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Influence of vision on upper limb reaching movements in patients with cerebellar ataxia

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Summary

The effects of vision on spatial and temporal characteristics of free unrestrained reaching movements of the arm were examined in 17 patients with ataxic syndromes due to degenerative disease of the cerebellum and its connections. Subjects were required to reach out and touch a visually presented target either in the dark or with the target and their finger visible. Overall, patients had prolonged reaction times and their movements were performed slower than normal. The spatial paths described by their fingertips were more circuitous, being of greater length than normal, a characteristic that was uninfluenced by visual conditions. Ataxic movements were less accurate than normal in two ways. First, there was greater spatial variability between repeat paths to the same target. The increased variability was present very early in the movement trajectory and at that stage was not influenced by visual feedback. Secondly, there were large constant errors at the end of movement, but only when moving in darkness. Patients with Friedreich's ataxia as well as those with intrinsic cerebellar degeneration showed the above abnormalities, although there were some quantitative differences between the two groups. We suggest these spatial errors arise because the cerebellum contributes either directly or indirectly to preparatory motor processes which, based on limb proprioceptive and retinal information, compute the pattern of muscle activity required to launch the limb accurately towards a target. Patients were largely successful at using visual guidance to make midflight adjustments to their movements in order to improve accuracy. This manifested as a reduction in spatial variability between repeat paths as the target was approached and a reduction in constant error. However, the visual correction mechanism did not appear normal. Under visual guidance, the end-phase of movement was often prolonged and characterized by excessive deviations or direction changes in the path. These deviations may be the expression of a visual guidance system producing corrections which themselves contain error requiring further correction. Thus, this process may be abnormal for the same reason that the initial pattern of muscle activity is misjudged.

Keywords: cerebellum; ataxia; Friedreich's ataxia; reaching; vision

Abbreviation: IRED = infrared-emitting diode

Introduction

Lesions of the cerebellum interfere with voluntary movement and produce a characteristic, often diagnostic, cluster of neurological signs. The physiological determinants of these signs are not known and the role of the cerebellum in motor control remains the subject of debate. The cardinal clinical features of cerebellar disease were described by Holmes over 50 years ago (Holmes, 1939). The ataxic arm is slow to start moving, moves slowly once under way, develops oscillations and jerky movements during movement (kinetic tremor) and towards the end of movement as the target is approached (intention tremor), with past pointing (dysmetria). Even while maintaining a posture the ataxic limb may begin to oscillate (postural tremor). Rapid alternating movements are fragmented and clumsy (dysdiadochokinesis). It is not clear whether these signs are all related to one fundamental deficit created by the cerebellar lesion or whether a series of different mechanisms is responsible, including voluntary adjustments to compensate for the underlying defect of movement. Reduced tone in antagonist muscles was considered by Holmes (1939) to be the major factor underlying hypermetria and ataxia on the grounds that most patients with acute cerebellar hemisphere lesions exhibited profound hypotonia.

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However, since patients with degenerative cerebellar disease have normal muscle tone yet display similar abnormalities of movement, factors other than tone must be important.

A number of studies have examined cerebellar movements with limb restraint and movement confined to one dimension. While such methods have been successful in determining some abnormal temporal characteristics, they have been relatively insensitive to disorganization of the spatial aspects of movement. Spatial errors are a fundamental clinical sign in cerebellar ataxia, yet there have been few studies of these aspects of movement in human cerebellar disease. The present study examined unrestrained reaching movements in a group of patients with degenerative disease of the cerebellum and its connections and clinical signs of upper limb cerebellar ataxia. The spatial characteristics of reaching movements were investigated in the context of the visual control of movement, following the hypothesis of Stein (1986) that the cerebellum plays an important role in the visual guidance of movement. Thus, we contrasted movements performed with vision of the hand and target with those performed in complete darkness. Some of these data have been presented to the Physiological Society (Day *et al.*, 1992; Day, 1994).

Methods

Subjects

With the National Hospital for Neurology and Neurosurgery and the Institute of Neurology Joint medical ethics committee approval, 17 patients with cerebellar signs associated with various degenerative diseases were studied. The patient group was diverse in terms of pathology, duration of illness and age (age range 22–68 years, mean ± SD 48.7 ± 13.0 years). Patients were classified into subgroups according to the diagnostic criteria of Harding (1996). Clinical details of these patients are summarized in Table 1. Prior to the experimental session, each patient underwent a standard neurological examination which was recorded on videotape. From these recordings, using a four-level rating scale (0 = normal, 1 = mild, 2 = moderate, 3 = severe) various motor features were assessed by two of the authors, who were unaware of the diagnosis. All patients had a cerebellar dysarthria and defects of eye movements (ocular dysmetria, square-wave jerks, or both) typical of cerebellar disease. The severity of arm ataxia and gait ataxia is shown in Table 1. Arm ataxia was judged by the presence of dysmetria on finger–nose testing, dysdiadochokinesia, and clumsiness of repetitive hand and finger movements. Gait ataxia was judged on spontaneous locomotion and heel–toe walking along a straight line. None of the patients had marked tremor. Tendon reflexes were absent in those with Friedreich's ataxia, who also exhibited extensor plantar responses. Pyramidal signs were present in three other patients (Table 1).

The patients' performance during the experimental session was compared with that of a group of eight healthy subjects (age range 28–43 years, mean ± SD 34.8 ± 5.2 years) recruited from departmental staff who were naive to the experimental set-up and procedure.

We suffered a loss of data for four of the patients, which meant their results were analysed only partially. The number of patients contributing to each analysis is indicated in the text.

Experimental procedure

Subjects were seated in a comfortable chair with their torso supported by the chair-back and arms. The head was supported and fixed facing forwards using a chair-mounted head clamp. This procedure was sufficient to eliminate any effects of postural instability on the arm movements whilst leaving the arm and shoulder free. In front was a horizontal row of seven 2 cm diameter target lights mounted 10 cm apart on a flat vertical board. The centre target light was aligned with the subject's midline at about the level of the mouth. The distance of the subject from the target board was adjusted so that all target lights could be comfortably reached by the index finger with no movement of the trunk. The index finger rested on a 3 cm diameter plate which was mounted 25 cm in front of and 25 cm below the centre target. The plate acted as a proximity detector and was adjusted to indicate when the finger was just touching it. An infrared-emitting diode (IRED) and a visible light-emitting diode were attached to a ring worn on the end of the index finger.

A target light was illuminated and after a delay of 3–4.5 s a tone (1 kHz for 100 ms) was sounded and the visible light-emitting diode on the finger turned on. Subjects were instructed to reach out and touch the illuminated target light as soon as they heard the tone. This long period between target presentation and the 'go' signal was used to ensure adequate time for preparation of the movement and to minimize reaction time. Subjects were urged to react to the tone without delay, but emphasis was placed on accuracy of final finger position rather than speed of execution of the movement. Within this constraint each subject was free to choose a movement path and movement speed that felt natural. All subjects, with the exception of one patient, used their right hand. The left hand was chosen for this patient as it was clinically more affected than the right hand. However, because of possible differences between limb movements in ipsilateral versus contralateral hemispace, the values obtained from right-sided targets of this patient were treated as if they were from left-sided targets and vice versa. The three-dimensional position of the finger tip in space was measured with a sampling frequency of 200 Hz, using a three-camera Selspot II system (Selcom AB, Sweden) which tracked the IRED on the finger.

For each block of trials eight movements were made to each of the seven targets (56 trials) presented in pseudorandom order. Three blocks were performed with a 10–20 min rest between each block. The first block of trials took place in ambient light conditions and served as a familiarization and practice session. The second block of trials was performed with the room blacked out except for the illuminated target and finger lights. For the third block the target and finger

Table 1 *Summary of patient details*

Case	Diagnosis	Sex	Age (years)	Arm ataxia	Gait ataxia	Pyramidal signs	Tendon reflexes	Sensory loss†
1*	PCD	M	51	3	3	–	+	–
2*	ILOCA	F	55	2	2	+	+	–
3*	ILOCA	M	48	2	2	–	+	–
4*	ILOCA	F	68	2	3	–	+	–
5	ILOCA	F	53	1	1	–	+	–
6	ARLOCA	F	57	2	3	–	+	–
7	ADCA	M	57	2	2	–	+	–
8	ADCA	M	60	2	1	–	+	–
9	ADCA	M	55	2	2	+	–	–
10	ADCA	F	55	2	2	–	+	–
11	FA	F	42	2	2	+	–	–
12	FA	F	25	1	1	+	–	–
13	FA	M	42	2	3	+	–	+
14	FA	F	27	2	2	+	–	–
15	EOCA	M	22	2	2	–	+	–
16	MSA	M	55	1	1	–	+	–
17	MSA	M	56	1	2	+	+	–

+ = present; – = absent; ADCA = autosomal dominant cerebellar ataxia type I; ARLOCA = autosomal recessive late-onset cerebellar ataxia; ataxia: 0 = normal; 1= mild; 2 = moderate; 3 = severe; EOCA = early-onset cerebellar ataxia with retained reflexes; FA = Friedreich's ataxia; ILOCA = idiopathic late-onset cerebellar ataxia; MSA = multiple system atrophy; PCD = paraneoplastic cerebellar degeneration. *Missing data, analysed partially; †reduced appreciation of joint position in the fingers.

lights were extinguished as the finger left the touch-plate. For this condition, therefore, movements were initiated with vision of the target but executed in complete darkness. Subjects were instructed to keep their finger on the target board and at the end of the data collection period the target and finger lights were turned back on to give feedback regarding the final end-point accuracy of the movement.

