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R.C. Miall · S. Price · R. Mason · R.E. Passingham
J.L. Winter · J.F. Stein

Microstimulation of movements from cerebellar-receiving, but not pallidal-receiving areas of the macaque thalamus under ketamine anaesthesia

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Abstract The motor thalamic areas receiving input from the globus pallidus (VA) and the cerebellar nuclei (VL) appear to have different roles in the generation and guidance of movements. In order to further test these differences, we used electrical stimulation to map the ventro-anterior and ventro-lateral nuclei of the thalamus in three ketamine anaesthetised monkeys. Movements were readily evoked from VL at currents of down to 10 μA. The movements were typically multijoint, and stimulation could evoke arm and trunk or arm and facial movement at the same current threshold. Evoked arm movements often involved multiple joints, with or without finger movements. Facial movements included the lips, tongue, jaw, eyebrows and, occasionally, the eyes. The thalamic map was topographic, but complex with at least two separate regions related to arm movement. Very few sites within the VA could stimulate movement, even at high currents. We therefore suggest that the cerebellar projections to motor regions of the cortex, which pass through the VL thalamic nuclei, have a different relationship and are closer to movement execution than the projections from basal ganglia via the ventro-anterior nucleus.

Key words Thalamus · Basal ganglia · Cerebellum · Electrical stimulation · Movement

Introduction

The basal ganglia and cerebellum appear to have different roles in the generation and guidance of movements (a recent collection of papers are provided by Mano et al. 1993). These two structures project to separate zones within the motor territories of the thalamus, which in turn project to overlapping regions within the motor cortical areas. One strand of evidence supporting this separation of function is the differential effects of electrical stimulation within the motor thalamus. In general, microstimulation within pallidal-receiving areas has been shown less likely to evoke motor responses, whereas in the cerebellar-receiving areas, movements can be evoked at low current thresholds. However, there are still some aspects of this microstimulation work that require clarification.

Unfortunately, the nomenclature of the motor thalamus is confusing, with at least three different schemes (Olszewski 1952; Jones 1985; Ilinsky and Kultas-Ilinksy 1987). In this paper we will use Ilinsky and Kultas-Ilinksy's (1987) scheme. They defined pallidal-receiving nuclei as lying within VA, (VApc, VAdc and VAmc), while the cerebellar-receiving nuclei were grouped together as VL. Their definition of VAmc and VApc were synonymous with Olszewski's (1952), but what they defined as VAdc, Olszewski had labelled as VLo. Olszewski defined the cerebellar-receiving nuclei as VPLo, VLps, VLc and Area X. Thus, we can abbreviate the pallidal-receiving nuclei to VA and the cerebellar nuclei to VL, and we will refer to VLo only as VAdc; we will occasionally refer to subdivisions within VL (VPLo, VLps, VLc or Area X).

Strick (1976) first recorded and stimulated within the arm area of the motor thalamus and reported that localised contractions of shoulder, arm and hand musculature could be seen at currents of 25 μA at about 30% of the sites tested, mainly within VL (VLc and VPLo), although some sites fell within VAdc (Olszewski's VLo). Strick did not report on the somatotopic details, but did find that even limited movement of the electrode would dramatically shift the response characteristics. He did not explore within VApa, VAmc or Area X. Anner-Baratti et al. (1986) also evoked movement from about half the sites tested within the motor nuclei at very similar stimulation levels (20 or 30 uA) and, although many of these fell within VAdc, the authors suggested that a proportion

R.C. Miall (✉) · S. Price · R. Mason · J.L. Winter · J.F. Stein
University Laboratory of Physiology, Parks Road,
Oxford OX1 3PT, UK
e-mail: chris.miall@physiol.ox.ac.uk
Tel.: +44-1865-282162, Fax: +44-1865-272469

R.E. Passingham
Department of Experimental Psychology,
South Parks Road, Oxford OX1 3UD, UK

