

# The cerebellum is not necessary for visually driven recalibration of hand proprioception

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## ABSTRACT

Decades of research have implicated both cortical and subcortical areas, such as the cerebellum, as playing an important role in motor learning, and even more recently, in predicting the sensory consequences of movement. Still, it is unknown whether the cerebellum also plays a role in recalibrating sensory estimates of hand position following motor learning. To test this, we measured proprioceptive estimates of static hand position in 19 cerebellar patients with local ischemic lesions and 19 healthy controls, both before and after reach training with altered visual feedback of the hand. This altered visual feedback, (30° cursor-rotation) was gradually introduced in order to facilitate reach adaptation in the patient group. We included two different types of training (in separate experiments): the typical visuomotor rotation training where participants had full volition of their hand movements when reaching with the cursor, and sensory exposure training where the direction of participants' hand movements were constrained and gradually deviated from the cursor motion (Cressman, E. K., Henriques, D. Y., 2010. Reach adaptation and proprioceptive recalibration following exposure to misaligned sensory input. *J. Neurophysiol.*, vol. 103, pp. 1888–1895). We found that both healthy individuals and patients showed equivalent shifts in their felt hand position following both types of training. Likewise, as expected given that the cursor-rotation was introduced gradually, patients showed comparable reach aftereffects to those of controls in both types of training. The robust change in felt hand position across controls and cerebellar patients suggests that the cerebellum is not involved in proprioceptive recalibration of the hand.

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## 1. Introduction

Adapting reaching movements to visual or mechanical perturbations of the hand leads not only to changes in motor output, but also to changes in sensory perception of the position and motion of the hand. That is, learning to reach with a rotated cursor or within a velocity-dependent force field leads to systematic changes in where people report feeling the location of their unseen hand in a purely perceptual task, in the direction of the perturbation (Cressman and Henriques, 2009, 2011; Ostry et al., 2010; Salomonczyk et al., 2011; Vahdat et al., 2011). In our visuomotor adaptation studies, the shifts in proprioceptive estimate of hand position are in the order of 20% of the size of the visuomotor distortion. Such changes in felt hand position are much smaller than the reach aftereffects following adaptation. Our lab (Cressman and Henriques, 2010; Salomonczyk et al., 2013) has further shown that similar changes in hand proprioception and reach aftereffects occur even after being exposed

to merely the discrepancy between visual and proprioceptive feedback of the hand. Others have also found that the predicted consequences of the hand movement changes with adapting reaches to altered visual feedback of the hand (Izawa et al., 2012; Synofzik et al., 2008). In other words, when subjects were asked to indicate the direction by which their unseen hand had moved following a volitional out and back reaching movement, they misperceived their outward movement as being again in the direction of the altered visual feedback during the training trials. Together these results suggest that motor learning is associated with some sort of sensory recalibration.

The goal of the current study is to investigate the possible neural structures that may underlie these different motor and sensory outcomes. Specifically, we are interested in the role of the cerebellum not only on motor plasticity but sensory plasticity as well. Patients with cerebellar damage show clear abnormalities when producing movements; including lack of coordination, increased variability and poorer accuracy, as well as deficits in sensorimotor learning (Bastian, 2006, 2008; Criscimagna-Hemminger et al., 2010; Donchin et al., 2012; Rabe et al., 2009; Straube et al., 2001; Timmann et al., 1996; Werner et al., 2010). Neurophysiological studies and theoretical

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models suggest that the cerebellum is involved in comparing predicted or intended movements (based on efference copies of the movement commands provided by the motor cortex) with actual movements (sensory inputs received from the spinal cord and brain), and making the appropriate corrections, as well as updates to these sensorimotor predictions (Bastian, 2006; Shadmehr and Krakauer, 2008; Shadmehr et al., 2010; Werner et al., 2009). As a consequence, the cerebellum plays a critical role in sensorimotor learning and many of the deficits in patients with cerebellar dysfunction can be attributed to a failure to predict or accurately estimate the consequences of motor commands, such as where the hand is and where it should be during and following the movement. For instance, people with an intact cerebellum have no difficulty in adapting reaching movements in response to consistent, predictable perturbations (Criscimagna-Hemminger et al., 2010; Sailer et al., 2005; Timmann et al., 1996; Werner et al., 2010; Werner et al., 2009). One such common perturbation involves altering visual feedback of the hand (by manipulating a cursor that is supposed to represent the unseen hand) while participants reach to visual targets. Compared to healthy individuals, patients with cerebellar dysfunction were unable to adapt (or adapt more poorly) their reaching movements in response to this false visual feedback of the hand (Burciu et al., 2014; Criscimagna-Hemminger et al., 2010; Donchin et al., 2012; Fernandez-Ruiz et al., 2007; Rabe et al., 2009; Taig et al., 2012; Werner et al., 2010, 2009).

Recent studies with patients with cerebellar damage have also begun to couple the location of the damage to the type of motor learning deficits. Werner et al. (2010) found that patients with local lesions to superior cerebellar artery (SCA) territory after cerebellar ischemic infarction appear to have greater deficits (poor learning rate, and smaller aftereffects) than patients with damage to posterior inferior cerebellar artery (PICA) territory when adapting to a visuomotor (cursor) rotation of 60°. Similarly Rabe et al. (2009) observed that SCA patients showed significantly lower levels of adaptation than PICA patients whose adaptation rates did not differ from that of healthy controls. These authors observed that patients with cerebellar degeneration in the more intermediate cerebellar zone of the posterior lobe have more difficulty adapting their reaches to a visuomotor distortion. Those whose locus of degeneration is in the intermediate and lateral zones of the anterior cerebellar cortex tend to be poorer at adapting their reaches to dynamic perturbations such as a velocity-dependent force field (Burciu et al., 2014; Donchin et al., 2012; Rabe et al., 2009). Thus, the locus of damage in the cerebellum appears to be associated with distinct motor learning impairments. It is possible that the resulting sensory or proprioceptive outcomes may also differ.

However, when the perturbation, and thus the error signals, are small and gradually increase in size, these deficits in motor adaptation can sometimes be greatly reduced even in the severest cases of cerebellar degeneration (Criscimagna-Hemminger et al., 2010; Izawa et al., 2012). These studies examined patients with predominantly hereditary cerebellar damage, with high ataxia scores. In this case, if the cursor rotation does not start at 45°, or 60° like in the other studies, but starts at 5° and only ramps up slowly, then even cerebellar patients can adapt their reaching movements in a way that more closely resembles that of healthy individuals. However, it is unknown whether this is true for all types of patients, including those groups that have particular difficulty adapting to a visuomotor distortion such as the SCA patients and patients with degeneration at locations known to interfere with a particular type of adaptation (i.e. visuomotor rotation vs force field). Thus, we separated the cerebellar patients in the current study into SCA and PICA groups, and tested their adaptation to a gradually introduced cursor rotation.

The role of the cerebellum in predicting the sensory consequences of the movement has been recently investigated in two studies. Both Synofzik et al. (2008) and Izawa et al. (2012) had cerebellar patients, and age-matched controls, estimate the direction of their unseen, but volitional hand movements. These estimates of the

outward hand movement were measured both before and after adapting reaches of the same hand to a visuomotor rotation. Both studies found that healthy controls showed a substantial shift in their estimation, or prediction, of their hand movement, while cerebellar patients showed a significant but much smaller change. The authors of these two studies interpret their results as suggesting that patients were impaired at updating or estimating the sensory consequences of their reach movements, suggesting that the cerebellum contributes to updating the forward model for estimates of hand movements. However, it is hard to dissociate predictive estimates and sensory estimates of hand movement in volitional reaches. It is possible that the mislocalization found in these studies could involve erroneous associations of proprioceptive signals with visual signals of hand position, that is, a deficit in fusing the two sensory estimates.

