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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.

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

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