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RESEARCH ARTICLE

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Perturbed step initiation in cerebellar subjects: 2. Modification of anticipatory postural adjustments

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Abstract Although ataxias of stance and gait are frequent manifestations of cerebellar disease, the number of human studies examining stance or gait in cerebellar subjects is limited. In the present study, we examined whether anticipatory postural adjustments were impaired in cerebellar subjects during perturbed and unperturbed step initiation. The first aim was to show possible abnormalities in timing, force and kinematic parameters of anticipatory postural adjustments in unperturbed stepping in cerebellar subjects. Second, we examined the ability of cerebellar subjects to modify anticipatory postural adjustments associated with step initiation in response to a backward translation. Finally, we asked whether cerebellar subjects (and controls) make use of predictive knowledge of perturbation amplitude in perturbed stepping. Only few abnormalities of anticipatory postural adjustments were found in cerebellar subjects compared to controls. Both in the unperturbed and perturbed step conditions, force production as well as step length and step velocity were reduced in cerebellar subjects compared to controls, suggesting compensatory slowing. Cerebellar subjects also appeared to be less able to use predictive information of perturbation amplitude to scale anticipatory postural adjustments than control subjects. Nevertheless, in unperturbed steps, temporal parameters of anticipatory postural adjustments were preserved in cerebellar subjects. When subjects voluntarily initiated a step in response to the surface translation, both control and cerebellar subjects adapted by executing the anticipatory postural adjustments for step more rapidly. Furthermore, both control and cerebellar subjects were able to use online information regarding perturbation amplitude to scale parameters of step initiation in perturbed stepping. Overall, our findings suggest that the cerebellum is neither critical for the basic motor program underlying unperturbed step initiation nor for many adaptive changes occurring during perturbed step initiation. Like its role in predictive scaling of automatic postural responses to external perturbations, the cerebellum appears to be important for predictive adaptation of anticipatory postural adjustments during step initiation.

Keywords Step initiation · Anticipatory postural adjustments · Perturbed stepping · Cerebellum · Adaptation

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Introduction

The role of the cerebellum in control of automatic postural responses, anticipatory postural responses prior to step initiation, and their interaction when automatic postural responses interfere with step initiation is largely unknown. When the body undergoes an external perturbation, an automatic postural response, triggered by sensory information, restores equilibrium. In contrast, during the execution of a voluntary movement, anticipatory postural adjustments, centrally initiated with the intention to move, promote movement to a new position.

The automatic postural responses for maintenance of stance equilibrium during a backward surface translation include activation of gastrocnemius resulting in a symmetrical forward displacement of the center of pressure (CoP) that moves the center of mass (CoM) back to its original position with respect to the feet (Horak and Nashner 1986; Horak et al. 1989). In contrast, the progress of gait initiation requires coordination of anticipatory postural adjustments to move the body mass forward and over the stance limb in preparation for single-limb support during the first step.

The anticipatory adjustments for step initiation include tibialis and hip abductor (e.g., tensor fasciae latae) activation resulting in CoP moving backward and lateral toward the swing limb to propel the CoM forward over

the stance limb. Subsequently, activation of the swing limb gastrocnemius results in heel-off (Crenna and Frigo 1991; Nissan and Whittle 1990; Burleigh et al. 1994; Burleigh and Horak 1996; McIlroy and Maki 1993, 1999).

When healthy subjects voluntarily step in response to a backward translation of the support surface, distinct modifications occur of both postural adjustments for step initiation and automatic postural responses (Burleigh et al. 1994; Burleigh and Horak 1996). Automatic postural responses to the perturbation interfere with the intended step, and therefore are reduced in magnitude. The anticipatory postural adjustments are shortened in duration because the translation results in a forward displacement of the body, requiring a faster initiation of step. Healthy subjects use prediction of translation velocity to proportionally suppress automatic postural responses and online velocity information to scale the magnitude of anticipatory postural adjustments when subjects are instructed to step in response to a perturbation.

Several central neural structures (e.g., motor cortex, basal ganglia, cerebellum, brainstem) may play a role in the dynamic interaction between the automatic postural responses to an external perturbation and anticipatory postural adjustments for goal-directed movements. The present paper is part of a study that investigated the possible role of the cerebellum.

Our previous studies showed that the temporal sequence of automatic postural responses and ability to scale responses to online perturbation velocity information are preserved in subjects with cerebellar disorders (Horak and Diener 1994). However, postural responses in cerebellar subjects are hypermetric and not proportionally scaled to the predicted amplitudes of perturbations. In a corresponding paper (Timmann and Horak 1998), we found that cerebellar subjects were not impaired in their ability to suppress postural responses when instructed to step forward in response to a backward surface translation. Although cerebellar subjects showed hypermetric and more variable postural responses than controls, the cerebellum did not seem critical for suppression of the early postural response with a centrally intended movement.

In the present study, we examined whether anticipatory postural adjustments for step initiation were impaired in cerebellar subjects. Postural adjustments associated with voluntary movements (e.g., rising on toes, arm movements in standing subjects) have been shown to be impaired in cerebellar subjects (Diener et al. 1989, 1990, 1992). Other authors, however, found normal anticipatory responses in cerebellar subjects unless they exhibit severe truncal ataxia (Traub et al. 1980; Gurfinkel et al. 1981).

The first aim of the present study was to show possible abnormalities in timing, force and kinematic parameters of anticipatory postural adjustments in unperturbed stepping in cerebellar subjects compared to healthy controls. Second, we examined the ability of cerebellar subjects to modify anticipatory postural adjustments associated with step initiation in response to a backward translation. Finally, we asked whether cerebellar subjects (and control subjects) make use of predictive knowledge of perturbation amplitude in perturbed stepping. Three different amplitudes of backward surface translations were presented in a blocked (or serial; predictable) and a random (unpredictable) order. Based on our previous work on automatic postural responses, we predicted that anticipatory postural adjustments will be scaled to stimulus amplitude based on prediction by a central set effect in the blocked, but not the random, condition in control subjects with less scaling by subjects with cerebellar disorders (Horak et al. 1989; Horak and Diener 1994).

Materials and methods

Subjects

Eight subjects with cerebellar disorders (mean age 42.6± 15.2 years; range 22–73 years; five women and three men) and eight control subjects (mean age 38.5±19.9 years; range 18–76 years; six women and two men) participated. All patients presented with isolated cerebellar disease at the time of the experimental testing. None of the control subjects had a history of neurological disease or revealed neurological signs upon neurological examination.

