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RESEARCH ARTICLE

**Rebecca M. C. Spencer · Richard B. Ivry ·
Howard N. Zelaznik**

Role of the cerebellum in movements: control of timing or movement transitions?

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Abstract Patients with cerebellar damage are impaired on a range of timed tasks. However, recent research has indicated that the impairment on temporal production tasks is limited to discontinuous movements. The present experiments were designed to compare two accounts for the increased temporal variability observed in these patients when producing discontinuous movements. First, the impairment on discontinuous movements may be the result of the requirements associated with transitioning between movement onsets and offsets, requirements unique to discontinuous movement production. Second, the impairment may reflect a requirement to represent the temporal goal in timed, discontinuous movements. Patients with unilateral or bilateral cerebellar lesions and matched control subjects performed a key-pressing task. In one condition, the participants pressed and immediately released the key. The other conditions required the participants to press the key, and after either a 550-ms or 950-ms delay, release the key. Individuals with cerebellar damage were impaired on the two timed conditions. These results do not support the transition hypothesis. Rather, they are consistent with the hypothesis that the cerebellum is essential for tasks requiring precise event-like temporal control.

R. M. C. Spencer (✉) · R. B. Ivry
Department of Psychology, University of California at Berkeley,
3210 Tolman Hall, #1650,
Berkeley, CA 94720, USA
e-mail: rspencer@socrates.berkeley.edu
Tel.: +1-510-6429226
Fax: +1-510-6425293

R. M. C. Spencer · R. B. Ivry
Helen Wills Neuroscience Institute, University of California at Berkeley,
Berkeley, CA 94720, USA

H. N. Zelaznik
Department of Health and Kinesiology and Purdue University Integrative Program in Neuroscience, Purdue University,
West Lafayette, IN 47906, USA

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Introduction

Patients with cerebellar lesions exhibit temporal impairments on tasks ranging from simple finger tapping (Ivry et al. 1988) to eyeblink conditioning (Woodruff-Pak et al. 1996). However, recent evidence suggests that this impairment is specific to movements that are discontinuous; the patients are unimpaired on measures of temporal control when producing continuous movements (Spencer et al. 2003). This dissociation was demonstrated through a comparison of two types of repetitive flexion/extension movements of the index finger both without surface contact. In one condition, the participants were instructed to insert a brief pause prior to each flexion. In the other condition, the participants produced smooth, continuous movements. An increase in temporal variability in the patients' performance was only evident in the former condition, the one that contained a discontinuity between successive cycles.

The dissociation between discontinuous and continuous movements can be understood in terms of how the movement goals are conceptualized (Ivry et al. 2002; Robertson et al. 1999; Zelaznik et al. 2000, 2002). The timing of periodic discontinuous movements is hypothesized to be controlled by a representation of the timing of salient events that demark each cycle. Thus, for finger tapping, an event representation might specify the onset of each flexion cycle or the target time for contacting a response surface (Billon et al. 1996). In contrast, continuous movements lack such an event structure. We propose that for these movements, temporal regularities are an emergent property, reflecting the operation of control parameters satisfying other movement constraints such as minimizing jerk (Hogan and Flash 1987) or spatial noise (van Beers et al. 2002).

Although the distinction between explicit and emergent timing was formulated at a psychological level of description, it has been demonstrated that cerebellar damage is associated with impaired performance on a range of motor and non-motor tasks that require precise timing (Ivry et al. 1988; Ivry and Keele 1989; Mangels et al. 1998; Woodruff-Pak et al. 1996). Notably, the tasks used in these studies lend themselves to an event-based description. For example, eyeblink conditioning requires timing the interval between the onset of the conditioned stimulus and the unconditioned stimulus. Similarly, perceptual tasks such as duration discrimination would appear to require an explicit representation of stimulus duration. Given these results, we predicted that patients with cerebellar lesions would be disproportionately impaired on discontinuous movement tasks given the hypothesized dependency of such tasks on an event representation in terms of temporal control. A priori, we did not know if cerebellar damage would disrupt performance on the continuous tasks. The results of Spencer et al. (2003) showed that the patients exhibited higher temporal variability on the discontinuous tasks, while performing similar to controls on comparable measures on the continuous tasks. Interestingly, this dissociation is not generically observed in patients with movement disorders. We have recently observed that in terms of temporal variability, patients with Parkinson's disease are unimpaired on both discontinuous and continuous repetitive movement tasks (Spencer and Ivry 2004).

In the current study, we further explore the temporal impairment observed in performance of cerebellar patients on discontinuous movements. As described above, this impairment could reflect lesion-induced noise in an event-based representation. Consider a task in which the participant is required to tap every 500 ms. According to the event timing hypothesis, the cerebellum provides the computation signaling the requisite timing for salient events that mark each cycle. Computational models suggest that precise timing is imposed by the cerebellar cortex and the output of the deep cerebellar nuclei (Medina and Mauk 2000). In this way, the nuclei not only facilitate the production of a selected response pattern, but ensure that the pattern has the appropriate temporal profile. In these models, timing does not reflect the operation of some sort of pacemaker system, but rather arises from the dynamics of time-varying physiological signals coupled with salient learning signals (Fiala et al. 1996; Medina and Mauk 2000). As such, damage to this system is expected to increase variability (i.e., noise), and this prediction is consistent with many experimental studies. Thus, in the tapping task, the output would, on average, continue to occur around the target interval, but the consistency of these signals would be reduced.

Alternative hypotheses to the event timing hypothesis can be generated upon consideration of the kinematic requirements for these two classes of movements. If the cycle duration is equated, the maximum velocity will be greater for discontinuous movements compared to continuous movements. However, patients with cerebellar lesions were unimpaired in making continuous flexion/extension movements of the index finger across a range of movement speeds, including conditions in which the maximum velocity for the continuous movements exceeded that obtained when similar movements were made discontinuously (i.e., with a slight pause before each flexion phase, see Spencer et al. 2003).

A second, alternative kinematic-based account centers on the idea that the patients' impairment in producing discontinuous movements may reflect the control requirements associated with transitions between movement onset and offset (Conrad and Brooks 1974; see also Meyer-Lohmann et al. 1977). By this movement transition hypothesis, the increased temporal variability exhibited by patients with cerebellar lesions during finger tapping or discrete circle drawing may result from a deficit in initiating and/or terminating each movement cycle. Previous research indicates that cerebellar lesions produce delays and increased variability in movement initiation (Day et al. 1998; Spidalieri et al. 1983; Botez-Marquard and Botez 1997). Furthermore, dysmetria, one of the cardinal symptoms of cerebellar ataxia, is characterized by an inability to accurately terminate ballistic movements (Hore et al. 1991). Electromyographic (EMG) analyses reveal a prominent breakdown in the onset of the braking action provided by the antagonist (Hallet et al. 1975).

Evaluating the merits of the event timing and movement transition hypotheses is difficult. First, event timing and transition control could be two independent functions of the cerebellum. If this were so, then we might expect to observe dissociations in performance of selected patients between impairments associated with event timing and impairments associated with transition control, assuming these functions were subsumed by distinct subregions of the cerebellum. Second, controlling the initiation and/or termination of a response may be the manner in which event timing is implemented. For example, if the movement goal is to tap every 500 ms, then this might be achieved by signaling the onset of a response every 500 ms. An impairment in representing the temporal goal would be expected to lead to increased temporal variability. Similarly, an impairment in implementing the initiation command could also lead to increased temporal variability.

One approach for assessing these hypotheses is to consider tasks that involve event timing without transition control. As noted above, temporal impairments associated with cerebellar damage are not limited to motor tasks. Patients with cerebellar lesions are also impaired on perceptual tasks that require precise timing. These include duration discrimination (Ivry and Keele 1989; Mangels et al. 1998; Nichelli et al. 1996) and the perception of speech sounds defined solely by temporal cues (Ackermann et al. 1997). An impairment in movement transitions would not be expected to influence performance on perception tests. Thus, the perceptual studies favor the event timing hypothesis.