Measurement and analysis

The beginning of a movement was defined as the time that the finger left the touch-plate. The end of a movement was defined as the time that the IRED on the finger passed through a vertical plane parallel to and just in front of the target board. This end-plane was taken to be 20 mm in front of the target, but because the IRED was situated over the back of the finger it crossed the plane when the finger was only some 2–6 mm (depending upon finger size and orientation) from the target board. Each movement was stored as a sequence of three-dimensional position data from which the velocity of the finger was calculated by digital differentiation. A number of temporal and spatial measures were derived from these data.

Reaction time

Reaction time was defined as the interval from the 'go' signal (tone) to the finger leaving the touch-plate. Movements were rejected if the reaction time was <100 ms or >1 s.

Movement time

Movement time was defined as the interval between the finger leaving the touch-plate and passing through the end-plane. Movements were rejected if the finger failed to cross the end-plane by the end of the recording period (3 s).

Peak speed

The speed of the finger was defined as the magnitude of the velocity vector, irrespective of its direction. Peak speed was the maximum value achieved during the movement phase.

Path length

Path length was defined as the sum of linear distances between adjacent data points along the movement path. The length of a straight line between the position of the finger at the beginning and at the end of each movement was calculated and used to normalize the path length.

Spread of paths

Spread of paths was used to estimate the spatial variability between paths to the same target at different stages of movement. The intention was to extract a spatial measure that was insensitive to temporal fluctuation. It was calculated by taking each movement path and cutting it into 20 equal lengths. The three-dimensional position of the finger at each cut was estimated using linear interpolation between raw data points. Each cut of a family of paths yielded a cluster of points which, in general, varied in all three dimensions. The spread of such a cluster, irrespective of its shape or orientation, was estimated by measuring the mean distance of all points in the cluster from the cluster's mean position. This measure of spread plotted against percentage of path

travelled gave a simple, one-dimensional estimate of how the spatial bundling of paths changed as the target was approached.

Cumulative direction change

An attempt was made to quantify the deviations along individual paths by measuring the direction the finger was moving at each sampling point and computing the angular difference in direction between adjacent points. Cumulative direction change was defined as the successive changes in direction summed over the movement path. The instantaneous direction of movement at each data point was calculated from the relative magnitudes of the three components of velocity. Direction change was taken to be the inclusive angle between each pair of adjacent vectors. Ideally, for a given path this measure should yield the same cumulated value irrespective of the speed at which the movement is executed, provided the sampling rate is high enough. For example, a constant speed movement that describes a quarter of a circle in space could, with an appropriate sampling rate, result in 91 data points with 1° of direction change between each pair. If the movement was repeated five times faster it would result in 19 data points with 5° of direction change between each pair. Thus, the cumulated direction change would be the same for both speeds. In practice, however, there is uncertainty associated with the velocity measure because of noise in the signal, and this introduces similar uncertainties to estimates of instantaneous direction. Furthermore, the effect of noise on direction measurements is dependent upon the magnitude of the speed at the time. At high velocities noise can be ignored whereas at very low velocities it may contribute to direction measurements.

Constant end-point error

Constant end-point error was assessed in two ways. The two-dimensional position of the finger was measured as it crossed the end-plane. The mean position was computed for repeat movements to each target, and the distance between the mean finger position and target location was measured for the two visual conditions separately. Because the IRED signalling finger position was placed on the fingernail and the one signalling target position was situated at the top of the target disc, the two positions would coincide in the vertical and horizontal directions only when the tip of the finger hit the target straight on. With any other finger orientation the position of the two IREDs would produce a small apparent error for an otherwise perfect placement of the finger. However, it is reasonable to assume that any such effect would be cancelled out when relative mean finger positions are considered. A second measure of constant error was taken, therefore, from the distance between the two mean finger positions obtained under the two visual conditions.

Data were analysed statistically using analysis of variance with repeated measures. When appropriate, group means were compared using Student's *t* test.

Results

Temporal characteristics

In all respects the patients' movements were slower than those of the healthy subjects. Patients took longer to initiate a movement (interval between tone and finger leaving touch-plate), achieved a lower peak speed and took longer to reach the end-plane (for statistical analysis see Fig. 1 and Table 2).

Effect of target location

Both peak speed and movement time were influenced by target location. When reaching for targets in the ipsilateral hemispace healthy subjects tended to move with an approximately constant movement time, the increase in distance for the more eccentric targets being compensated by moving with greater peak speed (Fig. 1). In contrast, targets situated in the contralateral hemispace were approached with approximately constant peak speed, which led to slightly longer movement times for the more distant targets. This behaviour has been reported previously by Fisk and Goodale (1985). Patients behaved slightly differently in that peak speeds were influenced less and movement times more by target eccentricity (group×target interaction; Table 2).

Effect of vision

When moving in darkness, healthy subjects tended to move with lower peak speed but with little effect on movement time. Patients, on the other hand, tended to move with marginally higher peak speed and shorter movement time. These changes in the patients' movement time with vision, which were reflected to some extent in the changes in peak speed, often appeared to stem from a prolonged end-phase of movement that occurred when they could see their finger and the target throughout (e.g. Fig. 1A).

Spatial characteristics

Subjects were free to choose any route for their finger. If the three required elements of lift, forward progression and lateral deviation were performed simultaneously then the finger would travel along a straight-line path to the target. However, paths were never straight but displayed a variety of curves (Figs 2 and 3). Furthermore, the finger took a different route each time an attempt was made to touch the same target, resulting in a family of curved paths, more or less tightly bundled, which ended up variably accurate. In general, lift and lateral deviation dominated the early part of the movement while forward progression dominated the later part. This had the effect of ensuring that the finger approached the target board approximately straight on.