of these might actually lie within 'islands' of VL (VPLo). They were only rarely able to evoke single-finger movement, more usually finding movement of more than one finger or of both the fingers and hand. They reported that "occasionally the microstimulation caused complex movement of the whole arm and hand" (p. 576) and that the "movements were frequently more complex" than those evoked by stimulation in the motor cortex (p. 577). However, Buford et al. (1996) then reported evoking only simple movements of shoulder, elbow, wrist or fingers with microstimulation in VL, along with responses in the muscles of the face, trunk and leg. They found stimulus thresholds for evoking movement ranged from 5 to 75 μA in their quiescent animals. No complex movements were found, and no somatotopic mapping was attempted. Buford et al. (1996) did report some effective stimulation sites within VAdc, often around its margin with VL (VLc or VPLo) or with VM (VLm). They explored VA more extensively in one animal, but, for about half of the sites within VA, they tested with stimulus strengths of only up to 50 μA. Where stimulation was ineffective in this animal, they report testing at stimulus currents of 75 μA or below for 50%, 100 μA for 30% and at 200 μA on 17% of occasions. Most recently, Vitek et al. (1996) also restricted stimulation mainly to the cerebellar nuclei, with only limited microstimulation in VA and with currents limited to 40 μA. They reported only 1% of effective stimulation sites in VA (and only 21% in VAdc), and all effective sites in VAdc were close to the borders with VL (VPLo). Again, they suggested that effective sites evoked single muscle or single joint movement. Table 1 below (in the discussion) summarises the stimulation parameters used in the various reports.

Thus, the preponderance of evidence favours the notion that only simple movements are produced by microstimulation within the cerebellar-receiving areas of the thalamus. However, the restriction of most stimulation studies (in alert animals) to currents of below 25–40 μA falls well within the threshold range that Buford et al. (1996) found necessary even within cerebellar territories. It is thus possible that stimulation sites within VA might be present, but with slightly higher thresholds. We have therefore attempted to map the motor thalamic nuclei in anaesthetised monkeys using electrical stimulation and aimed to include the bulk of VA within our search. In addition, the report by Anner-Berratti et al. (1986) suggests to us that there is still uncertainty whether the movements evoked are single joint or complex, and so we also sought to determine if any complex movements could be evoked by electrical stimulation of the motor thalamus. Some of these results have been reported in a conference abstract (Miall et al., 1993).

Materials and methods

Three adult rhesus monkeys (*Mucaca mulatta*) were anaesthetised with barbiturates, placed in a stereotactic head holder and then maintained under ketamine (6.3–9.1 mg/kg/h). A craniotomy was opened over the anterior thalamus on one side, and, in Monkeys 1 and 2, a ventriculogram was also taken to localise the thalamus. A tungsten stimulating electrode insulated with varnish (approx. 25 kΩ) was advanced through the dura using a mechanical micromanipulator to map the motor regions of the thalamus on a 1-mm grid in the horizontal plane (sagittal and coronal axes), with a dorsal-ventral step size of 0.5 mm. A reference electrode (a 23 gauge needle) was inserted under the scalp. Movements were sought using brief trains of cathodal current pulses (100 or 200 Hz, 0.3-ms duration, 300-ms trains). Current intensity was monitored on an oscilloscope as the voltage drop across a 10-kΩ resistor in series with the electrode. At each stimulation site, current intensities were increased from a low level (based on results at neighbouring sites) until movement could be observed reliably on each stimulation or until a current intensity of 300–500 μA was reached. Between three and five stimulation trains were applied at each threshold measurement. Visual observations were made by two or three observers; in some instances, we also tested for movement by tactile manipulation of the affected limb. Anaesthetic level, breathing rate and any spontaneous movements were carefully monitored throughout the procedure. Following microstimulation mapping, electrolytic marker lesions were placed at locations around the stimulation volume, and the animals were killed with an anaesthetic overdose. Stimulation sites were reconstructed from standard parasagittal histological sections stained with cresyl violet. Identification of the thalamic nuclei was based on the description given by Olszewski (1952). In monkey no. 3, sections were taken coronally, but poor histological staining precluded our identification of the individual thalamic nuclei. For this animal, we estimated the nuclear borders by superimposing scaled copies of Olszewski's maps onto the gross thalamic outline in coronal section.

Data presentation

For each animal, we recorded the threshold for stimulation of movement at each site, and these values were then entered into a statistical package (SAS Institute) to generate contour plots of threshold stimulation current for each sagittal or transverse plane. The contour plots were linearly interpolated from the original 0.5-mm or 1.0-mm resolution to 0.1-mm resolution in both axes. Thalamic borders, located with reference to the known position of the marker lesions within the histological sections, were then superimposed onto the contour plots. In the figures shown, the shaded rectangles represent the area of tissue sampled with the stimulating electrode (Fig. 2). Hence the shaded area alters in extent between some parasagittal sections.

Number of sites tested

In monkey no. 1, we tested 223 sites on 22 electrode tracks; for monkey no. 2 we tested 375 sites on 32 tracks; and for monkey no. 3, 184 sites on 34 tracks were tested.

Results

Stimulation at many sites evoked clear movement of the fingers, arm or leg on the contralateral side of the body. At some sites, we also noticed movements of the face, including the jaw, lips, eyelids and tongue. At a few sites, small movements of the eyes were detected, but these were neither easily evoked nor very consistent. Movements tended to be complex, with a graded onset, and clearly different from the simple, sharp movements that could be evoked by stimulation within the internal capsule. Our data support four principal findings.

