Exp Brain Res (2000) 135:179–188
DOI 10.1007/s002210000528

RESEARCH ARTICLE

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Effects of accuracy constraints on reach-to-grasp movements in cerebellar patients

Received: 13 March 2000 / Accepted: 11 July 2000 / Published online: 5 September 2000

Abstract Reach-to-grasp movements of patients with pathology restricted to the cerebellum were compared with those of normal controls. Two types of paradigms with different accuracy constraints were used to examine whether cerebellar impairment disrupts the stereotypic relationship between arm transport and grip aperture and whether the variability of this relationship is altered when greater accuracy is required. The movements were made to either a vertical dowel or to a cross bar of a small cross. All subjects were asked to reach for either target at a fast but comfortable speed, grasp the object between the index finger and thumb, and lift it a short distance off the table. In terms of the relationship between arm transport and grip aperture, the control subjects showed a high consistency in grip aperture and wrist velocity profiles from trial to trial for movements to both the dowel and the cross. The relationship between the maximum velocity of the wrist and the time at which grip aperture was maximal during the reach was highly consistent throughout the experiment. In contrast, the time of maximum grip aperture and maximum wrist velocity of the cerebellar patients was quite variable from trial to trial, and the relationship of these measurements also varied considerably. These abnormalities were present regardless of the accuracy requirement. In addition, the cerebellar patients required a significantly longer time to grasp and lift the objects than the control subjects. Furthermore, the patients exhibited a greater grip aperture during reach than the controls. These data indicate that the cerebellum contributes substantially to the coordination of movements required to perform reach-to-grasp movements. Specifically, the cerebellum is critical for executing this behavior with a consistent, well-timed relationship between the transport and grasp components. This contribution is apparent even when accuracy demands are minimal.

Key words Cerebellum · Reaching · Grasping · Coordination · Human

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Introduction

In normal subjects, the reach-to-grasp movement is a highly stereotypic, coordinated movement consisting of a well-executed arm trajectory (arm transport component), a precise orientation of the wrist in relation to the object, and careful scaling of grip aperture for grasping the object (grasp component; Jeannerod 1981, 1984; Jeannerod et al. 1998; Paulignan et al. 1997; Stelmach et al. 1994). Recent views on planning reach-to-grasp movements suggest that arm transport is planned based on analyzing visually the spatial properties of the target object such as distance and direction, whereas the grasp is planned based on the visual analysis of the object's intrinsic properties such as size and shape (Jeannerod et al. 1995). Furthermore, these two components may be controlled in part by two different sets of central structures. For example, the parietal cortex may play a more crucial role in planning the grasp during the visually guided reach-to-grasp movements (Binkofski et al. 1998; Faillenot et al. 1997; Jeannerod et al. 1994), since only the grasp is affected by a posterior parietal lesion (Jeannerod et al. 1994) or a lesion of the anterior lateral bank of the intraparietal sulcus (Binkofski et al. 1998).

One of the hallmarks of the reach-to-grasp movement is the precise temporal relationship with which the arm transport and grasp components are executed (Jeannerod 1981, 1984; Jeannerod et al. 1998; Marteniuk et al. 1990; Wallace and Weeks 1988; Wallace et al. 1990). Furthermore, the two components become more interdependent as the reach progresses (Saling et al. 1996; Timmann et al. 1996b). In addition, the spatial organization of the fingers required to fit the shape of an object becomes more stereotypic as the reach progresses (Paulignan et al. 1991; Santello and Soechting 1998). These findings emphasize that the reach-to-grasp movement is highly coordinated both spatially and temporally and that this coordination involves the regulation of limb transport as well as the organization of finger movements required to grasp and subsequently manipulate the target.

The cerebellum is a structure well known to be involved in the coordination of complex movements (Bloedel and Bracha 1995; Bloedel et al. 1996; Lu et al. 1998; Thach 1998; Thach et al. 1992, 1993; Van Kan et al. 1993, 1994), including the coordination of limb segments during reaching (Bastian et al. 1996; Holmes 1939; Milak et al. 1997). However, little is known about its contribution to regulating the intricate coordination required to perform reach-to-grasp movements. A few experiments have linked information processing in the cerebellum directly to the execution of reach-to-grasp behaviors. A recent PET study reported increased blood flow in the cerebellum during this type of movement when compared with the changes in cerebellar blood flow during visual discrimination of object shapes (Faillenot et al. 1997). Unitary studies and inactivation experiments also implicate the cerebellum in the control of reach-to-grasp movements. Studies in cats showed that movements consisting of reaching to and grasping a vertical bar are severely disrupted following cerebellar nuclear inactivation (Milak et al. 1997). Other experiments in monkeys showed that the cerebellum is involved in the control of the distal extremities at the termination of reach-to-grasp behaviors (Gibson et al. 1996, 1998; Van Kan et al. 1994). It was reported that some neurons in the interposed nuclei were active only when a hand movement is combined with the reach, suggesting that this nucleus is related to the control of grasp during the reach-to-grasp movement (Gibson et al. 1996; Van Kan et al. 1994).

