Can we improve slow learning in cerebellar patients?

Abbreviated title: Slow learning in cerebellar patients

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Conflict of interest statement: The authors declare no competing financial interests.

Acknowledgements: The study was funded by a grant of the German Research Foundation (DFG TI 239/16-1) awarded to OD and DT and a scholarship from the **E**ssener Ausbildungsprogramm "**L**abor und Wissenschaft" für den **A**erztlichen **N**achwuchs (ELAN) supported by the Else Kröner-Fresenius-Stiftung awarded to AM. We would like to thank Beate Brol for her support in the analysis of this experiment.

Abstract

We tested whether training paradigms targeting slow learning alleviate motor learning deficits of cerebellar patients compared to matched controls using four visuomotor tasks: standard, gradual, overlearning and long intertrial interval. We measured slow learning using spontaneous recovery, the return to learned adaptation after brief wash out of fast adaptation. Spontaneous recovery increased in both groups only in overlearning. A model of adaptation suggested that in controls the increase reflects changes in slow system dynamics. In contrast, because cerebellar participants plateaued more slowly than controls, added trials in models of cerebellar participants increased the level of slow learning. Whereas, under the model, slow learning became more resilient in controls, there was no change in its dynamics for cerebellar participants. Our results and modeling suggest that while residual slow learning does exist in cerebellar patients and can be expressed through increased training trials, the primary cerebellar deficit cannot be improved by overlearning paradigms.

1 Introduction

The cerebellar ataxias are a heterogeneous group of disorders clinically identified by cerebellar dysfunction. Patients exhibit a range of impairments in motor control, including incoordination of eye movements, dysarthria, limb incoordination, and gait disturbances (Mariotti et al., 2005), as well as impairments in the cognitive domain (Schmahmann and Sherman, 1998). While the genetic and pathophysiological underpinnings of many of the cerebellar ataxias are increasingly well understood (Jayadev and Bird, 2013; Matilla-Dueñas et al., 2014), treatment remains a major challenge with genetic therapies being at the horizon for only a subset of genetically defined ataxias (Scoles et al., 2017). Contemporary cerebellar therapy is aimed at alleviating motor symptoms to maintain activities of daily living (ADL), as no curative therapy currently exists (Ilg et al., 2014). Although the consensus is that cerebellar patients benefit from rehabilitation therapy, i.e. physical therapy, speech therapy and occupational therapy, little is known about the mechanisms underlying the improvements and how patients can benefit most (Fonteyn et al., 2014; Ilg et al., 2014). Providing effective care for ataxia patients can be especially challenging, since cerebellar patients suffer from well-known motor learning deficits (Maschke et al., 2004; Tseng et al., 2007) and initial studies suggest a relationship between motor learning deficits and the efficacy of neurorehabilitation programs (Hatakenaka et al., 2012). To develop training programs which are most beneficial for cerebellar patients, one needs to understand which learning abilities remain functional, and whether reduced learning abilities can be improved by certain interventions.

Much research on motor learning has focused on reach adaptation, leading to a well-characterized task that serves as good model for more general questions in motor learning and adaptation (Krakauer et al., 2019). In reach adaptation, two learning processes can be distinguished. A fast learning process -- thought to reflect explicit strategic and reinforcement

learning -- and a slow process -- thought to reflect implicit sensory error-based learning (McDougle et al., 2015; Smith et al., 2006). Although the cerebellum has recently been shown to contribute to both processes (Hull, 2020), it is thought to be primarily involved in sensory error-based learning. Indeed, previous work has found that cerebellar patients retain ability to use explicit strategy (Taylor et al., 2010) and reinforcement learning (Therrien et al., 2016). However, there have not been many studies exploring whether slow learning can be utilized by cerebellar patients. Early evidence indicated beneficial effects in gradual introduction of reaching movement perturbations in cerebellar patients (Criscimagna-Hemminger et al., 2010), but the results were not replicated in subsequent work (Gibo et al., 2013; Schlerf et al., 2013). Other paradigms shown to drive slow learning in healthy subjects have not been explored in cerebellar patients. We consider two additional such paradigms. The first is overlearning, continued training after asymptotic performance, which increases retention in healthy subjects as a function of the number of trials trained at asymptote (Joiner and Smith, 2008). The second is to use long intertrial intervals (ITI) between movements. This decreases the rate of learning in healthy subjects, but increases retention (Kim et al., 2015; Sing et al., 2009).

The aim of the present study is to test all the paradigms in the same sets of healthy subjects and cerebellar patients. We tested twenty patients with degenerative ataxia and twenty healthy age- and sex-matched controls on a visuomotor reaching adaptation task under four different training paradigms We tested their effects on the development of slow learning using a behavioral measure called spontaneous recovery. In spontaneous recovery, we measure the tendency of subjects to return to a learned perturbation after application of a short counterperturbation, a phenomenon that is thought to reflect retained slow learning following wash out of the fast component of the initial adaptation (Coltman et al., 2019; Smith et al., 2006).

In addition to the behavioral measure of slow learning, we also characterized it using the two-state model of Smith et al. (2006). Although this model has known limitations (Forano and Franklin, 2020; Petitet et al., 2018; Zarahn et al., 2008), it provides good fit to human behavior and successfully isolates the two main time constants of human learning. By using the model to characterize slow learning, we can gain insight into the changes caused by the behavioral paradigms.

Our interest was both in the ability of the different paradigms to drive slow learning in healthy subjects and in the differences between healthy subjects and cerebellar patients. Slow learning is particularly affected in cerebellar patients. We would like to know whether any paradigm that drives slow learning has the ability to leverage the remaining slow learning in hopes of ameliorating the deficit.

2 Methods

2.1 Participants

Twenty participants with cerebellar degeneration (9 females, 54.9 years ± 10.8 (SD), range 18 – 70 years) and twenty age- and sex-matched participants (9 females, 55.2 years ± 11.2 (SD), range 18 – 71 years) took part in the study. Cerebellar participants were recruited from the patients attending our ataxia clinic and matched controls were recruited via print advertisements distributed on the hospital campus. Only right-handed individuals were included, as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971). The severity of cerebellar symptoms in the group of cerebellar participants was assessed by one experienced neurologist (DT) and healthy age- and sex-matched controls were examined by AM. Cerebellar symptoms were scored on the International Cooperative Ataxia Rating Scale (ICARS; Trouillas et al., 1997), as well as the Scale for the Assessment and Rating of Ataxia (SARA; Schmitz-Hübsch et al., 2006). The group of cerebellar participants was diagnosed with diseases known to primarily affect the cerebellar cortex (Gomez et al., 1997; Timmann et al., 2009). Three age-matched controls were excluded and replaced due to neurological symptoms on their examination or minor extracerebellar pathology on their MRI. All participants gave informed oral and written consent. The experiment was approved by the ethics committee of the medical faculty of the University of Duisburg-Essen and conducted in accordance with the Declaration of Helsinki. The characteristics of the recruited cerebellar participants and matched controls can be found in **Table 1**.