Clinical data of the patient group have been given in detail in an accompanying paper (Timmann and Horak 1998). All cerebellar subjects suffered from chronic degenerative disorders (mean disease duration 25±20 years; range 3–60 years). Three subjects had autosomal dominant cerebellar ataxia (ADCA; Harding 1993); one had idiopathic cerebellar ataxia (IDCA); and four had autosomal dominant periodic ataxia (episodic ataxia type 2, EA-type 2; Griggs and Nutt 1995). Patients with periodic ataxia have been tested between attacks. All cerebellar subjects showed signs of gait and stance ataxia. Three had mild, three moderate, and two marked ataxia of gait; and five had mild and three moderate ataxia of stance based on a scale adapted from Klockgether et al. (1990). The Internal Review Board of Legacy Good Samaritan Hospital approved the study. All subjects gave informed written consent.

Methods

All subjects stood on a platform with two force plates that moved backward together under the control of a hydraulic servomotor. Subjects were tested under different conditions in which they stepped forward in response to a backward surface translation. The right leg was always the initial swing limb, and the left leg the initial stance limb. A platform with solid plates for stepping was used and all subjects stepped onto the moving plate. The test conditions were as follows:

Condition 1: Step to Cue

The plate of the initial swing limb (right leg) moved backward approximately 0.1 cm at 10 cm/s, which produced a reliable somatosensory cue, but did not elicit any automatic EMG response. Subjects were instructed to take a forward step with the right foot, as soon as they felt the plate begin to move, and continue the step through with the left foot. A total of ten steps to cue were collected.

Condition 2: Step to Perturbation

Subjects were instructed to step forward in response to three amplitudes of backward surface translations (3 cm, 6 cm and

12 cm), which were presented serially and then randomly. Subjects received seven trials of each amplitude in blocked presentation (total of 21 trials) and five trials of each amplitude in random presentation (total of 15 trials). The same sequence of amplitudes, going from the smallest to the largest (3 cm to 6 cm to 12 cm), was used in blocked presentation for all subjects. The first two trials of the blocked presentation were not analyzed, in order to study responses to predictable perturbation amplitudes. Ramp velocity was constant for all amplitudes at 15 cm/s. Platform perturbations did not induce ("force") stepping: Both cerebellar subjects and controls were able to maintain stance when instructed to stand in response to the same platform perturbations (see the Stance to Translation condition in Timmann and Horak 1998).

To ensure a consistent initial foot position, subjects stood in tracings of their feet made on the platform during quiet stance. To control that the weight distribution and the initial stance position were the same across all trials, initial body position was monitored visually as was the subject's *x* and *y* center of pressure (CoP) on an oscilloscope. At the beginning of each trial, subjects stood with arms folded across the waist and eyes open. Feet were on average 16±1.66 cm (range 14.2–18.3 cm) apart at the heels in the control group and 16.5±2.8 cm (range 12.3–19 cm) in the cerebellar group (P=0.48; unpaired t-test). The time between stepping trials, determined by the experimenter after the subject's CoP returned to quiet equilibrium position, varied between 10 and 15 s.

Force, EMG and kinematic data were collected for 3 s, including 250 ms before the perturbation.

Data analysis

Parameters of initial step initiation were compared between healthy control subjects and subjects with cerebellar disorders. First we were interested if step initiation was different between groups in an unperturbed step. Next, we analyzed if cerebellar subjects were impaired in their ability to adjust parameters of step initiation in perturbed stepping. Finally, we examined effects of different perturbation amplitudes and the use of predictive amplitude information in perturbed step initiation in controls and cerebellar subjects.

EMG activity

EMG activity was recorded using 2.5-cm surface electrodes spaced 2–4 cm apart on the right tibialis anterior (Swing TIB), left tibialis anterior (Stance TIB), right medial gastrocnemius (Swing GAS), left medial gastrocnemius (Stance GAS) and right tensor fasciae latae (Swing TFL). The first burst of GAS EMG activity in the Step to Perturbation condition represented the automatic postural response to forward sway (Fig. 3). A second burst in Swing GAS related to heel-off for step of the initial swing limb. The first burst of Stance and Swing TIB related to the postural preparation of voluntary step initiation (posterior excursion of the CoP). Latencies of automatic postural responses preceded the step-related TIB activity in perturbed steps in both the control and cerebellar group (for details see Timmann and Horak 1998, p. 80). The initial burst of the Swing TFL related to the lateral CoP shift during step initiation (towards the swing limb) (Burleigh et al. 1994). For data reduction, results of Swing TFL, Stance TIB, and Swing GAS will be reported.

Amplified EMG signals (×100) were bandpass filtered (70–2000 Hz) and full-wave rectified. They were then low-passed filtered with a time constant of 10 ms, amplified again, sampled at 400 Hz and stored for offline analysis. Although no attempt was made to calibrate EMGs on an absolute scale, amplifier gains were fixed throughout each experimental session.

Mean baseline amplitude was quantified over a fixed time window (100 ms) prior to onset of platform movement in each trial, multiplied by 75 ms (see below) and subtracted from integrated EMG areas (IEMG) of each muscle burst. IEMG areas were normalized by assigning an arbitrary value of 100% to each subject's mean IEMG value over a fixed time window (75 ms from burst onset) in the Step to Cue condition and by referencing changes in their IEMG to that value. EMG latencies were identified in single trials by placing a cursor at the earliest time an EMG burst lasting at least 25 ms deviated from the preperturbation EMG baseline level. Each EMG latency was measured with reference to perturbation onset.

Force and anticipatory step phases

Four strain gauges embedded in the corner of the plates measured the vertical forces exerted by each foot against the support surface. Forces were sampled at 500 Hz and stored for later analysis. Summation of the four strain gauge signals produced an estimate of vertical force (Fz). The initial increase in vertical force of the initial swing limb (Swing Fz) was analyzed. Before heel-off, an increase in Fz of the initial swing limb contributes to the lateral center of pressure (CoP) excursion towards the swing limb. Forward displacement of Fz produced by ankle dorsiflexion contributes to the posterior excursion of the CoP: Together, these ground reaction forces have the effect of propelling the body center of mass (CoM) diagonally forward and toward the stance limb.

The maximum initial increase of Swing limb Fz was defined with a peak-picking program. The initial rate of change (slope) of Swing Fz was quantified by calculating the slopes of the linear regression of the first 100 ms of force change. Forces were compared among subjects by normalizing changes in Fz as a percentage of total body weight.

A pressure-sensitive resistor, taped under the heel of the initial swing limb, determined the precise time of heel-off during step initiation. Foot-off was determined as the precise moment Fz equalled zero on the initial swing limb plate.

Three phases of anticipatory postural adjustments for step initiation were studied (Burleigh-Jacobs et al. 1997): *reaction time phase* (onset of cue or perturbation to initial increase of Swing Fz), *anticipatory phase* (initial increase of Swing Fz to onset of heel-off), and *push-off phase* (onset of heel-off to onset of foot-off of the initial swing limb).