To assess the cerebellum's contribution to reach-to-grasp movements in human subjects, we have undertaken a study examining the abnormalities in the performance of this behavior in patients with pathology restricted to the cerebellum. This objective in part is based on the fact that cerebellar dysfunction is known to affect the execution of movements that require coordination of several joints and body segments (Holmes 1939; Milak et al. 1997). When cerebellar patients perform multijoint movements, their joints are engaged in a serial but overlapping manner when compared with the parallel, comparatively simultaneous flexion and extension of joints observed in normal subjects during the same movement (Bastian and Thach 1995; Bastian et al. 1996; Becker et al. 1991; Massaquoi and Hallett 1996; Topka et al. 1998a). Others have described these abnormal movements as being decomposed into a sequence of elements, each of which is executed as a functionally separate unit (Dichgans and Diener 1984; Inhoff et al. 1989).

Haggard et al. (1994) reported data from one cerebellar patient, suggesting that the coordination of reach-to-grasp movements is disrupted following the occurrence of cerebellar pathology. Grip aperture either started in a more open position or rapidly approached full aperture very early during transport. Furthermore, the relationship between these components was abnormally variable from trial to trial. These initial observations together with the findings indicating that the cerebellum is involved in regulating temporal features of several types of movements (Ivry 1997; Ivry et al. 1988; Sakai et al. 1998, 1999; Takikawa et al. 1998) suggest that this structure may be critical for coordinating the temporal relationship between the aperture and transport of the arm.

Based on the implications from the above literature, we examined the hypothesis that cerebellar impairment disrupts the stereotypic relationship between arm transport and grip aperture and that the variability of this relationship is altered when greater accuracy is required. To test this postulate, two types of paradigms with different accuracy constraints of grasping were used. The reach-to-grasp movements were made to a dowel in one condition and to the crossbar of a small cross in the other condition. Since cerebellar patients have difficulty in generating accurate movements to specific targets in pointing tasks (Bastian et al. 1996; Becker et al. 1991; Bonnefoi-Kyriacou et al. 1998), it is possible that a spatial accuracy constraint might further disrupt the coordination between the transport and grasp components. The data will show that the temporal relationship between the arm transport and grasp movements are highly variable and that this variability is present even when accuracy constraints are minimal. A preliminary study has been presented elsewhere (Rand et al. 1999).

Materials and methods

Subjects

Six cerebellar patients having chronic, isolated cerebellar lesions and six age- and sex-matched healthy controls were tested in the present study. This study was approved by the Institute's Internal Review Board. A brief summary of the patient's clinical characteristics is shown in Table 1. All subjects signed a written consent prior to participation.

Procedure

For the experiment, the patients performed reach-to-grasp movements with the hand ipsilateral to the cerebellar pathology. All patients were right-handed, and all patients except patient 6 (Table 1) were tested with their right hand. However, the characteristics of the reach-to-grasp movements by patient 6 were similar to those made by other patients. All subjects were seated comfortably in front of a table top on which a target object was placed. The start zone was located approximately 30 cm laterally from the subject's midline at the end of an extended arm rest located on the same side as the hand used for reach-to-grasp movements. The target was centered in front of the subject 40 cm from the start zone. The subjects were asked to grasp either a dowel or the cross bar of a small cross, which were used to alter the accuracy requirements of reach-to-grasp movements. The diameter of the dowel was 2.5 cm; the cross consisted of a cross bar 2.5 cm in length, and both its vertical and horizontal components were 5 mm in diameter. The

Table 1 Summary of patients' clinical characteristics (*CT* computerized tomography, *MRI* magnetic resonance imaging, *PICA* posterior inferior cerebellar artery)

Subject	Diagnosis	Radiological findings	Deficits
Patient 1: male, 51 years	Right cerebellar arteriovenous malformation (resected in 1992)	CT: Large lesion involving the right cerebellar hemispheric cortex, vermis, and the cerebellar nuclei	Dysarthria, ataxia of right arm and leg, a significant intention tremor in the right arm
Patient 2: male, 55 years	Right cerebellar cortical lesion (surgically excised in 1995)	MRI: 11-mm lesion in the dorsolateral aspect of the right cerebellar hemisphere	Upper extremity cerebellar ataxia, intention tremor in the right arm
Patient 3: male, 35 years	Right cerebellar stroke in 1996	CT: A focal area of nonenhancing diminished attenuation within the right cerebellar hemisphere in the distribution of the right PICA	Cerebellar ataxia of right arm and leg; slight ocular dysmetria, especially on gaze to the right
Patient 4: male, 68 years	Right cerebellar stroke in 1998	CT: Focal hypodensity in the right medial and inferior hemisphere in the distribution of PICA	Truncal instability with eyes closed, mild gait ataxia, intention tremor of right arm, mild disdiadochokinesis on the right
Patient 5: male, 26 years	Post. Fossa medulloblastoma in 1997	MRI: 8–9 cm^3 mass removed, leaving a lesion extending from the tentorium into the superior hemisphere	No clinical signs were apparent
Patient 6: male, 53 years	Posterior fossa stroke in 1998	MRI: Lesion within the left cerebellar hemisphere that extended into the ipsilateral vermis	Truncal instability with eyes closed; very mild ataxic gait, mild dysmetria of the left arm