In the present experiments we designed three movement conditions to directly evaluate the event timing and movement transition hypotheses. The task required a keypress involving flexion then extension of the metacarpophalangeal joint of the index finger. Thus, the conditions each placed similar demands on processes associated with movement transitions. For two of the conditions, there was an added explicit timing requirement. In the *short* response condition, the participants were trained to hold the key in the depressed position for 550 ms; likewise, in the *long* response condition, the participants were trained to depress the key for 950 ms. In a third condition, *press*, the participants were instructed to simply press and release the key. The primary dependent variable for all three conditions was the temporal variability of the time during which the key was depressed.

The event timing and transition hypotheses lead to differential predictions regarding patient performance on this task. If patients with cerebellar lesions are impaired on tasks requiring event timing, then we expect that they will exhibit increased variability on the conditions requiring the key to be pressed for a specified duration. Correspondingly, this hypothesis predicts no impairment on the press condition given the assumption that there is no explicit temporal goal for a movement in which the onset and offset follow in immediate succession. Previous studies indicate that the maximum rate at which alternating movements can be performed is limited by how well individuals can selectively activate agonist/antagonist muscle groups rather than processes associated with temporal variability (Freund 1983; Keele et al. 1985). Alternatively, if patients with cerebellar lesions have difficulty on movements requiring transitions, then impairment should be evident on all three conditions. Moreover, this impairment should be especially pronounced in the press condition. We assume that the variability of the response period is composed of (at least) two sources: one associated with the transitions and another associated with timing the hold period. The contribution of the latter source should be greater in the short and long conditions, thus diluting the contribution to total variability to that associated with transitions. In contrast, there should be little (or no) variability associated with timing the hold period in the press condition. As such, variability here will primarily reflect variability associated with transitions.

In sum, the event timing hypothesis predicts that patients with cerebellar lesions will show increased variability in the two conditions in which the response offset is delayed, the short and long conditions, whereas the transition hypothesis predicts increased variability on all three conditions with the effect most evident on the press condition.

Table 1 Participants for experiments 1 and 2. *Years post* years post onset/lesion relative to the testing date, *Path* pathology of the cerebellar damage. Side of the lesion for unilateral cerebellar patients is indicated in parentheses. *CVA* cardiovascular accident, *TUM* tumor resection, *SCA* spinocerebellar ataxia (followed by genetic subtype), *ATRO* atrophy. The last four columns are ratings on the subscales of the International Cooperative Ataxia Rating Scale (Trouillas et al. 1997)

Subject code	Gender	Age	Dom. hand	Years educ.	Years post	Path	Posture/gait	Ataxia[a]	Speech	Occulomotor
Unilateral cerebellar patients										
LC01	M	54	R	13	6	CVA (L)	2	7	1.5	0
LC02[b]	M	66	R	12	11	CVA(R)	1	1	1	0
LC03	M	58	R	12	11	TUM(L)	7.5	6	1.5	4
LC04	M	46	L	18	3	CVA(R)	3	5	0	3
LC05	M	47	L	18	5	TUM(R)	10.5	15.5	3.5	3.5
LC06	M	77	R	18	11	CVA (R)	17.5	10.5	3	3
LC07	M	57	L	11	23	TUM(L)	7.5	6.5	5	3
Means	7 M	57.9	4 R:3 L	14.6	10		7	7.4	2.2	3.8
Bilateral cerebellar patients[b]										
AC01	F	56	R	18	3	ATRO	11	5.5	4	2
AC02	M	82	R	16	12	ATRO	14	5	3	0
AC04	M	47	R	18	9	SCA3	18	12.5	3	4
AC05	F	44	R	13	17	SCA3	18	5	3	5
AC06	M	64	R	17	44	ATRO	13	11	5.5	2.5
AC07	M	48	R	16	5	SCA2	12	10	3	1.5
AC08	M	54	R	16	12	ATRO	7	3	3	5
AC09	M	63	R	20	2	ATRO	4	4	3	2.5
AC10	M	73	R	12	43	ATRO	20	9	5	2
AC11	F	42	R	16	13	SCA6	20	8	4	3
Means	3 F:7 M	57.3	10 R	16.2	16		13.7	7.3	3.7	2.8
Controls[b]										
Means	8F:7 M	57.7	14 R:1 L	16.5						

[a]Ataxia ratings are for the impaired limb for unilateral cerebellar patients (=0 for unimpaired limb) and for both limbs for bilateral cerebellar patients (difference between limbs was never >0.5)

[b]LC02, bilateral cerebellar patients, and controls participated in experiment 1 only

Experiment 1

Method

Participants

Seven individuals with unilateral cerebellar lesions and ten individuals with bilateral cerebellar lesions participated in the experiment (Table 1). Fifteen neurologically healthy adults were also tested, selected to match the patients in terms of age and education.

Patients with unilateral lesions were recruited through referrals from outpatient clinics at local medical facilities. Reconstructions of the individual lesions, based on computed tomography (CT) or magnetic resonance imaging (MRI) scans, are presented in Fig. 1. Patients with bilateral damage were recruited in the same manner or through referrals from a local ataxia support group. When available, records were obtained concerning genetic subtyping. Medical histories were collected and patients were evaluated on neurological assessments of motor and cognitive function. Patients were excluded if there was a history of more than one significant neurological event or if there was evidence of cognitive or psychiatric impairment.

The work was approved by the local Ethics Committees of the University of California, Berkeley and the VA Medical Center in Martinez, California. Informed consent was obtained from all participants prior to testing.

Procedure

The response apparatus consisted of a response key and a restraint bar (Fig. 2a). The response key was 14 cm long × 2 cm wide. Situated 4-cm above and perpendicular to the key was a Plexiglas plate that served as a restraint bar. This served to define the starting position for each trial and to maintain a constant excursion distance of 4 cm for all movements. Participants were instructed to hold the top of the index finger against the Plexiglas plate between trials. A 2×2×8 mm receiver from the Ascension Technologies miniBIRD magnetic tracking system (Ascension, Burlington, Vt., USA) was taped to the side of the index finger.

There were three conditions: press, short, and long (Fig. 2b). In each condition, the movement phase was composed of a flexion phase in which the index finger pressed the response key and an extension phase in which the finger was lifted to the Plexiglas plate. The excursion distance of 4 cm ensured that the phases required sequential activation of flexor and extensor muscles; movement termination could not be achieved by simply terminating flexion and exploiting a mechanical rebound from the response key. Similarly, participants did not appear to use the mechanical properties of the restraint bar when returning to the home position, but rather, actively braked the extension phase. In this manner, we sought to create conditions that only differed in the delay imposed between the flexion and extension phases.

In the press condition, the word "PRESS" was presented on a computer monitor for a random interval between 550 and 950 ms. The screen was then blank for a random interval between 350 and 950 ms. An asterisk then appeared, serving as the imperative signal. Participants were instructed to press the key and then immediately lift the finger back to the starting position. In this manner, the task required that they switch from flexion to extension with minimal delay. The asterisk remained visible for 3 s, although responses were almost always completed much earlier.