Table 1

Overview Cerebellar participants and Control participants

Cerebellar participants							Control participants		
ID	**Age**	**Sex**	**Diagnosis**	**Disease duration**	**ICARS** (total/100)	**SARA** (total/40)	**ID**	**Age**	**Sex**
P01	18	M	ADCAIII	18 years	10.5	5	C01	18	M
P02	47	M	ADCAIII	25+ years	40	17.5	C02	43	M
P03	50	F	ADCAIII	25+ years	31	11.5	C03	50	F
P04	51	M	SCA14	25+ years	31	11.5	C04	50	M
P05	51	F	ADCAIII	19 years	29	12.5	C05	51	F
P06	52	F	SCA14	22 years	26.5	12	C06	53	F
P07	53	F	SCA6	2 years	23	9.5	C07	54	F
P08	53	M	SAOA	17 years	40	15	C08	53	M
P09	53	M	ADCAIII	17 years	36	11	C09	51	M
P10	54	F	SCA6	4 years	30.5	10	C10	56	F
P11	56	F	SCA14	25+ years	28	12	C11	58	F
P12	57	M	SCA6	11 years	38	11	C12	53	M
P13	57	M	SCA6	15 years	28	8	C13	59	M
P14	58	M	SAOA	25+ years	63.5	22	C14	61	M
P15	59	M	SCA6	5 years	23	9.5	C15	63	M
P16	60	F	SCA6	11 years	36.5	14	C16	60	F
P17	63	F	ADCAIII	23 years	33	13.5	C17	66	F
P18	66	M	SAOA	13 years	24.5	11	C18	66	M
P19	70	F	SAOA	7 years	32.5	12.5	C19	71	F
P20	70	M	SAOA	16 years	38	15	C20	67	M

Table 1: Cerebellar participants were age- and sex-matched with the controls on the right side of the table. SCA6 = spinocerebellar ataxia type 6; SCA14 = spinocerebellar ataxia type 14; SAOA = sporadic adult onset ataxia; ADCA III = autosomal dominant ataxia type III; ICARS = International Cooperative Ataxia Rating Scale (Trouillas et al., 1997); SARA = Scale for the Assessment and Rating of Ataxia (Schmitz-Hübsch et al., 2006). Disease duration is years since presentation of the first symptoms.

2.2 Task

All participants completed a standard reaching task with visuomotor perturbations. The experimental setup and task have been described previously in other studies from our group (Rabe et al., 2009). In short, participants were seated in front of an upright monitor and could,

with their right hand, move a two-jointed manipulandum freely in the horizontal plane (**Figure 1A**). Vision of the participant's arm was obstructed by a black cloth. Hand position and velocities were measured in a resolution of 10^6 counts per revolution and a sampling rate of 200 Hz (DMC-1826; Galil Motion Control). The location of the participant's hand was represented on the monitor by a green dot with a diameter of 5 mm. The origin and target locations were represented by a circle with a diameter of 10 mm, colored red and white respectively. At the start of each trial, the participant's hand was moved towards the origin location by the servomotors connected to the manipulandum. Then, after a delay of 2,000 ms, a target circle appeared at one of three possible target locations, located 10 centimeters away from the origin at an angle of 66°, 90° or 114° (**Figure 1B**). Participants were instructed to move the green dot from the origin towards the target with a "quick and accurate movement" as soon as the target appeared. When participants moved the cursor through an invisible boundary located 10 centimeters from the origin, their hand was gently brought to a stop by a simulated cushion, indicating the end of the movement. Following each movement, participants received feedback on whether they hit the target and moved with the correct velocity. The target turned yellow when moving too fast, blue when moving too slow, and green when moving with the correct velocity. Participants moved with the correct velocity when their movement and reaction time fell within a 250 ms window centered around 500 ms. The 250 ms window shrunk by 10% every time a movement had the correct velocity and increased by 10% when moving too fast or slow, adapting to a participant's individual capabilities. When participants also managed to hit the target, in addition to moving with the correct velocity, a "yahoo" sound was played.

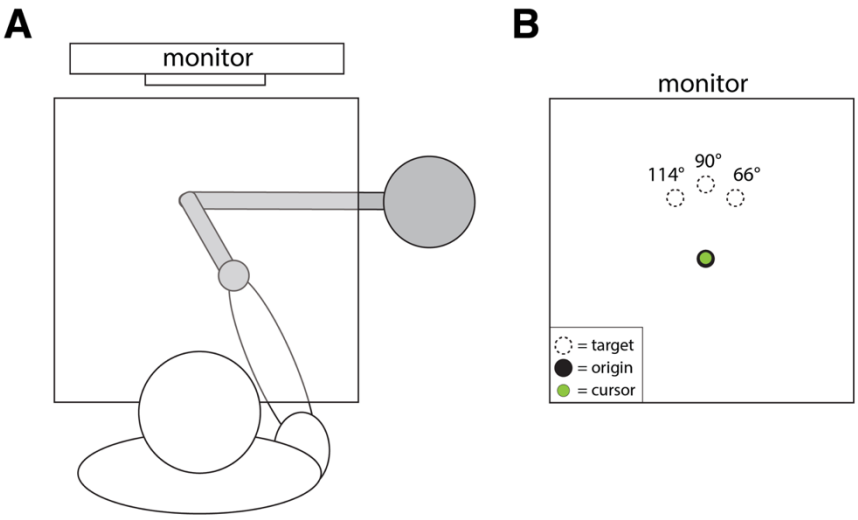

Figure 1*: A) Experimental setup. For illustrative purposes the tabletop is pictured here as transparent. In reality the tabletop was opaque to obstruct the view of the hand and robot arm. Additionally, a black cloth was draped over the shoulders of the participant and attached to the table to obstruct vision of the arm. B) Localization of origin and target circles on the monitor. One of the three target circles would pseudo-randomly appear at the start of a movement trial.*

The experimental task consisted of 4 different training paradigms. Each paradigm consisted of a baseline set, an adaptation set, and a washout set. All participants completed each of the training paradigms. The order of paradigms was counterbalanced with a Latin-squares design against first-order carryover effects (Williams, 1949). Every paradigm order was completed by 10 participants each (five cerebellar participants and five control participants, **Figure 2A**). Analysis of the effects of counterbalancing are presented in the supplementary materials. Furthermore, perturbation direction in the adaptation sets was balanced by flipping the direction of the perturbation (clockwise or counterclockwise) in every successive adaptation set. Participants were allowed to take 5- to 10-minute breaks between paradigms, but not after sets within a paradigm. Each baseline set consisted of 135 null trials, in which participants received veridical feedback on hand position, and 15 pseudo-randomly interspersed clamp trials, in which participants received perfect feedback regardless of movement error. Then, depending on the training paradigm, one of four adaptation sets followed. In the standard training paradigm, the adaptation set consisted of 108 adaptation trials, in which a visuomotor