height of the dowel and the cross was 10 cm. When reaching for the dowel, the subjects were permitted to grip it comfortably at any location along its vertical extent. When reaching for the cross, the subjects were required to grip the tip of each side of the cross bar. The subjects started the movement with the thumb and index finger closed. In response to a tone signal, subjects were asked to reach for either target at a fast but comfortable speed, grasp the object between the index finger and thumb, and lift it a few centimeters off the table. A block of 40 trials were recorded for each of the two objects, and the order of the tasks were counterbalanced across subjects. For each condition, the subjects practiced for several trials before initiating the recording session. Arm and finger positions during reach-to-grasp movements were recorded using an Optotrak 3D motion-analysis system. Infrared light-emitting diodes (IREDS) were placed over the shoulder, elbow, wrist, the proximal interphalangeal joint of the index finger, the interphalangeal joint of the thumb, as well as on the tip of these fingers. An additional IRED was placed on the object to be grasped in order to record its position and movement. Positions of the IREDS were sampled at a rate of 100 Hz.

Data analysis

Kinematic characteristics related to the grip component and the reaching component were analyzed. The reaching component was assessed based on the position of the IRED on the wrist. Wrist velocity during the reach was calculated as the first derivative of wrist position. The grip component was assessed based on the positions of IREDS over the index finger and thumb tips. Grip aperture was defined as the distance between the two IREDS on these fingers. Both the temporal changes in this measurement as well as its maximum were determined. In addition, target touch was identified as the onset of any movement of the target, as determined from the movement of the IRED placed on the object. The time at which the subjects began to lift the object was identified as the onset of vertical displacement off the table.

Reaching time was measured as the duration from movement onset to the time at which the subject touched the target. Manipulation time was measured as the time from target contact to the initiation of the lift. Other measurements were: duration from movement onset to onset of grip aperture, duration from movement onset to the time of wrist peak velocity, duration from movement onset to peak grip aperture, and duration from the wrist peak velocity to the maximum grip aperture. These durations were expressed as a percentage of reach duration.

Statistical analysis

For all parameters, differences between the control and patient groups as well as the differences between the cross and dowel conditions were evaluated statistically using an ANOVA (2 groups, 2 conditions, 40 trials) with repeated measures. A Newman-Keuls test was used for post hoc analysis. Furthermore, for two parameters, the time to peak grip aperture and the time from the peak of wrist velocity to maximum grip aperture, the Levene test was used to assess the homogeneity of variance for: (1) measurements between subject groups for each condition, and (2) measurements between conditions for each group. Before applying the Levene test to these measurements, intersubject variability was normalized by expressing each measurement as a percentage of that subject's mean for the same measurement for each condition. The significance level used for discussion of all data was $P \leq 0.05$.

Results

The qualitative differences in the kinematic features of the reach-to-grasp movements performed by cerebellar patients and control subjects were examined first by assessing the change in grip aperture and wrist velocity for both the dowel (Fig. 1) and cross (Fig. 2) conditions. Profiles of these parameters for seven consecutive trials in each condition are shown for one subject from each group. When the control subject reached for either the dowel (Fig. 1A,C) or the cross (Fig. 2A,C), the profiles of these parameters were highly consistent across trials. For the dowel condition (Fig. 1), the time of peak grip aper-

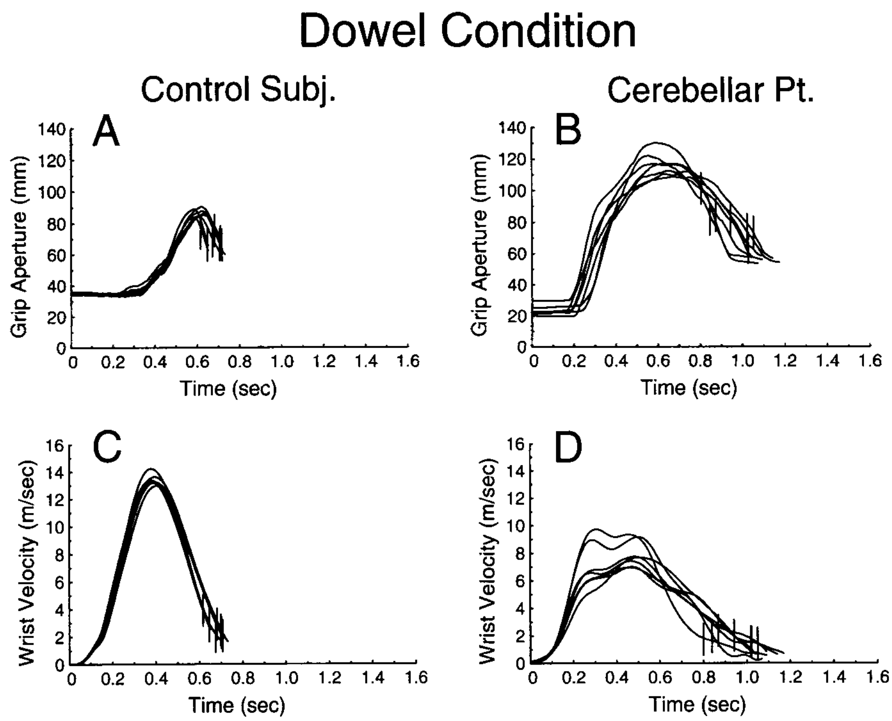

Fig. 1A–D Grip aperture (**A,B**) and wrist velocity (**C,D**) during reach in the dowel condition are plotted against time for seven consecutive trials (trials 12–18) for a control subject and a cerebellar patient. The *small vertical line* near the end of each record indicates the time the target is contacted by either finger. The end of the trace indicates the time the target is actually lifted