Kinematic data

Kinematic data were collected (60 Hz) with a three-dimensional Motion analysis system consisting of three high-speed video cameras. Reflective markers were attached to the subject's initial swing limb at the calcaneus and posterior to the subject's right heel on the translating surface. Computation of the marker's *x*, *y* and *z* trajectories was performed offline on a Sun workstation. The *x*, *y* and *z* trajectories were then low-pass filtered (Butterworth) with a cutoff frequency of 6 Hz. From the *x* and *z* trajectories the anterior-posterior (*x*) and vertical (*z*) displacement (i.e., step length and height) and peak velocities in the *x*- and *z*-directions in the sagittal plane were calculated.

Statistics

Step to Cue

Differences in EMG, force and kinematic parameters in step initiation were compared between the control and cerebellar groups with unpaired t-tests. P-values for effects were set at less than 0.05 for this and all subsequent tests unless otherwise stated.

Step to Perturbation

The latency and amplitude EMG, force and kinematic parameters were compared in the Step to Cue and Step to Perturbation conditions. In this part of the study we were not interested in possible effects of perturbation amplitude or prediction in the Perturbation condition. Therefore, the mean values of responses to the randomly presented amplitudes (3 cm, 6 cm and 12 cm) were entered into

statistical analysis. Univariate analyses of variance were calculated with group (control vs cerebellar) as the between-subjects factor and condition (Step to Cue vs Step to Perturbation) as the repeated measure.

Amplitude scaling in Step to Perturbation conditions

To quantify possible effects of amplitude scaling, changes in parameters of step initiation were analyzed comparing the three different perturbation amplitudes (3 cm, 6 cm, 12 cm) in the Step to Perturbation conditions. To analyze effects of amplitude prediction, differences between blocked and randomly presented amplitudes in the perturbation conditions were analyzed. Univariate analyses of variance were calculated with group (control vs cerebellar) as the between-subject factor and perturbation amplitude (3 cm vs 6 cm vs 12 cm) and condition (blocked vs random amplitude presentation) as the repeated measures. For all effects, the degrees of freedom were adjusted according to Greenhouse and Geisser if appropriate.

Results

Step to Cue

In the Step to Cue condition, a voluntary step was initiated with a stereotypic activation of Swing TFL and bilateral TIB followed by a GAS burst in the initial swing limb preceding heel-off. There were no significant differences between cerebellar and control subjects in the temporal characteristics of anticipatory postural adjustments for the initiation of a step (Fig. 1). Latencies to Stance TIB, Swing TFL and Swing GAS were not significantly different between groups (all P values >0.2; unpaired t-test; Fig. 2B).

Peak swing limb vertical forces (Swing Fz) and initial rate of change of Swing Fz appeared to be smaller and more variable in the cerebellar subjects compared to the control subjects shown in Fig. 1. Peak Swing Fz and rate of initial weight change, however, were not significantly different between groups (P=0.12 and P=0.76; Fig. 2C).

Timing of step phases appeared to be preserved in cerebellar subjects (Fig. 2A). The mean durations of the reaction time, anticipation and push-off phases were not significantly different between control and cerebellar groups (all P values >0.5).

Kinematic analysis of step parameters revealed a significantly reduced step length and step peak velocity in the x-direction in cerebellar subjects compared to controls (P=0.012 and P=0.01; Fig. 2D). There was no significant difference in step height and peak velocity in the z-direction (P=0.34 and P=0.19).

Linear regression analyses with EMG, force and kinematic parameters as dependent variables and clinical ataxia scores of stance and gait as independent variables revealed a tendency of more severely affected cerebellar subjects to initiate steps later than more mildly affected subjects (Stance TIB onset vs ataxia of gait: R=0.73, P=0.039; Swing GAS onset vs ataxia of gait: R=0.66, P=0.07; anticipatory phase vs ataxia of stance: R=0.64, P=0.08).

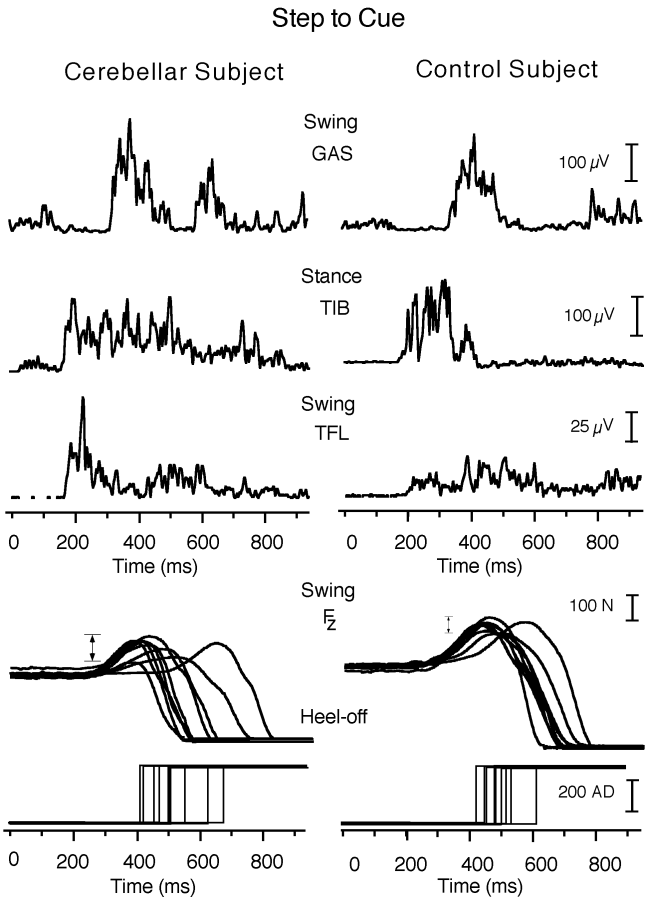

Fig. 1 Examples of representative EMG and force traces for a control and cerebellar subject ("VC," see Table 1 in Timmann and Horak 1998) in the Step to Cue condition. Subjects were instructed to take a forward step with the right foot as soon as they felt the surface cue. Note stereotypic activation of tibialis (*TIB*) and tensor fasciae latae (*TFL*) muscles followed by a gastrocnemius burst (*GAS*) in the swing limb in both subjects with no differences in latencies. Note reduced and more variable peak vertical forces (*Fz*) in the cerebellar subject compared to the control subject (indicated by *vertical arrows*). *The bottom trace* shows recordings of the heel-switch. Note increased variability of time of heel-off in the cerebellar subject compared to the control. EMG traces represent averages of the first five steps out of a total of ten steps. Swing Fz and heel-switch data represent individual traces of all ten steps. Zero ms indicates the onset of the platform cue (*Stance* initial stance limb, *Swing* initial swing limb)

In sum, timing of EMG onsets and step phases during step initiation appeared to be preserved in cerebellar subjects in the Step to Cue condition. There was a tendency of reduced force production of the swing limb in cerebellar subjects. Step length and peak velocity were significantly reduced in cerebellar subjects.