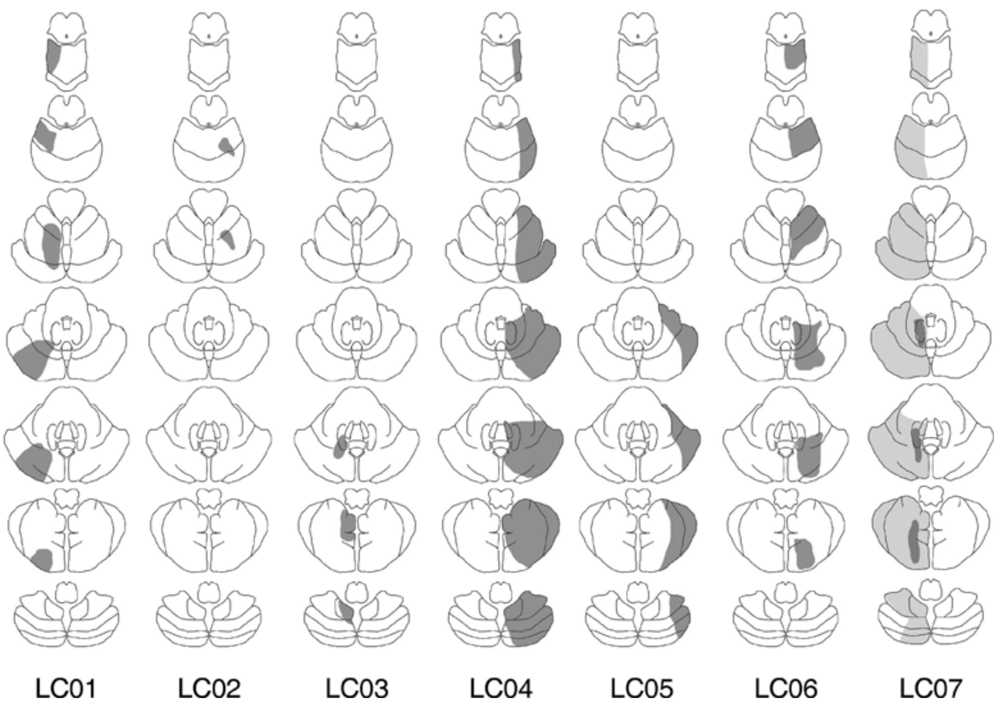

Fig. 1 Schematic reconstruction of the cerebellar lesions (in *dark gray*; *light gray area* represents secondary atrophy after tumor resection). Seven horizontal sections, arranged down the column from superior to inferior, are shown for each patient.

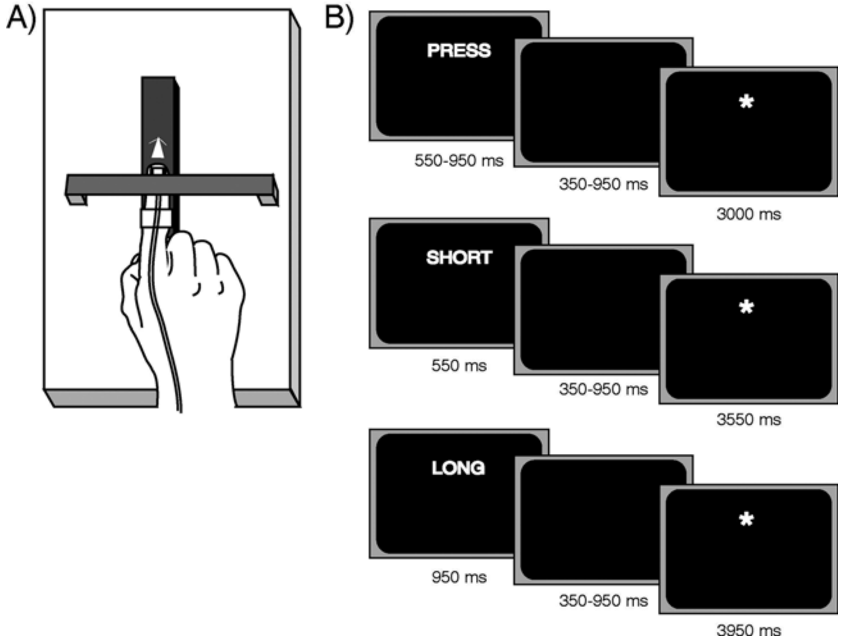

Fig. 2 Apparatus used for both experiments. **a** 4 cm above the response key was a plastic surface. Participants held the top of their finger against this surface between all movements within a block. All conditions required flexion of the finger to press and release the response key below the finger. **b** Stimuli for the three conditions. All conditions started with the presentation of the command, followed by a delay period, followed by the presentation of an asterisk which served as the go signal.

For the short and long conditions, participants were instructed to use the duration of the cue presentation to define the temporal goal for the subsequent movement. In the short condition, the word “SHORT” was presented on the computer monitor for 550 ms. In the long condition, the word “LONG” was presented for 950 ms. The screen was then blank for a random interval between 350 and 950 ms at which point the asterisk appeared. Participants were instructed to press and hold the key for an interval equivalent to the cue presentation, and then lift the finger back to the starting position. To roughly equate the delay from the response to the onset of the next trial, the asterisks remained visible for 3550 and 3950 ms in the short and long conditions, respectively.

Subjects performed two test blocks with each hand. Each block contained 20 trials of each condition, with the order of trials randomized. Two of the trials for each condition were catch trials; on these, no asterisk appeared. The catch trials were included to prevent participants from anticipating the imperative signal.

Practice was provided before each test block. The goal of the practice was to familiarize the participants with the task and provide training on the different responses required for the three conditions. Practice blocks consisted of six trials of a single condition, with the condition order counterbalanced across participants and within participants across blocks. That condition was repeated until the hold time for at least four of the six responses was within 25% of the cue duration for the short and long conditions. For the press condition, the hold time had to be less than 400 ms for all six responses. This criterion was chosen to ensure that there was no overlap between the press and short conditions. The instructions emphasized that this duration should be as short as possible in the press condition and on average, the hold time was around 200 ms. After each response, the duration of the hold time was displayed on the screen and the experimenter helped interpret this feedback for the participant. Practice continued until the participant had achieved the criteria for all three conditions. On average, cerebellar patients reached this criterion within 1.65 blocks of practice per condition. Control participants, on average reached this criterion within 1.35 blocks of practice. The quantity of practice trials was similar across conditions. The task performed first typically required the greatest number of practice trials.

The criterion training proceeded all four test blocks. An additional short training block was completed prior to the first test block with each hand. This block consisted of the random order presentation of 18 trials, 6 of each condition with 1 of these a catch trial.

Data acquisition

Two independent measures of the responses were collected. First, depression of the response key activated a microswitch and these events were detected and recorded by the computer with millisecond accuracy. The feedback provided to the participants was based on this measure. Second, kinematic data of the entire movement were obtained from the miniBird system, with a sampling rate of 138 Hz. Recording from both devices only occurred during the presentation of the imperative signal.

Results and discussion

Response categorization

The kinematic data were visually examined to identify and categorize the responses. There were six response categories. Correct responses were defined as those in which a single flexion/extension movement was initiated following the onset of the imperative asterisk and completed prior to the offset of this stimulus. Note that the evaluation of "correctness" did not consider the duration of the hold period. Responses that were initiated prior to the onset of the asterisk were classified "premature." Responses in which the key was still depressed when the asterisk was turned off were classified "too long." Responses in which there were multiple flexion/extension cycles were classified "multiple." There were infrequent trials in which a response was required but the participant failed to move (less than 1%); an unambiguous classification was not possible infrequently (less than 2%). From all subjects, only two responses were classified as a movement on the catch trials. Figure 3a presents examples of the kinematic records for correct and incorrect responses.

Overall, control participants' responses were classified as correct on over 95% of the trials. However, patients found the task quite challenging (Fig. 3b), as evidenced by an overall error rate of 17% for the bilateral cerebellar patient group (comparison to controls: $F_{(1,23)}$=25.84, P<0.001) and 10% for the unilateral group. Surprisingly, the error rate for the unilateral patients was similar between blocks performed with the contralesional and ipsilesional hands ($t_{(6)}$=0.65, P=0.27).

The majority of the errors were multiple responses (Fig. 3, hatched bars). It is possible that some of these were due to intentional tremor. However, on many of these trials, there was a significant delay between the two responses that would not be characteristic of tremor and the patients' verbal responses indicated that they were aware of having incorrectly made two successive responses. The second highest error category was the premature responses, occurring on approximately 5% of the patients' trials. It is unclear why the patients had difficulty waiting until the imperative signal to initiate their response as well as their tendency to press the key more than once.

Response key analyses

The primary analysis of temporal performance was based on the output of the microswitch, consistent with the fact that this measure was used to provide feedback during training. The analyses involve only correct responses (as defined above).