In the current study, we are interested in investigating the role of the cerebellum in recalibrating the proprioceptive-based perception of static hand position following similar visuomotor rotation training, as well as training to only a visual-proprioceptive discrepancy. We achieve the latter by removing the “movement component” of the visuomotor training. Participants’ hand movements toward the target were externally-constrained in direction, and this hand-movement direction was gradually deviated while the cursor continued to move directly to the target site. Our previous studies have shown that both types of training, with and without volitionally directed reaching movements, lead to changes in perceived hand position, as well as small but significant changes in reaching direction which were consistent with the direction of distortion (see Henriques and Cressman, 2012 for comparisons and explanation). These changes in proprioceptive hand estimates were measured using a purely perceptual task where subjects reported the position of their hand relative to a reference marker, both when the hand was displaced passively by the robot and when it was guided by the robot (Cressman and Henriques, 2009, 2010). The size of this shift in hand-proprioception was similar whether the hand was passively or actively displaced. Thus, given the role of the cerebellum on motor learning and motor control, our aim was to introduce a type of visual-distortion training, as well as a method for measuring proprioceptive estimation of the hand, that would have minimal motor confounds.

Here we tested patients both with chronic lesions in the SCA and in the PICA to determine whether the location of the lesions influenced the extent by which training with gradually altered visual feedback of the hand leads to (1) reach adaptation, and (2) the changes in hand proprioceptive estimates. We measured these changes both with training, using volitional movements and externally-guided hand movements. Our goal is to reveal the role of the cerebellum in visuomotor learning, and understand its contribution to both motor and sensory plasticity.

## 2. Methods

### 2.1. Participants

A total of 40 people, with normal or corrected-to-normal vision, participated in this study. The control participants ( $n=19$ , 11 females) had no history of relevant medical or psychiatric diagnoses. The patients ( $n=21$ , 4 females) were recruited out of a database of approximately 1900 documented cases with cerebellar lesions in the Neurology Department of the Klinikum Großhadern Munich, Germany. The diagnosis of the patients was made at the time of the onset of symptoms on the basis of standard clinical magnetic resonance imaging (MRI) protocols using a standard T1- and T2-weighted sequence. Included were all patients with an isolated left/right/bilateral sided cerebellar lesion excluding patients with involvement of the cerebral cortex and/or brainstem, as well as patients with other relevant neurological diagnoses such as epilepsy, polyneuropathy, neurodegenerative disorder, or chronic psychiatric diseases as well as paresis of the upper limb. Out of the 21 patients measured, one was removed since the patient had some difficulty using the equipment, and thus we did not obtain usable data for the tasks (proprioceptive estimate test). Another patient was also excluded since he was the only patient whose damage could not be attributed to a specific location or artery.

**Table 1**

Basic characteristics of patients. Age, sex (F-female; M-male), cerebellar disorder (PICA, infarct of posterior inferior cerebellar artery; SCA, infarct of superior cerebellar artery; AICA, infarct of the anterior inferior cerebellar artery), duration of disease (time since ischemic infarction in years), side most affected/arm tested (R-right, L-left), volume of the lesion (in cubic-centimeters), and total ataxia scores from SARA (Scale for the assessment and rating of ataxia; (Schmitz-Hubsch et al., 2006).

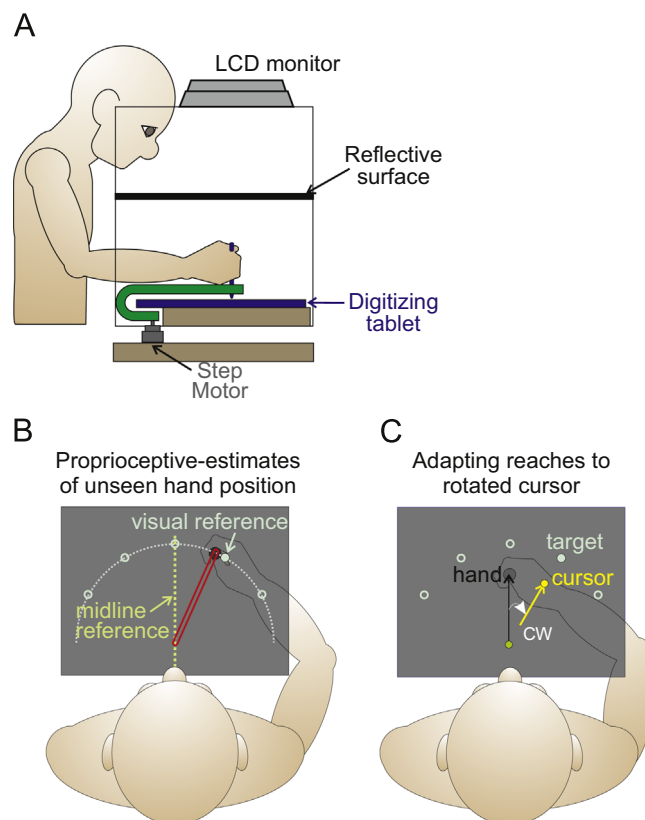
Patient	Age	Sex	Cerebellar disorder	Duration of the disease (years)	Side most affected/arm tested	Volume	Ataxia rating scale
01	81	M	PICA	2.8	L	unknown	3
02	68	F	PICA	3.9	L	unknown	1.5
03	68	M	SCA	6.5	L	1.5	1.5
04	58	M	SCA	3.2	L	4.4	1
06	48	M	SCA	8.2	L	15.6	6.5
07	71	F	SCA	6.4	L	6.0	12.5
08	67	M	SCA	1.5	L	unknown	1.5
09	78	M	PICA	5.4	R	unknown	2.5
11	72	M	PICA	4.7	R	3.0	4
12	52	F	PICA	8.5	L	25.2	7.5
13	74	M	AICA	7.8	L	47.8	4
15	47	F	SCA	3.2	L	13.3	1
16	72	M	PICA	6.4	L	5.7	1.5
18	72	M	PICA	14.9	L	13.8	7.5
19	64	F	SCA	8.4	L	7.7	4
20	49	M	SCA	14.1	L	unknown	2.5
21	36	F	PICA	7.5	R	unknown	1.5
22	73	M	SCA	4.7	R	76.8	4
23	75	M	SCA	8.0	R	4.4	2.5

Of the remaining 19 patients (see Table 1 for details), eight had lesions mainly in the area of the posterior inferior artery (PICA), nine in the area of the superior cerebellar artery (SCA), one in the anterior inferior artery area, and one in the SCA and PICA areas combined. All lesions were located in the cerebellar hemispheres sparing the midline. Patients participated in this study on average 82 months (range, 16–180) after the ischemic stroke. All patients scored from 1 to 12.5 (average of 3.67) on the SARA Ataxia scale, as measured by a neurologist prior to the experiment. We wanted to recruit patients with relatively moderate ataxia compared to degenerative cerebellar patients who frequently show also damage outside of the cerebellum. Also for practical purposes, externally guiding hand movements of severely affected patients would have required stronger forces which we wanted to avoid. Patients were on average 64.3 years old ( $\pm 12.2$ , SD), and their age did not significantly differ from that of the control group (57.9 years  $\pm 11.9$ , SD), ( $t(36) = -1.67$ ,  $p = 0.10$ ). All but one of the control participants were right-handed, and about half ( $n = 11$ ) were tested on their dominant hand. All of the patients were right-handed and were tested on their most affected (ipsilateral) arm (14 on their left/non-dominant hand).

## 2.2. Setup

Participants sat in a semi-dark room, on a height adjustable chair so that they could comfortably see and reach to all target and marker locations presented on an opaque, reflective surface. Head position was stabilized by a forehead-rest. Participants gripped a digitizing pen whose location was recorded on a 21 in. Wacom Cintiq 21UX digitizing tablet. Recording of pen position was event based, triggered by changes in positional signal (sampling interval between 6 and 8 ms). Visual stimuli were projected from a monitor (HPL2245wg, refresh rate 60 Hz) installed 44 cm above the tablet onto a reflective surface positioned in the center between the monitor and the tablet, thus appearing to lie in the same horizontal plane as the hand-held pen (see Fig. 1A). The room lights were dimmed and the participant's view of their hand and the tablet was blocked by the reflective surface. A key pad for entering two-alternative force choice (2-AFC) responses was placed either by the side of the opposite hand being tested for participants to key in their responses, or was placed near the experimenter so he could key the participants' verbal responses.