Step to perturbation

Both control and cerebellar subjects showed characteristic changes of step initiation on comparison of the Step to Cue and Step to Perturbation conditions. Both control subjects and cerebellar subjects took a faster and more

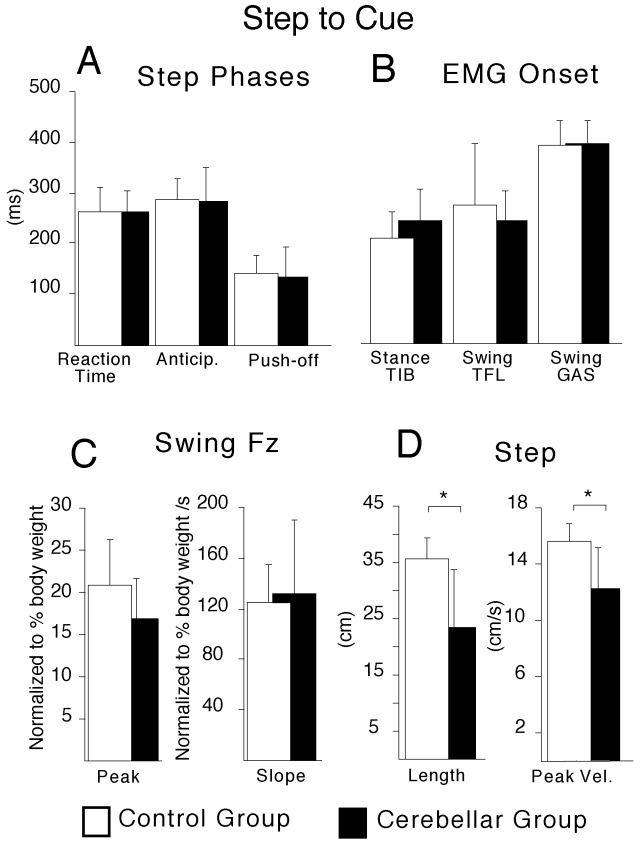

Fig. 2A–D. Step to Cue condition: group means (±SD) of the control (*open bars*) and cerebellar (*filled bars*) group are shown for **A** step phases (reaction time phase, anticipatory phase, push-off phase), **B** EMG burst onsets of tibialis (*TIB*), tensor fasciae latae (*TFL*) and gastrocnemius (*GAS*) muscles, **C** peak and initial rate of change of peak vertical forces of the initial swing limb (*Fz*) and **D** step length and step peak velocity in the *x*-direction. Note significant reduction of peak Fz, step length and step peak velocity in the cerebellar group compared to the controls (*Stance* initial stance limb, *Swing* initial swing limb)

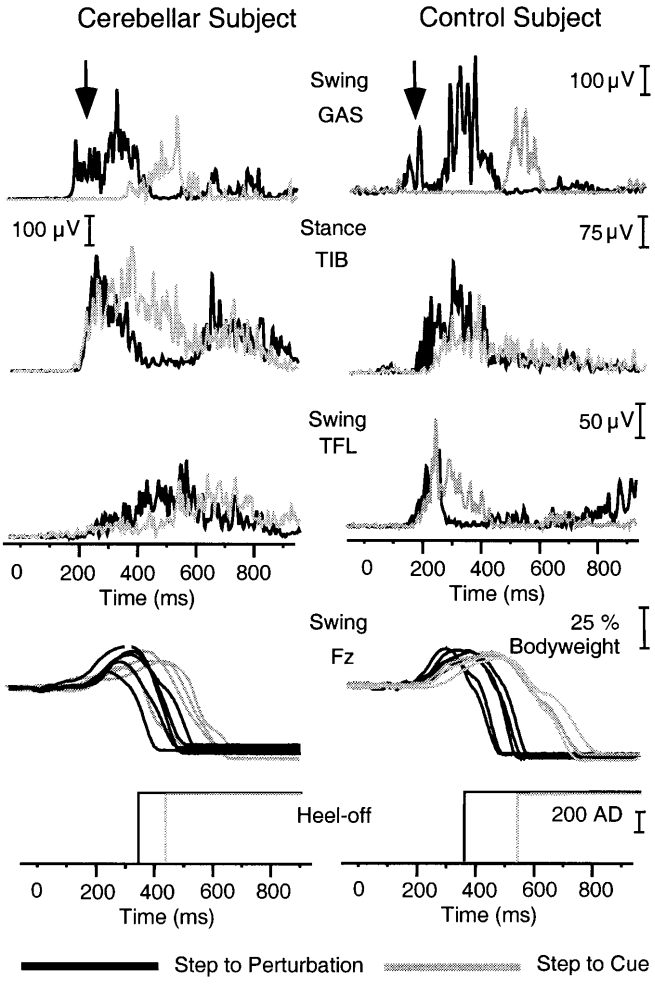

Fig. 3 Examples of representative EMG and force traces for a control and cerebellar subject ("MF," see Table 1 in Timmann and Horak 1998) for Step to Cue (*light grey*) and Step to Perturbation (*black*) conditions. GAS bursts for heel-off are preceded by automatic postural responses (*arrows*) in the Step to Perturbation condition. *The two bottom traces* show peak vertical forces (*Fz*) and recordings of the heel-switch. Note decreased onsets of GAS heel-off burst (*top trace*) and time of heel-off (*bottom trace*) in the Step to Perturbation condition compared to Step to Cue in both the control and cerebellar subject. Both the control and cerebellar subject showed a tendency to increase early muscle activity for gastrocnemius (*GAS*), tibialis (*TIB*) and tensor fasciae latae (*TFL*) and of the peak vertical forces (*Fz*) in the Step to Perturbation condition, whereas onset of TIB, TFL and Fz decreased in the control but not in the cerebellar subject. EMG and heel-off traces represent averages of the first five steps out of a total of ten steps in the Step to Cue condition and of the five steps in the 6-cm amplitude, random Step to Perturbation condition. Swing Fz data represent individual traces of each of the five steps. Zero ms indicates the onset of the platform movement (cue or perturbation) (*Stance* initial stance limb, *Swing* initial swing limb)

forceful step in the Step to Perturbation condition. Onsets of Swing GAS and heel-off were earlier in both the control and cerebellar patient shown in Fig. 3 (black = Step to Perturbation; light grey = Step to Cue). Peak initial force production was increased in the Step to Perturbation condition in both the control and cerebellar patient. Sizes of initial IEMGs were increased in the initial Stance TIB, Swing TFL and Swing GAS. The control, but not the cerebellar patient, showed a tendency to reduce the time of onset of Stance TIB, Swing TFL and initial weight change of the swing limb in the perturbed compared to the unperturbed step.

