

Cerebellar damage reduces the stability of motor memories

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A number of studies have shown that motor adaptation is impaired following cerebellar damage. However, the degree of impairment varies considerably from one study to another, with widely ranging results reported even within the same task. For example, three recent force field adaptation studies in reaching arm movements have reported very different levels of impairment ranging from 30-70%, as shown in Figure 1. Smith and Shadmehr (2005) reported a substantial 75% deficit in force field adaptation, but two more recent studies (Gibo et al 2013; Criscimagna-Hemminger et al 2010) found only 30-40% learning deficits in this task. Why would this be? Here we suggest that cerebellar damage reduces the temporal stability of motor memories. If this were the case, paradigms with longer inter-trial spacing might be more sensitive to cerebellar damage, as this damage would lead to greater decay of adaptation in the time interval between movements. Interestingly, the Smith and Shadmehr study was based on an 8-movement-direction paradigm whereas Gibo et al (2013) and Criscimagna-Hemminger et al (2010) employed only one or two movement directions, respectively. Correspondingly, the inter-trial intervals between consecutive movements in the same direction were 4-fold greater in the Smith and Shadmehr study, as shown in Figure 1.

We recently found that memories for force-field adaptation display a rapid but incomplete decay with the passage of time, suggesting distinct temporally-stable and temporally-labile components. Figure 2 illustrates this decay showing that 75% of the learned adaptation is temporally-stable, but that the remaining 25% decays rapidly with a time constant of less than 20 sec. We hypothesize that cerebellar damage may lead to a specific deficit in the formation of temporally-stable motor memories, altering the balance between stable and volatile memories, and increasing the reliance on temporally-volatile memories during motor learning. This would lead to greater decay for motor memories with the passage of time.

We tested this idea by reanalyzing the data from the Criscimagna-Hemminger et al (2010) and Gibo et al (2013) studies to examine the extent to which memory retention might be impaired with cerebellar damage. These data were originally analyzed to look at overall learning levels, but here we focused on trial-to-trial changes in learning that could reflect impairments in temporally-stable learning. Specifically, we took advantage of the fact that the effective inter-trial interval (ITI) between movement in the same direction varied considerably from one trial to the next in these studies by comparing retention on trials with different ITIs.

The Criscimagna-Hemminger et al (2010) study provided by far the richer dataset of the two, with 2 rest breaks of 30-60 seconds between blocks during the force training epoch, and random switching between two target directions that resulted in variable ITIs between consecutive movements in each target direction. When we compared performance in movements that were immediately preceded by movements in the same direction to ones where the preceding same-direction movement was more distant, we found greater decay in adaptation in cerebellar patients compared to controls (Figure 3b). Moreover, when expressed as a fraction of the adaptation observed on consecutive trials, memory decay on the non-consecutive trials was greater for cerebellar patients than control participants ($p < 0.01$). Rest breaks resulted in even greater ITIs which led to a pronounced memory decay in cerebellar patients that was greater than the corresponding decay observed in controls ($p < 0.01$) as shown in Figure 3b-c. Following these rest breaks, cerebellar patients retained just 27% of learning compared to consecutive-trial performance, whereas healthy control subjects retained 72%. The Gibo et al (2013) data are also consistent with impaired stable learning but do not provide statistically significant results, likely because there is only a single movement direction and only a single rest break. Although the variability was high, the data suggest that the cerebellar patients display reduced retention, displaying less than 10% retention following rest breaks, whereas controls retained about 60% (Figure 3e-f).

Together, our analyses suggest that the cerebellum may be critical for the formation of temporally-stable memories of motor adaptation. This raises the intriguing possibility that the cerebellum may provide a gateway to the formation of stable motor memories akin to the role of the hippocampus for stable declarative memory formation.