We used a custom-built track or railing on which a digitizing pen-holder could slide in order to guide the hand for certain paradigms described below (shown in green in Fig. 1A). Subjects could easily move along the length of this track but could not deviate with respect to the direction that was externally determined by a rotary stepper motor. Before each trial, this motor rotated the track by which participants moved the pen along. Subjects released the pen during this rotation, with the result that, prior to the movement they did not receive any proprioceptive information about this rotation. The track ended with a stopper, and in this way, the end location of the hand could also be specified if necessary. The motor was located just below the tablet, with the track located just above the tablet so that the center of



**Fig. 1.** Experimental set up and design. A: Side view of the experimental set up. B–C: Above view of the experimental surface visible to participants. B: In the proprioceptive estimate task, subjects actively pushed their hand out 20 cm along a constrained track (depicted in red) from the home position to a location along the arc (not shown to participant). The location of the hand was determined by the stepper motor (shown in A) which rotated the track in order to guide the unseen hand to its final location. Once the hand was there, a reference marker appeared/sounded, and participants judged the location of their hand with respect to a reference marker. Visual reference markers (circles) were located 0° and 15° CCW/left and CW/right of the midline. The body midline reference is indicated by the vertical dotted line (not shown to the participant). C: Visuomotor reach training task with rotated CW cursor (yellow circle). Reach targets (circles) were located 0° and 15° CCW/left and CW/right of the midline. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

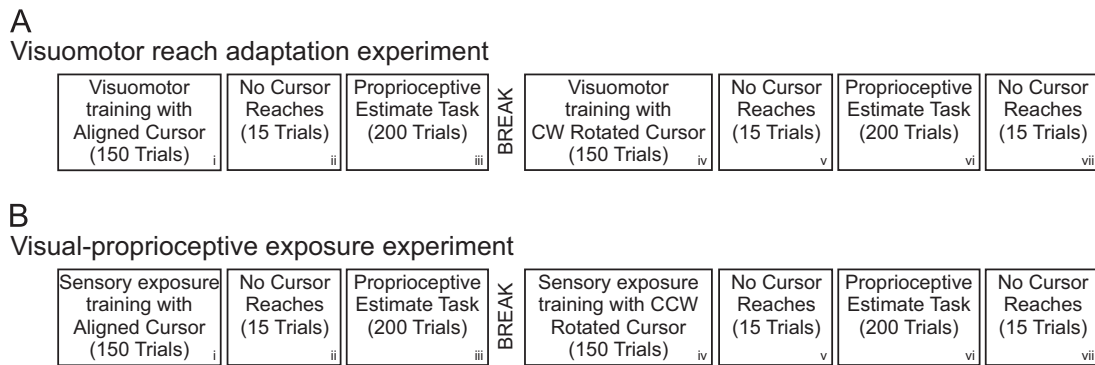
rotation of the track was located at a common home position. The constrained movements of the pen along the track were recorded on the tablet to ensure that the programmed direction of the motor was consistent with the direction of the pen-movement along this track; as well as to produce coordinated movements of the hand-cursor for certain paradigms.

## 2.3. Stimulus display

All tasks began with the hand at a home position (green dot, 1 cm in diameter, Fig. 1C) located at least 12 cm in front of the participant along the body midline. Targets (Fig. 1C) and visual reference markers (Fig. 1B) were represented by cyan dots (1 cm in diameters) located 20 cm in front of home position, along the midline, as well as 15° CW and CCW from this point. The hand-cursor was a yellow dot (Fig. 1C), also 1 cm in diameter.

## 2.4. General procedure

The study consisted of two experiments (run on separate days; details to follow) which each consisted of two blocks separated by a 45–60 min break. The first block (Fig. 2, boxes i–iii) served to collect baseline performance and thus includes training with an aligned cursor. The second block (Fig. 2, boxes iv–vii) involved training with a rotated cursor. Both of these training paradigms were followed by a paradigm for measuring proprioceptive estimates of hand position relative to a reference marker (boxes iii and vi) and a paradigm where subjects reached to displaced targets without visual feedback of their hand (no cursor-reaches, boxes ii, v and vii). The different experiments varied in the type of training participants received with both the aligned and rotated cursor: (1) Visuomotor



**Fig. 2.** Breakdown of the paradigms that make up the Visuomotor reach adaptation experiment (A) and the Visual-proprioceptive exposure experiment (B). Each experiment started with a block of paradigms that began with training with an aligned cursor (i), followed by no-cursor reaches (ii) and proprioceptive estimate task (iii). After a break, subjects performed a similar block of paradigms but this time training involved rotating the hand-cursor (iv), followed by no-cursor reaches (v) and proprioceptive task (vi). Experiments ended with a second set of no-cursor reaches.

reach adaptation (Fig. 2A), where subjects actively and freely reached to targets (Fig. 2A); (2) Sensory exposure (Fig. 2B), where the direction of hand movements toward the target were externally constrained. Thus, while both experiments involved a discrepancy between visual and proprioceptive feedback, only the Visuomotor reach adaptation experiment involved volitional movements. The order of these tasks for each experiment is illustrated in Fig. 2. Each experiment took less than 3 h including the break.

#### 2.4.1. Visuomotor training (Fig. 2A, illustrated in Fig. 1C)

This training paradigm resembled a typical visuomotor rotation paradigm where participants reached to targets first with a hand-cursor that was aligned with their unseen hand (baseline, panel i), and later with a cursor that was rotated 30° CW (panel iv) around the home position. The visuomotor rotation in the current study was introduced gradually by 0.75° per trial. Reaching was done by moving the pen along the tablet in order to actively move the yellow cursor to one of 3 targets. No external constraints restricted the direction of the movement. Participants were instructed to reach to the target as accurately as possible with the hand cursor.

Each trial began with one of the three targets appearing, which signaled the participant to begin their reaching movement. The target remained on until the cursor overlapped the target and its velocity dropped below 2 cm/s. Once this occurred, the target disappeared and a beep was sounded to indicate to the participants that the trial was done and that they should return their hand/cursor back to the start position. Each training set consisted of 150 trials, 50 reaches for each of the three targets.

#### 2.4.2. Sensory exposure training (Fig. 2B)

Like the Visuomotor rotation paradigm, the Sensory exposure training paradigm (Fig. 2B, boxes i and iv) also involved introducing altered visual feedback of the hand, but without requiring participants to volitionally direct the movement. Similar to our original paradigm (Cressman and Henriques, 2010), participants instead merely moved the pen along the motor-determined track, and the cursor moved synchronously with the pen. Independent of the actual direction of the track the cursor moved always directly toward one of three targets (same ones used in the Visuomotor training paradigm) which were briefly presented for 1 s before movement start. After the target disappeared, a 200 ms beep indicated that the participants should move the pen along the track until the cursor overlapped the remembered target site. This task to match the position of the track-guided cursor with the remembered location of the target was added to ensure that participants were paying attention to the hand-cursor. In the first (baseline) exposure training task, the cursor was aligned with the pen movement (Fig. 2B, box i). But in the second training task (Fig. 2B, box iv), the pathway of the cursor always moved directly to the remembered target, whereas the direction of the hand/pen movement was gradually rotated (using the Stepper Motor) so that the actual position of the hand motion was deviated by 30° CW (in 0.75° steps per trial) from the cursor. Thus, in the exposure training the cursor was rotated CCW relative to the hand and so in the opposite direction to the cursor motion in visuomotor rotation training for the other experiment. In this way, participants experienced a discrepancy between visual and proprioceptive sense of hand movements without actively directing their movements, and without having to adjust movements for any discrepancy between seen and actual movement. In fact, given that the cursor always moved toward the target, there was no explicit error as would have been the case in the Visuomotor rotation paradigm.