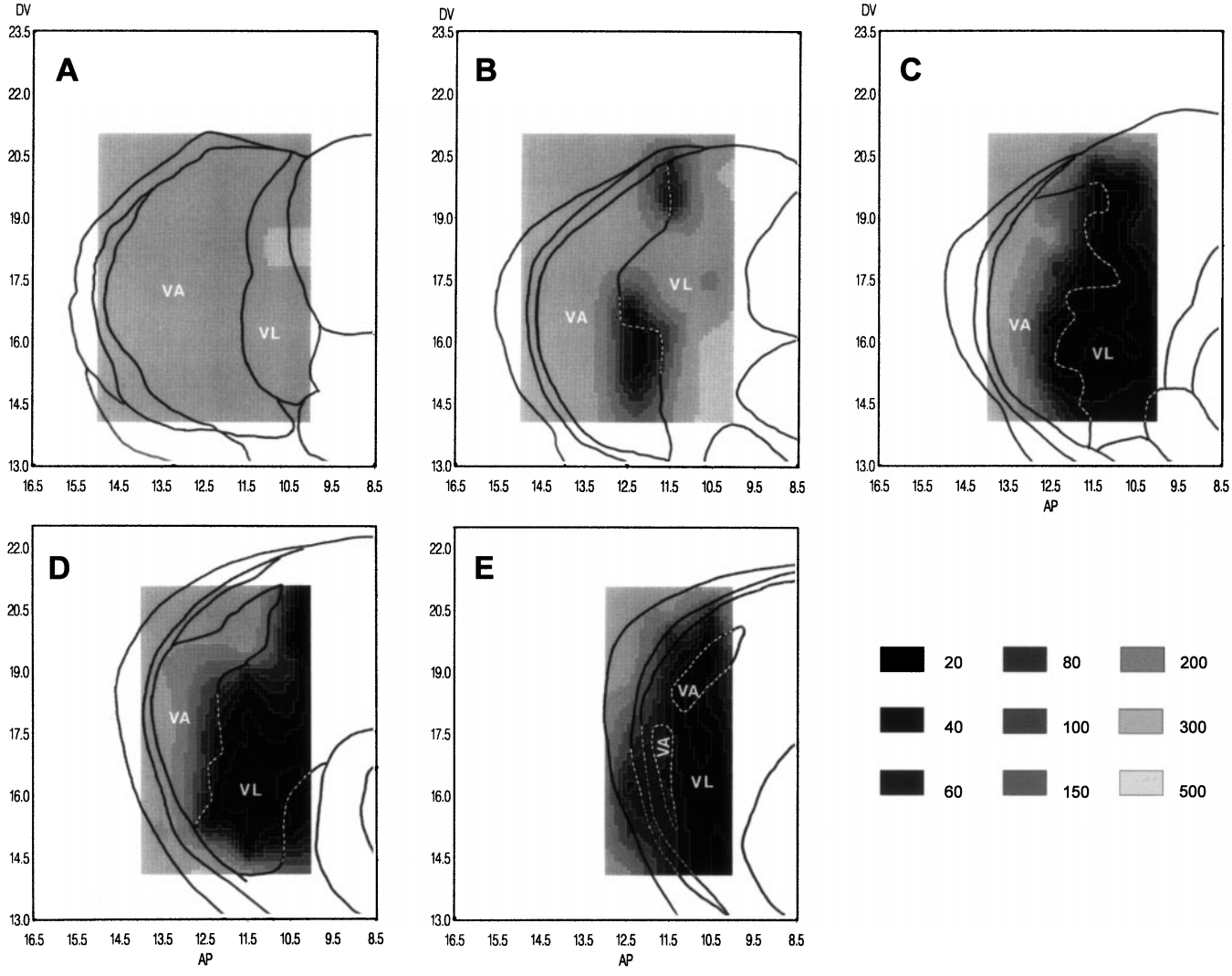

Fig. 1A–E Microstimulation map for monkey no. 1. The contour plot displayed in each panel depicts the area of tissue tested with electrical stimulation (*light grey areas*). The *darker regions* represent sites with low current thresholds, at which a movement of any body part was observed. Superimposed on the contour plots are the thalamic nuclear boundaries determined by post-mortem histological reconstruction. **A–E** Parasagittal sections at 1-mm separation from 4 mm lateral to the mid-line (**A**) to 8 mm lateral (**E**); the axes are plotted in mm with respect to stereotactic coordinates, anterior is towards the left. Contours are plotted at 20, 40, 60, 80, 100, 150, 200, 300 and 500 μA. Note how the excitable regions appear to lie adjacent to, but excluding VA

