Prediction and set-dependent scaling of early postural responses in cerebellar patients

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Summary
We reported previously that patients with cerebellar deficits were unable to scale the magnitude of their early automatic postural responses to the predicted amplitudes of surface translations based on central set from prior experience. The present study investigated whether this deficit in set-dependent amplitude scaling was based predominately on the cerebellar patient’s disability (i) to predict perturbation amplitudes on the basis of prior experience, (ii) to scale the gain or magnitude of upcoming postural responses or (iii) to habituate postural responses. The increase in size of the early postural response when a larger than actual platform amplitude was expected and decrease when a smaller one was expected was defined as a measure of set-dependent amplitude prediction. The suppression of the postural response when the same platform velocity was repeated was used as a measure of habituation. The correlation between the size of early postural responses and platform amplitudes when presented serially, but not randomly, tested the ability to scale the gain of postural responses based on prior translations based on central set from prior experience. Results show that although cerebellar patients could predict perturbation amplitudes based on prior experience, they could not use this prediction to modify precisely the gain of responses. The ability to habituate the magnitude of postural responses was not affected by cerebellar lesions. Thus, the cerebellum might not be critical for predicting upcoming events or for habituating to repeated postural stimuli, although it is important for accurate tuning of response gain based on prediction.

Keywords: posture; cerebellum; adaptation; habituation; human

Abbreviations: ADCA = autosomal dominant cerebellar ataxia; EA type 2 = episodic ataxia type 2 (autosomal dominant periodic ataxia); IDCA = idiopathic cerebellar ataxia; IEMG = integrated EMG

Introduction
The modification of automatic motor responses based on prediction of stimulus characteristics has been attributed to ‘central set’ effects (Evarts, 1975; Brooks, 1984; Hore and Vilis, 1985; Horak et al., 1989). A previous study from this laboratory had demonstrated that anterior lobe cerebellar disorders result in hypermetric postural responses associated with deficits in tuning initial postural response magnitude to perturbation amplitude based on prediction from immediate prior experience (Horak and Diener, 1994).

The aim of the present study was to investigate further why set-dependent amplitude scaling is disturbed in subjects with cerebellar dysfunction. Different mechanisms were investigated: (i) the inability to predict amplitudes based on prior experience; (ii) impaired scaling of response gain on the basis of prediction; (iii) the inability to habituate the response magnitude to repeated stimulation.

It has been shown previously that central mechanisms underlying the modification of postural responses based on prior experience are different for stimulus amplitude and velocity (Horak et al., 1989). Central set is necessary to code the intensity of initial responses to anticipated perturbation amplitudes because, at 100 ms latency, initial responses are executed before the completion of the perturbation amplitude. Initial postural response magnitude is tuned up or down based on the characteristics of the sequential experience. Normal subjects under-respond to the actual stimulus when they receive an amplitude displacement larger than expected, and they over-respond when they receive an amplitude...
displacement smaller than expected. There is no scaling of initial responses when perturbation amplitudes are randomized.

In contrast to the directionally specific effects of amplitude expectation, velocity expectation resembles habituation. Whether subjects expect a slower or faster perturbation than they actually receive, they over-respond to the unexpected velocity and suppress response to repeated velocities regardless of the characteristics of their prior experience (Horak et al., 1989). They over-respond, even if they expect a slower velocity than they receive. Velocity feedback, but not amplitude information, can be encoded into the earliest response of every trial as shown by responses which are scaled similarly whether perturbation velocity is randomized or blocked.

In this study, the effects of prior experience on automatic postural responses were examined by comparing responses to identical stimuli using two protocols: (i) presentation of expected and unexpected stimuli and (ii) presentation of serially and randomly changed stimuli. The first protocol focused on the subject’s ability to predict amplitudes based on prior experience. The second protocol focused on the ability to scale response gain or magnitude precisely on the basis of amplitude prediction. Both protocols were used to determine whether cerebellar subjects could habituate postural responses when the same perturbation velocities were repeated.

In the first protocol, the difference in size of the postural response when the same platform amplitude is expected and unexpected was defined as a ‘measure of amplitude prediction’. Exposure to a block of identical perturbations tested the ability of patients to set the gain of postural responses based on prediction by showing an ‘after-effect’ of abnormal gain when the perturbation amplitude was unexpectedly changed. A large difference in expected and unexpected perturbations (1.2 cm and 12 cm) emphasized the effects of prediction.