167 perturbation of 30° was introduced abruptly, and 12 pseudo-randomly interspersed clamp
168 trials (**Figure 2B**). The gradual paradigm contained 108 adaptation trials in the adaptation set,
169 where the visuomotor perturbation of 30° was introduced gradually over the course of the set,
170 increasing linearly each trial. The final 6 trials of the gradual adaptation set were at 30° of
171 visuomotor perturbation. In addition, 12 clamp trials were pseudo-randomly interspersed
172 (**Figure 2C**). The overlearning adaptation set consisted of 324 trials with a visuomotor
173 perturbation of 30° (three times the amount of the standard paradigm) and 36 interspersed
174 clamp trials (**Figure 2D**). The long intertrial interval (ITI) adaptation set included 120
175 adaptation trials with visuomotor perturbations of 30°, where instead of delay of 2 seconds
176 between each movement, the delay was increased to 15 seconds (**Figure 2E**). The adaptation
177 set of the long ITI paradigm did not include any clamp trials, thus trial-to-trial forgetting was
178 only dependent on the passage of time. Finally, all adaptation sets were followed by a
179 washout set. The first 12 trials of the washout set consisted of counterperturbation trials,
180 where the direction of the perturbation was flipped from the direction in the adaptation set.
181 Then, 60 clamp trials and 60 null trials followed.

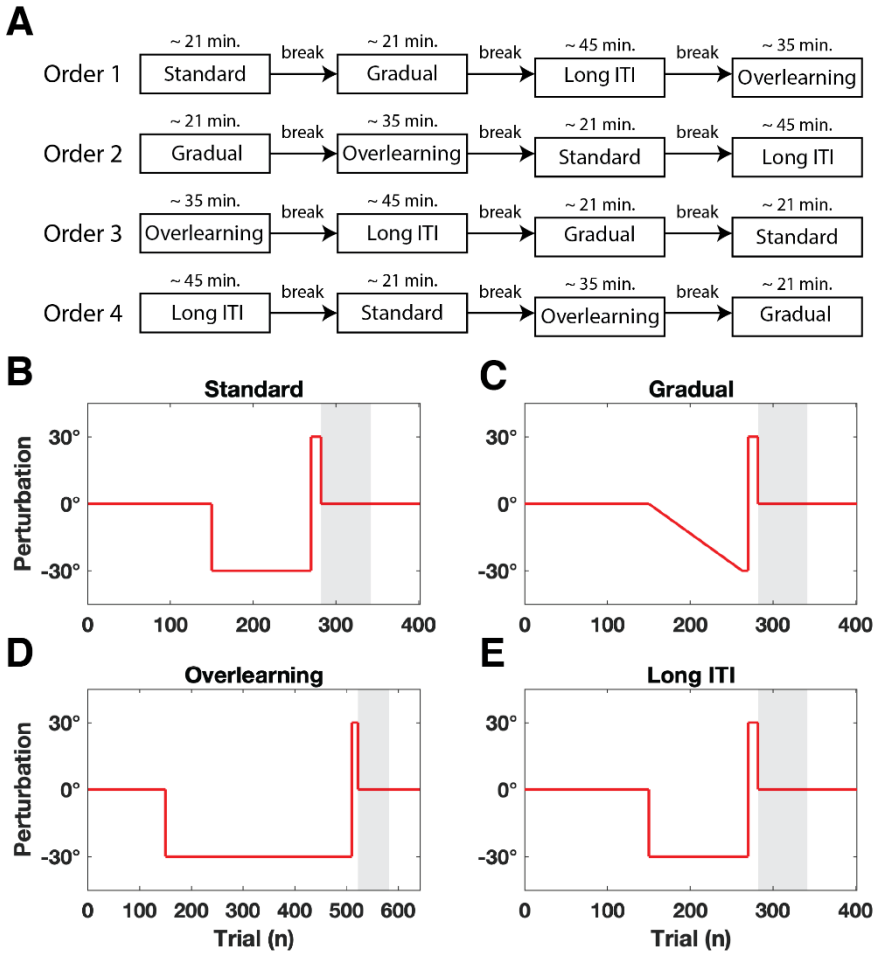

***Figure 2**: A) Overview of the paradigm orders. B–E) Trial structure of the experimental paradigms. Red line indicates the size and direction of the visuomotor perturbation. Direction of the perturbation is pictured here as clockwise for all paradigms, in reality perturbation direction was counterbalanced within participants. Grey area indicates the block of 60 clamp trials in the washout set. Not pictured are pseudo-randomly interspersed clamp trials during the baseline and adaptation phase.*

2.3 MR imaging

Cerebellar participants and age-matched controls were examined in a 3T combined MRI-PET system (Siemens Healthcare, Erlangen, Germany) with a 16-channel head coil (Siemens Healthcare) [TR = 2,530 ms; TE = 3.26 ms, TI = 1,100 ms; flip angle 7 deg; voxel size 0.5 × 0.5 × 1.0 mm^3]. All MR scans were evaluated by an experienced neuroradiologist (SLG). A voxel-based morphometry analysis was applied to the cerebellum of each participant as described previously (Hulst et al., 2015; Taig et al., 2012). The analysis was automated with an in-house program written for MATLAB 9.4 using the SUIT toolbox (version 3.2)

(Diedrichsen et al., 2009), implemented in SPM12 (http://www.fil.ion.ucl.ac.uk/spm/software/spm12).

2.4 Analysis of behavioral data

Behavioral data was analyzed in MATLAB 9.4 (MathWorks, Natick, USA). Our primary outcome measure was the reaching direction (in degrees) at the end of the movement (i.e., when participants hit the simulated cushion). The reaching direction was calculated by taking the angle between a straight line from the position of movement onset to the target and a straight line from the position of movement onset to hand position at the end of the movement. Movement onset was defined as the first moment when movement velocity exceeded 5cm/s. Reaching directions were corrected for movement biases by calculating the average reaching direction in each baseline set and subtracting this from the subsequent adaptation and washout sets of a training paradigm. For ease of interpretation, reaching directions were flipped towards the same direction, regardless of perturbation direction, in all figures and analyses. Furthermore, paradigms were reordered to a canonical order for each participant, starting with the standard learning paradigm, then gradual learning, overlearning and finally the long ITI paradigm, regardless of the order the participant encountered the paradigms. Statistical analyses were conducted using Markov Chain Monte Carlo (MCMC) methods in MATLAB and JAGS 4.3.0 (Plummer, 2003). A mixed-design model (ANOVA-like) was used to estimate the difference in reaching directions between factors. Participant group (cerebellar participant or control participant) was included as a between-subject factor. Movement phase and training paradigm were included as within-subject factors. Movement phases were defined as follows: baseline (all 150 trials in the baseline set), early adaptation (first 30 trials of the adaptation set), late adaptation (final 6 trials of the adaptation set) and recovery (all 60 clamp trials in the washout set). A random intercept for each participant and phase was included as well. The model ran on four separate chains with an adaptation phase

of 5,000 samples and burn-in phase of 25,000 samples, after which we collected 50,000 samples per chain. The MCMC procedure gives us a posterior distribution of credible parameter values, given the data. The 95% highest density interval (HDI) contains 95% of the mass of credible parameter values, where each value within the HDI has a higher probability density than any value outside the HDI. When the HDI falls completely within the Region of Practical Equivalence (ROPE), we accept the null value of the parameter and when the HDI falls completely outside the ROPE, we reject the null value of the parameter. The ROPE was set at $[-3.5°; 3.5°]$ to match the within group variability between subjects. Each parameter was visually and quantitatively checked to assure proper sampling of the posterior distribution using common MCMC diagnostics (Kruschke, 2010). First, trace plots were visually inspected for chain convergence. Next, the effective sample size (ESS), the potential scale reduction factor (PSRF) and the Monte Carlo Standard Error (MCSE) were calculated for all parameters. The PSRF was close to 1 for each parameter (max: 1.0002), MCSE was close to 0 for each parameter (max: 0.0001), and median ESS was generally large (>> 5,000), indicating convergence of the model run. The model code is available on https://github.com/thomashulst/paper-slowlearning.