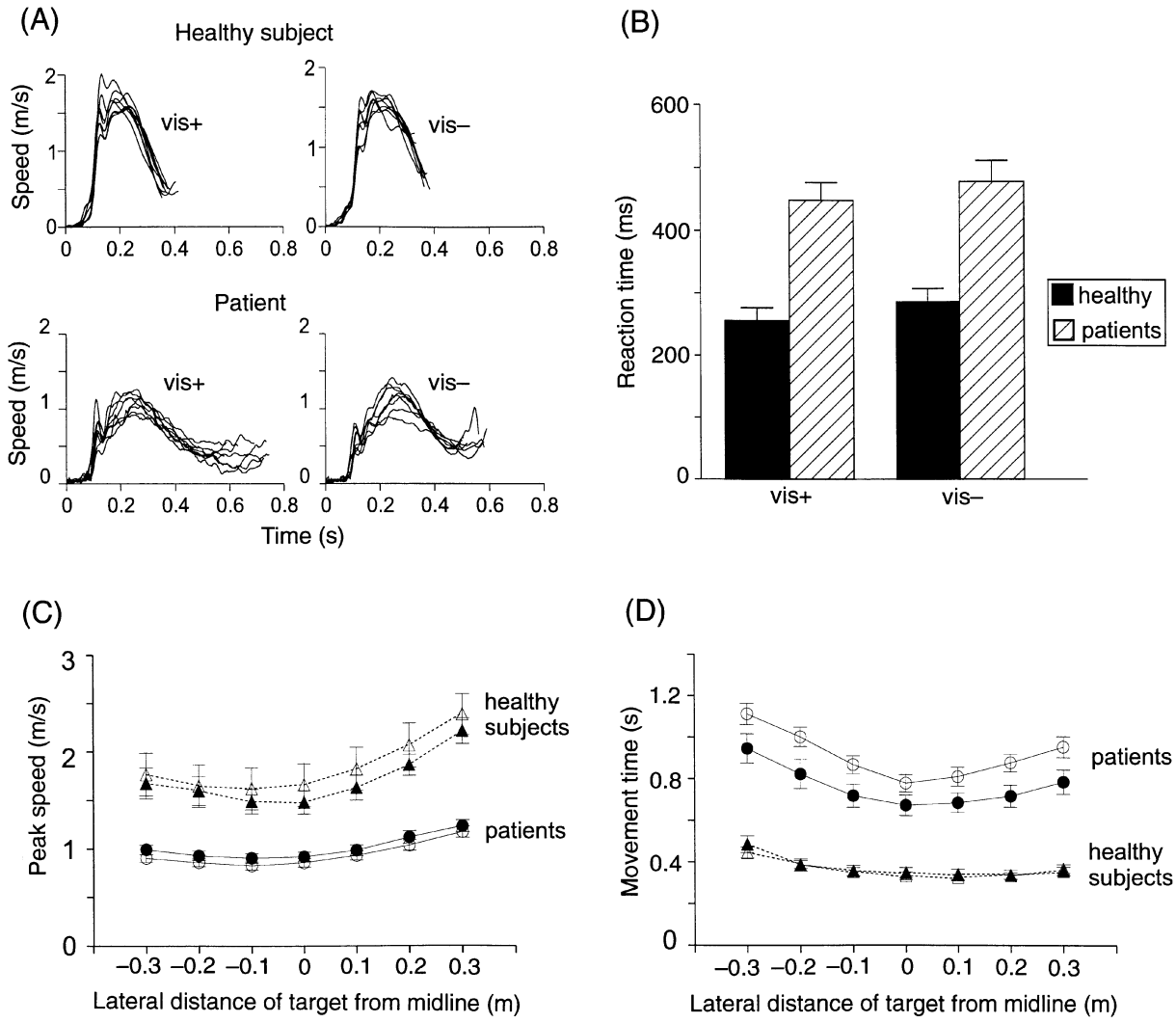

Fig. 1 Temporal characteristics of movements. **A** shows examples from a healthy subject and a patient (Case 14) of superimposed speed profiles of eight movements to one target (10 cm to the right of centre). Each trace has been realigned at 100 ms according to when the finger left the touch switch. Each trace ends when the finger passed through the end-plane. Left panels show records obtained when subjects could see both the target and their finger (vis+). Right panels show records obtained when subjects executed the movements in complete darkness (vis–). Note that peak speed was less and movement time greater for the patient. Also note that the movement time decreased for the patient when moving in darkness. Group mean (± SEM) data of reaction time, peak speed and movement time are shown in **B**, **C** and **D**, respectively. In **B** the reaction time for each subject has been averaged across all target locations and both visual conditions, whereas in **C** and **D** mean values for each of the seven targets are shown separately. In **C** and **D** open symbols denote movements performed with vision and closed symbols indicate those performed without vision.

Table 2 *Statistical significance of effect of visual condition (vision) and target location (target) on temporal and spatial parameters for the patients and healthy subjects (group)*

	Group	Vision	Target	Group × vision	Group × target	Vision × target	Group × vision × target
Reaction time	<0.001*	0.003*	0.014*	0.98	0.22	0.95	0.78
Peak speed	<0.001*	0.34	<0.001*	0.014*	<0.001*	0.018*	0.08
Movement time	<0.001*	0.045*	<0.001*	0.026*	<0.001*	0.43	0.71
Normalized path length†	0.001*	0.28	<0.001*	0.87	0.63	0.31	0.14
Cumulative direction change (1/4)	<0.001*	0.16	<0.001*	0.48	0.041*	0.07	0.35
Cumulative direction change (2/4)	0.008*	0.28	<0.001*	0.59	0.98	0.17	0.81
Cumulative direction change (3/4)	<0.001*	0.037*	0.21	0.09	0.09	0.76	0.32
Cumulative direction change (4/4)	<0.001*	<0.001*	<0.001*	0.002*	0.027*	0.037*	0.358

*Statistically significant ($P < 0.05$) comparisons; †path length normalized to straight line distance between start and end-point.

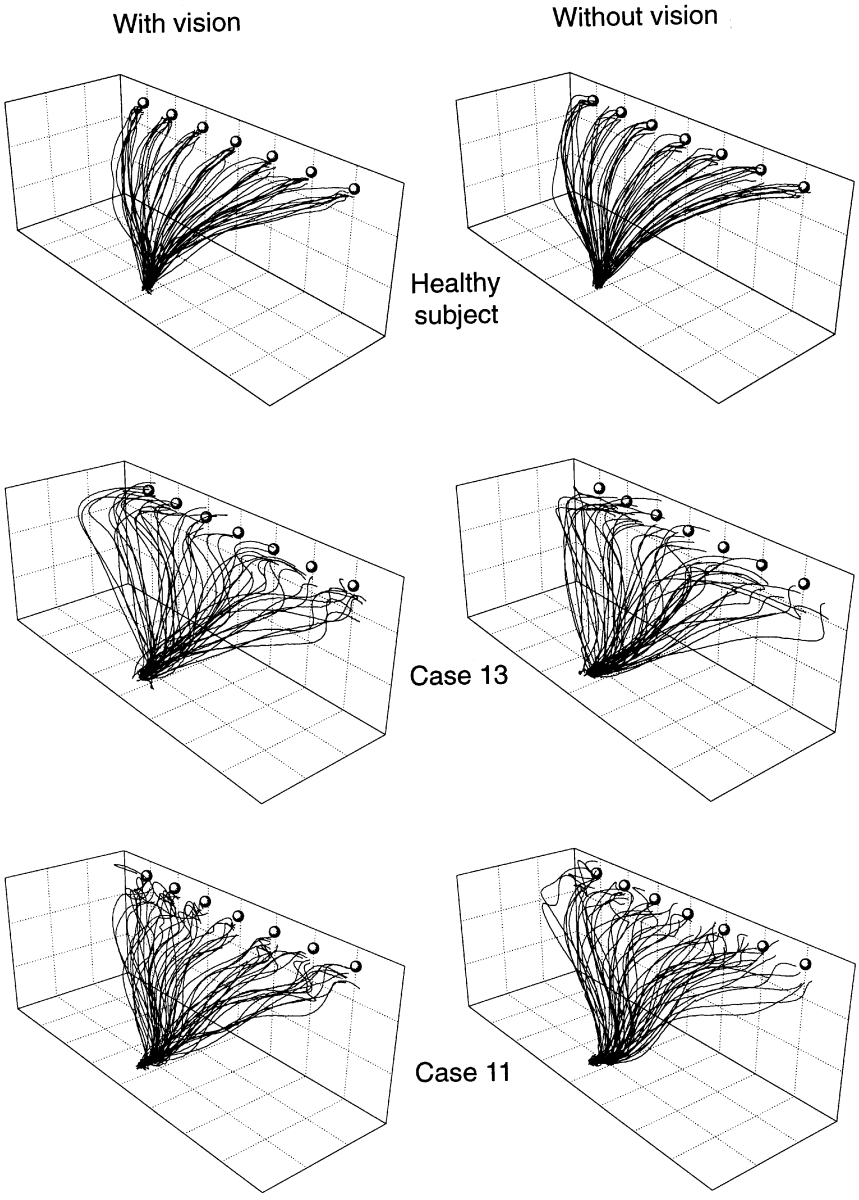

Fig. 2 Perspective view of movement paths of one healthy subject and two patients with Friedreich's ataxia. All movements within a block of trials have been superimposed. Panels on the left show movements performed with vision of target and finger. Panels on the right show movements performed in darkness. The circles indicate the position of the targets. The dotted grid projected onto each of the three planes consists of squares with 100 mm sides.

Path length

The path length was always greater than the straight-line distance, indicating that the route taken was never direct. However, for all targets the patients' path lengths were greater and therefore more circuitous than those of healthy subjects (mean + SEM path length expressed as a percentage of the straight-line distance and collapsed across targets and visual conditions: healthy subjects, 109.1 ± 2.1%; patients, 119.7 ± 1.6%; statistical analysis in Table 2). The amount of deviation from a straight line depended upon the location of the target but was insensitive to visual feedback conditions (Table 2). The least deviation from a straight-line path was observed for targets in the ipsilateral hemispace, with progressively greater deviation for more eccentric contralateral targets. In these respects patients behaved similarly to healthy subjects.

Variability of paths

The spatial variability (spread) between repeat paths to the same target varied as a function of distance travelled along the path in both healthy subjects and patients. Typically, the spread would increase steadily with distance, reach a maximum value and thereupon decrease until the end-plane