In the second protocol, correlations of initial postural responses with perturbation amplitude were compared when identical amplitudes were presented sequentially versus randomly. The correlation between the size of early postural responses and platform amplitudes was defined as a ‘measure of set-dependent scaling’ of postural response gain in the present study. This protocol emphasized the ability to tune the magnitude of early postural response gain gradually to subsequent small steps in expected perturbation amplitude on the basis of prior experience.

The ability to use ‘habituation’ to reduce the size of postural responses was tested by measuring the difference in size of response when perturbation velocity was expected and unexpected in the first protocol and by examining the gradual reduction in response with repeated velocities in the second protocol.

Material and methods

Subjects
A total of 12 cerebellar patients participated, six male and six female with a mean ± SD age of 47.4 ± 19.8 years (range 22–80 years). Ten patients were tested using the first protocol and 10 using the second, hence eight participated in both experiments. All patients showed signs of gait and stance ataxia (see Table 1). Three had mild, four moderate and five marked ataxia of gait, five mild and seven moderate ataxia of stance and six mild and six moderate lower limb ataxia (heel-to-shin-test) based on a scale adapted from Klockgether et al. (1990). Eleven patients presented with a form of degenerative ataxia: three had autosomal dominant cerebellar ataxia (ADCA; Harding, 1993), four idiopathic cerebellar ataxia (IDCA; two with an age of onset of >50 years) and four had autosomal dominant periodic ataxia [episodic ataxia type 2 (EA-type 2)]. Patients with EA-type 2 were tested between attacks. All of them presented with cerebellar oculomotor signs and mild lower limb ataxia at the time of testing. One patient had had sugery for an arterio-venous malformation of the right cerebellar hemisphere. None of the patients had sensory or peripheral vestibular deficits. All 12 patients had a pure cerebellar syndrome, except two who had minor additional pyramidal signs (brisk reflexes and extensor plantar responses). These two patients were included because their results did not differ from the group. As there were no significant correlations between our results and the amount of ataxia, the extent of the lesion, or type of cerebellar disorders, results are presented for the entire group of cerebellar subjects. No attempts have been made to classify the ADCA patients based on genetic diagnosis.

Eighteen healthy subjects without neurological or orthopaedic limitations were selected as controls; 11 female and seven male with a mean age ± SD of 48.2 ± 21.1 years (range 18–84 years). Ten control subjects, age- and sex-matched to the participating cerebellar patients, were tested with the first protocol and 10, matched in the same way, were tested with the second; hence two control subjects participated in both experiments. All subjects had a complete neurological evaluation by one of the authors.

All subjects gave informed consent for protocols approved by the Institutional Review Board.

Protocols
The effect of prior experience with stimuli of particular perturbation velocity or amplitude was examined in two separate protocols: (i) subjects were presented with expected stimuli, based on prior experience; versus unexpected stimuli; (ii) subjects were presented with predictably changed stimuli in series and a random presentation of the same stimuli.

Previous publications have described, in detail, the apparatus and methods used to impose displacements and quantify the resulting responses as well as the rationales of the applied protocols (Horak and Nashner, 1986; Diener et al., 1988; Horak et al., 1989; Horak and Diener, 1994). Results from the second protocol (serial versus random presentation of stimuli) have been reported previously for a group of cerebellar patients with anterior lobe atrophy (Horak and Diener, 1994). Because a different patient population...
Table 1 Diagnosis and ataxia score of cerebellar patients

<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Diagnosis</th>
<th>Ataxia score*</th>
<th>Extracerebellar signs</th>
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<td>1</td>
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<tr>
<td>MF</td>
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<tr>
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<td>35</td>
<td>ADCA‡</td>
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<tr>
<td>GH</td>
<td>Female</td>
<td>38</td>
<td>Resection of cerebellar AVM</td>
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<td>2</td>
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</tbody>
</table>

*1 = mild, 2 = moderate, 3 = marked, 4 = severe, 5 = most severe (based on a scale adapted from Klockgether et al., 1990); †IDCA = idiopathic cerebellar ataxia; ‡ADCA = autosomal dominant cerebellar ataxia; AVM = arterio-venous malformation.

was tested, a similar protocol was repeated in the present study in order to compare patient groups. Subjects stood on two platforms that moved backward together under the control of a hydraulic servomotor. They stood with arms folded in front, across the waist, eyes open and feet 6–9 cm apart at the heels. Strain gauges were embedded within the platforms to measure the torque (front-minus-back vertical-force changes) exerted by each foot and the anteroposterior horizontal shear forces.

