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Dissociation of 'on-line' and 'off-line' visuomotor control of the arm by focal lesions in the cerebellum and brainstem

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Abstract

Visuomotor control of the arm was assessed in a single case study of a subject with focal lesions in the cerebellum and brainstem. A dissociation between 'on-line' and 'off-line' visuomotor control was revealed: impairments in 'on-line' visuomotor control included inaccuracy of tracking velocity, increase in spatial pointing variability and a delay in simple reaction time; whereas the patient was able to adapt to a gain change in 'off-line' visual feedback during a pointing task, and his adaptation was less affected than that of control subjects by trial-to-trial random fluctuations in 'off-line' visual feedback. We conclude that focal damage in the cerebellar peduncles may be principally responsible for this dissociation.

Keywords: Visuomotor control; Tracking; Adaptation; Cerebellum; Brainstem

The cerebellum has complex functions concerned with sensorimotor integration and plays an important role in movement control by refining the motor command with temporal and spatial parameters [3,6,10]. In previous studies on a group of patients with multiple sclerosis (MS), we suggested that lesions in their cortico-cerebello-thalamo-cortical pathways were responsible for action tremor (AT) and impaired control of visually-guided tracking movements [8] and that AT was weighted predominantly towards the distal joint of the arm [7]. In the present report, we investigated impairment in the control of visually guided ramp tracking movements, of pre-programmed pointing movements, and of adaptation to a change in the gain of visual feedback, in one selected patient who had focal MS lesions in the cerebellum and brainstem clearly defined by magnetic resonance imaging (MRI).

A male patient, aged 46 years, right-handed, had a diagnosis of laboratory-supported definite MS. This patient was selected for the present study because he had limited symptoms rather than widespread motor deficits, and because MRI revealed focal lesions in the cerebellum and brainstem without lesions evident elsewhere in his brain. His major complaints were shaking in the upper limbs, inability to roll a cigarette, and unsteadiness when standing and walking. Clinically, AT, dysdiadochokinesis in the upper limbs, disequilibrium, weakness while standing and walking and reduced sensation below the knees were revealed. Subtle left internuclear ophthalmoplegia, but no severe nystagmus or diplopia which would interfere with the visual perception of the task were found. Ethical approval and informed consent were obtained for these studies. Focal lesions were revealed by T_2-weighted MRI images (TR 4055.0 ms, TE 90.0/2, 10 mm slices). Five healthy subjects without neurological deficits were also tested as normal controls. Ethical approval and informed consent were obtained for these studies.

Multiple focal lesions of hyperintense signal a few millimetres in diameter were seen in the white matter of the right cerebellar hemisphere and bilaterally in the cerebellar peduncles, mainly the middle and part of the inferior peduncle (Fig. 1, left) and the right cerebral peduncle (Fig. 1, right). The lesions in the right cerebellum were located latero-ventrally around the dentate nucleus [4], primarily affecting

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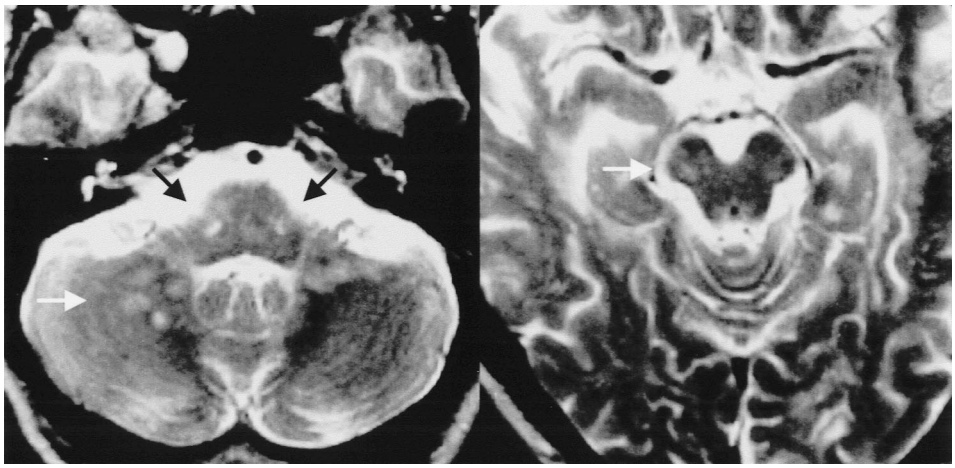