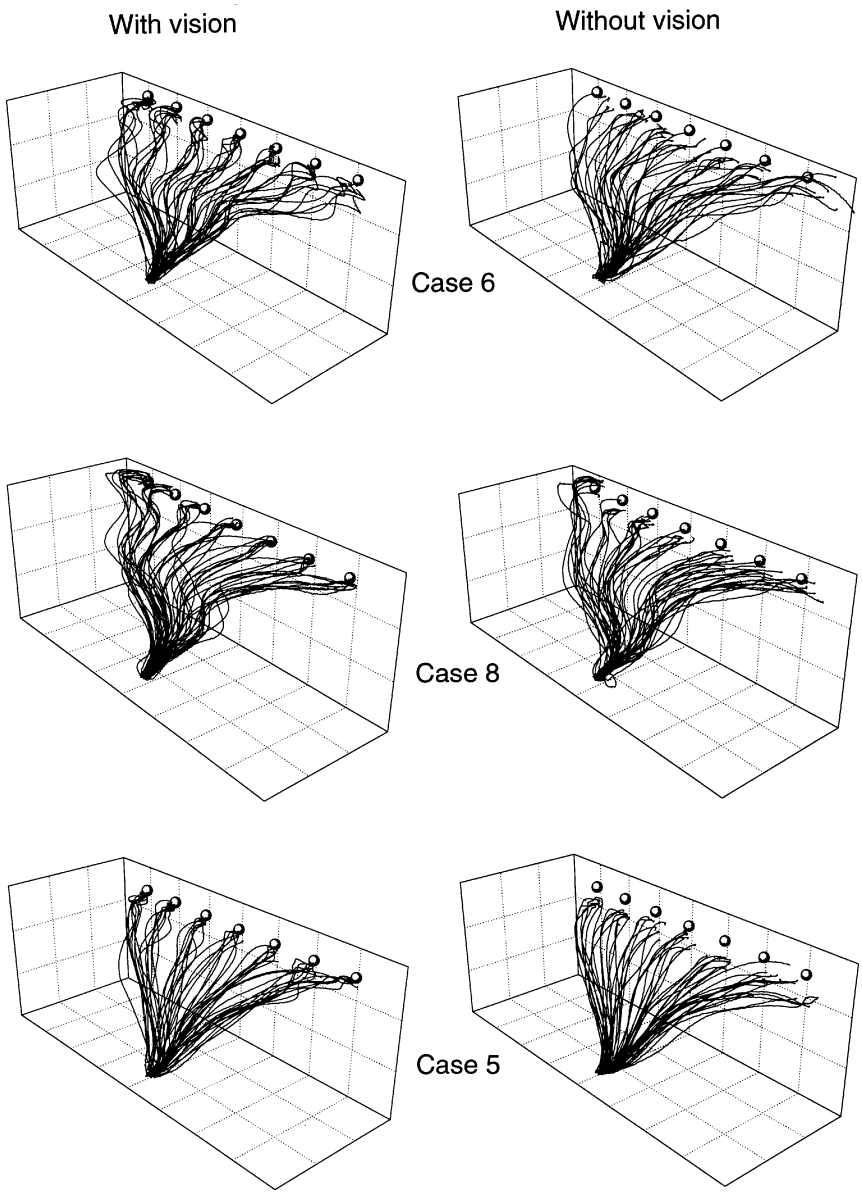

Fig. 3 Perspective view of movement paths of three other patients with cerebellar ataxia. Legend as for Fig. 2.

was reached (Fig. 4A). This pattern of divergence of paths followed by convergence was seen as often when moving in darkness as when visual feedback was available. More rarely, the paths would diverge steadily throughout, producing maximum spread at the end-plane.

For healthy subjects the maximum spread was about the same for the two visual conditions, but there was less convergence as the end-plane was approached when moving in darkness (Fig. 4C). This resulted in greater spread of the final finger position at the end-plane when visual feedback was not available. The greater convergence of paths with vision indicates that visual information was used to make mid-course adjustments to some or all of these movements.

The repeat paths of patients were characterized by being more loosely bundled throughout, giving greater maximum spread as well as greater end-plane spread compared with healthy subjects (main effect of group, $P = 0.004$; Fig. 4C). The greater spread of the patients' paths was apparent at an early stage of the movement, being statistically significant at the first cut of 5% distance along the path (Fig. 4B). This early spread, like the maximum spread, was not influenced by the visual feedback conditions.

The patients' paths, in common with those of the healthy subjects, converged under both visual conditions. However, visual feedback had greater effect than normal on the patients' end-plane spread [three-factor (group $\times$ vision $\times$ measurement plane) interaction, $P = 0.019$; Fig. 4C]. This greater reduction in end-point variability with vision may stem from the fact that the patients' movements were initially more variable and inaccurate, thereby allowing vision-based

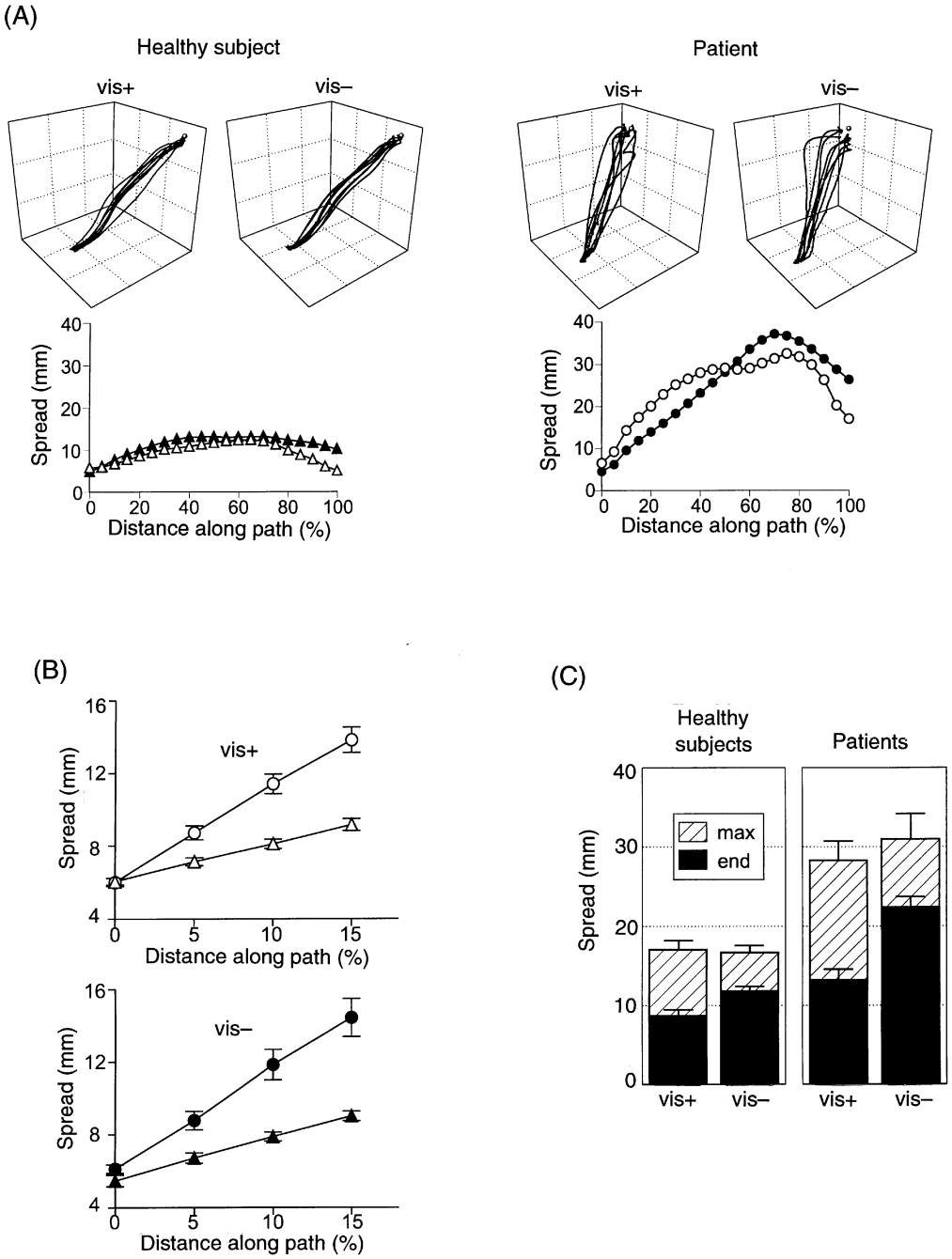

Fig. 4 Spatial variability between paths to the same target. The spread of paths was estimated at 5% intervals of the path. Two examples, one from a healthy subject and one from a patient (Case 14) are shown in **A**. The graphs at the top show perspective superimposed views of the paths. The dotted grid projected onto the three planes describe 100 mm squares. The graphs at the bottom of **A** show the spread of paths for the same examples plotted against the proportion of path travelled when vision was available (open circles or triangles) and when moving in darkness (filled circles or triangles). **B** shows the spread of paths at the initial 5% cuts. Triangles denote healthy subjects and circles denote patients. Movements were performed either with vision (open symbols) or without vision (closed symbols). Patients showed significantly more spread at the 5% cut either with vision ($P < 0.01$) or without vision ($P < 0.01$). **C** illustrates group mean ($\pm$ SEM) data of the maximum and the end plane spread of paths obtained by averaging these values across all targets for each subject.