Each trial began with the motor moving the track with the pen to the appropriate direction and then participants were cued to grip the pen (thus, the pen rotated in the home position prior to the participant gripping it). One of the targets appeared and participants moved their hand/pen along the track, which moved the cursor toward the target. When both the distance between cursor and

home position increased above 15 cm, and the speed of the cursor dropped below 2 cm/s, the cursor disappeared and a beep would sound to indicate the end of the trial thus signaling participants to move the pen again along the track to the home position. They released the pen at home position so the motor could position the track to its new location with respect to the new target. Each training set involved 150 trials, with 50 movements to each of the 3 targets.

#### 2.4.3. No-cursor reaching test (boxes ii, v and vi)

Following each of two training sets (aligned and rotated) for both experiments, participants produced open-loop reaches to the same three visible targets, without visual feedback of their hand (no cursor) (boxes ii and v in Fig. 2). These trials were included to determine if participants adapted their reaches in response to the misaligned cursor (i.e. exhibited aftereffects). Each trial began with the target appearing, which signaled to the participant to reach to the target. Once their unseen hand had stopped (moved < 1 cm) for 500 ms, and the reaching amplitude was at least 75% of the distance between home position and target, the reach was considered complete.

Since there was no visual feedback during either the outward or return reaches, in order to help participants return their hand to the home position, a smiley-face was placed on the home position dot which would rotate to indicate the direction of the pen on the tablet. Participants reached five times to each of the three targets without the cursor, for a total of 15 trials for each set of no-cursor reaches.

On top of the no-cursor reaches performed immediately after each of the two training paradigms for each experiment (boxes ii and v), a third set of no-cursor reaches for each experiment was also performed at the very end, following the second Proprioceptive estimate test (boxes vii in Fig. 2). We also ran this second measure of open-loop reaching following training with altered visual feedback of the hand. This was to determine if the resulting aftereffects following immediately after training persisted through the 20–30 min necessary to complete the Proprioceptive estimate test. Thus, we could assess whether motor adaptation persisted during the Proprioceptive estimate test.

#### 2.4.4. Proprioceptive estimate test (Fig. 2, boxes iii and vi, illustrated in Fig. 1B)

After the short set of no-cursor reaches, our goal was to assess whether training with altered visual feedback will lead to changes in participant's estimate of their hand position. As in our previous studies on this topic (Clayton et al., 2014; Cressman and Henriques, 2009, 2010, 2011; Mostafa et al., 2014; Salomonczyk et al., 2011, 2013), this proprioceptive estimate test involved participants having their unseen hand (while gripping the pen) moved or guided out along a particular direction to a specified location. In this case, their unseen hand was guided by moving the pen along the track (whose direction was determined by the motor, shown as a red trace in Fig. 1B). Once their hand had approached the specified location (along the arc shown in Fig. 1B but not shown to participants), either a dot would appear (visual reference marker) or a beep would sound. If it was a dot, participants would report using a two-alternative force choice paradigm (2-AFC) whether their hand felt it was left or right of the reference marker. If it was a beep, participants would judge whether their hand was left or right of their body midline (proprioceptive reference marker). The participants entered their 2-AFC into the keypad. The location of the three visual reference markers was the same as those for the reach targets in the other paradigm: one along the midline, and the other two located 15° on either side; 20 cm from home position.

The location of the unseen hand relative to each of the four reference markers was adjusted using an adaptive staircase algorithm (Kesten, 1958; Treutwein, 1995). For each of the reference markers, there were two staircases, one starting 30° to the left (CCW) of the reference marker and one starting 30° to the right (CW) and ending after 50 2-AFC trials. All the staircases were adjusted independently and randomly interleaved as outlined in Cressman and Henriques (2009, 2010), and consisted of a total of 200 trials for each set.

All participants were run on both experiments, first the experiment with the Sensory Exposure training, and then the experiment with the Visuomotor rotation training, at least 2 weeks later, and on average, approximately 3.5 months apart. Since the direction of the altered visual feedback was opposite in training paradigms of the two experiments, and sufficiently separated in time, there should be no effect (interference) of participation in the first experiment on results of the second experiment (Krakauer et al., 2005). The majority of controls and patients did not notice any visual perturbation; for Experiment 1 (Sensory Exposure training), 7 patients and 8 controls noticed some deviation in the cursor for the training while in Experiment 2 (Visuomotor training), 2 patients and 9 controls noticed the cursor misalignment. Of these, 1 patient and 5 controls (two of which were not naïve) noticed a perturbation for both experiments.

## 2.5. Data analysis

Our goal was to determine whether cerebellum patients showed similar changes in movement and estimates of hand position following training with both a visuomotor rotation and exposure to visual-proprioceptive misalignment as do neurologically intact controls. Most patients could be classified as having lesions that affect the PICA (8) or SCA (10). This included one patient who had a small PICA lesion on the right and a larger SCA lesion of the left, and tested with the left hand, was classified as SCA in our Group factor. Thus, the factor “Group” indicates healthy controls (19), PICA patients (8) and SCA patients (10). PICA and SCA patients did not vary in their ataxia scores ( $t(16)=0.50$ ,  $p=0.96$ ), nor with time since the lesion event ( $t(16)=-1.87$ ,  $p=0.85$ ) (see Table 1). For the illustrations, we include the single patient with damage to anterior inferior cerebellar artery (AICA), but do not include this person in the Group analyses.

Of the no-cursor reaches (Fig. 2, boxes ii, v, vii), we removed those reaches with directions whose distance from the median was more than 4 times the quartile-median distance. Every set of no-cursor trials for each participant had a minimum of 12 valid trials (out of 15). On average, 8% of these reaches were removed as outliers.

To assess changes in movements, we compared no-cursor reaches following training with an aligned cursor with those following training with a rotated cursor (Block, within-subject factor), for both patients and controls (Group, between-subject factor), across the three target locations (Target, within-subject factor), and the arm tested (Arm, between-subject factor) using a four way mixed ANOVA to include these four factors, for each of the two experiments.

To assess changes in proprioceptive estimate of hand position, as in our other papers (Cressman and Henriques, 2009, 2010), we first determined the hand location subjects felt as being congruent with the reference markers. This location was determined by fitting a logistic distribution to each subject's responses for each reference marker in each testing session and calculating the bias (the point of 50% probability). In addition to calculating bias, we also determined subjects' uncertainty (or precision) by finding the interquartile range of the logistic distribution (the uncertainty range). Next, we compared the proprioceptive biases (or estimate of hand position) following training with an aligned cursor to those following training with a rotated cursor (Block), for both patients and controls (Group), across the four reference markers (Markers: 3 visual, and the one body midline) and across the two arms tested (Arm) using a four way mixed ANOVA for both experiments.

To determine whether patients show poorer precision when estimating hand position than healthy controls, we compared the uncertainty range for these estimates using a four-way ANOVA (Group  $\times$  Block  $\times$  Arm  $\times$  Marker).

To compare baseline performance (no cursor reach errors and biases of felt hand positions) between the two arms, we compensated for the opposite directed hand-biases by flipping the sign of one of the arms. Since the cursor rotated in opposite directions for the two experiments, we did a similar flip when comparing the changes in open-loop reaches and hand proprioception across the two experiments. Likewise, when illustrating the change in hand proprioception and open-loop reaches (reach aftereffects) across experiments, we plotted these changes such that positive values were in the direction of distortion. When comparing across experiments, we used the change in proprioceptive estimates between Blocks and change in no cursor reaches between Blocks (reach aftereffects) as the dependent measure (to reduce the factors by one) and included experiment as a factor.

We also ran additional tests to characterize the general motor performance of the patient group (relative to the controls). To do so, we measured and compared the means and between-trials standard deviations of movement time, path length and endpoint errors of reaches during both closed-loop reaches made with the aligned cursor (the baseline training condition for the Visuomotor adaptation experiment) and the no-cursor reaches that followed, as well as those no-cursor reaches following baseline Sensory exposure training in the other experiment. For the baseline no-cursor reaches (from both experiments), we also looked at mean and variability of the reach endpoint errors of the patients as a function of Ataxia score. Again, we used a mixed design with Group, Arm, and Target location as the three factors.

