal mass remained on distal limb)	Shoulder free, elbow locked	If best proximal mass had not yet been determined
2	Best distal and best proximal masses added	Elbow and shoulder free	All subjects
	No masses added	Elbow and shoulder free	All subjects

This details the procedure for both experiments 1 and 2

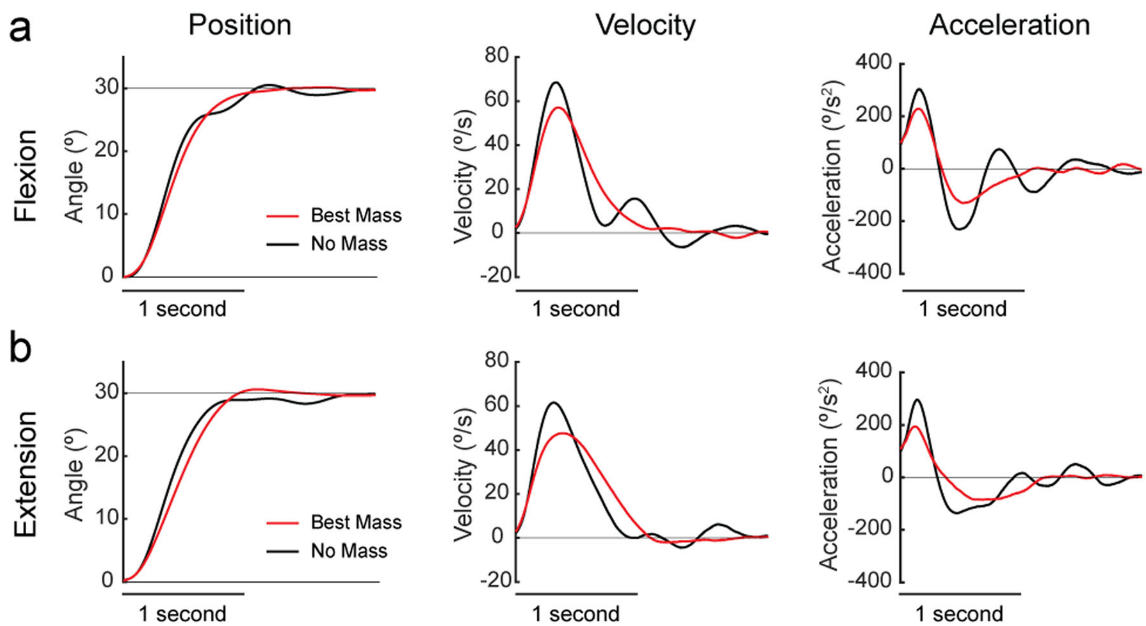

Fig. 2 Most improved subject's elbow movements with and without the optimal mass. Position, velocity, and acceleration are shown for a single subject's **a** elbow flexion and **b** extension movements, with and without the best mass. The red lines are mean reach data from P10 with 800 g applied. The black lines are from the same patient with no mass applied. This patient showed the most dramatic improvement out of all patients tested

velocity) and the tendency to undershoot (i.e., percentage of undershooting trials) and found that this was not the case ($r = -0.23$, $p = 0.44$). In other words, subjects who had a large percentage of reaches that undershot the target did not move more slowly.

We then tested whether systematically increasing the mass led to a linear change in the mean angle of the first correction, as would be predicted for the inertia mismatch hypothesis. A linear regression model was fit for each subject moving in the flexion and extension directions using the data from the standard masses of 0, 200, 400, 600, 800, and 1000 g. We then determined if the positive slope of the linear regression model was statistically different from zero. We found that 9 of 13 subjects showed statistically significant ($p < 0.05$) positive slopes with increasing mass for elbow flexion. The remaining four subjects' slopes were not statistically different from zero. In extension, only 4 of the 13 subjects had a statistically significant positive slope ($p < 0.05$) with increasing mass. The remaining nine subjects' slopes were not statistically different from zero. This suggests an asymmetric response to the added mass, which we did not expect based on our hypothesis.