2.5 State-space modeling

A two-state model of motor learning was fit to the reaching directions of all trials in each individual participant. This classical model was originally presented by Smith and colleagues (Smith et al., 2006) and posits a fast state (x_t^F), that learns and forgets quickly, and a slow state (x_t^S), that learns and forgets slowly, both adapting to the motor error. The model was fit using a Bayesian approach similar to that in van der Vliet et al. (2018). Details of the model and the Bayesian fitting procedure used to estimate individual subject parameters are available in the supplementary materials. The model code is available on https://github.com/thomashulst/paper-slowlearning.

We examined the internal model parameters to gain insight into the factors driving increased spontaneous recovery in the overlearning paradigm. To this purpose, we compared the estimated learning and forgetting rates of the fast system (BFast and AFast, respectively) and slow system (BSlow and ASlow) across paradigms and groups, both at the level of individual subjects and the population.

3 Results

3.1 Voxel-based morphometry (VBM)

First, the results of the structural MRI data were analyzed using VBM. **Figure 3** displays the difference in gray matter volume per voxel (in t-scores) between healthy participants and cerebellar participants. A resampling procedure (permutation test) was conducted to control the family-wise error rate. The significance threshold was determined to be 3.95, meaning that voxels with an absolute t-score higher than 3.95 were considered significant. No significant positive differences were found; thus, the figure displays negative t-scores only. The VBM analysis revealed a pattern of cerebellar degeneration in patients largely consistent with prior work (Hulst et al., 2015). The volume loss was largest in the anterior lobe of the cerebellum and the superior part of the posterior lobe (i.e., lobule VI). Cerebellar degeneration of the anterior cerebellum and lobule VI (i.e. the anterior hand area) are associated with motor learning deficits (Donchin et al., 2012; Rabe et al., 2009). Cerebellar degeneration was less pronounced in the inferior parts of the posterior lobe compared to earlier work (Hulst et al., 2015), which could be explained by younger cerebellar participants in the current study, with less severe ataxia scores.

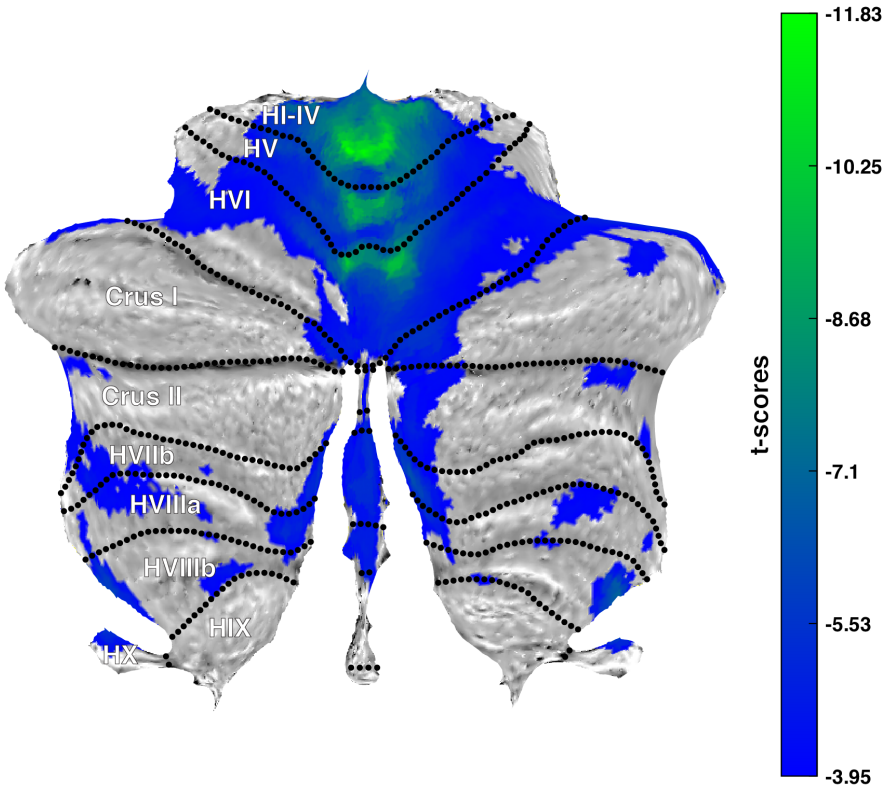

Figure 3*: Flatmap of the cerebellum. Colors indicate the gray matter volume difference per voxel between healthy participants and cerebellar participants in t-scores. Voxels that do not exceed the threshold* (-3.95) *are not colored, low significant t-scores are colored blue, and high significant t-scores are colored green. Flatmap template from Diedrichsen and Zotow, 2015.*

3.2 Average reaching directions

The average reaching directions for each paradigm in control participants and cerebellar participants are plotted in **Figure 4A** and **4C**. Differences in mean reaching directions per phase, paradigm and subject group were tested using the mixed-design model from the methods section and the most important results are described below.