Electromyographic (EMG) activity of eight representative ankle, knee and lower trunk antagonist muscles on the right were recorded using 2.5 cm surface electrodes spaced 2–4 cm apart on tibialis anterior, medial gastrocnemius, soleus, quadriceps femoris, hamstrings, rectus abdominis at the umbilicus and lumbar paraspinal at the level of the iliac crest. The results of tibialis anterior and gastrocnemius only will be shown, as these muscles demonstrated the major findings in previous studies using similar protocols to investigate healthy controls and cerebellar subjects (Horak et al., 1989; Horak and Diener, 1994). Amplified EMG signals were band-pass filtered (70–2000 Hz) and full-wave rectified, low-pass filtered (100 Hz) and stored for off-line analysis. Although no attempt was made to calibrate EMGs on an absolute scale, amplifier gains were fixed throughout each experimental session. Integrated EMG (IEMG) areas were normalized to allow meaningful comparison of changes between subjects and groups.

Postural perturbations consisted of backward-ramp translations of the platform, with velocities and amplitudes varied independently according to the protocols outlined below. The time between perturbations, determined by the experimenter after the subject’s centre of pressure returned to the quiet equilibrium position, varied between 10 and 15 s. Each protocol was performed on a separate day. Protocol 1 was performed first. The time interval between Protocols 1 and 2 was 2–4 months (average 3 months).

Protocol 1: expected and unexpected stimuli

The effect of expectation was examined by comparing responses that were preceded by 2–6 trials of the same stimulus (expected) with responses that were preceded by 3–7 trials of a different stimulus (unexpected). Each subject was presented with four blocks of 30 trials (total of 120 trials): two blocks for large (12 cm) and small amplitudes (1.2 cm) with constant velocity (20 cm/s) and two blocks for fast (20 cm/s) and slow (5 cm/s) velocities with constant amplitudes (6 cm). One block consisted of 30 trials in which five large amplitude trials were randomly interposed (unexpected trials) after three to seven trials of small amplitudes, another block of 30 trials in which five small amplitude trials were randomly interposed (unexpected trials) after three to seven trial blocks of the large amplitudes. Each subject was exposed to a similar protocol for expected and unexpected, slow and fast, perturbation velocities. The last trial in each block before each unexpected trial was selected to represent the expected condition. Five expected trials and five unexpected trials with the same stimulus parameters, but with different prior experience, were compared. To minimize the effects of presentation order, subjects received the four blocks at random.

Protocol 2: serial and random stimuli

To compare the scaling of postural responses to stimulus amplitude, four different amplitudes of platform displacements (1.2, 3, 6 and 12 cm) were presented serially and then randomly. Subjects received seven trials of each amplitude in serial presentation (total of 28 trials) and five trials of each amplitude in random presentation (total of 20 trials). The same sequence of amplitudes, going from the smallest to the largest (1.2 to 3 to 6 to 12 cm), was used in serial presentation for all subjects. The first two trials of
the serial presentation were not analysed in order to minimize the effects of ‘startle-like’ responses. Ramp velocity was constant for all amplitudes at 15 cm/s.

**Data analysis**

Force and EMG data were collected for 2 s in Protocol 1 and for 3 s in Protocol 2 including 250 ms before the perturbation. Torque responses were quantified in single trials by calculating the slopes of the linear regression of the first 75 ms of active torque (initial rate of change of torque). Onset of active torque, which included both the active response and passive elastic elements, was defined as the first significant change of torque slope after the displacement artifact with the use of a peak-picking program that differentiated the torque signal and identified peaks. Active torque responses were initiated ~50 ms after onset of the first gastrocnemius burst. Peak torque and torque integral >300 ms from active torque onset were also measured for each trial. Each (active) torque latency was measured with reference to perturbation onset (e.g. first platform shear artifact). Torque slope and integrals were normalized by assigning an arbitrary value of 100% to each subject’s mean torque values over a fixed time window (75 ms) in one condition and referencing changes in their torque to that value to eliminate the effect of subject’s size, strength and hypermetria. The mean torque value of each subject’s five individual trials in the expected, small amplitude condition (1.2 cm) was defined as 100% in Protocol 1. In Protocol 2, the mean value of the five individual trials in the expected, large amplitude condition (12 cm) was defined as 100%.