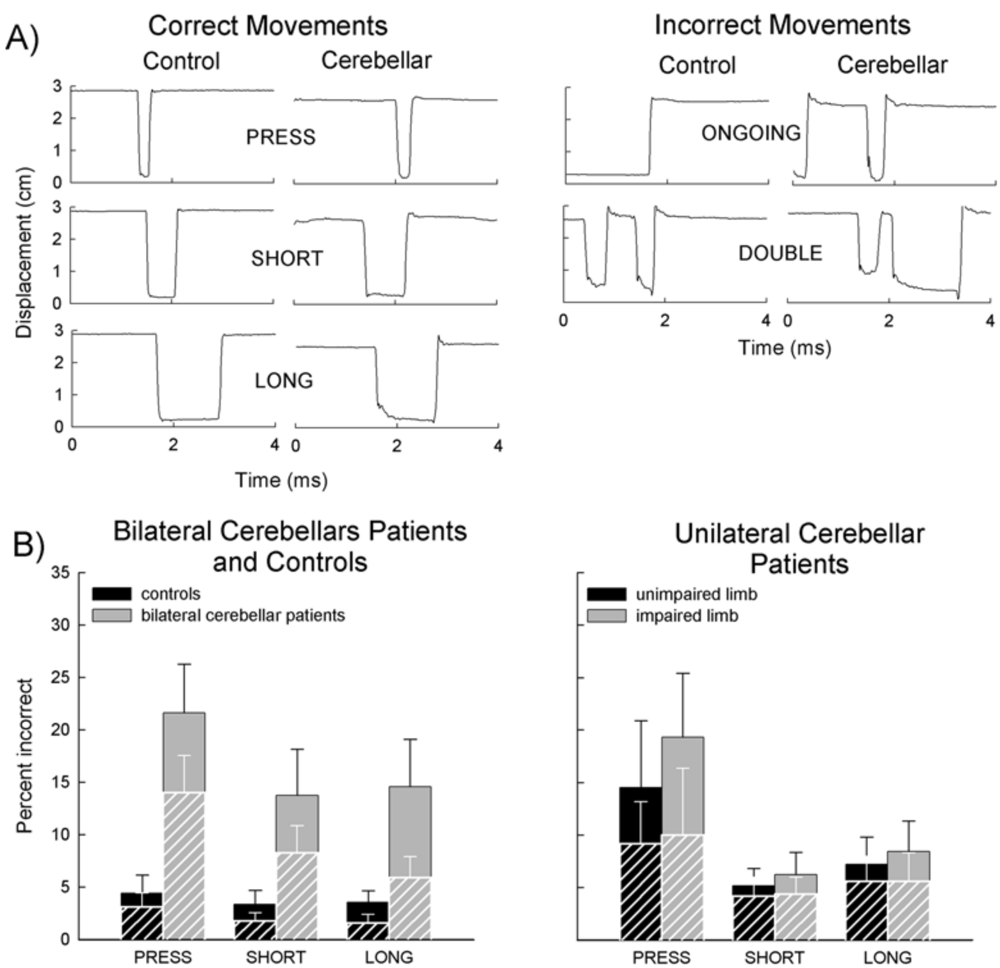

Fig. 3 **a** Trajectory categories produced by controls and patients. **b** Proportion of the movements classified as incorrect (anything other than a single movement after the presentation of the asterisk) and the proportion of the incorrect movements further classified as multiple movements (*hatched portion of the bars*).

Mean hold time

Hold time was defined as the interval from the activation to release of the microswitch (Table 2). No differences were observed between dominant and non-dominant hands for the control participants or the bilateral cerebellar patients; thus the data in Table 2 are collapsed across hands and subsequent analyses of variability use these composite scores. On average, the participants' responses approximated the goal hold time for the three conditions. The largest deviations from the goal were produced by the control and bilateral cerebellar groups on the long condition. Control participants were approximately 100 ms too slow on this condition while the bilateral group was 100 ms too fast.

Variability in hold time

The standard deviation of the hold time for each condition was calculated for each participant. The mean values are presented in Fig. 4.

The event timing and transition hypotheses make distinct predictions concerning the variability scores. The timing hypothesis predicts that the effect of cerebellar impairments will be most pronounced on the short and long conditions given the required insertion of a temporal delay. The transition hypothesis predicts that the impairments will lead to increased variability on all conditions, and that this should be greatest on the press condition. To evaluate these hypotheses, a 3 (movement type) × 2 (group) analysis of variance (ANOVA) was performed, with the group factor representing the between-subject factor, control participants versus bilateral cerebellar patients. There was a main effect of movement type, $F_{(2,74)}$=157.7, P<0.001, reflecting the fact that temporal variability increased as hold time increased. This scaling is consistent with findings in many other time production and perception tasks (Gibbon 1977; Ivry and Hazeltine 1995; Robertson et al. 1999).

The effect of group was significant, $F_{(1,74)}$=8.86, P=0.004, and most importantly, the movement type × group interaction was significant, $F_{(2,74)}$=3.29, P=0.04. As can be seen in Fig. 4, compared with the control group, the patients were more variable on the long condition ($t_{(23)}$=2.7, P=0.006) and were marginally more variable on the short condition ($t_{(23)}$=1.5, P=0.07). The 0.88 ms increase in variability for the patients in the *Press* condition was not significant ($t_{(23)}$=0.15, P=0.44).

A similar analysis was performed on the data from patients with unilateral lesions with the group factor replaced by hand (ipsilesional versus contralesional). The effect of movement type was again highly significant, $F_{(2,41)}$=78.9, P<0.001. However, there was no effect of hand, $F_{(1,41)}$<1, nor a movement type × hand interaction, $F_{(2,41)}$<1.

The lack of any difference between the ipsilesional and contralesional hands for the unilateral patients is puzzling. This comparison has provided a useful within-subject analysis in other studies of movement timing (Ivry et al. 1988; Spencer et al. 2003), with the consistent finding that temporal variability is increased in the ipsilesional hand. Given the lack of a hand effect, we performed an unplanned, post hoc comparison of the unilateral cerebellar patients' performance with their ipsilesional hand to the controls. Note that while the controls were selected to match the patients in the bilateral cerebellar patient group, they are similar to the unilateral group on age and education. The analysis yielded a similar pattern of results

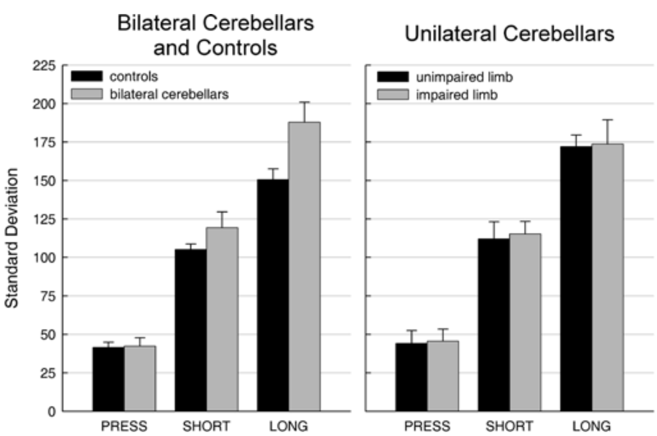

Fig. 4 Variability in hold time across conditions and groups for experiment 1.

Table 2 Mean hold times across groups and tasks for experiment 1 (standard error across subjects in parentheses)

	Press	Short	Long
Hold time			
Controls	187.4 (14.4)	613.6 (16.6)	1061.4 (26.2)
Bilateral cerebellar patients	198.0 (20.9)	531.3 (38.9)	856.1 (64.7)
Unilateral cerebellar patients			
Unimpaired limb	208.0 (28.9)	534.5 (32.0)	868.8 (36.6)
Impaired limb	177.6 (21.8)	547.3 (29.3)	917.7 (40.4)
Movement time			
Controls	390.1 (37.7)	875.0 (30.6)	1360.7 (36.3)
Bilateral cerebellar patients	456.0 (48.7)	911.1 (54.4)	1282.6 (68.0)
Unilateral cerebellar patients			
Unimpaired limb	378.8 (35.0)	788.9 (47.2)	1167.6 (38.4)
Impaired limb	388.7 (53.2)	866.8 (68.5)	1286.4 (76.7)

as obtained in the comparison of the controls and bilateral group: the movement type × group interaction was significant, $F_{(2,65)}$=4.02, P=0.02, due to an increase in variability on the short and long conditions (press: $t_{(20)}$=0.57, P=0.58; short: $t_{(20)}$=2.0, P=0.057; long: $t_{(20)}$=2.3, P=0.03). Indeed, a direct comparison of the unilateral and bilateral groups found no significant differences.