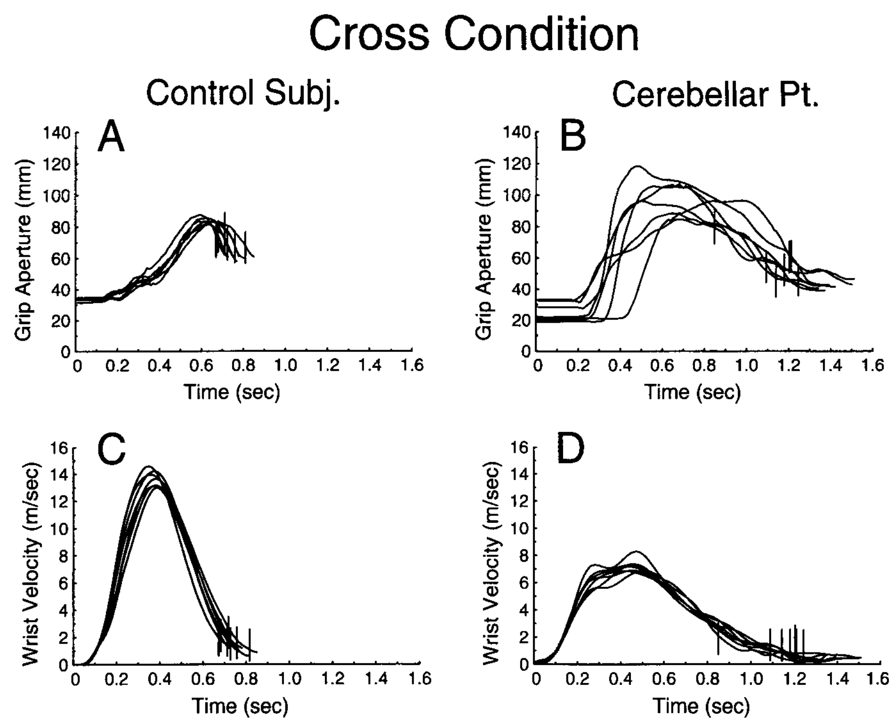

Fig. 2A–D Grip aperture (**A,B**) and wrist velocity (**C,D**) during reach in the cross condition are plotted against time for seven consecutive trials (trials 12–18) for the same control subject and cerebellar patient as in Fig. 1

ture was relatively fixed (Fig. 1A), occurring at approximately 85% of the transport phase. In the cross condition (Fig. 2), the peak aperture (Fig. 2A) occurred at an earlier time during the wrist transport phase (Fig. 2C) than in the dowel condition. In contrast, when the cerebellar patient reached for the dowel (Fig. 1B,D), grip aperture often began to open very early (Fig. 1C) and its time course was quite variable. In addition, the amplitude of the patient's peak grip aperture was much larger than that of the control. The patient's wrist velocity profile (Fig. 1D) showed comparable variation from trial to trial. Note that the time from peak velocity of arm transport to maximum grip aperture also was highly variable. The interval between the short vertical bar and the end of the trace reflects object manipulation time, the time from target touch with either finger to the onset of target lift. Notice that the aperture continued to decrease after target contact until the other digit also contacted the target. A comparison of A and B (Fig. 1) illustrates that this quantity was also larger and more variable for the patient than for the control subject.

Table 2 Mean ± SEM for the dowel and cross conditions for the control and cerebellar patient groups

	Dowel condition				Cross condition			
	Controls		Cerebellar patients		Controls		Cerebellar patients	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Reaching time (ms)	716.3	62.8	743.7	60.0	852.5	72.7	895.7	89.8
Manipulation time (ms)	41.3	14.4	93.7	28.7	71.0	10.5	171.8[b]	24.6
Amplitude of peak grip aperture (mm)	50.9	3.9	74.4***	6.7	46.0	2.4	59.9***	6.0
Time to grip aperture onset[a] (%)	21.5	3.1	8.3***	2.2	18.3	3.9	10.4**	3.0
Time to peak wrist velocity[a] (%)	45.8	1.1	43.4	3.3	41.1	1.4	37.5	2.4
Time to peak grip aperture[a] (%)	86.0	1.5	67.5***	4.9	80.3	2.3	65.3***	4.7
Time duration from peak wrist velocity to peak grip aperture[a] (%)	40.3	2.3	24.1***	2.4	39.2	1.6	27.8***	2.7

[a] Values are expressed as a percentage of reach duration
[b] No post hoc test was performed, because there was no significant interaction effect
*$P \leq 0.05$; **$P \leq 0.01$; ***$P \leq 0.001$

The patient's abnormalities were accentuated when an attempt was made to grasp the cross bar of the cross target (Fig. 2B,D). This subject clearly had difficulty in grasping the crossbar with the fingertips, and the movement slowed substantially compared with the movements to the dowel target (Fig. 1D). The time course of the aperture (Fig. 2B) was particularly variable when compared with the control subject's data (Fig. 2A).