We compared the performance of subjects moving without and with the optimized ("best") mass for flexion and extension movements (Fig. 3). Figure 3a shows the mean angle of first correction, which is our measure of dysmetria and Fig. 3b shows the mean peak velocity for all subjects. Nine subjects undershot the target in both flexion and extension movements when there was no mass added to the forearm. Four of the subjects (P03, P05, P06, and P12) overshot the target during their baseline flexion and/or extension movement (Fig. 3 dashed lines). These subjects theoretically should not benefit from adding mass; the forearm mass should be reduced to improve their movement, which was not possible in this paradigm. As such, we did not include them in the statistical analysis.

During flexion movements, paired t test showed significant improvement for patients who were hypometric in the no-mass condition ($t = -2.50$, $p = 0.04$, Fig. 3a, left). These patients did not show statistically significant slowing ($t = 0.26$, $p = 0.80$, Fig. 3b, left). Extension movements for some hypometric patients were improved, but the group improvement was not statistically significant ($t = -1.38$, $p = 0.21$, Fig. 3a, right). These subjects also did not show statistically significant slowing ($t = 0.42$, $p = 0.69$, Fig. 3b, right).

It should be noted that two of our hypermetric patients experienced an improvement in the flexion task with the addition of the best mass. This was unexpected based on our previous work, which predicted that their hypermetria would worsen. One possibility is that they improved because they slowed the movement down (Fig. 3b). Yet, when those same masses were applied in the extension condition, those subjects became more hypermetric (see subjects P05 and P06 in Fig. 3).

Finally, in preparation for the multi-joint condition, we locked the elbow with the optimal forearm mass and tested shoulder motions as described in the methods. This was done to determine if mass should be added to the upper arm segment. Masses were added using the same incremental scheme followed by PEST methods if necessary. Table 1

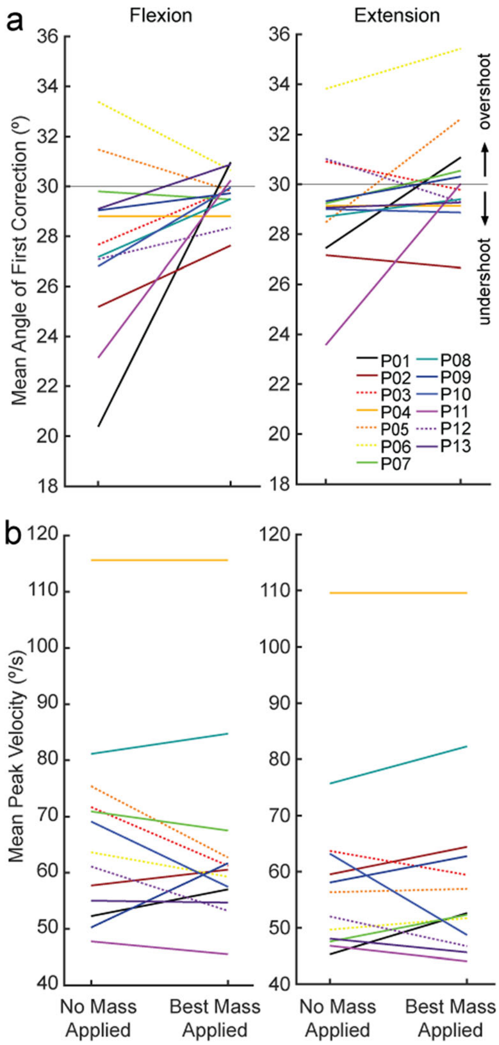

Fig. 3 Hypometric patients improve with best mass only in the elbow flexion condition. **a** The hypometric subjects (solid lines) improve with added mass in the elbow flexion condition ($p < 0.05$). The improvement for the hypometric patients in the elbow extension condition is not statistically significant ($p > 0.05$). The p values are computed using a paired t test (using the distance of mean angle of first correction from 30°) comparing the no mass and best mass conditions for the hypometric subjects. The hypometric subjects are classified as such because they are hypometric in both the flexion and extension conditions with no mass added. **b** The improvement exhibited in **a** is not simply a result of patients slowing their reaches, as there is no statistical difference in mean peak velocity between the no mass and best mass conditions