The dependency of temporal variability on interval duration provides an alternative way to compare the performance of the patients and control participants. As noted above, temporal variability increases with duration. Specifically, variance is linearly related to duration squared, an extension of Weber's law to the time domain (see Getty 1975). As outlined by Ivry and Hazeltine (1995; see also Ivry and Corcos 1993), the slope provides a measure of duration-dependent variability and the intercept a measure of duration-independent variability. Based on the event timing hypothesis, we would expect the slope values to be higher for patients with cerebellar lesions (i.e., greater duration-dependent variability).

We performed regression analyses on the data to obtain estimates of the slope and intercept.[1]

Calculated on an individual basis, the linear fit was reasonable: the percent of variance accounted for by the linear component (R^2) ranged from 0.68 to 0.99 with a median of 0.95. On the averaged functions, the R^2values were 0.91 and 0.96 for the control participants and patients with bilateral cerebellar atrophy, respectively. Most critical, the slope estimates for the patients were significantly greater than for the control participants, $t_{(23)}$=−3.72, P<0.001. The mean slope estimate for the patients was 0.045 (SE=0.007); the comparable value for the controls was 0.020 (SE=0.003). In contrast, on the estimate of duration-independent variability, the intercept values, the difference between groups was not significant, $t_{(23)}$=1.64, P=0.94. A similar pattern was obtained when the patients with unilateral lesions were compared to the control participants. When responding with their impaired hand, only the slope estimate was significantly greater, $t_{(20)}$= −2.66, P=0.008.

Kinematic analyses

While the instructions and feedback emphasized the task in terms of keypress duration, the miniBird system provided a complete kinematic record of the entire response. A velocity criterion was used to define movement onset and movement offset. The mean movement durations are presented in the lower half of Table 2. For the control participants, the mean response duration was 255 ms longer than the mean hold times. The speed movement varied across the three conditions. The difference between the movement duration and hold time was 203 ms, 262 ms, and 300 ms for the press, short, and long conditions, respectively. A similar pattern was observed for the patients with bilateral cerebellar degeneration. However, their movements were slower, with mean differences of 258 ms, 380 ms, and 427 ms across the three conditions. Although less pronounced, this measure indicated a difference between the ipsi- and contralesional hands in the unilateral cerebellar patients. Averaged over the three conditions, the response duration was 55 ms longer when these patients responded with their ipsilesional hand (245 ms versus 300 ms).

In terms of temporal variability, the results based on the kinematic measures correspond to those based on the hold times. Compared with controls, the bilateral cerebellar patients showed increased variability on the short and long conditions, but not on the press condition, (interaction: $F_{(2,74)}$=3.4, P=0.052). No differences were observed between the ipsi- and contralesional hands in the unilateral cerebellar patients.

Performance relative to disease severity

To determine whether disease severity was related to performance on this task, variability measures from the three conditions were correlated with the bilateral cerebellar patients' scores on the International Cooperative Ataxia Rating Scale (ICARS, Trouillas et al. 1997; Table 1). This score was positively correlated with temporal variability for all three movement types, although the magnitude of the correlation was small and not significant (Fig. 5). It should be noted that the ICARS scores include measures of upper and lower limb performance, eye movement control, and speech. None of the measures focuses on the fine control of finger movements that is required by the present task.

Summary of experiment 1

Experiment 1 contrasted two hypotheses for the timing deficits observed in patients with cerebellar lesions in tasks involving discontinuous movements. The results are at odds with the predictions of the transition hypothesis. Patients performed comparable to the control group on the press condition, the condition expected to disproportionately tax processes associated with response initiation, termination, and the transition from flexion to extension. In contrast, the results are consistent with the event timing hypothesis; patients with bilateral lesions of the cerebellum were more variable on the two conditions requiring a

[1] We used all three movement types in the regression analyses. However, we have assumed that the press condition does not entail an explicit timed component: the duration of these movements reflects the minimum time that the key is pressed during the transition from press to lift. Given this, one could argue that the press condition does not contain a duration-dependent source of variability and the slope analysis should be restricted to just the short and long conditions. We also calculated slope and intercept values using just these two points. The statistical outcomes were unchanged in this more restricted analysis. However, we report the regression based on all three conditions since it does not require an assumption regarding whether or not the press movement type involves "timing."

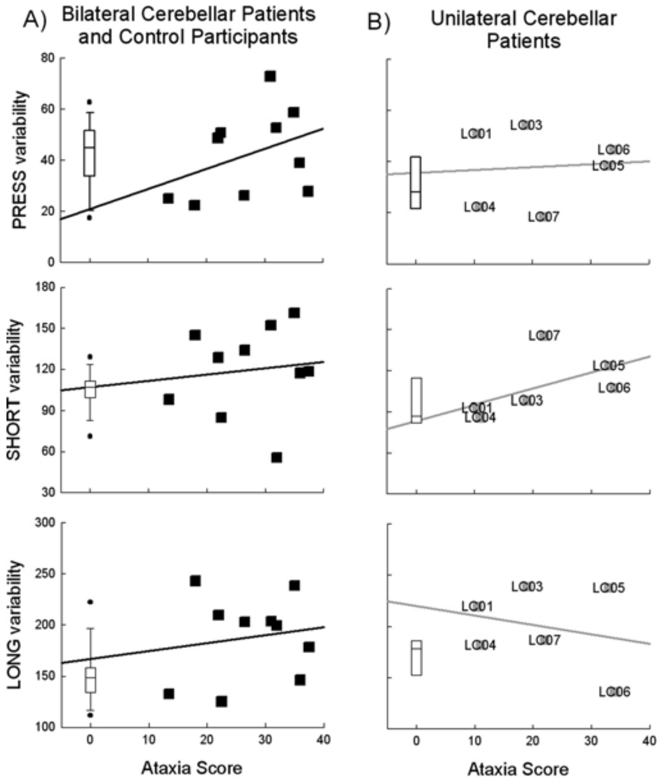

Fig. 5 Relationship of temporal variability on the three movement conditions and clinical ratings of cerebellar dysfunction as measured by the International Cooperative Ataxia Rating Scale (Trouillas et al. 1997). **a** Results for patients with bilateral cerebellar atrophy in experiment 1. **b** Results for patients with unilateral cerebellar lesions when performing with their impaired hand in experiment 2. Box plots at zero indicate the median and 90th percentile range of the control participants in experiment 1 (**a**) and the unilateral patients when performing with their contralesional limb in experiment 2 (**b**).

specified temporal delay. In addition, using the slope method of Ivry and Hazeltine (1995), the patients' deficit was selectively associated with an increase in duration-dependent variability.

The results for the unilateral cerebellar patients were ambiguous. The within-subject comparison failed to reveal a difference between the two hands in any of the conditions. However, a post hoc analysis demonstrated that the performance of these patients was similar to that of the bilateral lesion group. When compared to the control group, they too exhibited a selective deficit on the short and long conditions. Compared to control participants, the increase in temporal variability for the patients was greatest for the long condition, consistent with the hypothesis that their deficit was associated with imposing the temporal delay between flexion and extension.

Experiment 2

The null results obtained in the comparison of ipsi- and contralesional hands for the patients with unilateral lesions in experiment 1 were unexpected. Previous studies have consistently reported lateralized timing deficits in patients with unilateral lesions. Much of this work has involved simple tapping tasks in which the participants were required to produce isochronous intervals (Franz et al. 1996; Harrington et al. 2004, 1998; Ivry et al. 1988; Spencer et al. 2003, experiments 1 and 3). Other studies have used tasks with more isolated responses similar to what was used in experiment 1 (Hore et al. 1991; Timmann et al. 2000; Spencer et al. 2003, experiment 2). Thus, the failure to observe a difference between the two hands is not likely due to the novel task used in experiment 1.