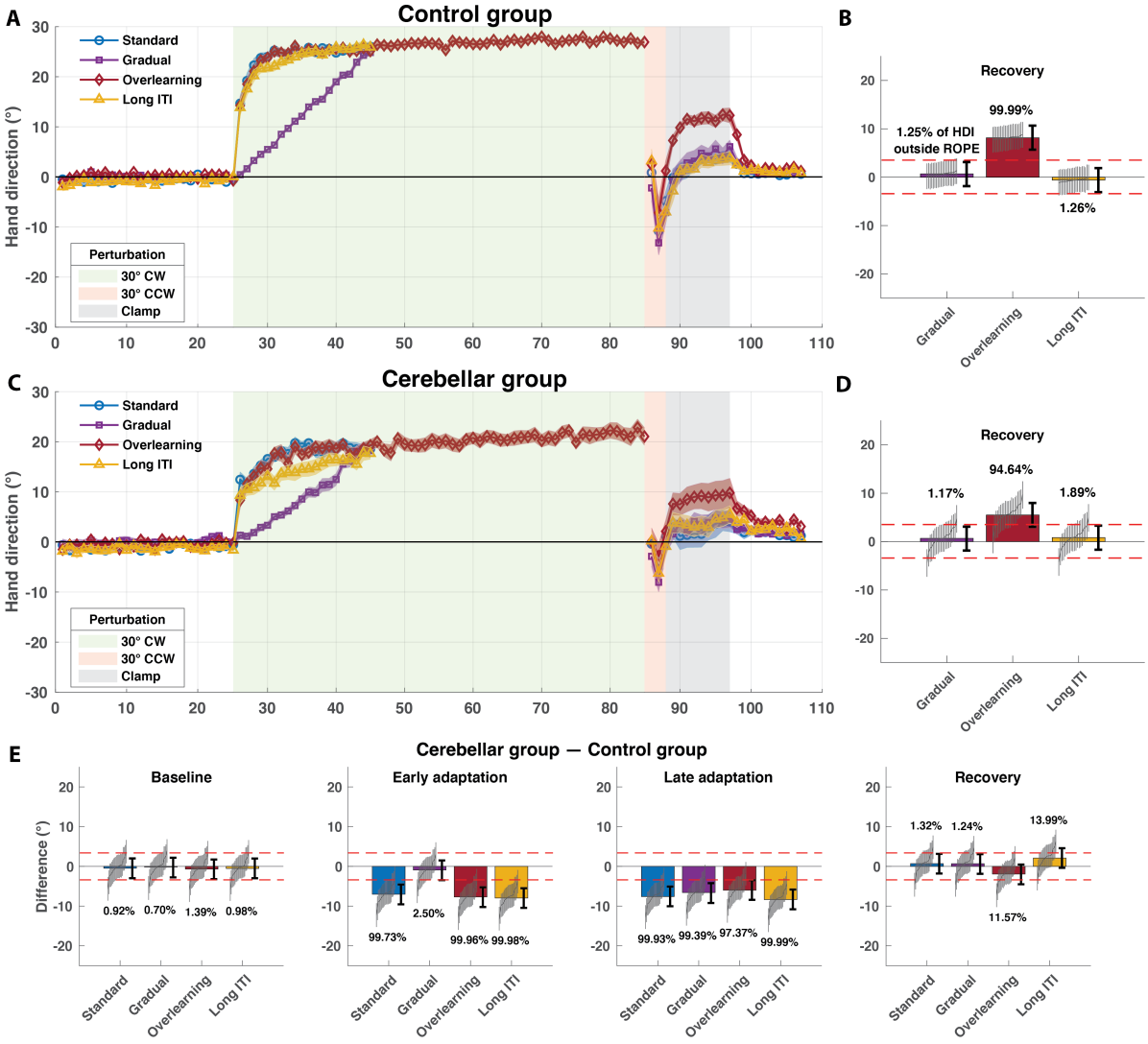

***Figure 4**: Average reaching directions of control participants and cerebellar participants. A) Reaching directions of control participants. Trials were binned per 6 trials. Shaded errorbars are mean ± SEM. B) Difference in reaching directions between the standard paradigm and slow learning paradigms during the recovery phase of control participants. Thin errorbars indicate HDI of individual participants, thick errorbars indicate HDI of group. % indicates percentage of HDI outside the ROPE. C) Reaching directions of cerebellar participants. D) Difference in reaching directions between the standard paradigm and slow learning paradigms during the recovery phase of cerebellar participants. E) Difference in reaching directions between cerebellar participants and control participants over all paradigms and phases of learning.*

As expected, reaching directions of control participants and cerebellar participants are practically straight during baseline in all training paradigms. When movements are perturbed by a visuomotor rotation, control participants learn the perturbation quickly, almost completely counteracting the rotation early and late in the adaptation set (barring the early phase of the gradual paradigm). Cerebellar participants adapt more slowly and much less,

counteracting about half of the rotation compared to healthy controls. In general, control participants counteract more of the perturbation than cerebellar participants, both early and late in the adaptation set (**Figure 4E**).

Behaviorally, the most salient difference between paradigms in control participants exists between the amount of spontaneous recovery in the standard paradigm versus the overlearning paradigm, i.e., there is more spontaneous recovery after overlearning than standard learning (**Figure 4B**). Similarly, the difference between the overlearning paradigm and the standard paradigm in cerebellar participants is highly suggestive of more spontaneous recovery after overlearning as well, though this difference is smaller and obscured by the larger variability in the cerebellar patients (**Figure 4D**). We hypothesized that the additional amount of spontaneous recovery in both groups could have two different causes. It might be due to more slow learning resulting from the prolonged activation of the slow system. Alternatively, the additional spontaneous recovery might occur despite similar levels of slow learning through increased retention in the slow system. These hypotheses will be explored in the next section.

3.3 Modelling

Since behavioral differences between the paradigms were mainly evident in overlearning and standard learning, we focus on comparing these paradigms. The model results for the other paradigms can be found as supplementary material. To assess how the differences in the learning and retention rate between training paradigms affect motor output (y_t) and the states (x_t^F and x_t^S), posterior predictive plots were generated from multiple random draws (n = 10,000) of the posterior distributions of each participant in the control and cerebellar group (**Figure 5**). The model captures the structure of a subject's behavior: rapid learning is followed by a plateau and the short period of counterperturbation leads to spontaneous recovery. The model also captures the increased spontaneous recovery in the overlearning

paradigm and the fact that this increase is much smaller for cerebellar patients than for controls. The amount of spontaneous recovery exhibited by the model in the two paradigms for both groups is shown by the blue bars in **Figure 5C and 5F**. The model predicts an increase of 6.12° in spontaneous recovery for controls and an increase of 2.04° for cerebellar patients.