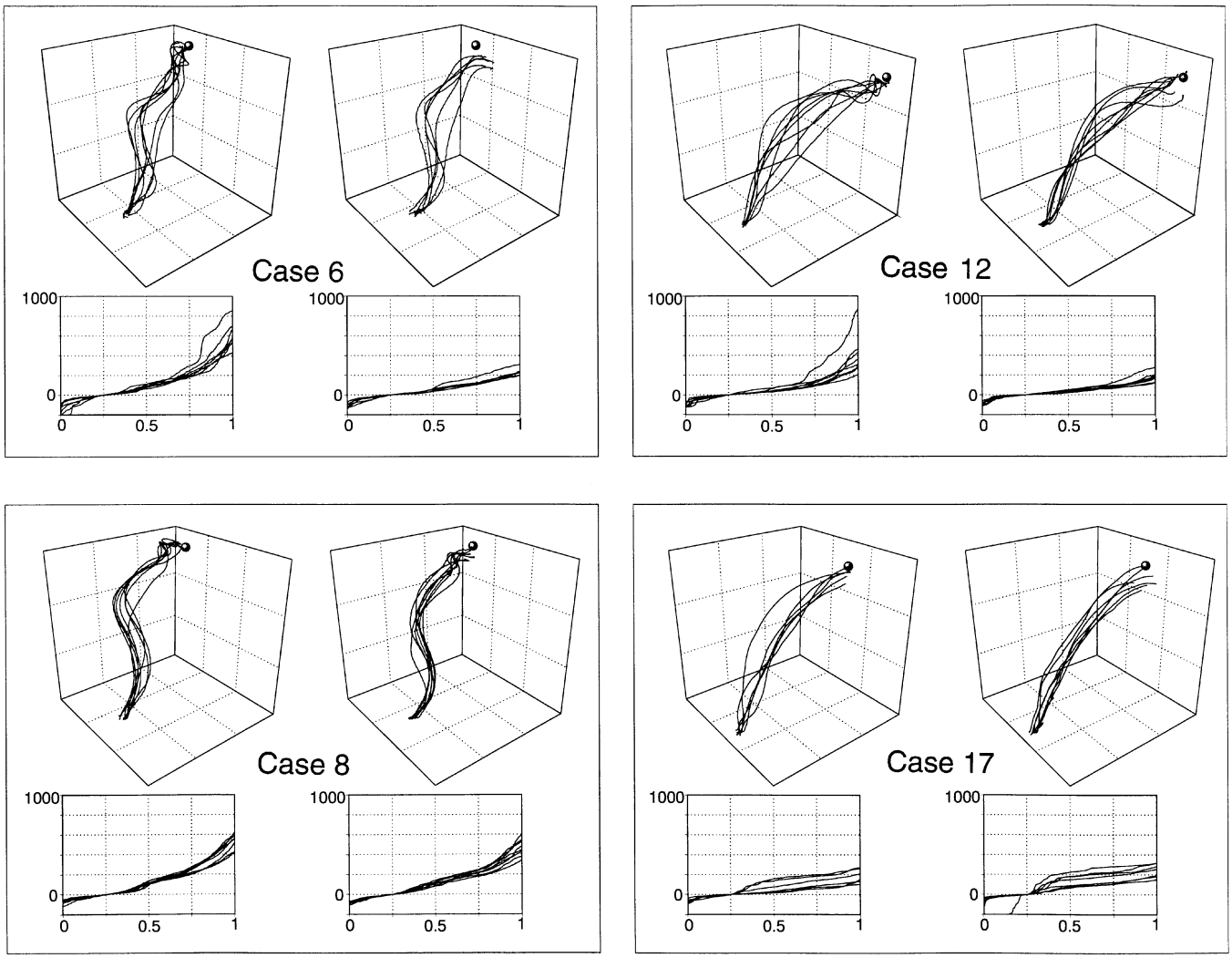

Fig. 5 Direction change along the path. Examples are shown of four patients who exhibited different types of behaviour. For each panel the top graphs illustrate perspective views of superimposed paths to a single target when vision was available (*left*) and when moving in darkness (*right*). Underneath is plotted superimposed the cumulative direction change (ordinate) against proportion of path travelled (abscissa) for each of these movements. These traces have been shifted vertically to align them at a point when 25% of the path had been travelled. Note that patients illustrated in top panels show a marked reduction in cumulative direction over the last quarter of the path when deprived of vision, whereas those illustrated in the bottom panels show little change.

corrections to have a more dramatic effect. Nevertheless, the implication is that patients had made substantial, and successful, midcourse adjustments to their paths based on visual information.

Direction changes

Visual inspection of the patients' paths showed that they would often curve and change direction in complex and idiosyncratic ways. Figure 5 shows examples of repeat movements to one target from four patients. One class of curve seemed relatively insensitive to visual feedback and would appear as snaking movements towards the target (e.g. Cases 6 and 8 in Fig. 5). When present, these deviations would be largely reproduced in every movement to the same target. A second class of curves was seen mainly towards the end of a movement and seemed to be relatively more affected by visual conditions, being less conspicuous when moving in darkness (e.g. Cases 6 and 12 in Fig. 5). These later deviations were more variable in their form for repeat movements to the same target. Case 17 (Fig. 5) showed neither of these types of behaviour. In Fig. 5, underneath each family of paths is shown the cumulative direction change for each movement plotted against normalized distance travelled along the path. These examples have been chosen to illustrate that cumulative direction change does appear to reflect deviations and curves in the path and to be a particularly sensitive indicator of the smaller deviations in the path that occur towards the end of the movement.

The group mean cumulative direction change over each quarter of the path to each target is shown in Fig. 6 (statistical analysis in Table 2). Greater quantities of direction change

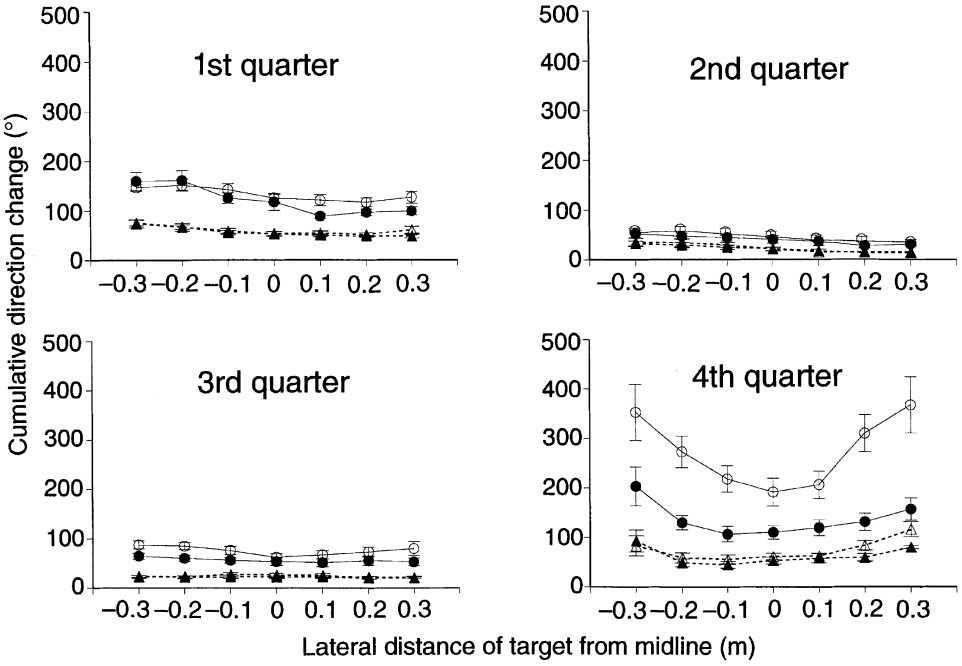

Fig. 6 Cumulative direction change over four quarters of the path to each of the seven targets. Mean (± SEM) values are shown separately for patients (circles, solid lines) and healthy subjects (triangles, dashed lines). Open symbols are from movements performed with vision and filled symbols from those performed in darkness.

occurred in the first and last quarters than in the second and third quarters. Some targets yielded greater direction changes than others, but this depended on which quarter of the path was considered. Nevertheless, for both visual conditions the patients' cumulative direction change was greater than normal for all four quarters of the movement path to all targets. A dramatic effect of vision occurred during the final quarter of the path. For the fourth quarter, both groups of subjects produced a greater amount of direction change when visual feedback was available, but the magnitude of this effect was considerably greater for the patients. With vision, the patients' mean cumulative direction over this final quarter increased with targets further from the subject's midline.

Constant end-point errors

An obvious feature of many of the patients' movements was a marked tendency to point consistently to the same wrong place on the target board when moving in darkness (Fig. 7). As illustrated in Fig. 7A, for the patient group overall there was a tendency to point below the targets in the dark. However, there were considerable differences within the patient group in the pattern of direction and amplitude of systematic errors to the different targets. Some examples are shown in Fig. 7B. The direction of error ranged from being similar for all targets (e.g. Case 3) to being clearly target-sensitive (e.g. Case 17). The amplitude of the error was usually influenced by target location but, again, the pattern varied between patients. For these reasons, the group behaviour was quantified by taking the mean magnitude of constant error averaged across all targets (Fig. 7C); the direction of error was not considered further.

When visual feedback was available the patients' constant errors (two-dimensional distance of mean finger position from target position at the end-plane) were not significantly greater than those of healthy subjects (*t* test; $P = 0.21$). When moving in darkness, the patients' constant errors were considerably greater than normal ($P = 0.001$). Because of potential difficulties in interpreting the distance between finger and target location (see Methods), the distance between the mean finger position with and without visual feedback was computed (i.e. irrespective of finger position relative to target). Again, this measure of constant error was significantly greater for the patients ($P < 0.001$).