One possible account of the null results for the within-hand comparison is based on the observation that the patients moved more slowly when using the ipsilesional hand. Perhaps a speed-accuracy trade-off attenuated any differences between the hands on measures of temporal variability. However, our post hoc analysis suggests that the patients with unilateral lesions were more variable when performing with either hand compared to the control participants. Why might the unilateral patients show a generalized impairment? One hypothesis relates to the demanding nature of our task, reflected in the high error rates for the patients. Ravizza and Ivry (2001) reported that the performance of patients with cerebellar lesions may be affected by competition for limited attentional resources (Kahneman 1973). In their study, the degree of impairment associated with cerebellar lesions on an attention shifting task was modulated by the motor requirements. When the motor requirements were high, the patients were impaired on a measure of attentional control. This impairment, however, was attenuated when the motor demands were reduced. A converse account of the resource hypothesis may be relevant when considering the deficits in experiment 1. The demands associated with monitoring stimulus duration and inserting the delay for the timed conditions may have reduced attentional resources available for controlling the responses.

Therefore, in experiment 2, we designed an easier task context. Rather than use a mixed block design, each of the three movement types was tested in separate blocks. Only the patients with unilateral lesions were tested. We predicted that under the reduced attentional demands, these patients would now exhibit greater timing variability on the timed conditions when using their ipsilesional hand. Note that we were not attempting to evaluate the attention hypothesis here; rather, we simply sought a within-subject replication of the between-group results obtained in experiment 1.

Method

Participants

Six of the seven patients with unilateral lesions from experiment 1 were available for experiment 2 (see Table 1). There was a delay of at least 2 months between the two experimental sessions.

Procedure

The procedure was identical to that used in experiment 1 with the exception that each response condition was blocked. Prior to each test block, the participants were informed of the forthcoming condition (press, short, or long) and then given practice. Test blocks consisted of 22 trials for that condition, 20 in which the asterisk appeared as an imperative signal and 2 catch trials. Subjects performed two test blocks of each of the three conditions with both limbs for a total of 12 test blocks.

Results and discussion

Response categorization

As in experiment 1, the kinematic data were used to classify the responses into the six response categories. The patients continued to have difficulty when using their ipsilesional, impaired hand (Fig. 5). The overall error rate of 11.5% for this hand was greater than when they used their contralesional, unimpaired hand (5.2%, $F_{(1,35)}$=6.4, P=0.02). Again, the majority of the errors were multiple responses (hatched bars in Fig. 6). Thus, blocking by condition had a mixed effect on error rates. The manipulation succeeded in differentiating between performance with the impaired and unimpaired hand. However, making the task easier did not have a noticeable effect on the error rate for the impaired hand.

Analysis of temporal performance

As shown by mean hold time, the participants properly produced the three types of responses (Table 3), although there was a tendency to depress the key for longer than the goal time for the short and long conditions. Most important, no differences in hold time were observed between the ipsi- and contralesional hands ($F_{(1,35)}$<1). This null effect is also found for the mean movement times, calculated from the kinematic records (lower half of Table 3).

The variability of hold time for the six conditions is presented in Fig. 7. The pattern of results in the within-subject comparison for the unilateral lesion patients in experiment 2 is similar to the results from the comparison of the bilateral lesion patients and the control group in experiment 1. While the movement type × hand interaction was not significant, $F_{(2,41)}$=2.2, P=0.13, planned comparisons showed that the patients were significantly more variable on the short, $t_{(5)}$=2.20, P=0.04, and long conditions, $t_{(5)}$=3.24, P=0.011. There was no reliable increase in variability for the ipsilesional hand on the press condition, $t_{(5)}$=0.84, P=0.22. The same pattern was evident when the response interval was defined from movement onset to movement offset, using the kinematic records.

As in experiment 1, a regression analysis was used to determine the source of increased variability when the patients performed with their impaired limb. R^2 values on an individual basis ranged from 0.87 to 0.99, and were 0.96 and 0.94 for the functions based on averaging across participants for the contra- and ipsilesional hands, respectively. The slope estimate was 0.024 (SE=0.003) for the contralesional hand and 0.039 (SE=0.007) for the ipsilesional hand. Thus, the patients exhibited a significant

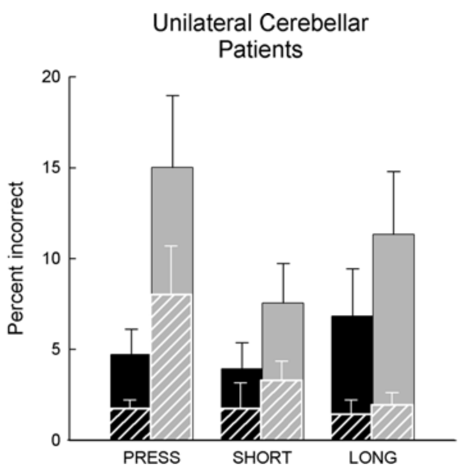

Fig. 6 Proportion of the movements classified as incorrect (anything other than a single movement after the presentation of the asterisk) and the proportion of the incorrect movements further classified as multiple movements (*hatched portion of the bars*) for experiment 2.

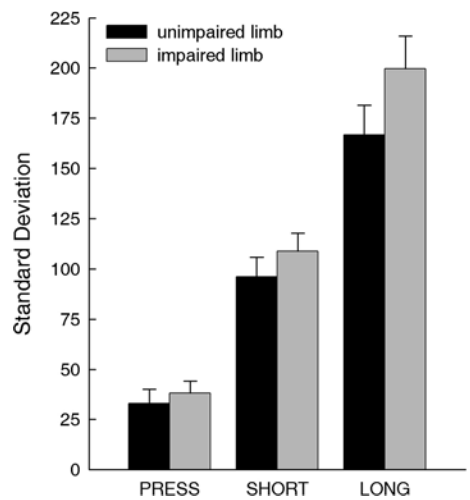

Fig. 7 Variability in hold time across conditions and groups for experiment 2.

Table 3 Mean hold times and movement times across limbs and tasks for experiment 2 (standard error across subjects in parentheses)

	Press	Short	Long
Hold time			
Unimpaired limb	182.7 (27.9)	614.5 (18.2)	1116.4 (62.9)
Impaired limb	194.5 (29.2)	613.3 (11.9)	1095.6 (77.6)
Movement time			
Unimpaired limb	316.4 (57.9)	844.2 (46.9)	1359.4 (72.6)
Impaired limb	329.8 (64.5)	888.5 (51.0)	1302.9 (120.3)

increase in the estimate of the duration-dependent source of variability ($t_{(5)}$=2.5, P=0.03). In contrast, the estimate of duration-independent variability, the intercept, did not differ between hands, $t_{(5)}$=−0.92, P=0.80.

Performance relative to disease severity

Temporal variability on the three conditions for each individual was correlated with their overall score on the ICARS (Fig. 5b). As was observed in experiment 1, the clinical assessment of cerebellar dysfunction failed to predict the patients' performance with their ipsilesional hand.

We also assessed whether individual differences might be related to lesion size or lesion location. Previous studies have associated increased temporal variability with lateral cerebellum (Ivry et al. 1988), and more specifically, with superior neocerebellum (Harrington et al. 2004). The small patient sample available for this study precludes any systematic analysis along these dimensions. Nonetheless, some observations suggest that there is no simple relationship between lesion size or location and performance (compare Fig. 1 and Fig. 5b). For example, the lesion for patient LC03 is primarily medial whereas the lesion for patient LC05 is lateral. Performance of these two participants was similar on all three conditions. In terms of lesion size, LC04 clearly has the largest lesion. However, he was the least variable on the short condition and had lower variability than the patient with the smallest lesion (LC03) on the long condition.

Summary of experiment 2

The results of experiment 2 provide further support for the event timing hypothesis. Patients with unilateral lesions of the cerebellum were selectively impaired on the two conditions requiring the insertion of a temporal delay when using their ipsilesional, impaired hand. No difference was observed between hands on the press condition, the condition we assume is most demanding on processes involved in controlling movement transitions. The regression analyses also converge with the between-group comparisons of experiment 1: the increase in variability for the ipsilesional hand was selectively associated with the estimate of duration-dependent variance.

It is not clear why the within-subject comparisons of temporal variability were reliable in experiment 2 but not in experiment 1. There are two notable differences between experiments 1 and 2. First, all of the participants in experiment 2 had also been in experiment 1; it is possible that the patients' previous experience with the task was most beneficial when they used their contralesional hand. Although between-experiment comparisons must be treated with caution, the mean standard deviation scores for both hands were lower in experiment 2, and the decrease was greater for the contralesional hand.