EMG latencies were identified by placing a cursor at the earliest time that EMG activity in a single trial deviated from the preperturbation EMG base-line level (mean DC level). Each EMG latency was measured with reference to perturbation onset (i.e. first platform shear artifact). Integrated areas under the rectified, filtered EMG were quantified and normalized independently for the early (0–75 ms) and late (75–300 ms) activity for gastrocnemius and tibialis anterior. In each protocol, the IEMG was normalized by assigning an arbitrary value of 100% to each subject’s mean IEMG values over a fixed time window (0–75 ms) in the expected condition (1.2 cm perturbation amplitude in Protocol 1 and 12 cm in Protocol 2).

We were interested in differences in the amount of prediction and scaling between the control and cerebellar group. To eliminate the effects of hypermetria in the patient group, only normalized torque and EMG data were entered into statistical analysis. The absolute amount and effects of dysmetria are considered separately at the end of the Results section. The following statistical analyses were performed for each protocol.

**Protocol 1: expected and unexpected stimuli**

Differences (delta-values, ‘measure of prediction’) were calculated between the mean values in expected and unexpected conditions for each variable and each individual subject. All delta-values for each variable, group (control or cerebellar) and stimulus condition were tested for being significantly different from zero (two-tailed, one-sample t test). The effect of stimulus parameters (slow/fast velocity conditions and small/large amplitude conditions) versus the group effects (control/cerebellar) were tested using two-way ANOVAs. $P < 0.05$ was considered significant.

**Protocol 2: serial and random stimuli**

The relation between postural response amplitude and perturbation amplitude (‘measure of set-dependent scaling’) was measured by calculating linear regressions between normalized rate of change of torque versus stimulus amplitude and normalized IEMG versus stimulus amplitude for each subject and each block of five individual trials. The slopes of these regressions provide a measure of the ‘gain’ of the postural response. The elevations of the regressions (ordinate-intercepts) of non-normalized values were used to measure relative ‘hypermetria’ of the response. Slopes of linear regressions in serial and random conditions and in the control and cerebellar groups were tested for significance (slope significantly different from zero) using a two-tailed, one-sample t test. Differences between serial and random conditions in each group were tested with two-tailed, paired t tests and between groups with two-tailed, unpaired t tests. $P < 0.05$ was considered significant.

The results from the smallest stimulus amplitude (1.2 cm) tests were excluded in subjects who presented with torque and EMG onsets above the mean $\pm 2$ SD of the control group data (mean torque onset$+2SD = 178$ ms; mean gastrocnemius onset$ + 2SD = 124$ ms), as it was likely that subjects received sensory feedback about the stimulus amplitude given the short duration of platform translation of 80 ms. In these subjects (two elderly controls and five cerebellar patients) linear regressions were only calculated for the other three stimulus amplitudes, 3, 6 and 12 cm.

**Results**

**Protocol 1: expected and unexpected stimuli**

**Effects of amplitude expectation: central set**

Automatic postural responses to identical stimuli were different when they were preceded by trials with the same (expected) stimulus amplitude rather than by trials with a different (unexpected) stimulus amplitude for both controls and cerebellar patients. The effect of unexpected stimulus amplitudes was dependent on the nature of prior experience: Both controls and cerebellar subjects over-responded to a given stimulus when larger amplitudes were expected and under-responded when smaller amplitudes were expected.

To demonstrate this effect, the average ankle torques and gastrocnemius IEMGs (Figs 1 and 2) for expected and unexpected amplitudes are superimposed. Amplitude
Postural reflexes and cerebellum

Fig. 1 Effect of expectation on averaged torque responses of 10 cerebellar and 10 age- and sex-matched control subjects for small and large amplitude perturbations. Torque-responses when amplitudes were expected (dark line) are superimposed on those when amplitudes were unexpected (grey line). The slopes of the linear regression of the first 75 ms of torque changes for expected and unexpected conditions are shown. The onset of the platform movement is indicated by the small shear artifacts in every trace at 260 ms.

![Fig. 1](image-url)

expectation could be demonstrated in every individual control and cerebellar subject (Fig. 1). The amount of prediction is indicated by the difference between the slope of the linear regression of the first 75 ms of torque changes for expected and unexpected amplitudes.