## 3. Results

### 3.1. Baseline movement parameters for patients and controls

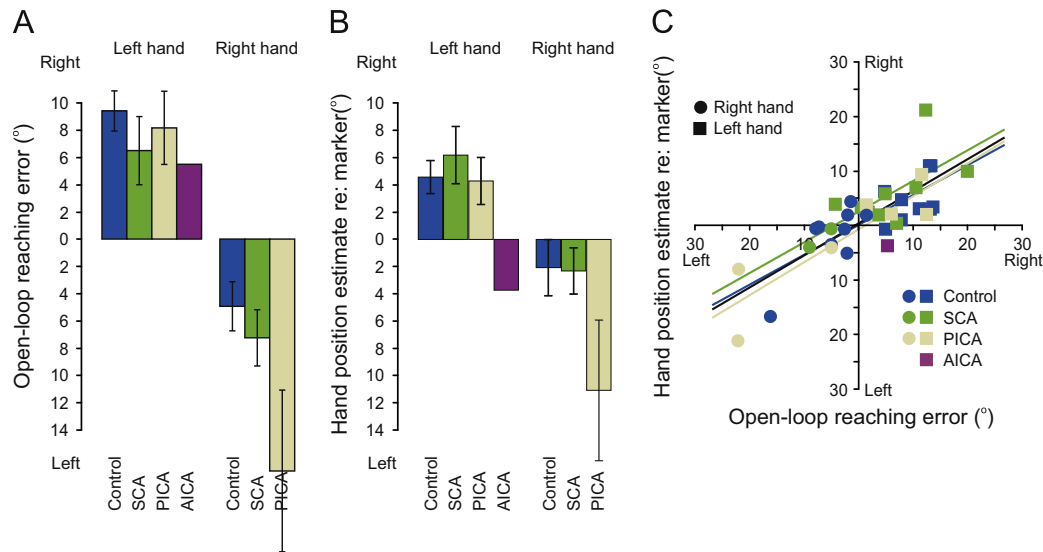
Our patient groups were highly functional, with reaching movements whose properties were similar to those of controls, both for the baseline reaching training (with aligned cursor) and the open-loop reaches. Specifically the means and the SDs of movement duration ( $1.79 \pm 0.86$  s, average and SD), peak velocity ( $31.58 \pm 11.26$  cm/s), and length of the hand path ( $20.97 \pm 2.70$  cm) did not vary between patients and controls for both closed-loop (without distortion) and open-loop reaches. Likewise, we did not find that these reaches were more curved or showed greater oscillations than controls, in that the ratio between the path length to the final reaching endpoint and the most direct path to this endpoint did not vary much from 1.0 for all groups (various two-way ANOVAs with factors Arm and Group,  $p > 0.05$ ). Perhaps this is not surprising given that there was no speed constraint and these movements were made with a pen on a surface (not in 3D).

Angular reach endpoint errors varied with arm used, such that people erred, on average,  $7.8^\circ$  left of the target when reaching with the right arm and  $8.0^\circ$  to the right when reaching with the left arm ( $F(1, 31)=52.3$ ,  $p < 0.001$ ). However, when we compared the magnitude (by flipping the sign of the results of one of the arms) of these errors, they did not differ overall ( $F(1, 31)=0.6$ ,  $p=0.418$ ), although this arm dependency varied as a function of group ( $F(2, 31)=3.86$ ,  $p=0.032$ ). This effect appears to be driven by a rather large angular endpoint error for 2 of the 3 PICA patients, on average  $17^\circ$  left, when reaching with the right affected arm (Fig. 3A, see 3C for the results of each participant). There was no significant effect of group across these (flipped) endpoint errors ( $F(2, 31)=1.62$ ,  $p=0.215$ ). The between-trial variance in the angular reach endpoints tended to be a bit larger for PICA patients ( $SD=3.30^\circ$ ), compared to SCA patients and controls ( $3.05^\circ$  and  $3.03^\circ$ ) but this did not reach significance ( $F(2, 31)=0.5$ ,  $p=0.59$ ). However, this variability in angular errors did increase slightly but significantly with increasing ataxia scores for SCA patients ( $r^2=0.64$ ,  $t(8)=3.76$ ,  $p=0.006$ ). This was not the case for the group of PICA patients ( $r^2=0.02$ ,  $t(6)=0.32$ ,  $p=0.759$ ).

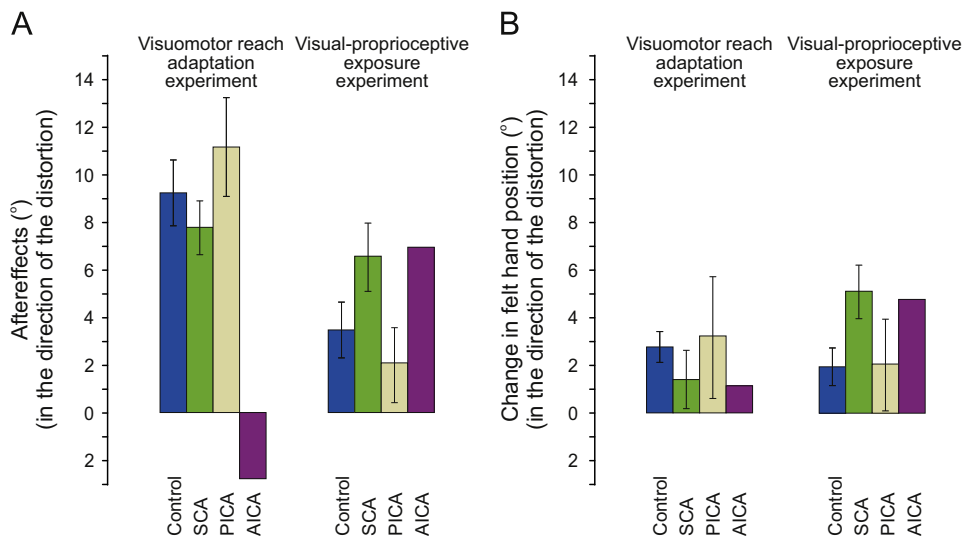
### 3.2. Proprioceptive sensitivity across patients and controls

The proprioceptive estimates of hand position relative to either a visual reference marker or a body (midline) reference marker, under baseline conditions (after reach-training with an aligned cursor) were also similar across patients and controls (Fig. 3B). Like reaches, these biases varied in opposite directions as a function of the arm tested,  $4.0^\circ$  left for the right hand and  $5.2^\circ$  right for the left hand ( $F(1, 31)=22.47$ ,  $p < 0.001$ ), although the size of these proprioceptive biases did not differ ( $F(1, 31)=0.01$ ,  $p=0.97$ ). While we did not find a significant difference between groups ( $F(2, 31)=1.59$ ,  $p=0.22$ ) or an interaction between group and arm ( $F(2, 31)=2.39$ ,  $p=0.11$ ), the baseline biases shown in the bars in Fig. 3B suggest that PICA patients may have mislocalized their right hand more than controls or SCA patients. But with 8 PICA patients, 3 of whom had their right affected arm tested, we could not detect such a significant difference. These biases also did not differ across the location and modality of the reference marker ( $F(3, 93)=1.62$ ,  $p=0.19$ ) (diamonds in Fig. 5). Moreover, biases in felt hand position correlated with the errors in open-loop reaches (Fig. 3C), with an overall  $R^2$  of 0.65 and  $R^2 > 0.5$  for all three groups, and an overall significant slope (shown in black) of 0.58 ( $p < 0.001$ ). The slopes for the controls and two patient groups (lines of fit in the corresponding colors) were parallel with this overall slope.