Statistical analysis revealed a significant reduction of Swing GAS onset in the Step to Perturbation condition compared to Step to Cue condition in both the control and cerebellar groups (Fig. 4C; condition $P<0.001$; ANOVA). There was no significant group effect and no significant group by condition interaction. In the perturbed step, there was a tendency to reduce onset of Swing TFL and Stance TIB in both the control and cerebellar group which appeared to be more pronounced in the control group (Fig. 4A, B, top row). However, analysis of variance revealed no significant condition, group or group by condition interaction effect (all P values >0.1).

The size of the initial EMG integral increased in Swing TFL, TIB and Swing GAS in both control subjects and cerebellar subjects (Fig. 4A–C, bottom

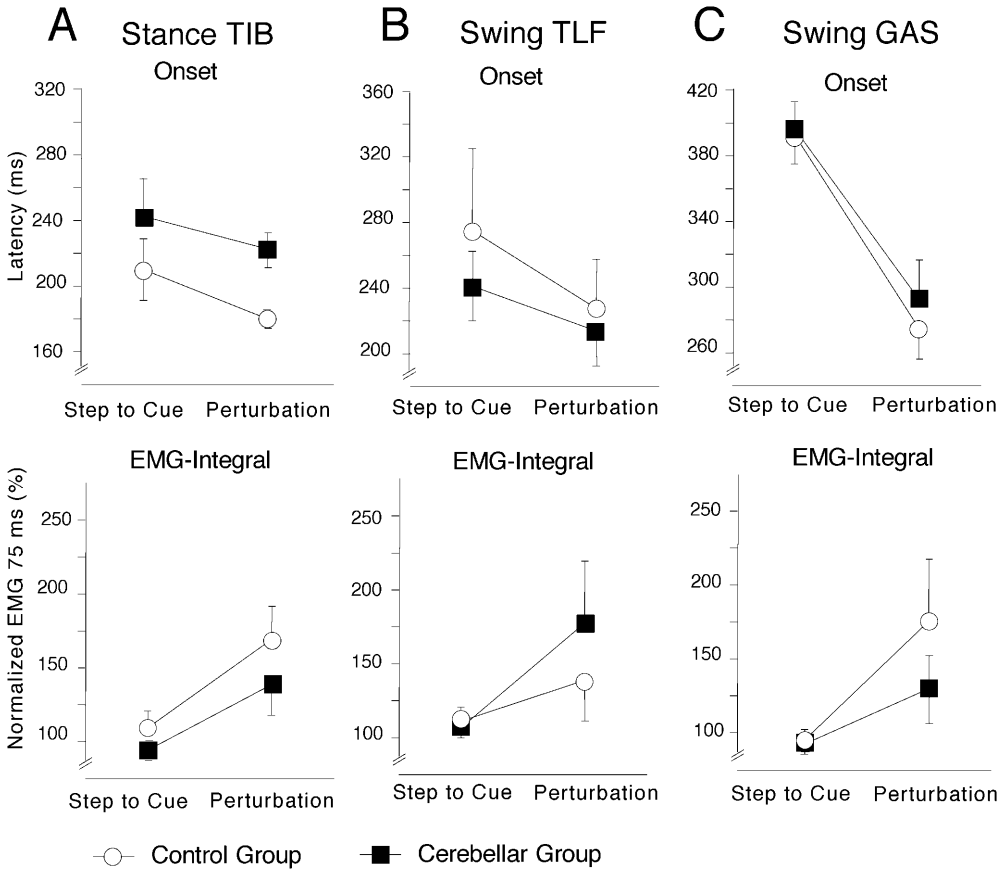

Fig. 4A–C Step to Cue and Step to Perturbation (*Perturbation*) conditions: group means (±SE) of the control (*open circles*) and cerebellar (*filled squares*) groups are shown for EMG burst onsets (*top row*) and normalized EMG integrals (*bottom row*) of **A** tibialis (*TIB*), **B** tensor fasciae latae (*TFL*) and **C** gastrocnemius (*GAS*) muscles (*Stance* initial stance limb, *Swing* initial swing limb)

row). Analysis of variance revealed significant condition effects (swing GAS P=0.038; Stance TIB P<0.001; Swing TFL P=0.069*)*, but no significant group and group by condition effects.

Changes of step phases are shown in Fig. 5A–C. Both control subjects and cerebellar subjects showed a tendency to reduce *reaction time* in the Step to Perturbation condition compared to the Step to Cue condition. The amount of reduction appeared to be less in the cerebellar group (filled squares) than in the controls (open circles; Fig. 5A). Analysis of variance revealed a condition effect which was close to being significant (P=0.098), but no significant group effect and no group by condition interaction. The most obvious finding was a clear reduction of the *anticipatory phase* in the Step to Perturbation condition in both control and cerebellar subjects (Fig. 5B; P<0.001; no significant group effect, no group by condition interaction). Although inspection of Fig. 5C suggested a tendency of control subjects but not cerebellar subjects to decrease push-off time in the perturbed step, changes of *push-off phase* were not significantly different between groups or conditions (Fig. 5C; all P values >0.5; no condition or group effect, no group by condition effect).

The peak initial Swing Fz showed a tendency to increase from Step to Cue to Step to Perturbation in both control subjects and cerebellar subjects (Fig. 5D); however, this did not reach statistical significance (P=0.59). There was a significant group difference (P=0.034) emphasizing generally decreased initial force production in the cerebellar subjects (see also Fig. 2C), but no group by condition interaction.

Both control subjects and cerebellar subjects increased peak step velocity in the *x*- and *z*-direction in the Step to Perturbation condition (P<0.01; Fig. 5E, F). Step peak velocity in the *x*-direction showed a significant group effect (P=0.0021), indicating generally slower step velocity in the cerebellar subjects (see also Fig. 2D). There were no significant group by condition interactions. Step length and height showed no significant change comparing the Step to Perturbation and Step to Cue conditions (P=0.6 and P=0.107). Again, step length was shorter in the cerebellar group regardless of the condition (group effect P=0.0021; see also Fig. 2D).

Linear regression analyses with EMG, force and kinematic parameters as dependent variables (i.e., differences in magnitude across the Step to Cue and Step to Perturbation conditions) and clinical ataxia scores of stance and gait as independent variables revealed no significant correlations, except for anticipatory phase. The reduction of anticipatory phase was significantly larger in perturbed steps in more severely affected cerebellar subjects (anticipatory phase vs ataxia of gait: R=0.75, P=0.031).