Comparison of behaviour between subgroups of patients

This heterogeneous group of patients was separated into subgroups according to well-defined diagnostic criteria (see Methods). A clinical assessment of various motor features of arm ataxia, based on videotape recordings of each patient, failed to reveal any clear differences between the patient subgroups. Thus, the severity of clumsiness of repetitive hand and finger movements, the proximal instability of the outstretched arms or the extent of dysmetria did not distinguish between the various types of cerebellar ataxia. Between subgroups, patients seemed to have similar clinical deficits, although these varied in severity from patient to

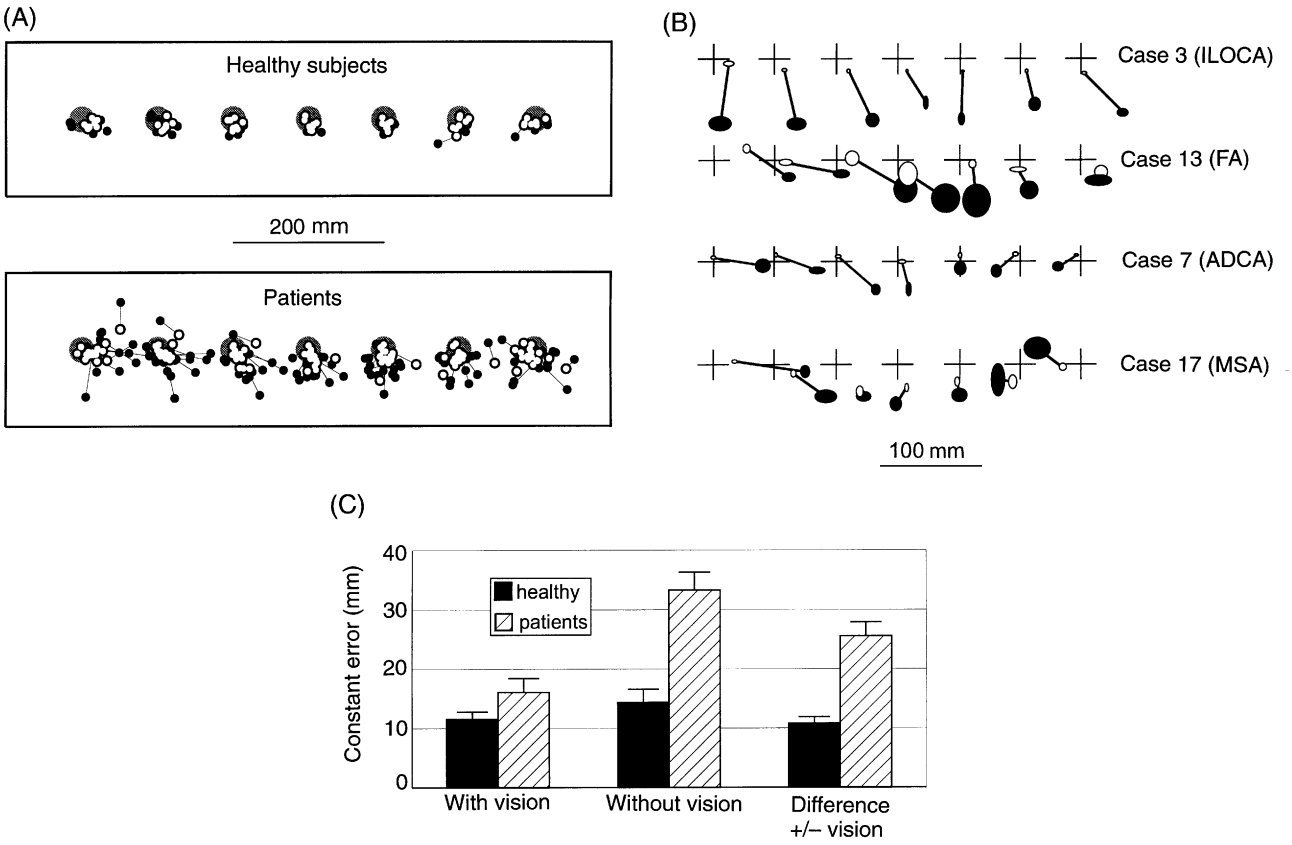

Fig. 7 End-point constant errors. **A** shows the mean final position of the finger as it passes through the end-plane for all subjects to each target. Open circles show the mean end position for movements performed with vision and filled circles for those performed in darkness. Data pairs from each subject are joined by a line. Large shaded circles indicate the position of the targets. **B** shows a variety of patterns of direction and magnitude of constant error seen in different patients. In this diagram each target is represented by a cross. Note that distance between targets is not to scale. The spatial distribution of final finger position to a target is represented by an ellipse. The centre of the ellipse is at the mean end position of the finger and the length of the horizontal and vertical axes of the ellipse is equal to 2×SEM of the horizontal and vertical distributions of finger end position. Open ellipses are from movements performed with vision and filled ellipses from those performed without vision. The overall magnitude of constant error is shown as group mean (+ SEM) data in **C** in which three measures of constant error are plotted. The first two measures indicate the distance between the mean final finger position and the target, with and without vision. The third measure indicates the distance between the mean final finger position with vision and that without vision, irrespective of target position. These data were obtained by averaging the values across all targets for each subject. ILOCA = idiopathic late–onset cerebellar ataxia; FA = Friedreich's ataxia; ADCA = autosomal dominant cerebellar ataxia; MSA = multiple system atrophy.

patient. However, for a number of the temporal and spatial parameters derived from the experimental session there were indications of differences between some subgroups.

Of particular interest was whether patients with a predominant disruption to the cerebellum and its outflow pathways differed from those patients with damage mainly to cerebellar inputs. For this analysis (Table 3), patients classified as having cerebellar ataxia due mainly to intrinsic cerebellar degeneration [subgroups ADCA (autosomal dominant cerebellar ataxia type I), ILOCA (idiopathic late-onset cerebellar ataxia) and ARLOCA (autosomal recessive late-onset cerebellar ataxia)] were lumped together and compared with patients with Friedreich's ataxia, in whom the major pathology lies in the spinocerebellar pathways. There were significant differences for all three temporal parameters. Patients with Friedreich's ataxia tended to have longer reaction times but moved faster and with shorter movement times. For the spatial parameters, path length and constant end-point errors were not significantly different between the two groups. However, the spatial variability of paths tended to be greater for patients with Friedreich's ataxia, whereas the amount of direction change with visual guidance over the final quarter was less for these patients.

Discussion

This study examined the temporal and spatial characteristics of upper limb ataxia in patients with various types of cerebellar degeneration, with particular reference to the influence of vision on ataxic movements. Free, unrestrained reaching and pointing movements of the arm, with emphasis on accuracy rather than speed, allowed the full expression of ataxia. Errors in the control and co-ordination of upper limb movement were reflected in the motion of the fingertip,

Table 3 *Comparison of some movement parameters* between patients with Friedreich's ataxia and patients with cerebellar ataxia due to intrinsic cerebellar degeneration (ADCA, ILOCA and ARLOCA)*

	RT	MT	VEL	MAX VAR VIS	MAX VAR NVIS	END VAR VIS	END VAR NVIS	CDC VIS	CDC NVIS
Friedreich's ataxia	482 (20)	728 (53)	1138 (55)	36.5 (4.5)	41.2 (6.9)	16.0 (1.9)	25.5 (2.6)	250 (31)	125 (21)
Cerebellar ataxia	410 (11)	907 (44)	920 (50)	24.0 (1.6)	26.6 (2.7)	10.5 (1.4)	20.0 (1.6)	361 (28)	163 (24)
P	0.007	0.036	0.025	0.015	0.052	0.043	0.092	0.032	0.29

CDC NVIS = cumulative direction change (degrees) without vision; CDC VIS = cumulative direction change (degrees) with vision; END VAR NVIS = spread of end position (mm) without vision; END VAR VIS = spread of end position (mm) with vision; MAX VAR NVIS = maximum spread of paths (mm) without vision; MAX VAR VIS = maximum spread of paths (mm) with vision; MT = movement time (ms) with and without vision combined; RT = reaction time (ms) with and without vision combined; VEL = peak speed (mm/s) with and without vision combined. *Mean (SEM).

in much the same way as ataxia is recognized during clinical examination. A number of differences were observed in the temporal and spatial characteristics of movements performed by patients compared with those of healthy subjects.

Temporal characteristics

Patients with limb ataxia took longer to initiate movement and movements were slower than normal, in keeping with the well-documented prolongation of reaction times and slowness of movement in human cerebellar disease (Holmes, 1939; Beppu *et al.*, 1984; Hallett *et al.*, 1991; Hore *et al.*, 1991; Bonnefoi-Kyriacou *et al.*, 1995; Bastian *et al.*, 1996) and in non-human primates with cerebellar dysfunction (Thach, 1975; Meyer-Lohmann *et al.*, 1977; Trouche *et al.*, 1980). The slowness of our patients may have been partly due to the instructions, which emphasized accuracy over speed. However, this is unlikely to be the main cause of slowness given the results of Bastian *et al*. (1996). In their experiments, subjects were asked to produce movements which were (i) slow and accurate, (ii) fast and accurate, or (iii) as fast as possible with no constraint on accuracy. They showed that cerebellar patients moved slower than normal for all three instructions. Nevertheless, Bastian *et al*. (1996) interpreted the slowness as a possible compensatory strategy, and this may also have been the case in the present study. Thus, moving at a slower speed may reduce or minimize other motor deficits.

Spatial characteristics

A number of spatial abnormalities were observed in our patients. First, the spatial paths described by the ataxic fingertip were more circuitous than normal, leading to longer path lengths. This has been described previously for arm movements of monkeys following cerebellar ablation (Gilman *et al.*, 1976) and for human subjects with cerebellar disease (Bastian *et al.*, 1996). Secondly, there were excessive changes in direction of the fingertip of ataxic limbs throughout the range of movement but especially during the last quarter of the movement. Thirdly, ataxic movements were less accurate than normal. Inaccuracy was present in two forms: increased spatial variability between paths to the same target, and the appearance of constant errors at the end of movement when moving in darkness. Constant pointing errors have been observed previously in monkeys after dentate nucleus cooling or ablation (Beaubaton and Trouche, 1982).