Given that both controls and patients had similar movements in the simple baseline reaching task and similar proprioceptive estimates



**Fig. 3.** Baseline performance averaged across Experiments for each Group (Controls, and SCA, PICA and AICA patients) and the two arms. A: Angular reach endpoint errors made during no-cursor reaches (box ii in Fig. 2). B: Proprioceptive estimates or biases of the hand (box iii). Error bars are SEM across participants. C: The relationship between hand position estimates and open-loop reaching errors. The black line is the slope fitted to all the data, while the colored lines are for each of the three Groups of participants. The unit slope is indicated by the dotted line.



**Fig. 4.** Change in open-loop reaches (A) and estimates in hand proprioception (B) for the Visuomotor reach experiment (left bars) and the Visual-proprioceptive exposure experiment (right bars) averaged across controls, and SCA, PICA and AICA patients. Error bars indicate SEM across participants.

of unseen hand position, the rest of the section involves looking at how reaches and hand proprioceptive estimates changed following both visuomotor adaptation and exposure to visual-proprioceptive discrepancies.

### 3.3. Change in open-loop reaches following visuomotor rotation training

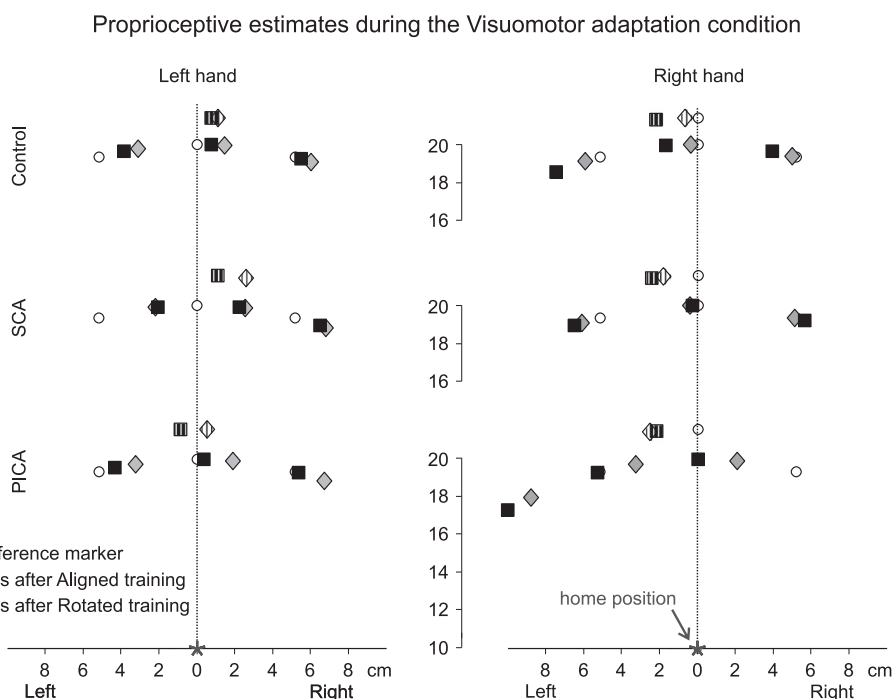
For the Visuomotor adaptation experiment, the changes in open-loop reaches following training with a rotated cursor were significantly more deviated in the direction of the rotated cursor than following training with an aligned cursor ( $F(1, 31) = 99.68, p < 0.001$ ) as illustrated by the left set of bars in Fig. 4A. These aftereffects, on average  $9.32^\circ (\pm 5.32 \text{ SD})$ , did not vary across patients and controls ( $F(2, 31) = 0.86, p = 0.43$ ), suggesting that aftereffects following reaching with a gradually rotated cursor were similar across the two groups. The change in open-loop reaches or aftereffects did not differ with the location of the target, ( $F(2, 31) = 2.08, p = 0.13$ ), and only tended to vary with the arm used ( $F(1, 31) = 3.91, p = 0.06$ ), such that the

aftereffects appear to be slightly larger when reaching with the right arm (rightward-pointed triangles) compared to the left arm.

We retested aftereffects with the final set of no-cursor reaches (Fig. 2, boxes vii) to see whether these motor changes had disappeared during the time of the proprioceptive estimate task. Not surprisingly, we found that these aftereffects were less than half of the size of those produced right after training ( $9.55^\circ$  vs  $3.95^\circ$ ,  $F(1, 31) = 25.63, p < 0.001$ ), but were still significantly different than the baseline no-cursor reaches ( $F(1, 31) = 18.71, p < 0.001$ ) suggesting that the effect of training persisted.

### 3.4. Change in proprioceptive hand estimates following visuomotor rotation training

As in our previous experiments (Clayton et al., 2014; Cressman and Henriques, 2009, 2010, 2011; Mostafa et al., 2014; Salomonczyk et al., 2011, 2013), we also found a significant change in the location where people felt their unseen hand following reach training with a rotated cursor (difference between diamonds and squares in Fig. 5A, and the



**Fig. 5.** Above view of 2-D proprioceptive estimates of the left and right hand for the Visuomotor adaptation experiment averaged across controls, SCA patients and PICA patients. Diamonds are the biases following aligned cursor training, while squares are those following rotated-cursor training. Striped symbols are those biases for the mid-line reference marker; which are offset vertically for better visibility. Circles are the visual reference marker locations.

left set of bars in Fig. 4B). Specifically, proprioceptive estimates were shifted in the direction of the rotated cursor by  $2.50^\circ$  ( $\pm 4.14^\circ$ , SD) following rotated-cursor training (Fig. 2A, box vi) compared to those following aligned cursor reach training (box iii) ( $F(1, 31)=8.81$ ,  $p=0.006$ ). However, this shift in hand proprioception again did not differ between the two cerebellar patient groups and healthy individuals ( $F(2, 31)=0.63$ ,  $p=0.54$ ). These changes in hand proprioception did not significantly vary with the arm tested, with the location, or the sensory modality of reference markers (interactions  $p > 0.05$ ).

### 3.5. Change in open-loop reaches following exposure to visual-proprioceptive discrepancies

Like in our original study (Cressman and Henriques, 2010; Salomonczyk et al., 2013), even when participants did not make free volitional reach movements, just being exposed to a discrepancy between the seen and the actual hand position as the cursor moved directly to the target, they also showed a change in their volitional open-loop reach errors. These reach aftereffects were about  $4.03^\circ$  ( $F(1, 31)=24.56$ ,  $p < 0.001$ ), as shown by the right set of bars in Fig. 4B. These aftereffects were present for both patients and healthy controls, in that this change in reaches did not vary with group ( $F(2, 31)=2.05$ ,  $p=1.45$ ). These changes in reaching movements did not vary with target, nor with the arm used.

Again, like those aftereffects produced following visuomotor adaptation of reaches, these aftereffects persisted through to the final set of no-cursor reaches (Fig. 2B, box vii) in that they continued to be significantly deviated compared to the baseline ( $F(1, 31)=6.11$ ,  $p=0.02$ ). Nonetheless, they were significantly smaller; about half of the size of those produced immediately after training ( $4.03^\circ$  vs  $2.27^\circ$ ,  $F(1, 31)=4.44$ ,  $p=0.044$ ).

When we statistically compared these reach aftereffects with those produced immediately following training with altered vision (by adding Experiment type as a factor), the changes in reaches did vary between the two experiments (and thus the two kinds of training) ( $F(1, 31)=32.59$ ,  $p < 0.001$ ). Specifically, the change in reaches following exposure to a visual-proprioceptive discrepancy was much smaller

(on average,  $4.03^\circ$ ,  $\pm 4.9^\circ$ , SD) than that produced following training arm movements to a visuomotor rotation (on average  $9.32^\circ$ ,  $\pm 5.31^\circ$ ), as can be seen by comparing the left and right set of bars in Fig. 4A. We also found that this difference in reach aftereffects across Experiments also significantly varied with Group ( $F(2, 31)=4.17$ ,  $p=0.025$ ). When we explored this further, we found that reach aftereffects were indeed significantly smaller for the Visual-proprioceptive Exposure Experiment compared Visuomotor-reach Adaptation Experiment for controls ( $p < 0.001$ ) and PICA patients ( $p < 0.011$ ), but not for SCA patients ( $p=0.397$ ;  $p$ -critical= $0.033$ ) whose reach aftereffects were only 25% smaller (but not significantly so). As we discuss below, reach aftereffects following exposure to a visual-proprioceptive discrepancy tend to reflect the change in hand proprioception. Given that SCA patients showed a relatively large change in felt hand position in this experiment, this may explain the larger reach aftereffects.