The directionally specific effects of amplitude expectation on the ankle torque and gastrocnemius IEMG response is illustrated in Fig. 2A and B. For both control and cerebellar subjects, the gastrocnemius response was too large when the amplitude was smaller than expected (Fig. 2A) and it was too small when the amplitude was larger than expected (Fig. 2B). The group mean early torque and gastrocnemius responses to the same stimulus are compared when the actual stimulus was expected and unexpected in Fig. 3. Normalization eliminated the absolute values which would reflect hypermetric responses in cerebellar patients. Torque and gastrocnemius IEMG responses were larger when (control and cerebellar) subjects expected a larger stimulus amplitude and smaller when they expected a smaller amplitude than they actually received.

The difference in early torque and gastrocnemius IEMG response between expected and unexpected amplitude conditions was significantly different from zero for both small and large amplitudes in the control group (all $P <$
Fig. 2 Differences in initial gastrocnemius IEMG from representative control and cerebellar subjects when a small (A) and a large (B) amplitude and when a fast velocity (C) was presented in expected (no shading) versus unexpected conditions (black shading). Averaged EMG responses from five single trials are demonstrated. Both control and cerebellar subject’s initial gastrocnemius EMG over-responded when larger amplitudes were expected and under-responded when smaller amplitudes were expected. In contrast, subjects over-responded in the fast velocity condition when they were expecting a slow velocity. Note that postural responses of the cerebellar subjects were larger than the controls.

Like the gastrocnemius IEMG, the antagonist, tibialis anterior IEMGs were larger when larger amplitudes were expected and smaller when smaller amplitudes were expected. The difference in the initial tibialis anterior IEMG between expected and unexpected amplitude conditions was significantly different from zero for small amplitudes in the control and cerebellar group ($P < 0.05$) and for large amplitudes in the control ($P < 0.05$). The difference of tibialis anterior IEMGs for large amplitudes did not reach significance in the cerebellar group ($P = 0.23$). There was no significant difference in the effect of expectation in early tibialis anterior IEMG between groups ($P = 0.5$).

The late (76–300 ms) torque response showed the same effects of expectation; integrated torque was larger when larger amplitudes were expected and smaller when smaller amplitudes were expected for both groups (all $P < 0.05$).

Late gastrocnemius and tibialis anterior IEMGs were also larger when larger amplitudes were predicted ($P < 0.05$), but were not smaller when smaller amplitudes were predicted (control: $P = 0.75$; cerebellar: $P = 0.28$). Thus, even later aspects of the postural response, when sensory information about the perturbation’s actual amplitude is available, show measurable effects of expectation.

**Effects of velocity expectation: habituation**

Unlike prediction of perturbation amplitude, initial torque and gastrocnemius IEMG responses were always larger when stimulus velocity was unexpected, whether subjects expected a faster or slower velocity than they actually received. Representative examples of gastrocnemius IEMG show that responses to unexpected velocities are too large, even when subjects expected a slower velocity than they actually received (Fig. 2C).

Figure 3A and B (fast velocity) demonstrates that group mean torque and gastrocnemius IEMG responses were smaller with repetition of the same, expected velocity, even when fast velocities were expected. These results are in contrast to Fig. 3A and B (large amplitude) demonstrating that mean torque and gastrocnemius IEMG responses were larger when
Effects of dysmetria on gain or prediction

The influence of postural dysmetria, reflected in response hypermetria and variability, on the ability of cerebellar subjects to use prediction (Protocol 1) and the ability to scale gain of postural responses (Protocol 2) was examined. Hypermetria of postural responses was quantified as the elevation (‘ordinate-intercept’) of individual linear regressions calculated between initial torque-responses (which were not normalized) and platform displacements when the amplitudes were presented serially (Protocol 2). The cerebellar group was significantly more hypermetric compared with the control group (control: 124.5±48 N m/s (mean±SD); cerebellar: 190.9±92 N m/s; one-tailed, unpaired t test P < 0.05). There was no significant correlation between the measure of hypermetria of automatic postural responses, however, and clinical scores of stance, gait or lower limb (heel-to-shin test) ataxia. For example, the cerebellar subject who showed the most hypermetric postural responses presented with only mild ataxia of stance and gait.