The group data shown in Table 2 demonstrate that the differences between the patient and control subject illustrated in Figs. 1 and 2 could be substantiated quantitatively at the group level. All significant differences were determined using the ANOVA described in the Materials and methods section. The reaching times for the control and patient groups did not differ significantly. However, reaching time was significantly longer for the cross than for the dowel condition across both groups ($F_{1,10}$=30.88, $P \leq 0.001$). Reach time was decomposed into the time to peak wrist velocity and the deceleration time. In addition, the percentage of the overall reach required to attain peak wrist velocity was determined (see Table 2). While this measurement did not exhibit any significant group main effect, it showed a significant effect of condition ($F_{1,10}$=21.68, $P \leq 0.01$). The percentage of reach time to peak wrist velocity became smaller when the subjects reached for the cross. No interaction between group and conditions was found for the reach time or for the percentage of reach time to peak wrist velocity. The manipulation time (Table 2) for cerebellar patients was significantly longer, indicating that they required more time to lift the target after touching it than control subjects ($F_{1,10}$=9.94, $P \leq 0.01$). In addition, the manipulation time was significantly longer for the cross than that for the dowel condition ($F_{1,10}$=10.27, $P \leq 0.01$). Although there was a greater difference between the two groups for the cross condition than for the dowel condition, there was no statistically significant interaction between group and condition.

The amplitude of peak grip aperture, namely the distance between the index finger and thumb, also was calculated. The data in Table 2 show that this quantity was greater for the patients than for the controls ($F_{1,10}$=6.94, $P \leq 0.05$). The mean amplitudes for each group are plotted in Fig. 3A. The ANOVA showed that the maximum grip aperture for the cross condition was significantly greater than that observed for the dowel condition ($F_{1,10}$=86.21, $P \leq 0.001$) and that there was an interaction between group and condition ($F_{1,10}$=21.35, $P \leq 0.001$). As can be seen in Fig. 3A, the patients showed an accentuated increase in grip aperture when they reached for the dowel, despite the fact that the final aperture was the same for both manipulanda. In contrast, the comparable increase was smaller for the control group. Post hoc comparison

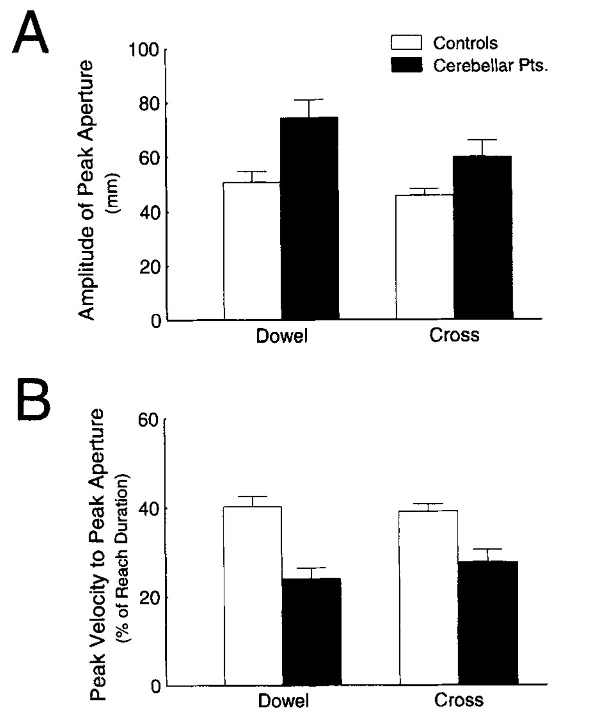

Fig. 3A,B Effects of changing the accuracy constraint on the amplitude of peak grip aperture (**A**) and the interval from the time of peak wrist velocity to the time of peak grip aperture (**B**). Means for each subject group are plotted for each condition. The *error bars* indicate the SEM

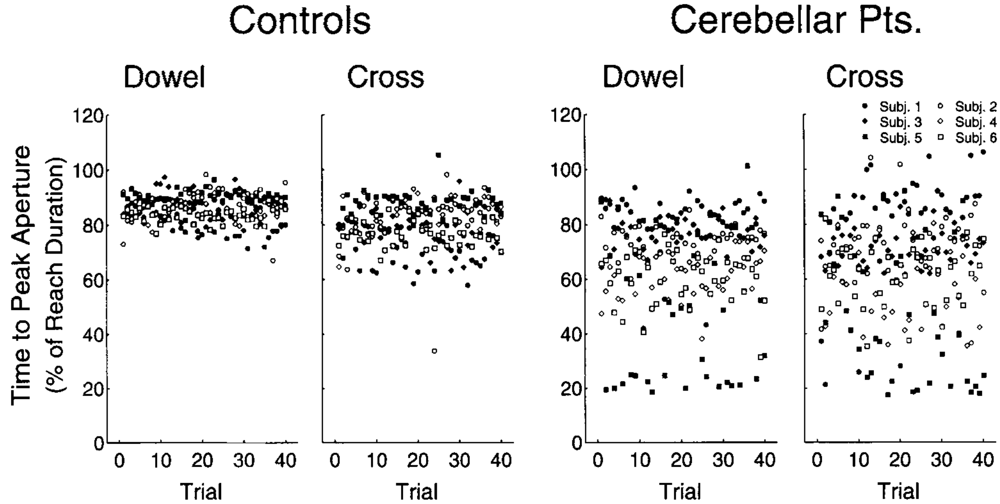

Fig. 4 The time from movement onset to peak grip aperture was plotted for the dowel and the cross conditions across all trials for all controls and patients. This value was expressed as a percentage of reach duration