Fig. 1. T_2-weighted MRI scans showing multiple small and focal lesions in the white matter ventrally around the right dentate nuclei (white arrow, left half), in the bilateral inferior cerebellar peduncles (black arrows) and in the right cerebral peduncle (white arrow, right half).

efferent fibres from the ipsilateral cerebellar cortex; afferent cerebellar fibres may also have been affected. The lesions in the bilateral middle/inferior peduncles would have disrupted connections between the cerebellum and neighbouring brainstem structures, perhaps including olivo-cerebellar fibres. The focal lesion in the right cerebral peduncle would have damaged part of the corticospinal tract. No obvious lesions were found elsewhere in the brain although spinal lesions cannot be excluded without spinal scans.

In the 'on-line' wrist and arm ramp tracking tasks, a small hollow square target moved either horizontally for wrist tracking and reaction time tasks or circularly for arm tracking at a constant speed on a computer screen. The subject moved a low-resistance joystick to control a continuously displayed cursor either (a) by wrist flexion and extension with the forearm supported or (b) by moving the whole arm around at the shoulder joint while keeping the elbow straight [7,8]. Tremor (AT) was quantified by calculating the standard deviation of the movement velocity (SD-MV). AT was scored as distal or proximal using the ratio of wrist SD-MV relative to whole arm SD-MV. Tracking accuracy was quantified as the absolute percentage error in the movement velocity (EV) relative to the target velocity. For perfect smooth tracking the SD-MV and EV would both be zero. The frequency composition of the tracking records was computed using a Fourier transform. Visually-cued simple reaction times (SRT) were also measured using rapid wrist flexion or extension.

In the 'off-line' arm pointing task, the subject was instructed to move the right arm in a single forward movement from a fixed starting position to reach one of three visual targets presented 20 cm away from the starting position on a digitizing board; one target was central, two others were 30° to left and right. View of the arm was blocked, and arm position was displayed at the completion of each movement with a visual cursor. The digitizing table has been previously described [11]. After practise, baseline pointing movements were recorded without terminal feedback. The target/movement amplitude ratio (TM ratio) was calculated for each movement. In an exposure phase the ratio between movement amplitude and the visual feedback was then increased from 1.0 to 1.5, and assessed in a final test session without terminal feedback. Adaptation was measured as the percent change in TM ratio before and after the imposed gain change. For perfect adaptation, the change in TM ratio would be 100%. Spatial variability (SV) in final position of each movement along the movement direction was calculated, and expressed as a percentage of the mean TM ratio. For perfect pointing without a gain change, the TM ratio and SV would be 100 and 0%. Finally, in some sessions, visual

Table 1
Motor impairments assessed by visually guided tasks

		MS patient	Normal controls (mean ± SD)
1. Tracking tasks			(n = 10)
Action Tremor (SD-MV, %)			
Wrist	L	184.3*	65.8 ± 13.8
	R	156.9*	
Arm	L	41.9*	20.7 ± 3.2
	R	37.4*	
Wrist/arm AT ratio			
	L	4.4*	3.2 ± 0.5
	R	4.2*	
Tracking accuracy (EV, %)			
Wrist	L	2.0	5.6 ± 1.5
	R	12.8*	
Arm	L	36.0*	12.4 ± 12.5
	R	0.1	
Simple reaction time (ms)			
	L	423.1*	
	R	403.3*	264.6 ± 23.3
2. Pointing tasks			(n = 11)
Spatial variability (%)		16.0*	10.3% ± 2.1
Adaptation (%)		68	55% ± 36.7
Noise threshold (%)		75	30

*Values in the patient are beyond the 95% confidence range (mean ± 1.96 SD) in controls.

'noise' was added to the cursor position by shifting randomly, on a trial-to-trial basis, the position of the cursor. The level of noise was varied from ±10, ±30, ±50, ±75 and ±100% of the movement amplitude, and its effect on gain adaptation assessed.

Results of arm tracking and pointing movements are listed in Table 1, with values from the patient that are beyond the 95% confidence range of controls defined as abnormal.