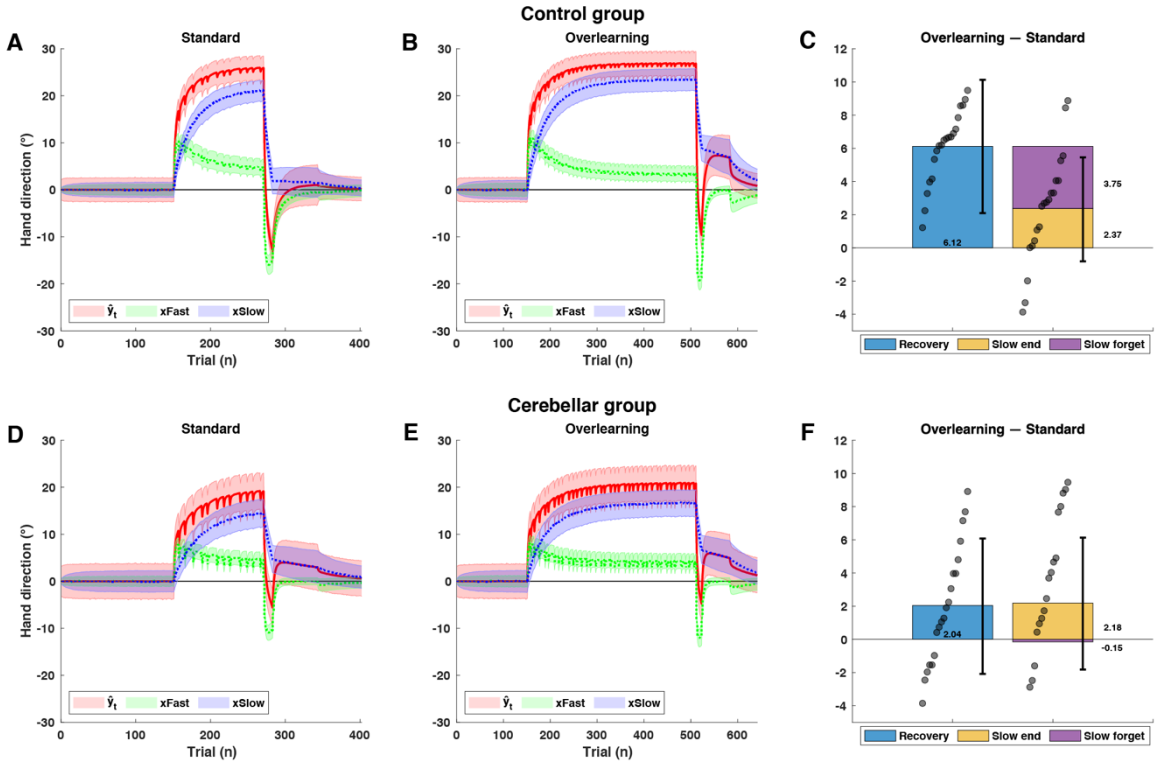

***Figure 5**: Posterior predictive plots of control participants in the A) standard and B) overlearning paradigm. The average model output ($\hat{y}_t$) is displayed with a solid red line, the average fast state (x_t^F) with a dotted green line, and the average slow state (x_t^S) with a dotted blue line. The shaded errorbars indicate the variability around the average posterior predictive (2.5th percentile – 97.5th percentile of simulated data). Panel C) shows the difference in spontaneous recovery of the slow system between the standard and overlearning paradigm (blue bar) and the difference in the amount of slow learning at the end of the adaptation set (yellow bar). The purple bar is the difference in the drop of slow learning after the counterperturbation trials between the standard and overlearning paradigm. Grey circles on the blue bar indicate individual differences in spontaneous recovery, the thick errorbar is the HDI of the group. Grey circles on the yellow bar indicate individual differences in slow learning at the end of adaptation, the thick errorbar is the HDI of the group. Panels D), E) and F) display the same plots for cerebellar participants instead.*

The results of the model support the intuitive idea that spontaneous recovery reflects slow learning. For both groups, fast learning is essentially 0 during the spontaneous recovery phase. However, the results of the model are not entirely consistent with our initial hypothesis

336 that increased spontaneous recovery reflects increased slow learning at the end of adaptation.
337 The yellow bar in **Figure 5C** shows the difference in the amount of slow learning in the
338 model at the end of adaptation in the standard paradigm vs the overlearning paradigm. Slow
339 learning in controls is only 2.37° higher in the overlearning paradigm than in the standard
340 paradigm, a difference similar to that in cerebellar patients (2.18°). Indeed, in controls, the
341 model predicts that increased spontaneous recovery reflects primarily a reduced drop in slow
342 learning after the counterperturbation trials (i.e., less forgetting of the slow system). As
343 depicted by the purple bar in **Figure 5C**, the slow forgetting for controls in the overlearning
344 paradigm is 3.75° smaller than in the standard paradigm. Thus, for controls, about 61.3% of
345 the increased spontaneous recovery comes from a reduced drop in slow learning during the
346 counterperturbation phase and only 38.7% from increased buildup of slow learning during the
347 elongated adaptation set. In contrast, for cerebellar patients, practically all increased
348 spontaneous recovery is a result of added buildup of slow learning.
349 To understand how the model generated less slow forgetting after counterperturbation trials in
350 the overlearning paradigm in control participants, we examined how learning and retention
351 parameters changed between the standard and overlearning paradigm (**Figure 6**). As the
352 figure shows, the model suggests that, in controls, slow retention (ASlow) is higher in
353 overlearning than in the standard paradigm and the slow learning rate (BSlow) is actually less
354 (**Figure 6A**). This result is consistent across control participants and contrasts with the
355 learning rate and retention in the fast state, which are largely unchanged between the
356 paradigms. While the model also ascribes a decreased slow learning rate to some cerebellar
357 subjects, there are a few cerebellar subjects who do not show such a shift (**Figure 6B**).

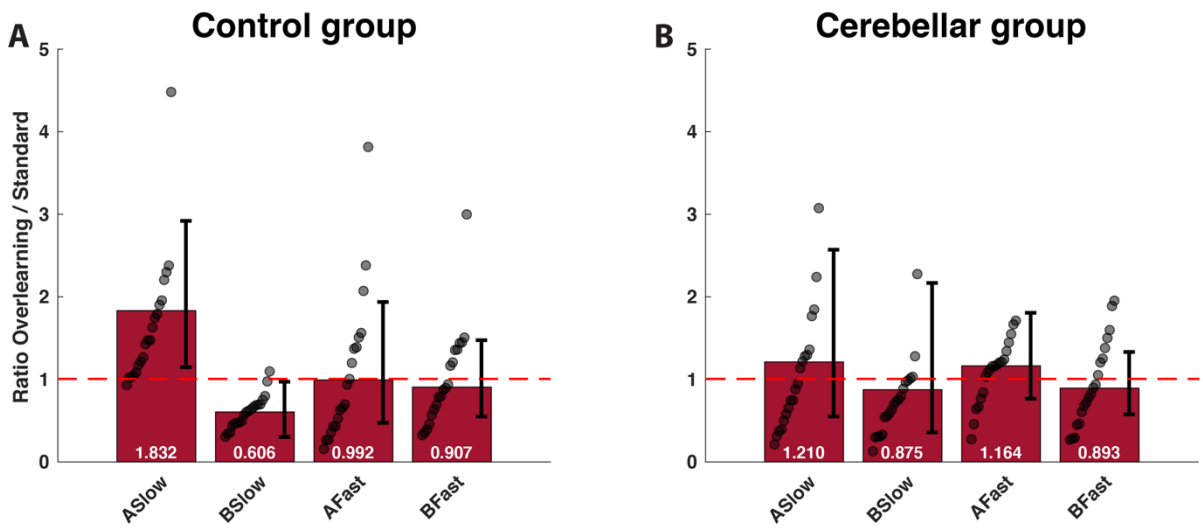

Figure 6: *Change in learning and retention parameters between paradigms. The change in parameters is expressed as a ratio between the standard and overlearning paradigm. For A parameters the ratio was taken as* $\frac{1-A_{\text{standard}}}{1-A_{\text{overlearning}}}$*, for B parameters the ratio was taken as* $\frac{B_{\text{overlearning}}}{B_{\text{standard}}}$*. This choice was made so that in both cases we are showing ratios of rates (forgetting rate and learning rate) and also so increased slow learning in overlearning would lead to larger numbers for both parameters. The gray circles represent ratios for individual participants, the thick black errorbar is the HDI of the population parameter. The red line indicates a ratio of 1. A) Control participants. B) Cerebellar participants.*