In sum, both control subjects and cerebellar subjects decreased the time of Swing GAS onset and the duration of the anticipatory phase in the Step to Perturbation

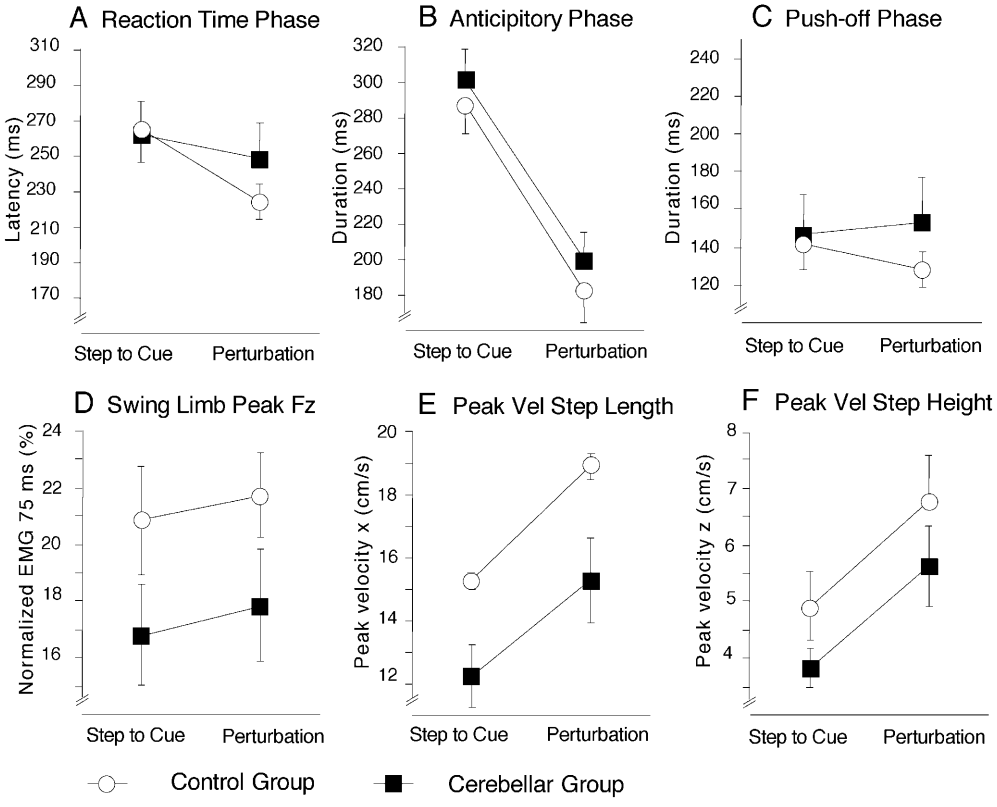

Fig. 5A–F Step to Cue and Step to Perturbation (*Perturbation*) conditions: group means (±SE) of the control (*open circles*) and cerebellar (*filled squares*) groups are shown for durations of **A** reaction time phase, **B** anticipatory phase, **C** push-off phase, **D** peak vertical force (*Fz*), **E** peak step velocity in *x*-direction and **F** peak step velocity in *z*-direction

condition compared to the Step to Cue condition. In addition, initial EMG amplitude of Stance TIB, Swing TFL and Swing GAS were increased and the velocity of the step was faster. Regardless of the condition, cerebellar subjects took slower and shorter steps with less initial vertical force production of the swing limb.

Amplitude scaling in step to perturbation conditions

Both control subjects and cerebellar subjects showed significant adjustments of step initiation to increasing perturbation amplitudes in the perturbed step conditions.

The most consistent findings were a decrease of Swing GAS onset and a decrease of the anticipatory phase with increasing perturbation amplitude (Fig. 6A, B). Moreover, step height, length and peak step velocities in the *x*- and *z*-directions increased with increasing perturbation amplitudes (Fig. 6C, D). Analysis of variance revealed significant amplitude effects (all *P* values <0.001). There were no significant group by amplitude interactions. Step length and peak velocity in the *x*-direction showed a significant group effect, reflecting generally shorter and slower steps in the cerebellar subjects (see also Figs. 2D, 5E).

To verify the effects of scaling of step initiation parameters to perturbation amplitude based on prediction in the blocked condition, the three different amplitudes were presented in a blocked and a random order. In the case of predictive scaling, one would expect amplitude effects in the blocked, but not the random, conditions. Closer inspection of Swing GAS onset and duration of anticipatory phase in Fig. 6A, B suggested that in control subjects (open columns) effects of amplitude scaling were present in the blocked, but not in the random, condition. In cerebellar subjects, however, blocked and random conditions showed no clear difference. It appeared that scaling was present in both the 3-cm blocked and random conditions.

Analysis of variance revealed no significant group (control vs cerebellar) or condition (blocked vs random) effects. However, the amplitude (3 cm vs 6 cm vs 12 cm) by condition (blocked vs random) interaction was close to statistical significance (Swing GAS onset P=0.077; anticipatory phase P=0.098), hinting at possible effects of prediction.

Post hoc analysis of variance of Swing GAS onset showed a significant amplitude effect in the blocked condition (P=0.029), but not in the random condition (P=0.72) in control subjects. In the cerebellar subjects, however, there was a significant amplitude effect in both the blocked and random condition (P=0.037 and P=0.046). Post hoc analysis of duration of anticipatory phase showed a significant amplitude by condition interaction in the control group (P=0.037) but not in the patient group.

On closer inspection of the scaling data in Fig. 6A, B, cerebellar subjects showed differences in responses only between the short duration 200-ms/3-cm amplitude translation compared to the longer 6-cm/400-ms and 12-cm/800-ms duration translations. Because of their longer reaction times (i.e., onset of perturbation to initial