In the 'on-line' tracking tasks, the patient had AT in both arms evident as increased SD-MV. There was a pronounced 4 Hz peak in the frequency spectra. The wrist/arm AT ratios were higher than that in normal controls, suggesting that his tremor was predominantly distal in both arms. EV was elevated during right wrist tracking and left arm tracking. Visually cued reaction time was prolonged in both arms.

In the 'off-line' pointing tasks, the patient's pointing movements were dysmetric (under- and over-shoot) and the variable error of his pointing was increased with respect to controls. However, neither average movement amplitude (constant error) nor his level of adaptation was significantly different from that of the normal controls. Adaptation was maintained at this level even when faced with up to 75% random visual feedback noise, while controls showed a significant reduction in adaptation with only ±30% noise.

These results suggest that the patient displayed a dissociation between 'on-line' visuomotor control and 'off-line' control. Despite his dysmetria with increased variable pointing errors, his tremor, increased tracking errors and prolonged reaction times, the patient had no increase in constant pointing error and was able to adapt his movement amplitude to a gain change in the visual feedback even in the presence of significant visual 'noise'.

This dissociation may be illuminated by correlating the visuomotor impairments of the arm to the focal lesions in the cerebellum and brainstem. The bilateral arm AT and disturbances in equilibrium and walking were very likely caused by the symmetrical lesions in the middle/inferior cerebellar peduncles. These lesions would have damaged the fibres connecting the cerebellum and neighbouring brainstem structures, including the lateral and inferior vestibular nuclei, reticular formation and inferior olive. They could also be responsible for his slight internuclear ophthalmoplegia in the left eye. However, he had no palatal tremor despite the obvious axial involvement in his clinical symptoms, so the lesions appear to have spared medial cerebellar areas contributing to oculomotor and palatal control [1]. His 'closed-loop' tracking movements and the delay in visually cued reaction times may have been further impaired by increased delays in the feedback loop caused by conduction blockage [7,8]. Thus, these lesions may be mainly responsible for his impaired 'on-line' control of movement. Complimentary to previous cerebellar studies [5,9], we suggest that impaired on-line control of visually guided tracking movement can occur both because of damage in the superior cerebellar peduncles which contain ascending outflow to the motor cortex, and as a consequence of damage in the inferior and middle cerebellar peduncles which contain spinocerebellar afferents and brain stem-cerebellar connections.

In our pointing task, movements were performed 'open-loop' with respect to visual feedback, and in the patient were dysmetric with increased variable errors. This may result from abnormal sensory-motor processing by the damaged cerebellum coupled with the fact that he was not able to use visual guidance to make mid-flight adjustments in order to improve accuracy [2]. However, his average movement amplitude over a number of trials (constant error) was not significantly different from the controls, suggesting that he was able to scale his basic motor commands. In other words, he was able to adequately program his movements even though he had difficulty in executing them accurately. He was, moreover, able to adapt his movements when the gain of the 'off-line' terminal feedback was modified. Based on these results and on cerebellar patients studied in a dart-throwing task [9], it appears that partial damage to the middle and superior cerebellar peduncles or to the cerebellar nuclei does not affect adaptation to changes in the visual feedback, whereas damage to the inferior olive, the inferior peduncle or the cerebellar hemisphere supplied by the inferior posterior cerebellar artery does affect adaptation. Adaptation may rely on the intact cerebellar cortex to efficiently process various sensory inputs including limb proprioceptive and retinal information for other motor systems in order to adapt. Lesions in the inferior peduncle could selectively disrupt this process by degrading the proprioceptive afferent inflow or by blocking input from the inferior olive. Interestingly, our patient was able to adapt despite much greater random visual noise in the terminal feedback of his movement, perhaps because his movements are normally so variable. Over a period of time, he may have become 'tuned' to this noisy situation allowing update of the control processes despite increased variable errors. This is possible if the control process uses an average measure of error, sampled over many trials; if the patient used a longer average which would be more robust, he would be less disturbed by the trial-to-trial variations. In contrast, controls may use a shorter average, better tuned to their normal low-variance performance, and hence suffer when exposed to even moderate noise levels.

Finally, we suspect that the focal lesion in the right cerebral peduncle mainly involving the corticospinal tract may be the reason that motor impairments are noticeably worse in the left than right side.

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