### 3.6. Change in proprioceptive hand estimates following exposure to visual-proprioceptive discrepancies

Again as in our original study, exposure to visual-proprioceptive discrepancies (where the hand movement-direction was constrained) also lead to a shift in estimated location of the unseen hand in the direction of the visual discrepancy, of about  $2.86^\circ$  ( $\pm 4.0^\circ$ , SD) ( $F(1, 31)=11.83$ ,  $p=0.002$ ), as illustrated by the right set of bars in Fig. 4B. This shift in felt hand position did not vary across groups ( $F(2, 31)=0.86$ ,  $p=0.43$ ), but did vary with the arm tested ( $F(1, 31)=4.63$ ,  $p=0.04$ ), with a larger change of the left compared to the right arm ( $4.06$  vs  $0.87$ ) for both patients and controls. The change in hand proprioception also varied with reference marker location ( $F(1, 31)=3.32$ ,  $p=0.02$ ), being a bit smaller for the marker on the left (on average  $1.54^\circ$  difference) compared to those in the center (both body midline and visual marker) and to the right (all of which were over  $3^\circ$  different).

Consistent with our previous results (Cressman and Henriques, 2009, 2010), in the healthy controls, the proprioceptive recalibration following this Sensory discrepancy exposure training did not differ from that produced following Visuomotor rotation training. When

Experiment was added as a factor (and the opposite distortions adjusted for), the changes in biases did not significantly differ across the two experiments ( $F(1, 31)=0.15, p=0.90$ ). There was no further interaction of Experiment with Group ( $F(2, 31)=1.59, p=0.221$ ) on these changes that consistently occurred across the two experiments.

### 3.7. Proprioceptive uncertainty

Patients showed a marginally larger uncertainty range than controls ( $F(2, 31)=2.79, p=0.077$ ), with a range of  $8.95^\circ (\pm 4.74, \text{SD})$  for SCA patients,  $8.34^\circ (\pm 3.92, \text{SD})$  for PICA patients compared to that of controls,  $6.01 (\pm 2.85, \text{SD})$ . Not surprisingly, we did not see any changes in uncertainty across aligned and misaligned training ( $F(1, 31) < 1$ ). The small differences between the two arms, a range of  $6.34^\circ$  for the right arm and  $7.89^\circ$  for the left arm, did not reach significance ( $F(1,31)=0.129, p=0.72$ ). There was also no significant difference in this uncertainty across the different reference marker locations and marker modality ( $F(3, 31)=1.19, p=0.316$ ).

Combining patients: The same pattern of results that we described above were also found when we combined the 10 SCA patients, 8 PICA patient and the single AICA into one patient group ( $n=19$ ).

## 4. Discussion

Several decades of research have shown that motor learning relies on both cortical and subcortical, specifically cerebellar, processing. The goal of our study is to investigate whether proprioceptive recalibration of the hand following training with altered visual feedback of the hand also involves cerebellar processing. Perceptual estimates of unseen hand location were measured in patients with PICA and SCA infarcts, along with age-matched healthy controls. These estimates of hand proprioception were assessed both before and after training their reaching movements (Visuomotor adaptation training), and externally-guided hand movements (Sensory discrepancy exposure training) with a rotated cursor. We found that patients and controls showed comparable reach aftereffects following both types of training with gradually-introduced visual distortion, although, like our previous results, these reach aftereffects were significantly smaller when measured after training with only the cross-sensory discrepancy. Moreover, cerebellar patients also showed small but significant changes in felt hand position following both types of training and the magnitude of this proprioceptive recalibration was similar to that found in controls. Our results suggest that the cerebellum does not seem essentially to be involved in recalibration of hand proprioception following training with altered visual feedback of the hand. Likely, this recalibration is occurring in cortical areas such as the posterior parietal cortex.

### 4.1. Baseline performance

Like in the related studies of [Izawa et al., \(2012\)](#) and [Synofzik et al., \(2008\)](#) we found that cerebellar patients did not differ from controls in their baseline performance; both in their ability to localize their unseen hand and reach to targets with and without cursor. The size of these reach errors and proprioceptive biases was similar across our study and the two mentioned above.

### 4.2. Motor changes following training with altered visual feedback of the hand

Many studies have demonstrated the importance of the cerebellum in the adaptation of limb movements to various perturbations. For instance, patients with damage to the cerebellum show deficits in adapting their saccades, arm movements, and locomotion when

compared to controls ([Bastian, 2008](#); [Fernandez-Ruiz et al., 2007](#); [Straube et al., 2001](#); [Timmann et al., 1996](#)). Recent work has begun to correlate the location of the damage with the extent of impairment in learning different perturbations. Specifically, [Burciu et al. \(2014\)](#), [Donchin et al. \(2012\)](#), [Rabe et al. \(2009\)](#) and [Werner et al. \(2010\)](#) have found that in general patients with infarcts in SCA (and related areas) have more difficulty adapting to a visuomotor distortion than PICA patients and controls, while those with PICA infarcts are more likely to have problems adapting to a velocity-dependent force field. Yet, all these studies showing deficits had the perturbation abruptly introduced. Likewise, [Synofzik et al. \(2008\)](#) found that cerebellar patients showed no reach aftereffects when the cursor-rotation was introduced in quick-steps (i.e. a full  $30^\circ$  rotation within 6 trials). In contrast, recently, two studies from the Shadmehr lab, using velocity-dependent force perturbation ([Crisimagna-Hemminger et al., 2010](#)), and a  $30^\circ$  rotation ([Izawa et al., 2012](#)) that was gradually introduced over many trials, showed that patients with cerebellar degeneration were able to produce reach aftereffects similar to those of controls. Although some studies show no such advantage for cerebellar patients when again adapting to a force-field perturbation ([Gibo et al., 2013](#)) and for visuomotor rotation when participants are not shown the cursor during the reach, but only at the end do they see the entire hand path ([Schlerf et al., 2013](#)). In the current study, we found patients could adapt to a gradually introduced cursor rotation; that is, both SCA and PICA patients produced similar reach aftereffects to those of controls following a gradual introduction to the cursor rotation. Further neurophysiological evidence for this comes from a recent transcranial magnetic stimulation (TMS) study ([Schlerf et al., 2012](#)). This study demonstrated that cerebellar excitability in healthy individuals does not modulate across learning when subjects adapted to a gradually introduced visuomotor rotation, but did modulate when the rotation was abruptly introduced. Thus, our results are consistent with some of the recent evidence suggesting that cerebellar patients are less impaired when adapting to visual perturbations that are gradually introduced, particularly when the cursor concurrently moves with the hand during the reach training.

Likewise, the gradual introduction of the visual-proprioceptive discrepancy in our Visual-proprioceptive exposure experiment also lead to significant reach aftereffects that were equivalent between patients and controls. As in our previous studies ([Cressman and Henriques, 2010](#); [Salomonczyk et al., 2013](#)), the reach aftereffects from our Visual-proprioceptive experiment were significantly smaller than those that result from the more traditional Visuomotor rotation experiment. These findings are compatible with our theory that adaptation of active reaching is driven by two types of errors (training signals). First, the mismatch between the actual and expected sensory consequences of motor commands, and second the visual-proprioceptive discrepancy (see ([Henriques and Cressman, 2012](#))). This suggests that at least the visual-proprioceptive discrepancy signal is persevered in cerebellar patients, and likely the cerebellum is not involved in this signal.