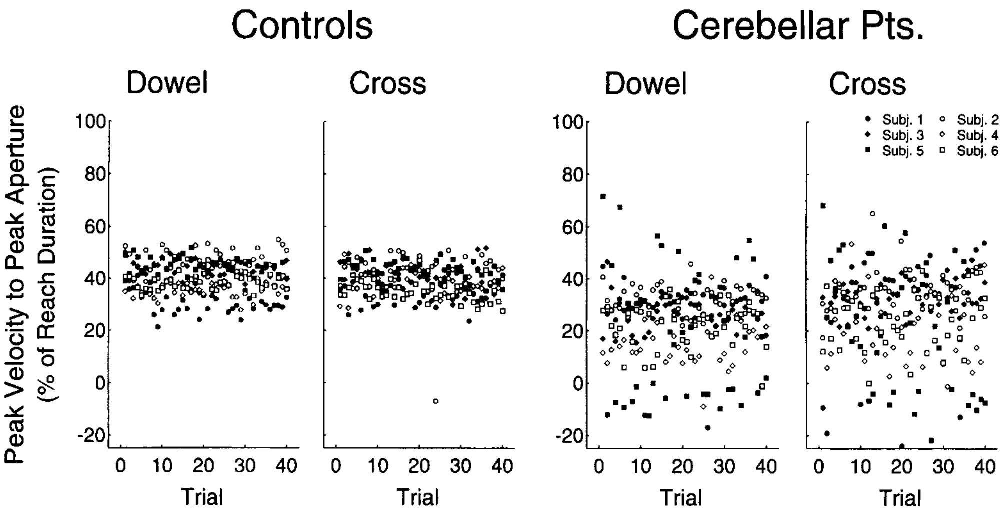

Fig. 5 The interval from the time of peak wrist velocity to the time of peak grip aperture was plotted for the dowel and cross conditions across all trials for all controls and patients. This value was expressed as a percentage of reach duration

revealed that the difference between conditions was significant for both control group ($P \leq 0.01$) and patient group ($P \leq 0.001$). To examine whether there was any group difference in the time required to initiate the movement of the fingers during reaching, the percentage of reach time before the onset of a change in grip aperture (grip aperture onset) was measured. As seen in Table 2, the patients had an earlier grip onset time in both conditions than the controls. The ANOVA revealed that there was a significant difference between groups ($F_{1,10}=6.31$, $P \leq 0.05$). However, there was neither a statistically significant difference between conditions nor a significant interaction between group and condition.

In order to determine whether the subjects produced reach-to-grasp movements with a consistent relationship between the arm transport and grip aperture components, the times from movement onset to peak grip aperture and from peak wrist velocity to peak grip aperture were measured. The time from movement onset to peak grip aperture was expressed as the percentage of reach duration. Across two conditions, the control subjects required an average of 83% of the reach duration to produce a peak grip aperture, while the patients required an average of 66%. This difference between the two groups was significant ($F_{1,10}=10.89$, $P \leq 0.01$). When reaching for the cross, this quantity decreased modestly for both groups, and the main effect of condition was significant ($F_{1,10}=21.91$, $P \leq 0.001$; Table 2). To demonstrate differences in the consistency of this measure between groups, the values are plotted across all trials for all controls and patients (Fig. 4). The patients showed a greater variability than controls in the time during reach at which the grip aperture was maximum. Comparing the variances of this measure between subject groups using the Levene test revealed that the variability across 40 trials in the patients was significantly larger than that in the controls both for the dowel condition ($F_{1,478}=87.08$, $P \leq 0.0001$) and for the cross condition ($F_{1,478}=110.47$, $P \leq 0.0001$). When reaches were made to the cross, both groups increased the variability of this measurement significantly (control group: $F_{1,478}=37.46$, $P \leq 0.0001$; patient group: $F_{1,478}=8.24$, $P \leq 0.01$).

The time from peak wrist velocity to the time of peak grip aperture also was expressed as a percentage of reach duration. The values are plotted across all trials for all controls and patients in Fig. 5. The Levene test revealed that the patients' variability across 40 trials was significantly larger than that of the controls ($F_{1,478}$=109.95, $P\leq0.0001$ for the dowel condition; $F_{1,478}$=124.79, $P\leq0.0001$ for the cross condition). When reaches were made for the cross, the controls increased the variability of this measurement significantly compared with the dowel condition ($F_{1,478}$=6.44, $P\leq0.05$). In contrast, for the patient group the variability between the two conditions did not differ significantly.

The mean duration across each group is plotted in Fig. 3B for each condition. The control subjects spent an average of 40% of reach duration between peak wrist velocity and peak grip aperture across the two conditions, while the patients spent an average of 26% (Table 2). This difference was significant ($F_{1,10}$=19.08, $P\leq0.01$); no condition effect was found. However, an accentuated decrease in this duration was observed when the patients reached for the dowel, and the interaction effect between group and condition was significant ($F_{1,10}$=10.20, $P\leq0.01$).