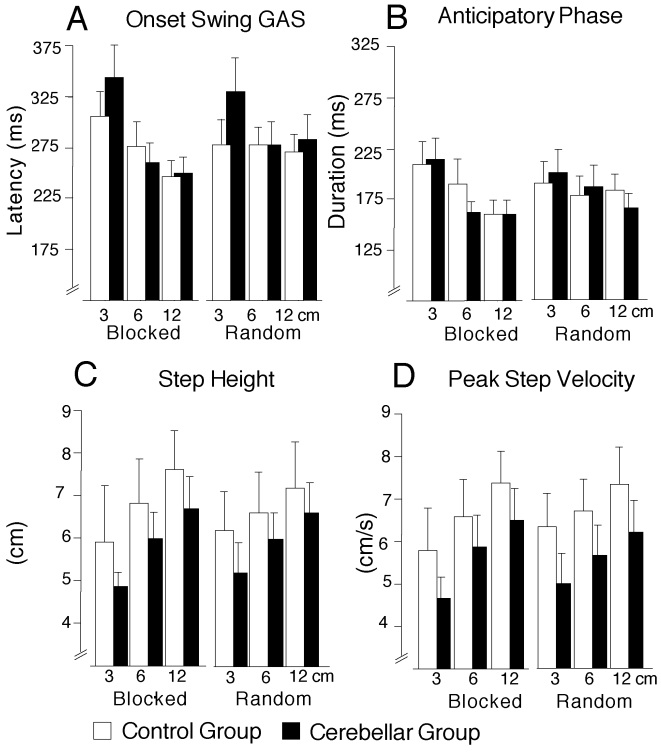

Fig. 6A–D Effects of amplitude scaling in the Step to Perturbation conditions: group means (±SE) of the control (*open bars*) and cerebellar (*filled bars*) groups are shown for **A** onset of gastrocnemius (*GAS*) heel-off burst, **B** duration of the anticipatory phase, **C** step height and **D** peak step velocity in *z*-direction for the three amplitude conditions in the blocked (predictable) and random (unpredictable) orders. Note decreasing gastrocnemius (*GAS*) heel-off burst onset and duration of the anticipatory phase with increasing amplitudes in the blocked but not the random condition in the control group. Cerebellar subjects appeared to scale for the blocked *and* random 3-cm conditions, suggesting use of online information in both conditions. Both control subjects and cerebellar subjects increased step height and peak step velocity with increasing perturbation amplitudes in the blocked *and* random conditions

increase of Swing Fz) to step initiation (274.0±69.0 ms), cerebellar subjects, but not control subjects with reaction times of 229.1±32.0 ms, could have used online feedback about translation duration/amplitude in both the blocked and random 3-cm condition. Cerebellar subjects, however, seemed less able to use predictive information in the 6-cm and 12-cm blocked amplitude conditions than control subjects.

Closer inspection of kinematic step parameters showed amplitude changes in both the control and cerebellar group regardless of the blocked or random presentation (Fig. 6C, D). Both control subjects and cerebellar subjects appeared to use online information to adjust kinematic step parameters regardless of whether predictive amplitude information was available or not. Analysis of variance revealed no significant group or condition (blocked vs random) effects and no significant group by condition interactions (all *P* values >0.2).

There were no significant correlations between EMG, force and kinematic parameters of amplitude scaling (i.e., slopes of individual linear regression analysis) and clinical ataxia scores of stance and gait (all *P* values >0.05).

In sum, both control and cerebellar subjects changed parameters of step initiation to increasing perturbation amplitudes. Early in step initiation, control subjects appeared to use predictive information of perturbation amplitude to scale the onset of swing GAS and the duration of the anticipatory phase. Cerebellar subjects appeared to be less able in the use of predictive information. Both control subjects and cerebellar subjects used online information of perturbation amplitudes to adjust kinematic step parameters to increasing perturbation amplitudes.

Discussion

The present study of anticipatory postural adjustments in unperturbed and perturbed stepping revealed few abnormalities in subjects with cerebellar disorders compared to control subjects. Subjects with cerebellar disorders had reduced force production as well as reduced step length and step velocity compared to control subjects. In addition, subjects with cerebellar disorders appeared to be less able than control subjects to use predictive information of perturbation amplitude to scale anticipatory postural adjustments. In contrast, both in the unperturbed and perturbed step conditions many aspects of spatial-temporal coordination and of adaptation of step initiation to postural perturbations were normal in subjects with cerebellar disorders. In unperturbed voluntary steps, the temporal parameters of postural adjustments in step initiation were preserved in cerebellar subjects. When subjects voluntarily initiated a step in response to the surface translation, both control and cerebellar subjects adaptively shortened the anticipatory postural adjustments to step more rapidly. Furthermore, cerebellar subjects, like control subjects, were able to use online information of perturbation amplitude to scale kinematic step parameters in perturbed stepping.

Intact coordination of voluntary step initiation

In step initiation, cerebellar subjects showed less peak vertical force production in the initial swing limb than control subjects and took shorter and slower steps. Reduced initial force production appeared to be a compensatory strategy rather than a primary cerebellar deficit. Less initial force production resulted in less forward and lateral movement of the CoM towards the stance limb and, therefore, reduced lateral postural instability and size of subsequent steps (Crenna and Frigo 1991; Burleigh and Horak 1996; McIlroy and Maki 1999). Patients with chronic cerebellar disorders may have learned to execute step initiation slower and less forcefully to compensate for their hypermetria of gait. These findings agree with recent studies of gait in cerebellar subjects that described reduced peak ankle plantar-

flexion (attributed to a reduced push-off) and short and slow steps (Gilman et al. 1981; Palliyath et al. 1998; Earhart and Bastian 2001). Since it is known from studies of finger force control that cerebellar subjects are able to produce different force levels, but have difficulty building up force quickly, the preserved rate of change of vertical force in the cerebellar group argues against a primary cerebellar deficit of reduced anticipatory postural forces (Mai et al. 1988; Mueller and Dichgans 1994a, 1994b; Serrien and Wiesendanger 1999).

Reduced force production in step initiation is not a unique finding in cerebellar disorders. Decreased force production, decreased velocity of movement, and slowed execution of the anticipatory postural adjustments have been described in self-generated step initiation in patient's with Parkinson's disease (Crenna et al. 1990; Burleigh-Jacobs et al. 1997). Unlike in cerebellar disease, reduced force production in Parkinson's disease is likely a primary deficit from centrally determined bradykinesia.

Temporal characteristics of unperturbed step initiation were preserved in cerebellar subjects. These results agree with the most common theories of neuronal control of initiation of locomotion. Activation of the spinal locomotor networks is produced primarily by an excitatory drive from populations of reticulospinal neurons located in the pons and medulla, which can be activated via two inputs in the mesencephalic and subthalamic locomotor regions (for recent review see Orlovsky et al. 1999). Although recent animal studies demonstrated that stimulation of midline cerebellar areas can also evoke locomotion (Mori et al. 1998, 1999), the main function of the cerebellum is thought to be the coordination of stepping limb movements. Similarly to step initiation, we found preserved temporal characteristics of automatic postural responses to backward translation in cerebellar subjects (Timmann and Horak 1997, 1998). Areas within the brainstem, but not the cerebellum, appear to be critical for the basic motor programs underlying automatic postural adjustments during stance and step initiation.