Movement was evoked from cerebellar territories

Movements were readily evoked from distinct regions within the thalamus, in and around the cerebellar receiving territory of VPLo, with current thresholds in one animal as low as 10 μA. In the second animal, many sites had thresholds below 40 μA; in the third animal the lowest stimulation thresholds found were approximately 75 μA. We suspect that the differences between these three animals reflect subtle differences in the stimulation electrode and in the animal's reaction to anaesthetic, rather than a fundamental difference in the responses of the thalamus. The level of anaesthetic clearly influenced the current threshold measured. If a site with a low threshold was tested immediately after a supplementary dose of ketamine, the threshold sometimes rose by more than 200 μA before falling again to the original levels. Thus, we took care to maintain as constant a level of ketamine anaesthetic as possible, administering frequent, small volumes. We were also careful to return to most sites where stimulation was not at first effective, but which were adjacent to areas where stimulation had evoked movement, to reconfirm the threshold at two different times. Usually, this was possible while raising the electrode from its maximal depth following the initial descent.

In all three animals, more rapid movements were found at those areas with the lowest current thresholds. In other sites, the movements were often slow and gradual. However, the most rapid movements evoked were from stimulation sites outside the thalamus (probably from direct stimulation of descending fibres within the internal capsule). Thus, we could distinguish the effects seen from within the thalamus from the direct stimulation via the internal capsule.

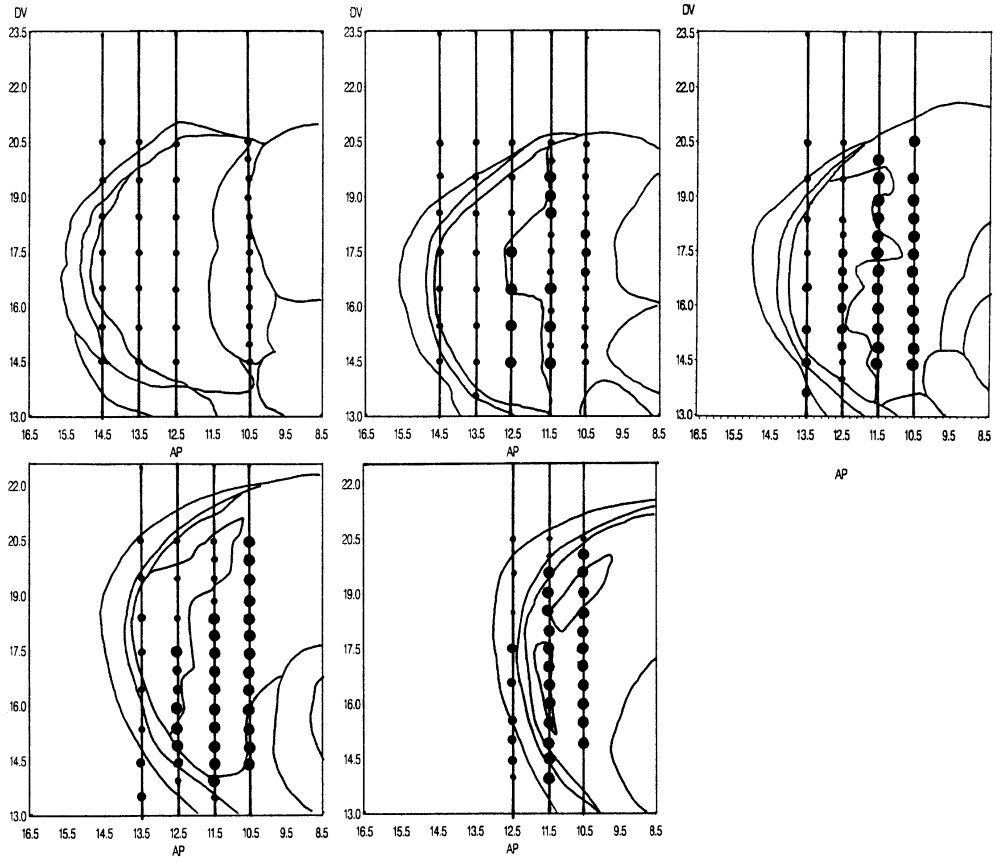

Fig. 2A–E Microstimulation sites for monkey no. 1. The electrode tracks and stimulation sites tested are plotted on the histological outlines corresponding to Fig. 1. Sites at which the stimulation threshold for any observed movement was 200 μA or more are marked with the *smallest dots*, sites where the threshold was 100–200 μA are marked with *medium dots* and sites where the threshold was under 100 μA are plotted with *large dots*