Discussion

Kinematic deficits

This study is one of the first to assess quantitatively the specific alteration in the kinematics of the precision grip that result from cerebellar pathology in human subjects and is the first to examine this question using different, well-controlled accuracy constraints. When cerebellar patients reached for the target, they exhibited impairments in several parameters tested, including the timing of grip opening (Table 2) and the time from the peak wrist velocity to peak grip aperture (Fig. 3B). Both the onset of their grip aperture and the peak grip aperture (Table 2) occurred early during the reach. Furthermore, the interval from peak wrist velocity to peak grip aperture was much shorter for the patients than controls, and for the patients this interval was disproportionally shortened in the dowel condition (Fig. 3B). These results indicate that cerebellar patients increased their aperture rapidly and reached maximum aperture very early during transport compared with controls. They also transported the hand closer to the object before initiating a phasic closure and the grasp. These data extend and substantiate quantitatively the previous observation made in a single cerebellar patient by Haggard et al. (1994). This deficit may reflect an abnormality in velocity control, consistent with previous reports (Conrad and Brooks 1974; Gilman et al. 1976; Hallett et al. 1991).

Cerebellar patients also displayed an abnormally wide opening of the thumb and index fingers during reach (grip aperture; Fig. 3A), a finding also observed in the single patient of Haggard et al. (1994). This abnormality is substantially different from that observed in patients with Parkinson's disease, whose grip aperture is abnormally narrow (Castiello and Bennett 1994; Castiello et al. 1999; Gentilucci and Negrotti 1999). The data further showed that the increased maximal grip aperture observed in the cerebellar patients was accentuated in the dowel condition even though the final aperture required to grasp the dowel and cross was the same (Fig. 3A). It is known from studies of normal subjects that the peak grip aperture increases when reach-to-grasp movements are made more rapidly (Wallace and Weeks 1988; Wing et al. 1986), with peripheral vision (Sivak and MacKenzie 1990), or without vision (Chieffi and Gentilucci 1993). This wider grip aperture was interpreted as reflecting a compensatory strategy in which subjects increased the safety margin for grasping the object successfully at the end of a fast reaching movement. Thus, the accentuated peak grip aperture in the dowel condition observed in patients could reflect an accentuation of a compensatory strategy seen in normal subjects. However, it also is possible that the wider grip aperture in cerebellar patients reflects the hypermetria seen in several types of movements performed by this group of subjects (Flament and Hore 1986; Hore et al. 1991; Topka et al. 1998a, 1998b). In these previous studies, hypermetria occurred at the *termination* of a discrete movement directed toward a certain target. In the present study, a movement component, grip aperture, was modified *during* the movement. Consequently, the abnormal scaling of grip aperture preceded target contact, and its disruption affected its relation to other features of the ongoing behavior. Thus, when the cerebellum is dysfunctional, the scaling of the more distal movement component, grip aperture, is disrupted during the execution of the other component, wrist transport. In addition, the scaling of this measurement is appreciably more variable than observed for normal subjects. Our results, however, do not differentiate between hypermetria and an abnormal compensatory strategy as a basis for these findings, and it is possible they are linked in the performance of this task. These findings extend previous observations regarding the cerebellum's contribution to the coordination of complex movements by emphasizing its importance for implementing a consistent strategy when executing a complex motor behavior.

Another impairment in reach-to-grasp movements observed in cerebellar patients was a difficulty in manipulating the object with the thumb and index fingers after the arm reached the target. Compared with normal subjects, cerebellar patients took longer to lift the object after grasping it (Table 2). This suggests that there is a general difficulty in coordinating the index finger and thumb when performing a precision grip to lift the object at the end of a reaching movement. Other related abnormalities in the regulation of grip have been reported. These include abnormalities in the organization and timing of precision grip when contacting a stationary object (Bastian and Thach 1995; Goodkin et al. 1993) and when manipulating an object in different contexts (Babin-Ratté et al. 1999; Mai et al. 1988; Müller and Dichgans 1994; Serrien and Wiesendanger 1999). These deficits in performing the grasp probably contribute to increasing the manipulation time observed in the present experiment. In addition, the coordination of finger grip, the application of grip force, and the lifting the object have to be achieved in smooth succession after the hand is transported to the object. Disrupting the coordination of this sequence may also contribute to this abnormally long manipulation time. Finally, this deficit may also reflect delays in movement initiation reported following cerebellar pathology (Beaubaton and Trouche 1982; Conrad and Brooks 1974; Trouche and Beaubaton 1980).

Increased variability of reach-to-grasp movements in cerebellar patients

As expected, normal subjects showed highly consistent profiles for grip aperture and wrist velocity for reaches to both the dowel and the cross targets. In agreement with the previous studies (Jeannerod 1981, 1984; Jeannerod et al. 1998; Marteniuk et al. 1990; Wallace and Weeks 1988; Wallace et al. 1990), the relationship between the peak velocity of the wrist and the peak aperture of the fingers was highly invariant throughout the experiment.