Second, the three conditions were blocked in experiment 2. We hypothesized that the lack of a difference between hands in experiment 1 might be related to noise associated with the high attentional demands of the task. Blocking was expected to make the task easier. The error rates, at least for the contralesional hand, suggest that this manipulation was effective. Nonetheless, the unilateral lesion patients continued to make many errors when using their ipsilesional hand, even under the blocked format. Notably, the error rate was highest in the press condition. Thus, the lack of a difference between performance with the two hands on measures of temporal variability is qualified by the fact that the patients still produced a large number of errors when using their impaired hand.

General Discussion

Patients with cerebellar lesions exhibit increased temporal variability on a range of movement tasks (Hore et al. 1991; Woodruff-Pak et al. 1996; Ivry et al. 1988). Recently, we reported a dissociation between the temporal control of discontinuous and continuous movements: cerebellar lesions were associated with increased timing variability only on the former (Spencer et al. 2003). This dissociation was most striking in a modified tapping task in which the patients made repetitive flexion/extension movements of the index finger in midair without contacting a response surface. When the participants were required to insert a brief pause prior to each flexion phase, patients with cerebellar degeneration exhibited higher timing variability than control participants and patients with unilateral lesions were more variable when using their ipsilesional hand. In contrast, neither group showed a deficit when the instructions emphasized that the movements should be made as smoothly as possible.

In the present study, we evaluated two accounts of the patients' deficit on discontinuous movement tasks. The event timing hypothesis assumes that the cerebellum is essential when task constraints require the representation of a temporal goal. For example, in the air tapping condition with a pause, the cerebellum may compute the interval separating the events that define each cycle. The absence of a deficit when the movements are made continuously is hypothesized to reflect the fact that such movements lack an event structure (see Ivry et al. 2002; Zelaznik et al. 2002). In contrast, the transition hypothesis attributes the increased variability to the control demands associated with initiating and/or terminating each movement cycle when a pause is required in the air tapping condition (or in table tapping, where people spontaneously insert a pause). The absence of abrupt transitions when the movements are made continuously may account for the normal performance of the patients in such conditions.

The results of the present experiments fail to support predictions derived from the transition hypothesis. If the patients had difficulty with movement transitions, we expected they would exhibit increased temporal variability on all three conditions because each requires the initiation and termination of a single keypress. Moreover, the deficit should be greatest in the press condition, which required a rapid transition from flexion to extension after the key was pressed. Contrary to these predictions, the patients were unimpaired on the press condition: The patients with bilateral cerebellar damage performed similar to the controls and the unilateral patients did not show a difference between the ipsi- and contralesional hands in experiment 2.

In accord with the event timing hypothesis, the patients exhibited increased variability on the two conditions requiring the insertion of a pause between the downstroke and upstroke. We assume this increased variability reflects the effect of the lesions on the ability to control the timing of the delay between the downstroke and upstroke for an interval matched to the stimulus duration. This deficit is consistent with previous findings that cerebellar lesions disrupt the operation of an internal timing system in both perception and action (see Ivry et al. 2002). In the current studies, this impairment might affect the patients' ability to represent the stimulus duration, the ability to translate this temporal goal into an action, or both processes.

While the instructions regarding the hold time clearly differentiate the press condition from the short and long conditions, it is important to note another difference between these conditions. The response duration in the press condition is shorter than in the short and long conditions. The literature on motor and perceptual timing demonstrates that timing variability is proportional to the duration being timed, a form of Weber's law (Gibbon 1977; see also Ivry and Hazeltine 1995). Indeed, the current results demonstrate that variability increased with response duration and the rate of increase was larger for the patients than the control participants. It is possible that the reduced overall variability in the press condition lowered the sensitivity of this condition in detecting differences resulting from the lesions. While we cannot rule out this hypothesis,[2] we believe the observed dissociation is strengthened by the fact that the results were in accord with the predictions of the event timing hypothesis in both experiments 1 and 2. Moreover, the transition hypothesis predicts that the patients would be disproportionately affected in the press condition. Our reasoning here is that variability associated with movement transitions would contribute greatest in the condition in which other sources (i.e., variability associated with the pause) are minimized.

The patients with unilateral lesions did not show a difference between the two hands in experiment 1; as revealed by our post hoc comparison of this group to the control participants, the unilateral patients were more variable with both hands on the short and long conditions. The reason for the bilateral timing deficit in patients with unilateral lesions remains unclear given previous work showing that the motor timing impairments in unilateral patients is restricted to the ipsilesional side (Franz et al. 1996; Ivry et al. 1988), and furthermore, the impairment was significantly greater on this side in experiment 2. It is possible that the bilateral deficit in experiment 1 resulted from the demanding nature of our task. Ravizza and Ivry (2001) have shown that patients with either bilateral or unilateral cerebellar lesions are impaired on an attention shifting task when the motor demands are relatively great. This finding suggests that performance deficits may reflect the allocation of limited resources. When motor demands are high, relatively fewer resources are available for non-motor functions and this shift is exaggerated in people with motor impairments. Perhaps the reverse effect was present in experiment 1. The demanding nature of the task, as indicated by the high error rates, may have reduced resources required for controlling the movements.

Further evidence of the demanding nature of the task is provided by the unexpectedly high error rates of the patients in both experiments. Errors were not scored in terms of whether the participants' responses matched the temporal goals for the three conditions. Rather, they represent trials in which the kinematic records indicate multiple responses or in which the participants initiated the response prior to the imperative signal. Despite extended practice blocks, these types of errors occurred on approximately 15% of the trials for the patients with bilateral lesions and around 10% of the trials for the patients with unilateral lesions. Experiment 1 was undoubtedly attention demanding. The participant had to attend to the instruction cue, the length of the instruction presentation, and the onset of the imperative signal. When using an impaired limb, the patients faced the additional demands associated with producing the movements. We examined this hypothesis in experiment 2 by testing the three conditions in separate blocks, thus reducing the demands associated with monitoring the stimulus duration. The results of this manipulation were mixed; the error rates were significantly higher when the unilateral cerebellar patients used their ipsilesional hand compared with their contralesional hand. However, the overall rates remained high and similar to that observed in experiment 1. Thus, by the attentional hypothesis, we would have to conclude that even under blocked conditions the patients' resources were taxed by the task.

The most frequent type of error was multiple responses. Superficially, the secondary movements might be indicative of intentional tremor, a cerebellar symptom present in most of the patients. However, it is unlikely that tremor would be of sufficient size to produce multiple keypresses (requiring a 4-cm excursion) and the timing of these movements did not resemble that associated with intentional tremor (Hore et al. 1991). In addition, premature responses cannot be attributed to tremor.

We consider a third, novel explanation for the increased error rate observed in the patients' performance. Some of the errors may reflect deficient processes controlling the inhibition of planned movements. In the Ravizza and Ivry (2001) study of attention shifting, participants were

[2] The effect size for the short and long conditions was used to estimate the power for identifying differences in the press condition given our group sizes. Power was low in experiment 1 (12% chance that we would detect significant difference between means in the press condition). This value increased to 62% in experiment 2.

required to respond to target stimuli and withhold responses to irrelevant stimuli. Similar to the early responses and the multiple movements reported here, Ravizza and Ivry noted exceptionally high occurrences of “false alarms”—that is, responses to irrelevant stimuli. Inhibition of a response, whether waiting for a relevant stimulus in the attention shifting task or waiting for the imperative signal in the present task, may involve cerebello-prefrontal pathways. In a similar vein, the multiple responses may reflect trials in which the participants failed to inhibit an initial response, and then attempted to correct for this with a subsequent, task-appropriate response.

In conclusion, the primary findings of these experiments provide new support for the event timing hypothesis of cerebellar function (Ivry et al. 2002; Spencer et al. 2003). This hypothesis proposes that the cerebellum provides a representation of the timing of critical events. In the current task, this form of representation is required when a stimulus-defined interval must be imposed between the downstroke and upstroke of a keypress. In contrast, the press condition does not require “explicit” timing; the short delay between these two phases of the movement is an emergent property, reflecting the time required to make the transition from flexion to extension. The event timing hypothesis provides a parsimonious description of the deficit associated with cerebellar lesions in a range of motor and non-motor tasks. For example, Spencer et al. (2003) hypothesized that the dissociation between repetitive, discontinuous and continuous movements is due to the fact that the former involves event timing whereas in the latter, timing is emergent. Similarly, non-motor deficits associated with cerebellar lesions such as those observed on duration discrimination tasks (Ivry and Keele 1989; Mangels et al. 1998) and eyeblink conditioning (Gerwig et al. 2003; Woodruff-Pak et al. 1996) can be attributed to noise in timing critical events defined by the stimuli.