Movement could not be evoked from basal ganglia territories

Few movements could be evoked from within the main body of the basal ganglia territories (VA), even at high currents (300–500 μA). Figures 1 and 2 show contour maps and the microstimulation sites, respectively, through the areas of VA and VL for monkey no. 1, in which the current threshold has been calculated for a stimulation of movement of any body part. In this animal, no movement was evoked from any region within VA, except an area that, on histological reconstruction, lay within 0.5 mm of the border between VA and VL (Fig. 1B, lower dark region). Monkey no. 3 also showed the same result, with sites for evoked movement lying close to the expected locations of VL (mapped with respect to the edges of the thalamus, although we could not reconstruct the exact VA/VL border in this animal). In monkey no. 2 (Fig. 3), there was one active site within the body of VAdc (the dark region at bottom left of Fig. 3B and D), at which both facial and arm movements were evoked. In contrast, movement could be consistently evoked across a broad region of VL posterior and lateral to VA, mainly lying within VPLo.

There was a complex topographic map

The contour plots shown in Figs. 1 and 3 indicate a complex three-dimensional volume within which movement could be evoked. By separately plotting the contour plots for each body part (e.g. the fingers, wrist, elbow, shoulder, trunk, legs or face), we were able to explore the topography within this region more clearly. Figures 4 and 5 indicate the areas in which movements of the arm (including hand and fingers) were elicited compared with movements of the face (including tongue or eyes). In general, these two maps are complimentary – the areas in which arm movement were evoked at low thresholds tended to be spatially separate from areas for low-threshold stimulation of the face. This separation was not complete, however, and there is some overlap of these zones. The low-threshold ‘hot spots’ were smaller than the complete volume from which movement could be evoked, so the degree of overlap is dependent on the current threshold chosen. Of the five local peaks seen in the contour map for face movement (Fig. 5C), one corresponded to a peak in the map for arm movement (Fig. 5A), while another was in an adjacent site (0.5 mm dorsal-ventral). The remaining three were clearly different. Likewise, of six peaks found for stimulation of arm movement (Fig. 5B), one corresponded to a facial movement site, one differed by the same 0.5-mm dorsal-ventral separation and the others were distinct (Fig. 5D).

The areas evoking arm movement tended to be more anterior and extended more dorsally to those for the face. In Fig. 4, there is also the suggestion that the arm area (Fig. 4A,B) forms a curved volume around the more central face area (Fig. 4C,D). This was also seen in monkey no. 3 (not