These changes in model parameters may be the cause of the change in model behavior between the two tasks, but it is also possible that changes in model behavior reflect the extended adaptation phase in the overlearning paradigm. To test the effect of the changes in the model parameters on model behavior, we generated posterior predictive data for the overlearning paradigm using parameters from the standard paradigm and for the standard paradigm using parameters from the overlearning paradigm. The results of this are shown in **Figure 7**. The figure shows that control participants have much smaller spontaneous recovery in the overlearning paradigm when using parameters from the standard paradigm (**Figure 7A**). Similarly, spontaneous recovery in the standard paradigm is larger using parameters from the overlearning paradigm (**Figure 7B**). Out of the total difference in the spontaneous recovery of controls between paradigms, practically all of it seems to come from the difference in parameters (**Figure 7C**). In other words, the changes in parameters primarily cause reduced slow forgetting during the counterperturbation and they have little effect on

level of the slow at the end of adaptation. A similar analysis of the model fit to cerebellar patients produces different results (**Figure 7D-F**). In the case of cerebellar patients, there is almost no difference in the amount of spontaneous recovery caused by swapping parameters. Thus, the model does not provide a good explanation for the increase in spontaneous recovery in the cerebellar patients.

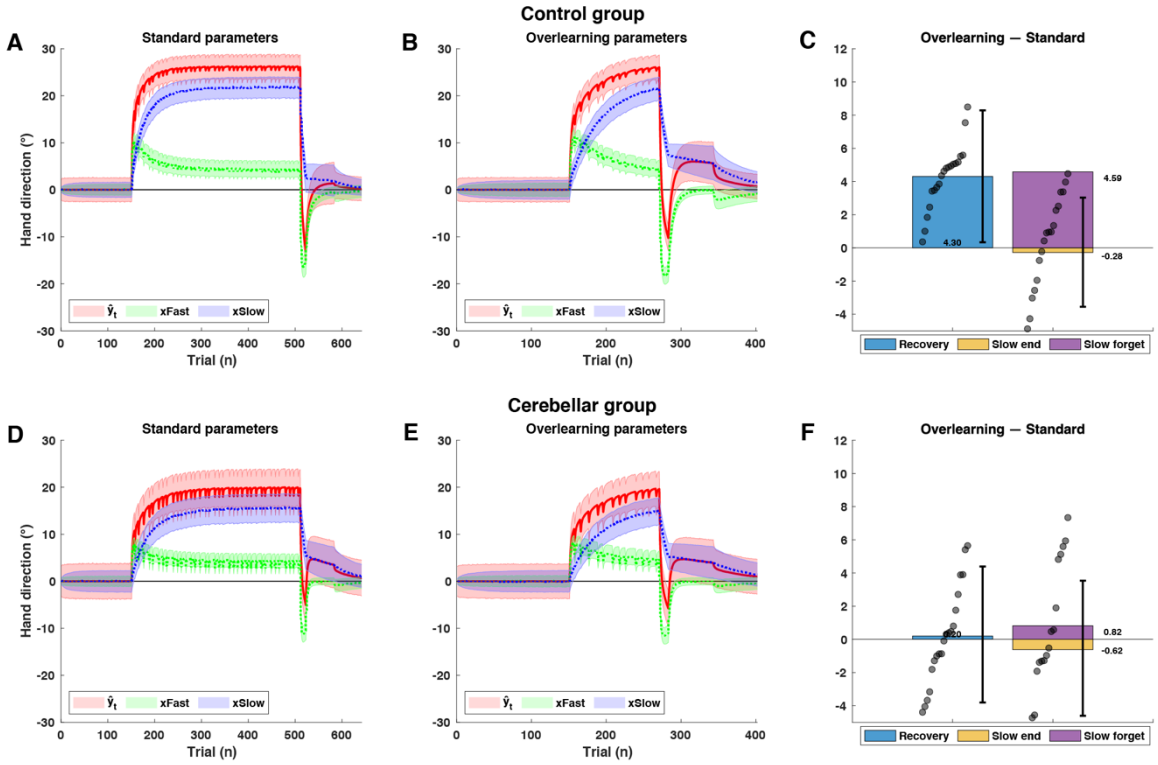

Figure 7: *Posterior predictive plots generated using incongruent parameters. That is, the posterior predictive plots for the overlearning paradigm were generated from the parameters fit to the standard paradigm and vice versa. A) Control participants with standard parameters in the structure of the overlearning paradigm and B) overlearning parameters in the structure of the standard paradigm. The average model output ($\hat{y}_t$) is displayed with a solid red line, the average fast state (x_t^F) with a dotted green line, and the average slow state (x_t^S) with a dotted blue line. The shaded errorbars indicate the variability around the average posterior predictive (2.5th percentile – 97.5th percentile of simulated data). Panel C) shows the difference in spontaneous recovery of the slow system between the standard parameters and overlearning parameters (blue bar) and the difference in the amount of slow learning at the end of the adaptation set (yellow bar). The purple bar is the difference in the drop of slow learning after the counterperturbation trials between the standard and overlearning parameters. Grey circles on the blue bar indicate individual differences in spontaneous recovery, the thick errorbar is the HDI of the group. Grey circles on the yellow bar indicate individual differences in slow learning at the end of adaptation, the thick errorbar is the HDI of the group. Panels D), E) and F) display the same plots for cerebellar participants instead.*

399 **4 Discussion**

400 We tested 3 paradigms that have been thought to increase slow learning in both controls and
401 cerebellar patients. For each we examined spontaneous recovery after a short
402 counterperturbation, a phenomenon that has been taken as a hallmark of slow learning (Smith
403 et al., 2006). We find that only one paradigm, overlearning, increased spontaneous recovery
404 and that it did so in both controls and cerebellar patients **(Figure 4)**. Intuitively, increased
405 spontaneous recovery might been taken as a sign that the level of slow learning is higher at
406 the end of adaptation. We tested this by fitting a two-state model of motor adaptation to our
407 data using a Bayesian fitting procedure and generating posterior predictive data to model the
408 behavior of the subjects. Our model showed increased spontaneous recovery, especially in
409 control subjects **(Figure 5)**. However, this did not result from a higher level of slow learning
410 at the end of adaptation. Rather, overlearning led to a smaller drop in the slow learning during
411 the counterperturbation. This seemed to be because, in controls, the model parameter for
412 retention of slow learning (ASlow) was higher during overlearning than during the standard
413 paradigm and the model parameter for slow learning rate (BSlow) was lower during the
414 overlearning than in the standard paradigm **(Figure 6)**. We verified that the change in
415 parameters was the primary driver of the change in model behavior by using parameters from
416 the standard model in the overlearning paradigm and vice-versa. This showed that increased
417 spontaneous recovery in the model came primarily from changes in the parameters rather than
418 the difference in the number of trials performed by the model **(Figure 7)**. Our model was not
419 able to explain the increased spontaneous recovery in cerebellar patients and did not show
420 strong changes in the parameter values in cerebellar patients going from the standard
421 paradigm to overlearning. Taken together our results indicate that extended training – as used
422 in our overlearning paradigm – can increase the resilience of slow learning to a
423 counterperturbation in cerebellar patients and controls and that the increased resilience is