We have shown here that the integrity of the cerebellum is not essential for the control of the transitions associated with simple keypresses. However, it should not be interpolated that all isolated movements do not require the temporal control we associate with the cerebellum. As shown in Spencer et al. (2003, experiment 2), patients with cerebellar lesions are impaired on a task in which they must draw a single circle. One difference between their circling task and the press condition used in the present study is that the participants were given a target duration for the circling task. By the event timing hypothesis, the cerebellum was required to represent this target duration. Hore and colleagues have also shown that throwing requires precise timing between the proximal movements producing arm rotation and the release by the fingers of the ball (Hore et al. 1996). Patients with cerebellar lesions are highly variable in the timing of release onset (Hore et al. 1991; Timmann et al. 2000). Throwing may represent a movement that reveals the interface between event timing and movement transitions. Skilled performance requires learning the appropriate timing for the different components of the action. The contribution of the cerebellum to motor learning may involve the representation of the timing for these transitions.

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References

Ackermann H, Graeber S, Hertrich I, Daum I (1997) Categorical speech perception in cerebellar disorders. Brain Lang 60:323–331

Billon M, Semjen A, Stelmach GE (1996) The timing effects of accent production in periodic finger-tapping sequences. J Mot Behav 28:198–210

Botez-Marquard T, Botez MI (1997) Olivopontocerebellar atrophy and Friedreich’s ataxia: neuropsychological consequences of bilateral versus unilateral cerebellar lesions. Int Rev Neurobiol 41:555–573

Conrad B, Brooks VB (1974) Effect of dentate cooling on rapid alternating arm movements. J Neurophysiol 37:792–804

Day BL, Thompson PD, Harding AE, Marsden CD (1998) Influence of vision on upper limb reaching movements in patients with cerebellar ataxia. Brain 121:357–372

Fiala JC, Grossberg S, Bullock D (1996) Metabotropic glutamate receptor activation in cerebellar Purkinje cells as substrate for adaptive timing of the classically conditioned eye-blink response. J Neurosci 16:3760–3774

Franz EA, Ivry RB, Helmuth LL (1996) Reduced timing variability in patients with unilateral cerebellar lesions during bimanual movements. J Cogn Neurosci 8:107–118

Freund H-J (1983) Motor unit and muscle activity in voluntary motor control. Physiol Rev 63:387–436

Getty D (1975) Discrimination of short temporal intervals: a comparison of two models. Percept Psychophys 18:1–8

Gerwig M, Dimitrova A, Kolb FP, Maschke M, Brol B, Kunnel A, Boring D, Thilmann AF, Forsting M, Diener HC, Timmann D (2003) Comparison of eyeblink conditioning in patients with superior and posterior inferior cerebellar lesions. Brain 126:71–94

Gibbon J (1977) Scalar expectancy theory and Weber’s law in animal timing. Psychol Rev 84:279–325

Hallet M, Shahani BT, Young RR (1975) EMG analysis of patients with cerebellar deficits. J Neurol Neurosurg Psychiatry 38:1163–1169

Harrington DL, Haaland KY, Hermanowitz N (1998) Temporal processing in the basal ganglia. Neuropsychology 12:3–12

Harrington DL, Lee RR, Boyd LA, Rapcsak SZ, Knight RT (2004) Does the representation of time depend on the cerebellum? Effect of cerebellar stroke. Brain 127:1–14

Hogan N, Flash T (1987) Moving gracefully: quantitative theories of motor coordination. Trends Neurosci 10:170–174

Hore J, Watts S, Tweed D, Miller B (1996) Overarm throws with the nondominant arm: kinematics of accuracy. J Neurophysiol 76:3693–3704

Hore J, Wild B, Diener H (1991) Cerebellar dysmetria at the elbow, wrist, and fingers. J Neurophysiol 62:563–571

Ivry RB, Corcos DM (1993) Slicing the variability pie: component analysis of coordination and motor dysfunction. In: Newell KM, Corcos DM (eds) Variability and motor control. Human Kinetics, Urbana, IL, pp 415–447

Ivry RB, Hazeltine RE (1995) Perception and production of temporal intervals across a range of durations: evidence for a common timing mechanism. J Exp Psychol Hum Percept Perform 21:3–18

Ivry RB, Keele SW (1989) Timing functions of the cerebellum. J Cogn Neurosci 1:136–152

Ivry RB, Keele SW, Diener HC (1988) Dissociation of the lateral and medial cerebellum in movement timing and movement execution. Exp Brain Res 73:167–180

Ivry RB, Spencer RM, Zelaznik HN, Diedrichsen J (2002) The cerebellum and event timing. Ann N Y Acad Sci 978:302–317

Kahneman D (1973) Attention and effort. Prentice Hall, Engle Cliffs, NJ

Keele SW, Pokorny RA, Corcos DM, Ivry RB (1985) Do perception and motor production share common timing mechanisms: a correlational analysis. Acta Psychol (Amst) 60:173–191

Mangels JA, Ivry RB, Shimizu N (1998) Dissociable contributions of the frontal and neocerebellar cortex to time perception. Cogn Brain Res 7:15–39

Medina JF, Mauk MD (2000) Computer simulation of cerebellar information processing. Nat Neurosci 3:1205–1211

Meyer-Lohmann J, Hore J, Brooks VB (1977) Cerebellar participation in generation of prompt arm movements. J Neurophysiol 40:1038–1050

Nichelli P, Alway D, Grafman J (1996) Perceptual timing in cerebellar degeneration. Neuropsychologia 34:863–871

Ravizza S, Ivry RB (2001) Comparison of the basal ganglia and cerebellum in shifting attention. J Cogn Neurosci 13:284–297

Robertson SD, Zelaznik HN, Lantero DA, Bojczyk KG, Spencer RM, Doffin JG, Schneidt T (1999) Correlations for timing consistency among tapping and drawing tasks: evidence against a single timing process for motor control. J Exp Psychol Hum Percept Perform 25:1316–1330

Spencer RMC, Ivry RB (2004) Comparison of patients with Parkinson's disease or cerebellar lesions in the production of periodic movements involving event-based or emergent timing. Brain Cogn, in press

Spencer RMC, Zelaznik HN, Diedrichsen J, Ivry RB (2003) Disrupted timing of discontinuous but not continuous movements by cerebellar lesions. Science 300:1437–1439

Spidalieri G, Busby L, Lamarre Y (1983) Fast ballistic arm movements triggered by visual, auditory, and somesthetic stimuli in monkey. II. Effects of unilateral dentate lesion on discharge of precentral cortical neurons and reaction time. J Neurophysiol 50:1359–1379

Timmann D, Watts S, Hore J (2000) Causes of left-right ball inaccuracy in overarm throws made by cerebellar patients. Exp Brain Res 130:441–452

Trouillas P, Takayanagi T, Hallett M, et al. (1997) International Cooperative Ataxia Rating Scale for pharmacological assessment of the cerebellar syndrome. J Neurol Sci 145:205–211

van Beers RJ, Baraduc P, Wolpert DM (2002) Role of uncertainty in sensorimotor control. Philos Trans R Soc Lond B Biol Sci 357:1137–1145

Woodruff-Pak, DS, Papka M, Ivry RB (1996) Cerebellar involvement in eyeblink classical conditioning in humans. Neuropsychology 10:443–458

Zelaznik HN, Spencer RM, Doffin J (2000) Temporal precision in tapping and circle drawing movements at preferred rates is not correlated: further evidence against timing as a general purpose ability. J Mot Behav 32:193–199

Zelaznik HN, Spencer RM, Ivry RB (2002) Dissociation of explicit and implicit timing processes in repetitive tapping and drawing movements. J Exp Psychol Hum Percept Perform 28:575–588