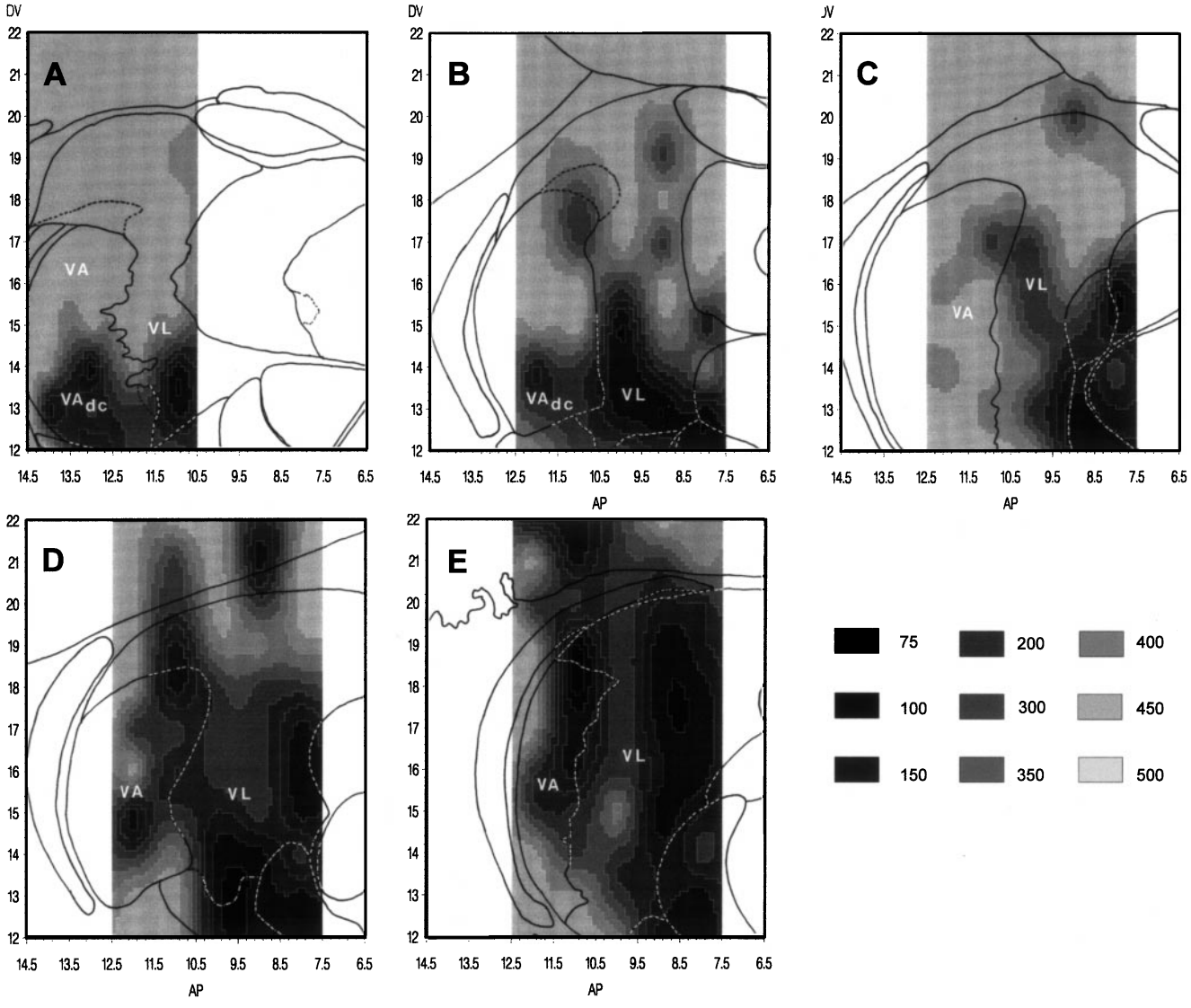

Fig. 3A–E Microstimulation map for monkey no. 2; data are presented in the same format as Fig. 1, except contours are plotted at 75, 100, 150, 200, 250, 300, 350, 400, 450 and 500 μA

shown), but was less clear in monkey no. 2 because of the more complex volume of face-related stimulation sites in that animal (Fig. 5). We did not see sufficient areas that evoked trunk or leg movement in each animal to be clear of their topography; those sites that did consistently generate leg and or truck movement tended to be towards the ventral posterior margins of VL (within VPLo).

On the nature of movements evoked

Movements evoked by stimulation were typically multijoint and not single muscle or single joint. Even at threshold, most movements were 'complex' in this sense. Examples are shown in Figs. 4 and 5, where the sites for stimulation of facial and arm movements overlap, even at the lowest currents used. Thus, we saw regions evoking arm and trunk movement, or arm and facial movements, at the same current threshold.

Facial movements included the lips, tongue, jaw, eyebrows and, occasionally, the eyes. In some instances, we observed movement of the lower jaw, tongue and around the throat, implicating many different muscles. In other instances, we saw movement of the lips (upper and lower) with movement of the eyebrows, again involving different muscle groups. Arm movements often involved all joints, with or without finger movements.

Figure 6 shows two parasagittal contour plots for monkey no. 1, in which separate plots have been drawn for movements of the fingers, wrist, elbow or shoulder. A distinct region can be seen at the top right of each panel (upper row), at which movement of all joints was evoked at the same threshold (<20 μA). In contrast, the lower region in each of these panels shows adjacent, overlapping, but not exactly matching regions for finger, wrist and elbow. In the lower row of the figure, both elbow and shoulder movements were evoked from the same elongated zone, whereas wrist and finger move-