Effect of vision on ataxia

The main aim was to identify and measure characteristics of ataxia and to ascertain which of those characteristics are affected or influenced by vision. In the time domain, ataxic movements were slower and had a more prolonged end-phase when patients were able to see their finger and the target compared with when they moved in darkness. This was in contrast to the healthy subjects, who tended to move faster when vision was available. The extra slowing of the patients with vision was probably a compensatory manoeuvre which enabled them to perform more accurately and to give them the time needed to correct their movements in midflight. In the spatial domain, the difference between the vision and no-vision conditions was most apparent towards the end of the movement. Thus, with vision the variability between paths was reduced as the target was approached and constant errors at the end of movement were eliminated. These findings suggest strongly that the patients were able to use visual information successfully to improve their accuracy. However, one striking effect in the patients was the dramatic increase in the amount of direction change over the final quarter, when visual feedback was available. This was one characteristic of ataxia that was clearly exacerbated when the limb was moving under visual guidance. Other spatial characteristics, such as the patients' long, circuitous paths, were the same length irrespective of whether vision was available or not. Similarly, the variability between paths, which was present at the beginning of movement, remained unchanged by visual conditions for most of the movement.

These various characteristics of ataxia correlate with the fundamental clinical signs of an ataxic limb. The following

discussion explores some possible explanations of the influence of vision on these measurements and the implications of these findings for mechanisms underlying ataxia. For this purpose we shall split the movement into (i) movement preparation, (ii) movement execution, and (iii) movement correction, and discuss each phase separately.

Disorders of movement preparation

Under the conditions of our experiment, visual information would be critical and used at an early stage in preparing movement. The required final finger position is specified by presentation of a visual target just before each movement. When attempting to move the finger to the target in darkness this early retinal image provides the only source of information about the destination of the fingertip. During darkness, the motor instructions to the arm must be either completely determined before movement commences or else adjusted during movement according to a memory of the target location together with an assessment of the developing limb trajectory. In either case, processing of the initial retinal image of target position is required in order to relate the target position to the finger position. One possibility is that both target and finger position are represented internally in a common frame of reference by taking into account the position of the image on the retina and the relative positions of all the body segments linking the eyes to the finger (Soechting and Flanders, 1989*a*, *b*). This internal representation could then be used for the final stage of computing appropriate muscle activity to take the finger to the target. The movement errors of our patients may arise from errors occurring within these preparatory processes.

Similar types of spatial error were seen in patients with Friedreich's ataxia and in patients with cerebellar ataxia, although some subtle differences were observed between the two groups. Those with Friedreich's ataxia had longer reaction times and greater path variability, whereas patients with intrinsic cerebellar degeneration were slower and showed greater end-phase oscillation. The pathology is quite different for these two groups, the brunt of the damage falling on spinocerebellar pathways in Friedreich's ataxia and on the cerebellum and its output pathways in cerebellar ataxia (Harding, 1996). If the cerebellum contributes in some way to the computation of goal-directed muscle activity then its dysfunction in patients with cerebellar ataxia might well lead to the spatial errors observed. Similarly, distortion of proprioceptive information denoting limb position, due to damage to spinocerebellar pathways in patients with Friedreich's ataxia, may create similar types of spatial error.

A number of diverse findings have pointed to a role of the cerebellum in movement preparation. Ataxic patients show prolongation of reaction time (Holmes, 1939; Beppu *et al.*, 1984; Bonnefoi-Kyriacou *et al.*, 1995), abnormalities of the premovement readiness potential (Shibasaki *et al.*, 1978), problems planning movement sequences (Inhoff *et al.*, 1989) and abnormalities in the programming of ballistic movements (Hallett *et al.*, 1975, 1991; Hore *et al.*, 1991). The present results provide a further link between ataxia and disordered preparatory processes. During the interval between target presentation and movement initiation the brain computes the motor pattern required to move the limb to the target. In agreement with other studies (see above), part of this interval (the reaction time) was prolonged in the patient group. Two types of spatial error can occur in this early computation. The output may contain random or variable errors such that when the same movement is attempted on different occasions the limb will move in a different direction each time. The output may also contain a constant error which is identical each time the same movement is attempted and which consistently takes the limb in the same, wrong direction. Both types of error were present in the ataxic movements of the patient group. Variable error was reflected in the spread of paths measured at an early stage of the movement. Constant error was reflected in the mean final position of the finger achieved in darkness without corrective visual feedback. We suggest that both types of error reflect programming errors encoded in the initial movement commands.

Disorders of movement execution

Once the movement is computed the limb is launched into its initial trajectory. Vision has no effect on this part of the movement. As the movement develops the finger describes a more or less curved path. The route taken by patients' fingers was more circuitous than normal. Often patients would move their finger along paths that snaked towards the target in an idiosyncratic and repeatable manner. Again, vision had no measurable effect on the route taken. At what point, in darkness, proprioceptive feedback comes into play to alter the limb trajectory is difficult to judge. Therefore, it is not possible to deduce whether the abnormal paths were the natural consequence of inappropriate programming of muscle activity or the result of proprioceptive feedback incorrectly modifying the central commands. Nevertheless, this behaviour probably arises from the faulty interjoint co-ordination reported previously in patients with cerebellar damage (Holmes, 1939; Becker *et al.*, 1991; Bastian and Thach, 1995; Bastian *et al.*, 1996). In these patients, the elbow and shoulder joints tended to move sequentially rather than simultaneously. Bastian *et al.* (1996) suggested that this deficit was due to an inability of cerebellar patients to take account of the dynamic interaction torques that occur between the joints of a multijointed limb. They suggested further that such relatively independent joint movement is a compensatory strategy aimed at simplifying the movement because of the patients' inability to accurately move both joints simultaneously. Whatever the reason for such decomposition of movement, inco-ordination of this sort would lead to the type of curved paths observed in our patients. An important point from the current perspective is that this characteristic of ataxia was immune from visual influence.

Disorders of movement correction

Illumination of the target and finger provided the subject with an opportunity to assess the accuracy of the developing movement and make fine adjustments based on the visual information received. The dramatic improvement in mean end-point accuracy coupled with the convergence of repeat paths with vision indicated that patients used visual information successfully to make midflight adjustments. A similar reliance upon visual information for accurate performance has been reported for ataxic patients performing single-joint tracking tasks (Beppu *et al.*, 1987; Cody *et al.*, 1993; Haggard *et al.*, 1995). However, the present results suggest that the end-phase of the movement, during which adjustments occurred under visual guidance, was not normal. It was often prolonged and characterized by excessive deviations or wobbles in the path. This phenomenon was reflected in the increased cumulative direction change over the last quarter of the path, which was less apparent when patients moved in darkness. Comparable effects of vision in generating some of the oscillations of ataxic arm movements have been described previously for pursuit or tracking arm movements of patients with cerebellar degeneration (Beppu *et al.*, 1987), patients with severe head injury (Haggard *et al.*, 1995) and for a single patient with a cerebellar neoplasm performing a whole-arm reaching movement (Haggard *et al.*, 1994).

Arguably, the large cumulative direction change could accrue from the poorer initial accuracy of the patients' movements creating the need for larger midflight adjustments. However, we favour the view that the end-phase deviations seen in the majority of patients were abnormal and the large cumulative direction change was greater than that warranted by the initial inaccuracy. This implies that the excessive end-phase deviations seen in many patients result from errors in the visual guidance mechanism even though, paradoxically, this mechanism was used successfully to improve final accuracy. The operation of such visual correction requires correct judgement of the pattern of muscle activity required to put the arm back on target. These deviations, therefore, are likely to be the expression of a visual guidance system producing corrections which themselves contain errors requiring further correction. It is possible that this process is erroneous for the very reasons that the initial pattern of muscle activity was misjudged.

Computation versus adaptation of movement by the cerebellum

Our results suggest that one core deficit responsible for ataxia is an inability to calculate the correct muscle forces required to direct the upper limb with accuracy to a visual target, either when the limb is moved from rest or when corrections are made once the limb is under way. This suggests that the cerebellum contributes directly or indirectly to the processes that transform the retinal image and limb position information into motor instructions.

The cerebellum receives limb proprioceptive information directly via spinocerebellar pathways. It does not receive direct visual input but receives powerful inputs from the posterior parietal cortex (area 7) via the pons (Glickstein *et al.*, 1985). Area 7 receives information from visual areas of cortex and is thought to play an important role in transforming visual space from retinotopic coordinates into a head or body coordinate system (Andersson, 1985). Cerebellar output nuclei project to the motor and premotor areas of the cortex via the thalamus. Therefore the cerebellum is well placed to operate on limb position information and on body-referenced visual information regarding target location, and to contribute to the final stage of assembling the motor commands that take the finger to the target.

Some firing properties of cerebellar neurons are compatible with this idea. First, the time of activation of the cerebellum is appropriate. In the monkey, cerebellar nuclei neurons usually fire well before the onset of movement (Thach, 1970*a*) and tend to fire before movement-related neurons in the cerebral motor cortex (Thach, 1975). Cooling the dentate nucleus produces a delay in the firing of movement-related motor cortical neurons and a similar delay in the reaction time to movement (Meyer-Lohmann *et al.*, 1977). Secondly, the firing patterns of cerebellar neurons carry spatial information regarding the intended movement direction. The firing rate of cerebellar nuclei neurons and Purkinje cells is usually different for movements in different directions (Thach, 1970*a*, *b*, 1978; Harvey *et al.*, 1977, 1979). Furthermore, the firing pattern of many different types of cerebellar neurons contains detailed directional information at an early stage during the reaction time interval between presentation of a visual target and initiation of the movement (Fortier *et al.*, 1989).