Figure 5A shows that the greater the amount of hypermetria in cerebellar patients, the lower the gain or slope of their set-dependent amplitude scaling (R = 0.74, P < 0.05, slope = -0.031). In contrast, the greater the hypermetria, the larger the directionally specific difference between expected and unexpected amplitudes based on prediction (Fig. 5C and D) (small amplitude: R = 0.9, P < 0.001, slope = 0.45; large amplitude: R = 0.7, P < 0.05, slope = 0.7). The variability of the response magnitude also increased significantly with increasing hypermetria in the cerebellar group (R = 0.09, P < 0.001, slope = 0.14 (Fig. 5B)). In summary, the ability to scale set-dependent amplitudes was
Fig. 5 (A) Negative correlation of hypermetria with set-dependent scaling of early postural responses the cerebellar patients. Individual subjects are indicated by their initials. Hypermetria was quantified as the elevation (ordinate-intercept) of linear regressions between torque-responses (which were not normalized) and platform amplitudes. Set-dependent scaling represented the slopes of those regressions. (B) Positive correlation of postural response hypermetria with variability in cerebellar patients. Response variability was defined as the SD of the initial rate of change of torque in the blocked amplitude conditions. Positive correlation of hypermetria with prediction of large (C) and small (D) amplitudes in cerebellar patients: Prediction was defined as the delta value, i.e. the difference between the responses in the expected and unexpected conditions.

worse in cerebellar patients with the largest response hypermetria and variability. In contrast, the most hypermetric subjects showed the largest values of directionally specific prediction (Subjects D.F. and J.N.; Fig 5).

Unlike cerebellar subjects, control subjects showed no significant correlation between hypermetria (ordinate-intercept) and set-dependent scaling ($R = 0.02, P = 0.95$, slope $= -0.001$). Furthermore, they showed no significant correlation between the measure of hypermetria and variability (SD) ($R = 0.3, P = 0.4$, slope $= 0.08$). Only two control subjects participated in both experiments, thus there were not enough subjects to calculate a meaningful correlation between the measure of hypermetria and prediction.

Variability of response magnitude was significantly larger in the cerebellar subjects than in the control subjects. SDS as a measure of variability were significantly higher in the cerebellar group compared with the control group for initial torque responses in the blocked amplitude conditions (control: $34.1 \pm 12$ N m/s (mean $\pm$ SD); cerebellar: $45.4 \pm 13$ N m/s; one-tailed, unpaired $t$ test $P < 0.05$). Figure 6A and B represent group data on a trial by trial basis for the control and cerebellar group in Protocol 2. Both the cerebellar and control groups seem to search around an aimed torque value, with the cerebellar group’s trial to trial excursions appearing larger than the control group’s. The difference in variability on a trial by trial basis between control and cerebellar subjects becomes more obvious in the individual plots, demonstrated by representative examples for a typical control (C) and cerebellar subject (D). Non-normalized values show hypermetria in cerebellar patients. All seven trials per amplitude condition are illustrated here, although only trials 3–7 were entered into the statistical analysis. Note the larger trial-by-trial variability in cerebellar patients compared with control subjects. Note also the obvious decrease in initial rate of change of torque comparing Trials 1 and 2 in both groups, indicating habituation of a ‘startle-like’ response. Platform amplitude: 1 cm, filled circles; 3 cm, open circles; 6 cm, filled triangles; 12 cm, open diamonds.

Effects of habituation of the first ‘startle-like’ response
Figure 6A and B demonstrates a remarkable reduction in response size comparing the first and second trial of the first (1.2 cm) amplitude block in both control and cerebellar subjects. The reduction in size of postural responses from the first to the second trial has been attributed to habituation of a ‘startle-like’ response (Hansen et al., 1988). This habituation effect is present for both the control and cerebellar groups. The difference between the first and second trial in the 1.2 cm amplitude condition was significantly different.
from zero for both the control and cerebellar group (both \(P < 0.05\)). There was no significant difference in reduction of the rate of change of torque between the first and second 1.2 cm trial comparing the control and cerebellar subjects (\(P = 0.5\)).

**Discussion**

In the present study, we investigated whether cerebellar deficits in set-dependent amplitude scaling are due to deficits in predicting, based on prior experience or in motor performance, namely, deficits in accurately adjusting postural response gain. Our results showed that difficulty in scaling response magnitude to stimulus amplitudes was due to difficulty in modifying response gain precisely and not to difficulty in predicting the upcoming stimulus or to habituation deficits.