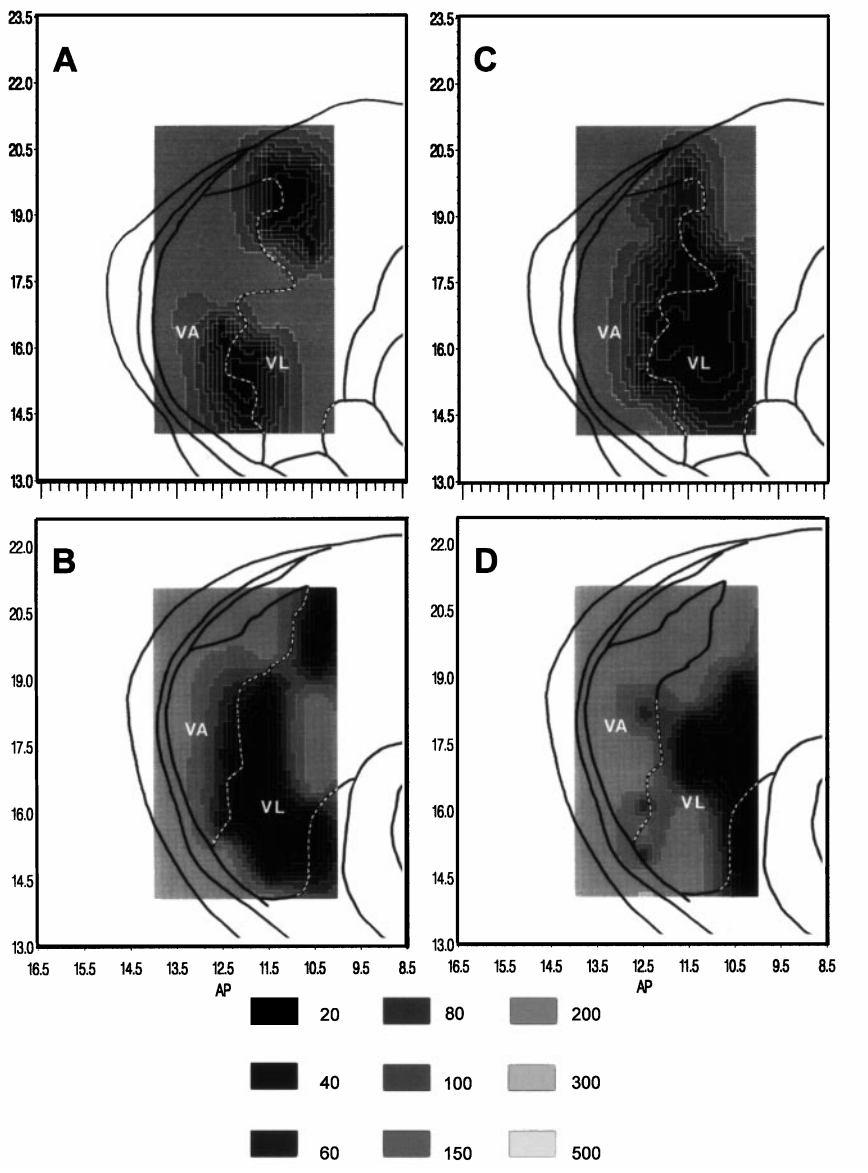

Fig. 4A–D Microstimulation maps for movement of the arm (*left column*) or the face (*right column*) at two parasagittal slices in monkey no. 1. Contour levels are as in Fig. 1. The *top row* are 6 mm lateral to the mid-line, the *bottom row* are 7 mm lateral

ments were obtained adjacent to this zone. Similar results were seen in all three monkeys.

Discussion

These experiments in the anaesthetised monkey have confirmed earlier reports that the stimulus threshold needed to evoke movement from the pallidal-receiving VA regions of the thalamus is higher than in the adjacent cerebellar-receiving VL regions. Except for the report by Buford et al. (1996), VA has been only previously tested at microstimulation currents of up to 40 μA. Buford and colleagues then reported many VL sites with thresholds above 40 μA; at least one excitable site had a stimulation threshold that varied from around 75 to over 200 μA on two successive days (Buford et al. 1996). This site lay on the border between VAdc and VL (VPLo), but they confirmed that it received inputs from the cerebellar nuclei with WGA-HRP, and so it would be expected to have a low current threshold. Buford et al. (1996) did in fact sample territory within VA, and on occasions used currents of up to 200 μA without evoking movement. However, only a total of 48 sites were tested at 200 μA in one animal, not all within VA. Strick (1976) also mentioned that evoked responses varied quite dramatically with the alertness of the animal. Thus, even in the awake animal, evoked responses may fluctuate dramatically, and for this reason we felt that the previous negative results for stimulation within VA at currents of 25–40 μA required confirmation.

At most sites we tested a wide range of stimulation currents (up to 300 μA at most sites, but up to 500 μA on occasions). At these high current levels, it is clear that the physiological threshold for stimulating movement would have been exceeded. In fact, these currents would be expected to spread a distance of about 1 mm from the stimulating electrode (Ranck 1975) and so activate any neighbouring sites for movement. Thus, we can be rea-