In contrast, grip aperture and wrist velocity were highly variable from trial to trial among the cerebellar patients, and the relationship of these measurements also varied considerably (Figs. 4, 5). These abnormalities were present regardless of the accuracy requirement. This variability is highly characteristic of the uncoordinated reach-to-grasp movements observed in cerebellar patients: a high variability not only of specific kinematic measurements but also of the relationship between the transport and grip components of the task. These results are consistent with the view that the cerebellum is involved in regulating the temporal relationship among the components of reach-to-grasp movements. Furthermore the increased manipulation time observed for cerebellar patients (Table 2) may reflect a general deficit in timing successive components of a movement. These interpretations are supported by several studies illustrating the cerebellum's contribution to the timing of other types of movements (Ivry 1997; Ivry et al. 1988; Sakai et al. 1998, 1999; Takikawa et al. 1998; Timmann et al. 1999). One recent study is particularly pertinent. Timmann et al. (1999) demonstrated that the timing of another skilled movement requiring coordination between hand and arm, overarm throwing, also is impaired in cerebellar patients. In this study, cerebellar patients displayed a high variability in the time of ball release during throwing, suggesting that patients were impaired in determining the precise onset of finger opening (grip release) during the throwing movement of the arm. Our data extend this observation by showing that the timing deficit characterizing cerebellar dysfunction affects the relationship of ongoing components of this complex movement, the transport and the grip aperture of a goal-directed reaching task.

The large variability of movement profiles across trials may reflect an abnormality in on-line processing of proprioceptive information regarding arm and hand position during the reach-to-grasp movements. Recent studies suggest that cerebellar patients have deficits in the processing of kinesthetic information during the movements (Grill et al. 1994, 1997; Shimansky et al. 1997). For example, Grill et al. (1997) demonstrated that cerebellar patients required a longer time to process the index finger's position of one hand before using this information to initiate a movement of the finger on the other hand. During reach-to-grasp movements, information regarding the state of grip aperture and the state of arm position is probably processed online in order to update the internal representation of the limb and hand required for coordinating the two major components of this task. A deficit in using kinesthetic cues to generate an internal representation of traced objects also has been reported for cerebellar patients (Shimansky et al. 1997). Therefore, it is possible that deficits in processing kinesthetic information regarding arm and finger movements may have contributed to the observed variability in the reach-to-grasp movements displayed by cerebellar patients in the present experiment.

In addition to the movements required for grasping, cerebellar dysfunction is known to disrupt the coordination of other multijoint limb movements (Bastian and Thach 1995, Bastian et al. 1996; Becker et al. 1991; Goodkin et al. 1993; Thach et al. 1993; Topka et al. 1998a, 1998b). These studies demonstrated the disorganization of shoulder and elbow movements during discrete arm-pointing movements. For example, Bastian et al. (1996) reported that, when cerebellar patients performed a two-joint (elbow and shoulder) reaching movement in a slow, accurate manner, the primary phase of the movement at each joint started at different onset latencies. The authors speculated that this strategy may be used by cerebellar patients to compensate for difficulties in controlling interactive torque between the two joints (see also Milak et al. 1997 for related observations and conclusions). Since reach-to-grasp movements also employ the concurrent control of shoulder and elbow movements, this explanation also may apply to some of the abnormalities observed in the present study. It is possible that the parallel processing between the shoulder and elbow joint, together with the coordination of grip aperture, is particularly dependent on the cerebellum for concurrent, accurate execution of reach-to-grasp movements.

In the present study, the patients' cerebellar lesions are quite varied in location. Yet the observations were comparable across subjects. Our study is not alone in demonstrating this aspect of cerebellar deficits in patients. A group of cerebellar patients with widely distributed lesions often display related abnormalities when their performance on a specific task is examined (Bracha et al. 1997; Kargerer et al. 1998; Rand et al. 1998; Timmann et al. 1996a). Together with the present findings, these data suggest that several different cerebellar regions contribute to the control of a single type of movement, in this experiment the reach-to-grasp movement. This suggestion also is consistent with our previous observations in a study examining the effects of inactivating different cerebellar nuclear regions on a reaching task in cats (Milak et al. 1997). Inactivating separately each of the three primary cerebellar nuclear regions produced ataxia of the same reaching movement. However, kinematic analysis of the data revealed that there were some differences in the specific measurements affected by inactivating each nucleus.

In summary, the present results demonstrate that cerebellar patients have an impaired capacity to coordinate temporal features of the reach-to-grasp movement required to scale the arm transport and grasping components appropriately, and that this impairment is present regardless of whether the accuracy constraints of grasping are high or low. These data also indicate that these kinematic measurements characterizing their reach-to-grasp movements are considerably more variable than those of control subjects. This finding is highly consistent with observations in our previous study examining another type of stereotypic movement, locomotion (Rand et al. 1998). This experiment, which examined adaptive responses to locomotor perturbations, demonstrated that patients with cerebellar lesions were unable to acquire corrective responses consisting of well-timed EMG patterns of lower limb muscles. Furthermore, a recent study in cats (Milak et al. 1997) showed that the inactivation of specific cerebellar nuclei resulted in substantial trial-to-trial variations of joint angular velocities involved in a series of reaching, grasping, and manipulating movements. All of these observations are consistent with the postulate that the cerebellum is critical for optimizing the temporal relationships among multiple limb segments during goal-directed movements.

Acknowledgements The investigators wish to thank Mr. S. Morrissy for his technical assistance. This study was supported by NIH grants RO1 NS 21958 and RO1 NS 36752. In addition, Dr. M. K. Rand was supported by the Flinn Foundation Program in motor control.

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