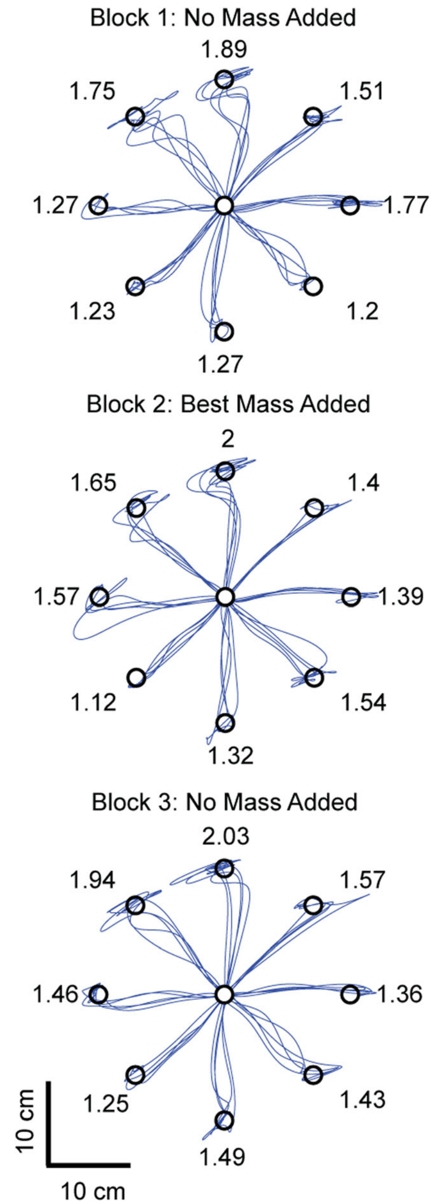

Fig. 4 Most-improved subject's reaching trajectories. Data are shown from P03. The improvement was calculated as the sum over all targets of the differences in mean path length between block 2 and block 3. The numbers indicate the mean path inefficiency

provides the optimal forearm and upper arm masses that were determined and used in the multi-joint experiment.

Effect of Mass on Multi-Jointed Reaching

The addition of the best masses did not improve, and may have worsened, reaching in the multi-joint task. The primary outcome measure for improvement was the path length of the fingertip from the central start target to each end target. This is reported in terms of path inefficiency, which is the ratio of the path length taken to the minimum path length possible. For a straight reaching movement, the path inefficiency would be equal to 1, and for a curved movement, it would be greater than 1. Figure 4 shows the reaching paths from the subject who showed the best result—that is, the added mass slightly improved some reaches and slightly worsened others. The average path inefficiency values are provided for each direction before mass was added, with the mass, and after the mass was removed. Qualitatively, the trajectories of the reaches show similar oscillations at the end target in both the baseline and in the best mass conditions.

Across all subjects, the average path inefficiency either increased (i.e., worsened) or did not change substantially with added mass (Fig. 5a). We performed a two-way ANOVA on