### 4.3. Change in predictive vs sensory estimates following training with altered visual feedback of the hand

The role of the cerebellum in predicting the sensory consequences of the self-generated movement have been recently investigated in two studies. In a [Synofzik et al. \(2008\)](#) study, after training to reach with a rotated cursor, both patients and controls made out-and-back movements in a self-specified direction in the right-upward quadrant of the workspace without visual (cursor) feedback of the unseen, right hand, and after each movement, they indicated the perceived direction of this movement. Both controls and patients continued to show a perceptual shift of these self-generated yet unseen hand movements, this shift was significantly smaller in patients than controls (15% of the distortion vs 50%).



Note, these patients showed a small change in perceived hand movements, even in the absence of any reach adaptation. In a similar paradigm, [Izawa et al., \(2012\)](#) showed that both controls and patients also produced changes in localizing their unseen hand movements after successfully adapting their reaches to a gradual 30° visuomotor rotation. That is, when participants had to report their perceived outward movement, this time by pointing to the remembered location with the opposite hand once the reaching hand had returned to the home position, healthy controls showed a sizeable change in the perceived direction of the prior reaches (about 15°), while patients showed only half of the change in this localization task. The authors of these two studies interpret the reduced perceptual shift in cerebellar patients as suggesting that the cerebellum is involved in updating or estimating the sensory consequences of their reach movements.

However, given the difficulty of isolating only the efferent-based predictions (sensory consequence) from afferent-based estimates (sensory feedback) of the produced movement, it is possible that the reduction in the perceptual shift in their cerebellum patients was not exclusively due to a failure to predict the sensory consequences. The perceptual/localization tasks of [Synofzik, et al. \(2008\)](#) and [Izawa et al. \(2012\)](#) cannot measure purely predictive estimation of hand movement, since proprioceptive feedback of the remembered hand movements was also available. Thus, their tasks could also be assessing change in felt hand position, or proprioceptive recalibration rather than exclusively efferent-based predictions. Our study addresses this possibly by using a proprioceptive estimate task that does not involve movement or motor prediction in estimating hand position. If the cerebellum is also involved in proprioceptive recalibration we would have expected a decrease in the change of felt hand position in patients in the current study. But, we did not; both cerebellar patients and controls show equivalent significant changes in felt hand position in this purely perceptual task. The absence of such a decrease in our results contributes to the distinction between predictive and proprioceptive recalibration, and simultaneously removes this efference-af-ferece confound thereby ratifying the original interpretation.

Nonetheless, both [Synofzik, et al. \(2008\)](#) and [Izawa et al. \(2012\)](#) studies showed that cerebellar patients did show a partial, yet significant, 6–8° shift in their sense of hand direction following training. It could be, as mentioned by [Izawa et al. \(2012\)](#) that this change may reflect changes in proprioceptive estimates of the hand position. In other words, the 2–3° shift in proprioceptive estimates that we find in patients (as well as controls) could partly account for the remaining 6–8° perceptual shift found in patients in the [Synofzik, et al. \(2008\)](#) and [Izawa et al. \(2012\)](#) studies. In summary, while the reduced perceptual change found in patients (compared to controls) in these studies is probably due to some impairment of the cerebellum in predicting sensory consequences, the perceptual change that still persists in patients may reflect a recalibration of hand proprioception for which the cerebellum is not necessary.

Consistent with the hypothesis that the cerebellum is not involved with proprioceptive recalibration of static hand position, we also found similar changes in felt hand position in the Visual-proprioceptive Exposure experiment. Given that training involved only externally-guided movements with the visual discrepancy, this Sensory exposure training should not have led to changes in prediction of movement consequences but reflect true sensory recalibration. Moreover, the similar proprioceptive recalibration that we found in both of our experiments (and thus both types of training), as well as our previous studies ([Cressman and Henriques, 2009, 2010](#); [Salomonczyk et al., 2011, 2013](#)), also suggests that the proprioceptive recalibration does not depend on the (movement) error signals that are also available when adapting reaches to a visuomotor rotation. Instead proprioceptive recalibration likely relies on the cross-sensory discrepancy signals that are common to both types of training. Thus,

while the movement-related error signals necessary to update forward models and modify the resulting movements are likely handled by the cerebellum (and perhaps other cortical areas), the integration and recalibration of cross-sensory signals for state estimation likely occurs in the posterior parietal cortex ([Shadmehr et al., 2010](#)).

#### 4.4. *Proprioceptive changes following training with altered visual feedback of the hand*

Changes in proprioceptive estimate of static hand location in the current study were smaller, about 2–3°, than those we have found in our previous studies ([Clayton et al., 2014](#); [Cressman and Henriques, 2009, 2010](#); [Cressman et al., 2010](#); [Salomonczyk et al., 2011, 2013](#); [Salomonczyk et al., 2012](#)), which were usually about 6°. We have two possible reasons for this. One has to do with the amplitude of the hand displacement for measuring proprioceptive estimate, as well as the reaching movements. It was 20 cm in the current study, but in our previous studies (cited above), as well as most other studies assessing visuomotor adaptation (e.g. [Izawa et al., 2012](#); [Synofzik et al., 2008](#)) or even somatosensory changes following force-field adaptation ([Ostry et al., 2010](#)), the distance tested was around 10–12 cm. While we introduced a larger movement in hope to better extract possible deficits in cerebellar patients, it is possible that proprioceptive recalibrations are limited to about 1 cm of lateral shift. This 1 cm corresponded to roughly 6° for 10–12 cm hand displacement (as in our other studies) but 3° for 20 cm displacement (as in this study). Also, because we did not have access to the same robot that we and others have used for similar perceptual tasks ([Cressman and Henriques, 2009](#); [Cressman et al., 2010](#); [Ostry et al., 2010](#); [Salomonczyk et al., 2011](#); [Salomonczyk et al., 2012](#)) we were somewhat limited in switching between tasks (introducing and removing the track and stepper motor). Thus, we could not easily include the usual procedure of interleaving reach-training trials with the perceptual tasks (also used by [Izawa et al., 2012](#); [Synofzik et al., 2008](#)). And without the interleaved training trials, we cannot rule out that some of the change in hand proprioception may have decayed across the 20 or so minutes necessary to complete 200 proprioceptive estimate trials. This, as well as the amplitude of the movements tested, can reasonably explain our smaller (but still significant) angular changes in felt hand position.

#### 4.5. *Motor changes vs sensory changes*

As in our previous studies in healthy individuals ([Cressman et al., 2010](#); [Henriques and Cressman, 2012](#); [Salomonczyk et al., 2011](#); [Salomonczyk et al., 2012](#)), we found no significant relationship between reach aftereffects and proprioception recalibration across groups in our study following visuomotor adaptation ( $r^2=0.1$ ,  $p > 0.05$ ). This is opposite to the usual significant correlation we find between these measures following Sensory exposure training both in this study ( $r^2=0.3$ ,  $p < 0.001$ ) and our other studies ([Cressman and Henriques, 2010](#); [Salomonczyk et al., 2013](#)). We explain the latter by suggesting that the small reach aftereffects following Sensory exposure training are associated with the perceptual change ([Henriques and Cressman, 2012](#)). In the current study, this can also be seen even at the Group level, in that changes in open-loop reaches in the right panel of [Fig. 4A](#) are similar to changes in felt hand position in the right panel of [Fig. 4B](#). Even more convincingly, we also find that the patterns of generalization for proprioceptive recalibration differ from those of reach aftereffects following visuomotor adaptation ([Cressman and Henriques, in press](#); [Mostafa et al., 2014](#)). Likewise, we can also infer that changes in perceived hand movements may be independent of reach adaptation from the [Synofzik et al. \(2008\)](#) and [Izawa et al. \(2012\)](#) studies. While both studies show significant and similar shifts in perceived hand direction, they showed opposite results for the patients reach adaptations. This supports our conclusion that the brain

areas or networks involved in motor changes are different than those involved in sensory or perceptual changes.

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