424 smaller in cerebellar patients than in controls. Modelling results suggest that the mechanism
425 of increased resilience may be different in cerebellar patients and controls.
426 Our primary result is that the overlearning task was the only paradigm that led to more
427 spontaneous recovery than the standard tasks. There was logic to thinking the other tasks
428 would also lead to greater spontaneous recovery. Gradual adaptation has long been thought to
429 decrease the rate at which retention washes away compared to abrupt adaptation
430 (Criscimagna-Hemminger et al., 2010; Huang and Shadmehr, 2009; Kagerer et al., 1997;
431 Kluzik et al., 2008; Michel et al., 2007; Wong and Shelhamer, 2011) although there have been
432 some studies that did not find such an effect (Klassen et al., 2005; Werner et al., 2014). A
433 recent paper suggests that the apparent effects on retention in the gradual condition actually
434 reflects secondary effects either of training duration or level of learning (Alhussein et al.,
435 2019). This is entirely consistent with our results. Our expectation regarding an effect of long
436 ITIs is rooted in the history showing increased retention following spaced learning compared
437 to massed learning (for a review see Smolen et al., 2016), that has been documented long ago
438 also in motor adaptation (Taub and Goldberg, 1973). Indeed, recent work has suggested that
439 long ITIs should drive stronger retention in adaptation (Kim et al., 2015; Zhou et al., 2017).
440 However, in these studies, effects are small and individual subject variability is large with
441 delays on the order of 15 sec. In both studies, details of the experimental protocol were also
442 quite different from our own. Thus, it might be possible to see effects with a long ITI, but it
443 would require delays that are quite long and a different task. In sum, our results are consistent
444 with other results in the literature raising doubts about whether either gradual adaptation or
445 long ITIs drive the slow learning system.
446 Overlearning – the continued practice once performance has plateaued – has long been known
447 to increase retention (for review see Driskell et al., 1992). The effect of the number of training
448 trials on retention of motor adaptation has been confirmed more recently (Joiner and Smith,

2008; Yamada et al., 2019). Indeed, as mentioned, Alhussein (2019) showed that previously reported effects of gradual adaptation on slow learning are, to a large extent, mediated by the number of training trials. Our findings are consistent with these previous findings. However, the effects shown previously are different from ours. First, Joiner and Smith (2008) and Yamada (2019) both show increased retention after 24 hours, while Alhussein (2019) measures the rate of decay of performance in a no feedback condition immediately after training. Ours is the first paper to our knowledge to show an effect of overlearning on spontaneous recovery.

Our second basic result is that spontaneous recovery was also increased in patients, although in a manner that was less pronounced than in controls. Consistent with many previous findings, cerebellar subjects learned slower than controls and reached a lower level of adaptation at the end of the adaptation **(Figure 4)**. During spontaneous recovery, their performance was close to that of controls for all paradigms, including the overlearning. This suggests that overlearning does cause some increased slow learning in patients as well as controls.

Our third basic result comes from our modeling which suggests that overlearning changes the parameters of the slow system in controls. Joiner and Smith (2008) ascribe most of the effect of overlearning to an increase in the level of slow adaptation with increased number of training trials. This contrasts with our interpretation: most of the effect reflects slow adaptation becoming more resistant to change as overlearning progresses. The differences may arise from the length of training in the two studies. Joiner and Smith (2008) show an effect that begins to level off near 100 training trials and the group with the most training only does 160 training trials. Our study had one group with around 108 training trials and another with 324 training trials. Thus, it is possible that what they see reflects a slow rise in the level

473 of the slow adaptation system, but that after this system reaches a plateau increased training
474 begins to change its responsiveness.
475 Model results also suggest that at the end of the standard paradigm, the slow system of
476 cerebellar patients has not yet reached plateau and some increase is still possible in the slow
477 learning system. The model suggests that cerebellar patients have less slow learning than
478 controls and more slow forgetting. Fast learning of cerebellar patients and controls is quite
479 similar, consistent with earlier experimental findings (Taylor et al., 2010; Wong et al., 2019).
480 The idea that the history of adaptation influences its dynamics is not new (Shadmehr and
481 Brashers-Krug, 1997). Our suggestion that overlearning may lead to increased resiliency in
482 the slow system is in line with previous research specifically suggesting that environmental
483 consistency affects adaptation dynamics (Avraham et al., 2019). Indeed, previous work has
484 also used changing fit of the two state model as evidence of changes in learning parameters
485 (Mawase et al., 2014).
486 Conclusions drawn from our research must be tentative due to a number of limitations. One
487 important caveat is that our design is a within subjects design with each subject doing all tasks
488 on the same day. We addressed this limitation in different ways. First, we used washout at the
489 end of each session to reduce transfer (Caithness et al., 2004; Krakauer et al., 2005; Nguyen et
490 al., 2019; but see also Kitago et al., 2013; Villalta et al., 2015). Second, order of the tasks and
491 perturbation direction was counterbalanced between subjects and we tested for order effects
492 (see supplementary materials). We do not believe that our central result is sensitive to possible
493 inter-session effects. A second concern is that subtle details of the task – such as the fact that
494 the gradual adaptation group did not spend any time in the plateau or that the long ITIs may
495 have been too short -- may have specifically influenced our results. This possibility cannot be
496 ruled out. A third concern is one that is characteristic of all patient studies: patients are
497 variable, disease etiology is complex, and we are specifically studying chronic lesions.

Perhaps the most salient limitation of our study is in the interpretation of the modeling. The modeling work cannot be conclusive, and alternative explanations exist. Overlearning may engage additional learning mechanisms that are not accounted for by the two-state model. For instance, Therrien et al., (2016) has shown that reinforcement learning can be selectively engaged in the adaptation task, and that this can affect the way subjects behave during error clamps (Shmuelof et al., 2012). Additional mechanisms to consider are use-dependent learning (Diedrichsen et al., 2010) or model-free learning (Huang et al., 2011). Finally, a recently published model uses dynamic formation of specific adaptation memory to explain many of the dynamics of adaptation (Heald et al., 2020). Thus, our findings and modeling work lend credence to the idea that extra practice makes learning more resilient, but they do not conclusively identify the mechanisms based on comparison of alternative models.

In sum, our research shows that spontaneous recovery is specifically affected by overtraining in cerebellar patients and controls. We hypothesize that, in controls, this is primarily driven by changes in the dynamics of slow adaptation while in cerebellar patients it reflects changes in the amount of slow adaptation achieved. That is, while residual slow learning does exist in cerebellar patients, we do not see evidence that the primary cerebellar deficit can be improved by overtraining paradigms.

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