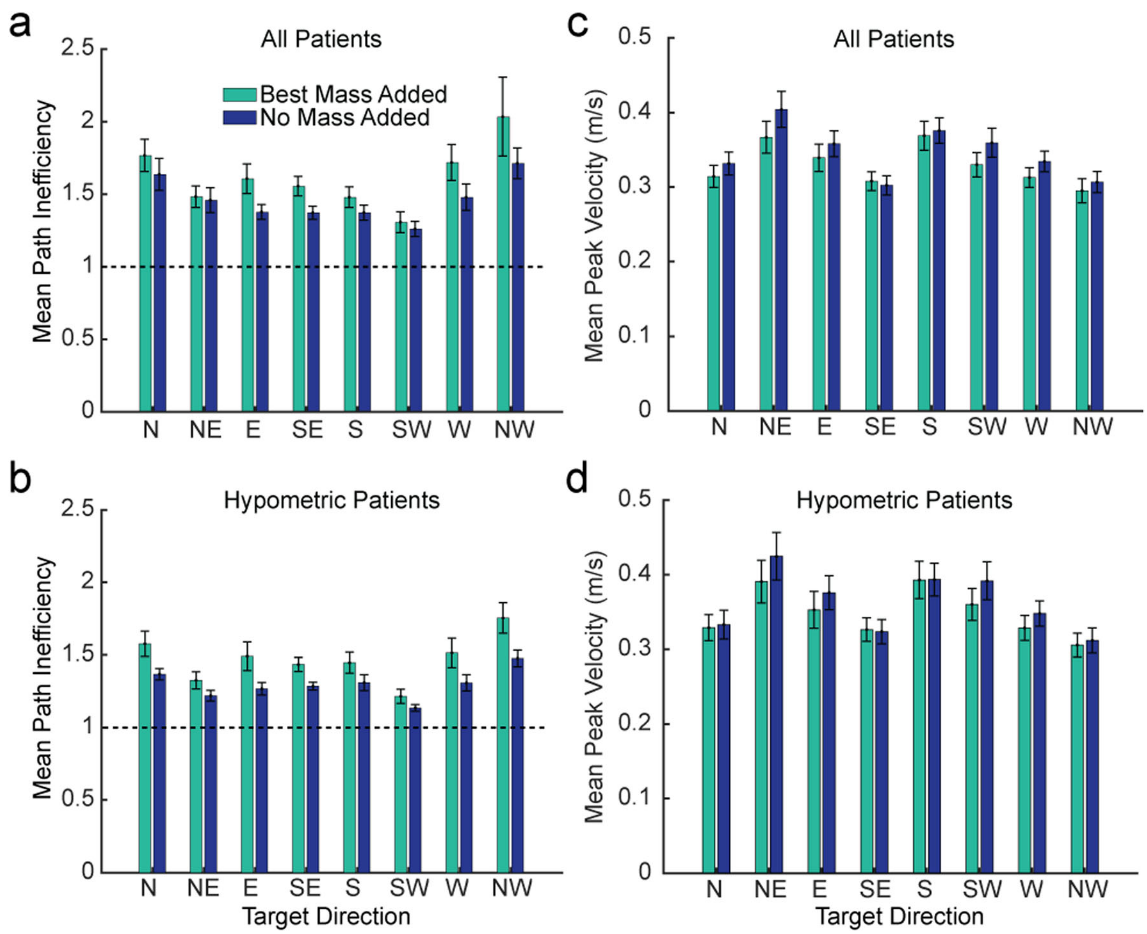

Fig. 5 Addition of individualized best masses does not improve reaching in multi-joint task. A higher mean path inefficiency indicates reaches are more circuitous. Error bars represent standard error of the mean. Reaches which were not completed within the time limit are also included here (to prevent losing data from individual subjects who had difficulty competing the task within the allotted time). **a** When all subject data are analyzed, there is no improvement observed in any direction with addition of the best masses. The dashed lines indicate the minimum possible path inefficiency. **b** When the data from the subset of patients who were hypometric in both the elbow flexion and extension task are analyzed separately, there is still no improvement in average path inefficiency with addition of the best masses. **c**, **d** The mean peak velocity is unchanged when mass is added

the data from all 13 patients to determine the effect of mass and target location on the path inefficiency. In Fig. 5a, there was no difference in path inefficiency based on either mass ($F = 0.53$, $p = 0.47$) or target location ($F = 1.77$, $p = 0.10$). When we assess the subset of nine subjects that were hypometric at baseline in the single-joint experiment (i.e., those that theoretically should improve with increased mass) we still see that the average path inefficiency was similar or worse with the mass (Fig. 5b). We performed another two-way ANOVA on the data from the nine hypometric patients in Fig. 5b, and found no difference in path inefficiency based on mass ($F = 2.93$, $p = 0.09$). However, there was an effect of target location on path inefficiency ($F = 2.11$, $p = 0.05$).

Note that this is not an effect of changes in movement velocity as the peak velocity was unchanged with the addition of mass (Fig. 5c, d). We performed a two-way ANOVA to determine the effect of mass and target location on peak velocity. In Fig. 5c, when analyzing all 13 patients, there was no effect of mass ($F = 0.04$, $p = 0.85$) or target location ($F = 1.18$, $p = 0.31$) on peak velocity. In Fig. 5d, when analyzing the nine hypometric patients, there still was no effect of mass ($F = 0.05$, $p = 0.82$) or target location ($F = 0.91$, $p = 0.50$) on peak velocity.