**Set-dependent gain control and prediction**

As in our previous study, this group of cerebellar patients showed difficulties scaling response magnitudes to relatively small differences in predictable displacement amplitudes (1.2 to 3 to 6 to 12 cm; Protocol 2) based on prior experience (Horak and Diener, 1994). To reduce the possible influence of cerebellar motor performance deficits, the ability to predict was investigated using more marked differences in perturbation amplitudes (1.2 cm and 12 cm) in Protocol 1 (Horak et al., 1989). In this protocol, both healthy subjects and cerebellar patients over-responded, when they expected, on the basis of prior experience, a larger displacement than they actually received and under-responded when they expected a smaller displacement than they received. This protocol measured predominantly the ability to predict, because the subject’s ability to tune response magnitude to subsequent perturbations gradually was not assessed. However, it should be noted that these effects of prediction can only be recognized by effects of scaling. Cerebellar patients clearly adjusted the magnitude of their responses up or down based on directionally specific prior experience.

Since there was no significant difference in the amount of amplitude prediction between the control and cerebellar groups, the cerebellum might not be critical for generating and storing a ‘memory’ of previous perturbation characteristics (and/or the subject’s response to them). However, the majority of the patients had degenerative, diffuse lesions of the cerebellum. Therefore, it might be argued that effects of prediction were made possible by unaffected parts of the cerebellum and/or mechanisms of compensation. Although this cannot be excluded, it seems unlikely, because the amount of prediction was not diminished in proportion to the severity of motor involvement.

In fact, the two most hypermetric patients demonstrated the highest measures of directionally specific prediction (Subjects D.F. and J.N.; Fig. 5); they over-responded the most, when they expected, on the basis of prior experience, a larger displacement than they actually received and under-responded the most when they expected a smaller displacement than they received. Furthermore, the amount of prediction (‘over-’ and ‘under-responding’) increased significantly with increasing hypermetria in the cerebellar patients. There was a clear trend for prediction to be larger in the cerebellar than control group. However, they were not able to tune precisely, or even in the correct direction, the gain of the responses appropriate for the anticipated amplitudes. These findings suggest dysmetric gain-control despite the presence of predictive information.

In contrast to predictive capabilities, the ability of cerebellar patients to scale response gain decreased significantly with increasing motor performance deficits, i.e. hypermetria and variability. Both hypermetria and increased variability seem to be involved in impaired anticipatory postural gain control in cerebellar dysfunction. Although some scaling was apparent within a set of seven trials, when individual trials of the blocked scaling experiment (Protocol 2) were examined, the large trial-by-trial response-magnitude variability in cerebellar patients did not allow for significant correlations. Thus, imprecision in adjusting the gain of postural responses on the basis of prior experience might well reflect a motor output deficit for the cerebellum.

It should be emphasized that, despite obvious impairment, a certain degree of anticipatory amplitude scaling was preserved in our group of cerebellar patients. In particular, six out of 10 cerebellar subjects showed a trend towards positive correlation in Protocol 2 and all cerebellar patients were able to adjust the gain of response magnitudes based on expectation from prior experience in Protocol 1, when large differences in expected and unexpected perturbations were presented.

Overall, these results suggest that the underlying cause of predictive scaling deficits reported earlier for the anterior lobe cerebellar patients lies with gain control and not with ability to develop predictions based on prior experience (Horak and Diener, 1994). It is unlikely that the cerebellar patients in our previous study were qualitatively different from the patients in the current study since both groups showed the same amplitude-scaling deficits and no latency deficits. The patients in our previous study, however, had clinically more severe anterior lobe signs and larger amounts of postural hypermetria and even more severe problems with predictive amplitude scaling. The amount of hypermetria, defined as the ordinate-intercept of the linear regression for the non-normalized initial rate of change of ankle torque versus displacement amplitude, was \(191\pm92\) N m/s (mean±SD) in the current study and \(308\pm135\) N m/s in our previous study. This difference in hypermetria might reflect a difference in cerebellar pathology: The majority of patients in the present study had degenerative, diffuse lesions of the cerebellum compared with the previously tested subjects who had primarily anterior lobe (alcoholic) cerebellar atrophy which is thought to affect primarily Purkinje cells (Victor et al., 1959).
However, the lack of correlation of clinical scores of cerebellar ataxia of stance and gait with the degree of hypermetria of automatic postural responses was an unexpected finding. For example, the cerebellar subject who showed the most hypermetric postural responses presented with only mild ataxia of stance and gait. To our knowledge, previous studies did not attempt to correlate clinical scores of cerebellar ataxia with measures of automatic postural responses. The role of hypermetric automatic postural responses in the development of cerebellar ataxia might be limited to certain tasks which are not particularly tested in a routine neurological examination. The present findings might be another example of functional compartmentalization (Dichgans and Diener, 1985) of the cerebellum. Different parts of the cerebellum might be involved in the control of automatic postural responses and of stance and gait.