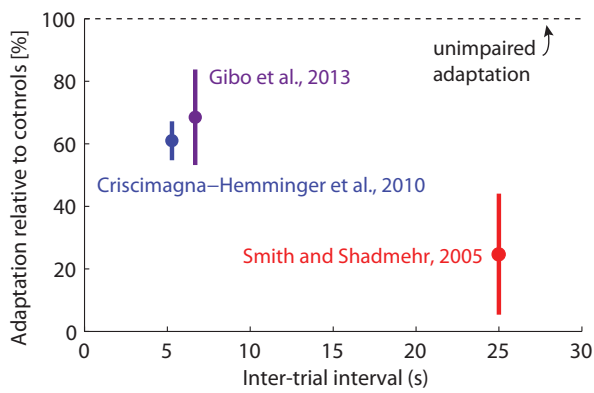


Figure 1: Previous work shows wide ranging deficits for cerebellar patients. The average adaptation for severe cerebellar patients is shown as a % of unimpaired adaptation estimated from healthy controls data, and it is plotted against the median inter-trial interval for the three different previous studies. Cerebellar patients' performance was most impaired when inter-trial intervals were highest.

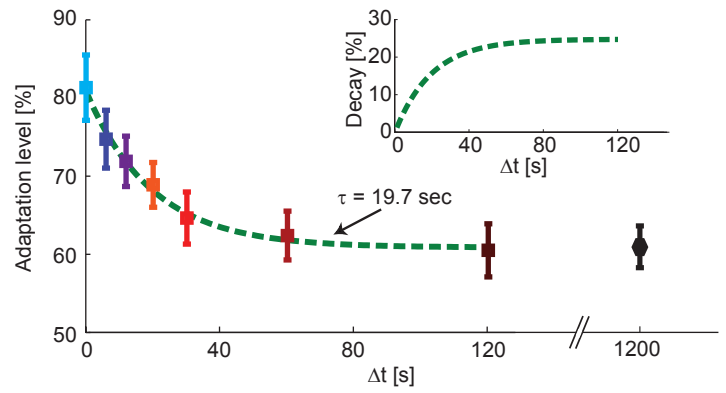


Figure 2: Time-dependent decay of motor adaptation. Subjects were trained to asymptote, tested for retention after a variable time delay Δt , and repeatedly retrained and retested to obtain decay curves. We found that adaptation consists of a temporally-labile component, which accounts for about 25% of overall adaptation and decays quickly ($\tau = 19.7$ sec), and a temporally-stable component which accounts for about 75% of overall adaptation.