Preservation of adapting step initiation to perturbations

Not only were the spatial-temporal patterns of voluntary step initiation intact in cerebellar subjects, their ability to adjust the pattern of voluntary initial step initiation to postural perturbations was also intact. When subjects initiated a step in response to the backward surface translation, both cerebellar and healthy subjects executed the anticipatory adjustments for step more rapidly and increased the velocity of the initiated step. These results suggest that the cerebellum is not essential for adapting motor programs based on online somato-sensory information indicating forward falling during step initiation.

The present findings bear similarities to those of our previous studies of adaptive control of early automatic postural responses to various platform perturbations. First, in an accompanying paper we demonstrated that cerebellar subjects were not impaired in their ability to suppress automatic postural responses when subjects were instructed to step, instead of maintain stance, in response to a surface translation (Timmann and Horak 1998). Furthermore, cerebellar subjects' ability to adapt to changing perturbation amplitudes, velocities, stance width and direction of the perturbation (translation vs rotation) was generally preserved, despite their increased variability and postural hypermetria (Horak and Diener 1994; Timmann and Horak 1997; Mummel et al. 1998; Timmann et al. 1998).

Our findings of preserved adaptive changes of postural responses and anticipatory postural adjustments are somewhat contradictory to findings of impaired adaptation of arm movements and locomotion in cerebellar subjects (Hore and Vilis 1984; Manto et al. 1994; Deuschl et al. 1996; Martin et al. 1996; Rand et al. 1998; Timmann et al. 2000). For example, Rand et al. (1998) described that cerebellar subjects were able to adapt their locomotor responses to repeated changes in treadmill speed although they showed a much less consistent motor pattern than that of normal control subjects. Earhart and Bastian (2001) investigated stepping on an inclined surface and found that the cerebellum appeared to be critical for fine-tuning of motor programs involving multiple joints to adapt to changes in the environment. Our findings in anticipatory postural adjustments and automatic postural responses suggest that the cerebellum may be less influential in adaptation of more automatic responses involved in postural control. Adaptive postural changes are likely to be primarily controlled by centers within the brainstem and spinal cord (Timmann and Horak 1997, 1998).

However, there are other possibilities which may to some extent account for the preservation of adaptive changes. First, cerebellar subjects were examined with relatively mild cerebellar ataxia of stance and gait. Although most EMG, force and kinematic parameters were not significantly different comparing the more mildly and more severely affected cerebellar subjects (except anticipatory phase, which showed an even larger reduction in perturbed steps in the more severely affected subjects), it cannot be excluded that adaptive changes may be more impaired in a group of more severely affected cerebellar subjects. Second, patients suffered from long-standing degenerative disorders and the effects of compensatory strategies cannot be excluded. Third, postural adjustments in our studies were primarily studied for movements around the ankle joint and in the anteroposterior direction. Because cerebellar deficits may be more prominent in the control of lateral stability (McIlroy and Maki 1999) and across multiple joints (Thach et al. 1992, Thach 1998; Goodkin et al. 1993), future studies should include assessment of lateral movements of the trunk and coordination between leg, trunk and head movements.

Predictive scaling of anticipatory postural adjustments

The present study extends our previous findings in healthy subjects on perturbed stepping to predictable and unpredictable perturbation velocities to the effects of predictable and unpredictable perturbation amplitudes. In brief, Burleigh and Horak (1996) showed that control subjects used online velocity information for modification of anticipatory postural adjustments when steps were initiated in response to surface perturbations. In the present study, we found that control subjects also utilized online amplitude information to modify kinematic parameters such as step length and height associated with perturbed step initiation. Furthermore, amplitude prediction seemed to be important for scaling postural adjustments as shown by scaling the magnitude of the GAS activation and duration of the anticipatory phase when perturbation amplitudes were blocked, and thereby predictable, but not when amplitudes were randomized. Thus, immediate afferent velocity information is used in healthy control subjects to modify anticipatory postural adjustments, whereas both online and predictive amplitude information are utilized to modify step initiation.

The ability to use online amplitude information to modify anticipatory postural adjustments for step initiation was preserved in cerebellar subjects. However, the ability to use amplitude prediction to scale these postural adjustments based on prior experience appeared to be impaired in cerebellar subjects. Cerebellar subjects were less able to use predictive information in the 6-cm and 12-cm blocked amplitude conditions than control subjects (see Fig. 6A, B). However, long reaction times to step initiation made it difficult to test the hypothesis that cerebellar subjects have difficulty using prediction of perturbation amplitude. The longer reaction time and later onset of stance leg TIB in cerebellar subjects compared to control subjects (see Figs. 2B, 4A, B) allowed cerebellar subjects (but not controls) to make use of online information of perturbation amplitude in both the blocked and random 3-cm condition.

The present findings for predictive scaling of postural adjustments for step initiation are consistent with our previous work demonstrating the importance of the cerebellum for predictive scaling of automatic postural adjustments triggered by surface displacements (Horak and Diener 1994; Timmann and Horak 1997). Subjects with cerebellar disorders showed an inability to scale postural response magnitude based on amplitude prediction but were able to scale based on online perturbation velocity information (Horak and Diener 1994). In a more recent study, we found that impaired amplitude scaling was due to inability to consistently scale motor output (i.e., hypermetric and variable postural responses) rather than to a primary deficit in recognizing or using predictive amplitude information (Timmann and Horak 1997).

When subjects intend to step forward in response to a backward surface translation, automatic postural responses triggered by the perturbation impede forward stepping and are inhibited in both control subjects and subjects with cerebellar disorders (Burleigh et al. 1994; Timmann and Horak 1998). Prediction of the velocity of translation is used to suppress the automatic postural responses proportionally for increasing velocities of perturbations (Burleigh and Horak 1996). In an accompanying paper, we found that neither controls nor cerebellar subjects used amplitude information to proportionately reduce the magnitude of initial postural responses to backward translations when subjects are instructed to step instead of maintain stance in response to a backward surface translation (Timmann and Horak 1998). The amount of postural response reduction was the same regardless of (predictable and unpredictable) perturbation amplitude in both controls and cerebellar subjects. The CNS, therefore, appears to use predictive knowledge of perturbation velocity, but not perturbation of amplitude, to modify automatic postural responses in perturbed steps.

Conclusions

Coordination of voluntary step initiation and many types of adaptive changes to voluntary steps initiated in response to perturbations appeared to be preserved in subjects with cerebellar disorders. Deficits in force production and step length were likely due to compensatory slowing in chronic cerebellar subjects. Although use of online sensory adaptation was preserved, use of amplitude prediction to modify step initiation in perturbed stepping appeared to be impaired in cerebellar subjects. Overall, the role of the cerebellum in the control of automatic postural control (e.g., anticipatory postural adjustments and automatic postural responses) appears to be more limited than its role in control of voluntary arm movements.

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