The results presented here agree somewhat with findings regarding the cerebellar role in the predictive control of voluntary saccades; Ito (1984) concluded, that it is unlikely that the cerebellum, alone, ‘makes the prediction’, since cerebelllectomy does not abolish volitional, predictive saccades. Cerebellar lesions, however, do make saccades inaccurate (dysmetric), just as the postural responses became inaccurate (hypermetric) in our cerebellar subjects. The saccade-deficits in the cerebellar subjects are also similar to the set-dependent deficits of arm posture in monkeys with cerebellar nucleus lesions (Hore and Vilis, 1985). Hore and Vilis (1985) suggested that the cerebellum modifies the magnitude of the agonist response based on expectation of perturbation duration from prior experience.

Habituation

Habituation differs from adaptation in that it refers to a generalized waning of a response as a result of repeated stimulation rather than specific tuning, up or down, depending on the nature of prior experience (Harris, 1943). The two manifestations of postural habituation in our task were an initial, large reduction between trials one and subsequent trials and an over-response to novel displacement velocities, even when a smaller velocity was expected based on prior experience (Hansen et al., 1988; Horak et al., 1989). In the present study, cerebellar dysmetria did not significantly affect the ability to reduce the magnitude of early postural responses between the first presented trial and subsequent trials. Both control and cerebellar subjects also overresponded to the same platform velocity when it was unexpected, although they expected a smaller velocity based on prior experience. Again, there was a trend for the amount of ‘over-responding’ to be larger in the cerebellar group, suggesting dysmetric gain control.

On the basis of the present findings, habituation of postural responses does not require the integrity of the cerebellum. These results agree with findings of the neural changes responsible for short-term habituation of the acoustic startle response which have been suggested to occur in the brainstem and spinal startle reflex pathways, but not the cerebellum (Lopiano et al., 1990; Rothwell et al., 1994).

Concluding remarks

The data presented here suggest that impaired set-dependent scaling of automatic postural responses in cerebellar dysfunction might represent deficits in motor control of postural response gain. Perhaps hypermetric postural responses are a sign that the cerebellar ‘rheostat’ is out of order and, therefore, precision tuning of postural responses is impossible. Postural response gain, however, is not stuck at a high level, since modulation of gain upwards and downwards was possible when large differences between actual and expected stimulus parameters were presented.

In fact, the main role of the cerebellum in automatic postural responses may be gain control, since Horak and Diener (1994) have demonstrated that the temporal synergy of multijoint postural organization is not affected in cerebellar dysfunction. Furthermore, the processing of concurrent sensory feedback to scale the gain of automatic postural responses seems to be unimpaired in cerebellar patients; it has previously been shown that the use of on-line velocity feedback to scale the magnitude of postural responses was not affected in patients with anterior lobe syndrome (Horak and Diener, 1994), despite the presence of dysmetria. In addition, both this and the previous study showed that cerebellar patients are capable of scaling their dysmetric postural responses to displacement amplitude as soon as afferent feedback is available.

Our finding of impaired postural reflex gain control in cerebellar patients is consistent with the suggestion that the cerebellum participates in the modulation of gain of various different reflex loops (MacKay and Murphy, 1979). Bloedel and Ebner (1985) have also suggested the ‘gain change hypothesis’ to explain cerebellar function, with the climbing fiber system exercising ongoing gain control over the output of the cerebellar cortex and nuclei.

However, the cerebellum may play a different functional role in automatic postural synergies, in which the spatiotemporal organization may be more rigidly hardwired by brainstem or spinal mechanisms, than in voluntary arm movements in which cerebellar dysmetria is associated with impaired temporal synergic organization (Hore et al., 1991). Furthermore, there was no significant correlation between hypermetria of automatic postural responses and clinical measures of dysmetric arm movements or ataxia of gait or stance. Thus, the functional role of the cerebellum in regulating automatic postural responses, and more complex or voluntary tasks, is likely to be different. Further studies need to be performed to examine the functional role of hypermetric automatic postural responses in cerebellar ataxia of stance and gait.

In conclusion, the role of the cerebellum in set-dependent amplitude scaling of automatic postural responses relates to its importance in accurately modifying the response gain.
based on prior experience. The ability to predict displacement amplitudes seemed unaffected, but the use of predictive information might be impaired. In addition, the cerebellum does not appear to be critical for habituation of postural responses.

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