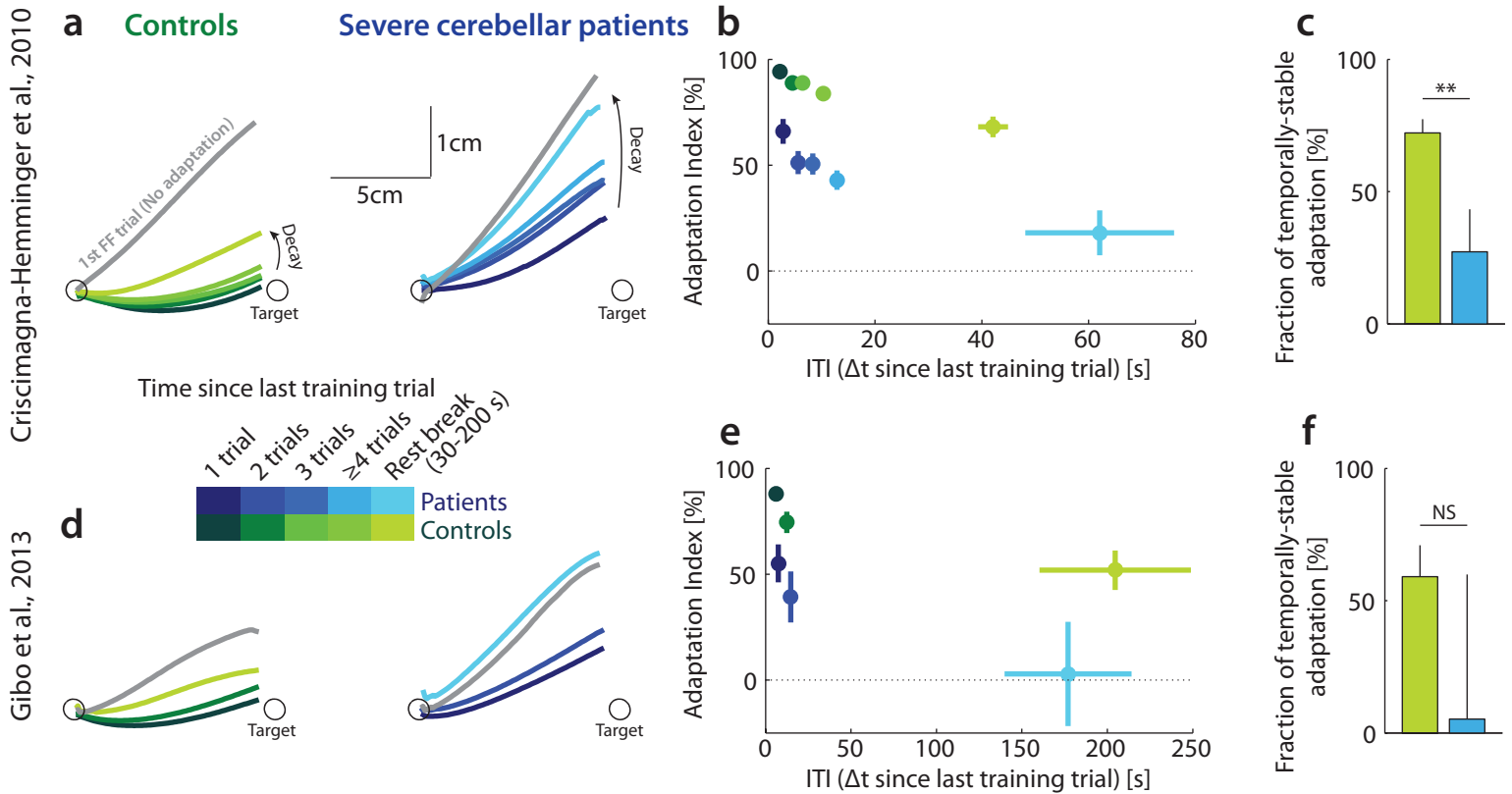


Figure 3: Cerebellar damage increases the temporal volatility of motor memories.

(a): Average paths from the Criscimagna-Hemminger et al. (2010) study for each type of inter-trial interval, as was defined by the distance to the most recent trial on the same direction (1, 2, 3 or ≥ 4 trials, or after a rest break). Controls are shown on the left; Severe cerebellar patients are shown on the right (ICARS index > 40). Note that patients are able to considerably reduce errors compared to the initial exposure to the force-field when the ITIs are low. However, while both patients and controls show increasing deviations (decaying performance) with increased ITI, these deviations increase much faster for the cerebellar patients. While the performance of controls after a rest break (which indicates temporally-stable adaptation) is still much better than the performance during the initial force-field exposure, in contrast, the performance of patients after a rest break is nearly as bad as during initial force-field exposure, indicating higher temporal volatility of motor memories.

(b): Decay of adaptation with increased ITI. Note how controls' adaptation decay to a nonzero level in line with the data shown in **Figure 2** whereas patients' adaptation decays close to zero. The adaptation index was calculated as the % improvement from the angular error that was experienced during initial force-field exposure.

(c): Fraction of overall adaptation that is temporally-stable. Overall adaptation was measured during consecutive same-direction learning trials (darkest shades in **a** and **b**). Temporally-stable adaptation was measured after rest breaks. The motor adaptation for controls is about three times more stable compared to patients ($72 \pm 5\%$ for controls vs. $27 \pm 16\%$ for patients, $p < 0.01$).

(d)-(f): Analogous to **(a)-(c)** but for the Gibo et al. (2013) study illustrating similar results.