In essence, the above idea presupposes that the spatial errors arise from a distortion introduced by diseased structures which continue to exert influence on movement production. An alternative possibility is that the cerebellum is not directly involved in the computation of goal-directed muscle activity but instead exerts an indirect, adaptive influence on this computation. The movement errors reported here, especially the constant end-point errors, may then represent a failure to adapt or recalibrate the visually and proprioceptively determined motor pattern. Thus, rather than the diseased structures distorting the computation, they may fail to contribute to its refinement. This would help to explain why chronically disabled patients had apparently not learned to compensate for their constant reaching errors and why the misreaching in the dark persisted even though feedback of the error was provided at the end of each movement. Interestingly, Beaubaton and Trouche (1982) demonstrated similar constant errors in monkeys following dentate nucleus cooling or ablation, and that after dentate ablation the errors remained remarkably stable over several months, even after limb oscillations and dispersion of end position had recovered. It is also in keeping with other experimental findings, for example, the failure of some cerebellar patients to show the

normal adaptation of arm movements to visual input that occurs when wearing displacing prisms for a period of time (Weiner *et al.*, 1983; Martin *et al.*, 1996).

Conclusions

We suggest that one key aspect of ataxic reaching movements is a failure to compute with accuracy, from visual and proprioceptive information, an appropriate pattern of muscle activity to drive the finger to a specific location in space. This leads to excessive variable and constant spatial errors of the fingertip as it is launched towards the target. Although ataxic patients are able to use visual guidance of the limb to improve their accuracy, the same deficit may underlie the abnormal deviations of the limb as the target is approached under visual guidance. Thus, midflight, visually based corrections to the movement also contain errors requiring further correction. However, it appears unlikely that all facets of ataxia stem from a single pathophysiological mechanism. Some of the abnormal characteristics, such as slowness and decomposition of movement (which contributes to the excessively circuitous paths of the finger), may even result from voluntary, compensatory strategies (Bastian *et al.*, 1996).

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References

Andersen RA, Essick GK, Siegel RM. Encoding of spatial location by posterior parietal neurons. Science 1985; 230: 456–8.

Bastian AJ, Thach WT. Cerebellar outflow lesions: a comparison of movement deficits resulting from lesions at the levels of the cerebellum and thalamus. Ann Neurol 1995; 38: 881–92.

Bastian AJ, Martin TA, Keating JG, Thach WT. Cerebellar ataxia: abnormal control of interaction torques across multiple joints. J Neurophysiol 1996; 76: 492–509.

Beaubaton D, Trouche E. Participation of the cerebellar dentate nucleus in the control of a goal-directed movement in monkeys. Effects of reversible or permanent dentate lesion on the duration and accuracy of a pointing response. Exp Brain Res 1982; 46: 127–38.

Becker WJ, Morrice BL, Clark AW, Lee RG. Multi-joint reaching movements and eye-hand tracking in cerebellar inco-ordination: investigation of a patient with complete loss of Purkinje cells. Can J Neurol Sci 1991; 18: 476–87.

Beppu H, Suda M, Tanaka R. Analysis of cerebellar motor disorders by visually guided elbow tracking movement. Brain 1984; 107: 787–809.

Beppu H, Nagaoka M, Tanaka R. Analysis of cerebellar motor disorders by visually-guided elbow tracking movement. 2. Contribution of the visual cues on slow ramp pursuit. Brain 1987; 110: 1–18.

Bonnefoi-Kyriacou B, Trouche E, Legallet E, Viallet F. Planning and execution of pointing movements in cerebellar patients. Mov Disord 1995; 10: 171–8.

Cody FW, Lovgreen B, Schady W. Increased dependence upon visual information of movement performance during visuo-motor tracking in cerebellar disorders. Electroencephalogr Clin Neurophysiol 1993; 89: 399–407.

Day BL. Influence of vision on the trajectory of human arm pointing movements in three-dimensional space. J Physiol (Lond) 1994; 476.P: 23P.

Day BL, Thompson PD, Harding AE, Marsden CD. The influence of vision on the accuracy of reaching movements in patients with cerebellar disease. J Physiol (Lond) 1992; 452: 271P.

Fisk JD, Goodale MA. The organization of eye and limb movements during unrestricted reaching to targets in contralateral and ipsilateral visual space. Exp Brain Res 1985; 60: 159–78.

Fortier PA, Kalaska JF, Smith AM. Cerebellar neuronal activity related to whole-arm reaching movements in the monkey. J Neurophysiol 1989; 62: 198–211.

Gilman S, Carr D, Hollenberg J. Kinematic effects of deafferentation and cerebellar ablation. Brain 1976; 99: 311–30.

Glickstein M, May JG, Mercier BE. Corticopontine projection in the macaque: the distribution of labelled cortical cells after large injections of horseradish peroxidase in the pontine nuclei. J Comp Neurol 1985; 235: 343–59.

Haggard P, Jenner J, Wing A. Co-ordination of aimed movements in a case of unilateral cerebellar damage. Neuropsychologia 1994; 32: 827–46.

Haggard P, Miall RC, Wade D, Fowler S, Richardson A, Anslow P, et al. Damage to cerebellocortical pathways after closed head injury: a behavioural and magnetic resonance imaging study. J Neurol Neurosurg Psychiatry 1995; 58: 433–8.

Hallett M, Shahani BT, Young RR. EMG analysis of patients with cerebellar deficits. J Neurol Neurosurg Psychiatry 1975; 38: 1163–9.

Hallett M, Berardelli A, Matheson J, Rothwell JC, Marsden CD. Physiological analysis of simple rapid movements in patients with cerebellar deficits. J Neurol Neurosurg Psychiatry 1991; 53: 124–33.

Harding AE. Cerebellar and spinocerebellar disorders. In: Bradley WG, Daroff RB, Fenichel GM, Marsden CD, editors. Neurology in clinical practice. 2nd ed. Boston: Butterworth-Heinemann; 1996. p. 1773–92.

Harvey RJ, Porter R, Rawson JA. The natural discharges of Purkinje cells in paravermal regions of lobules V and VI of the monkey's cerebellum. J Physiol (Lond) 1977; 271: 515–36.

Harvey RJ, Porter R, Rawson JA. Discharges of intracerebellar nuclear cells in monkeys. J Physiol (Lond) 1979; 297: 559–80.

Holmes G. The cerebellum of man. Brain 1939; 62: 1–30.

Hore J, Wild B, Diener HC. Cerebellar dysmetria at the elbow, wrist, and fingers. J Neurophysiol 1991; 65: 563–71.

Inhoff AW, Diener HC, Rafal RD, Ivry R. The role of cerebellar structures in the execution of serial movements. Brain 1989; 112: 565–81.

Martin TA, Keating JG, Goodkin HP, Bastian AJ, Thach WT. Throwing while looking through prisms. I. Focal olivocerebellar lesions impair adaptation. Brain 1996; 119: 1183–98.

Meyer-Lohmann J, Hore J, Brooks VB. Cerebellar participation in generation of prompt arm movements. J Neurophysiol 1977; 40: 1038–50.

Shibasaki H, Shima F, Kuroiwa Y. Clinical studies of the movement-related cortical potential (MP) and the relationship between the dentatorubrothalamic pathway and readiness potential (RP). J Neurol 1978; 219: 15–25.

Soechting JF, Flanders M. Sensorimotor representations for pointing to targets in three-dimensional space. J Neurophysiol 1989a; 62: 582–94.

Soechting JF, Flanders M. Errors in pointing are due to approximations in sensorimotor transformations. J Neurophysiol 1989b; 62: 595–608.

Stein JF. Role of the cerebellum in the visual guidance of movement. Nature 1986; 323: 217–21.

Stein JF, Glickstein M. Role of the cerebellum in visual guidance of movement. [Review]. Physiol Rev 1992; 72: 967–1017.

Thach WT. Discharge of cerebellar neurons related to two maintained postures and two prompt movements. I. Nuclear cell output. J Neurophysiol 1970a; 33: 527–36.

Thach WT. Discharge of cerebellar neurons related to two maintained postures and two prompt movements: Purkinje cell output and input. J Neurophysiol 1970b; 33: 537–47.

Thach WT. Timing of activity in cerebellar dentate nucleus and cerebral motor cortex during prompt volitional movement. Brain Res 1975; 88: 233–41.

Thach WT. Correlation of neural discharge with pattern and force of muscular activity, joint position, and direction of the intended movement in motor cortex and cerebellum. J Neurophysiol 1978; 41: 654–76.

Trouche E, Beaubaton D. Initiation of a goal-directed movement in the monkey. Role of the cerebellar dentate nucleus. Exp Brain Res 1980; 40: 311–21.

Weiner MJ, Hallett M, Funkenstein HH. Adaptation to lateral displacement of vision in patients with lesions of the central nervous system. Neurology 1983; 33: 766–72.

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