To rule out any effect of learning, fatigue, or other ordering effects, five subjects also completed the task without added mass before repeating the task with the best mass, and finally repeating it again without mass. No ordering effect was apparent. If the subjects were learning the task, we would expect a progressive decrease in path inefficiency between the first trial without mass, the second trial with mass, and the final trial without mass. This did not occur.

Discussion

In this study, we showed that we could not systematically reduce reaching ataxia via individualized weighting of patients' arms. Our approach was to (1) systematically add mass to the forearm and upper arm segments to optimize the effect on single-jointed movements and (2) determine if the optimized mass combination improved multi-jointed reaching movements across many directions. The results clearly showed some immediate benefit of weighting on single-jointed elbow movements, but no benefit (or worsening) of multi-jointed reaching movements.

These experiments were motivated by a previous study from our group supporting the theory that a mismatch in the brain's internal model versus actual arm inertia could explain cerebellar reaching deficits [4]. That work investigated single-joint elbow flexion movements and corrected the "mismatch" by altering the inertia of the arm using a robot. The arm inertia could therefore either be increased or decreased in order to match an estimate of individual subjects' internal model representation. Increased inertia was found to correct for undershooting and decreased inertia corrected for overshooting.

Here, we tested a more clinically viable method of altering inertia via weighting the arm, and thus could only expect to correct undershooting. Before discussing patients, we think that it is helpful to explain why the addition of a mass would tend to increase the amplitude of reaching, since it may seem counterintuitive. When mass is added, one might think that the subject would generate the same torque about the elbow as in the no-mass condition, and thus the amplitude of the reach would be smaller. Indeed, if the movement were generated by a purely open-loop (feedforward) torque, the overall amplitude would be diminished. However, a subject's arm lags behind the intended trajectory, he/she would increase the torque to try to "catch up," building up momentum in the arm. To stop the arm, he/she would again apply an insufficient counter torque, thus resulting in an increased movement amplitude.

Similar to what was seen previously, we were able to correct single-joint elbow flexion movements that undershot the target [4]. However, our results were not robust for elbow extension movements, which surprised us since we expected that the optimal inertia should be the same, irrespective of movement direction. This is even more apparent in the multi-jointed reaching movements, where the added masses either did not change or worsened reaching movements. No subject showed systematic benefit—the patient with the best response is shown in Fig. 4 and this individual worsened on four of the targets. The lack of any benefit was clear no matter if we considered the entire group, or if we analyzed the subgroup of patients who showed hypometria only. Note that the only single subject with a focal cerebellar lesion (P10) also had a similar pattern of hypometria and response to the weights compared with the rest of the group. Importantly, the peak velocity of all movement types did not change with and without the added weight. This means that the beneficial effect of the mass on elbow flexion movements was not due to subjects slowing down. Likewise, the poor effect of the mass on elbow extension and reaching movements could not be explained by subjects speeding up. This suggests that the hypothesized inertial mismatch model cannot fully account for patient deficits.

Instead, this work suggests that there might be deficits in both the parameters, such as inertia, and the structure of the patients' putative internal model. It would be challenging to identify all the possible parametric and structural deficits in the internal model on a patient-by-patient basis due to the exponential growth of the number of combinations to be assessed. Furthermore, it may be impossible and almost certainly impractical to translate a given patient's deficit into an optimal (passive) weight distribution that improves reaches over a broad range of movements. Instead, an actuated system, such as a robot, would likely be necessary to help subjects compensate for identified mismatches in model parameters and structure.

One might be concerned that the weights that we chose were not large enough to alter movement substantively. We do not think that this is not the case. First, we added masses up to ~ 50% of the human forearm's mass and ~ 25% of the total arm's mass, which we think is a non-trivial amount [5, 7]. Second, we see a systematic increase in movement amplitudes with progressive increase in the weights, suggesting that weighting does indeed have, at least in part, the expected effect. Finally, we used weights that were effectively similar to what was used in the previous study from our lab, and we were able to reproduce the same effect in elbow flexion movements [4].

Conclusion

Here, we were unable to improve cerebellar patient reaching movements with individually optimized weighting. This suggests that treatments aimed at using weights to improve limb ataxia may not be beneficial.

Compliance with Ethical Standards

All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Conflict of Interest The authors declare that they have no conflict of interest.

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