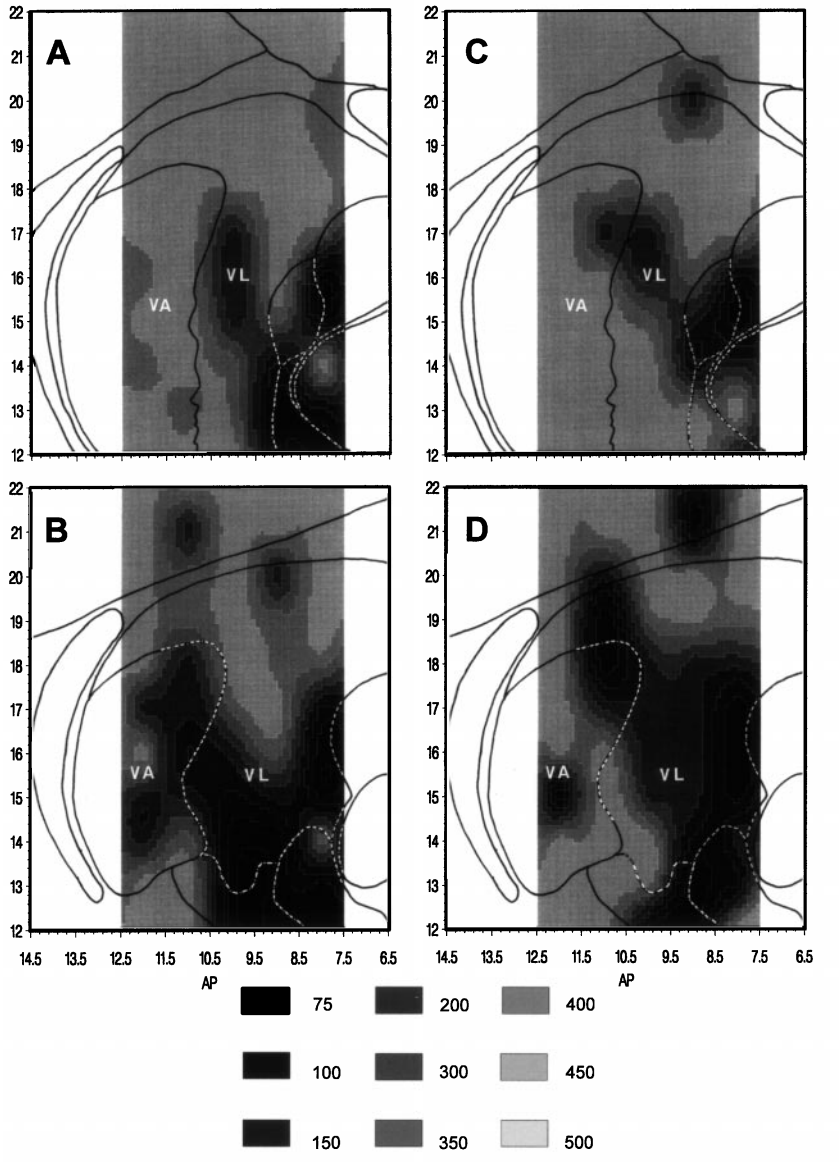

Fig. 5A–D Microstimulation maps for movement of the arm (*left column*) or the face (*right column*) at two parasagittal slices in monkey no. 2. Contour levels are as in Fig. 3. The *top row* are 6 mm lateral to the mid-line, the *bottom row* are 7 mm lateral

sonably confident that our failure to evoke movement within VA is genuine and not merely related to the stimulation parameters used, the depth of anaesthetic or of the precise location of the electrode.

In contrast, movements were stimulated from many of the non-basal ganglia thalamic sites tested, and the threshold for evoking movement in VL (VPLo) ranged from as low as 10 μA in one animal, 30–40 μA in a second, but also up to 150–200 μA at some sites in any one animal. The movements observed were often complex and often had a gradual onset. Thus, we believe that they are unlikely to have been evoked simply by stimulation of motor cortical efferents. These movements appear to be rather different from those observed by Strick (1976), Buford et al. (1996) and Vitek et al. (1996), who reported only simple movements of single joints or single muscles. Buford et al. (1996) also reported that their movements were brief; Strick (1976) and Vitek et al. (1996) did not report on movement speed. Our results appear somewhat closer to those of Anner-Baratti et al. (1986), who evoked combined finger and wrist movements from a limited number of sites near the border of VAdc and VL at current thresholds of 30 μA or below. The responses we observed appear similar to those of Mitz and Wise (1987), who used microstimulation in the SMA and reported that, at half the sites tested, the responses were complex (motion about ‘contiguous’ or ‘non-contiguous’ joints), whereas at the remaining sites motion around a single joint was seen. They also reported stimulation of orofacial movements similar to those we observed (the lips, tongue, jaw, eyebrows and around the throat) and, at the most rostral SMA sites that they tested, saccadic eye movements. Microstimulation evoked brisk movements at the vast the majority of sites they tested, although a small percentage were quite gradual in onset.

We did not explore a range of stimulation parameters (stimulus rate, pulse width, profile etc.; Table 1), but it seems unlikely that the differences in the speed of evoked

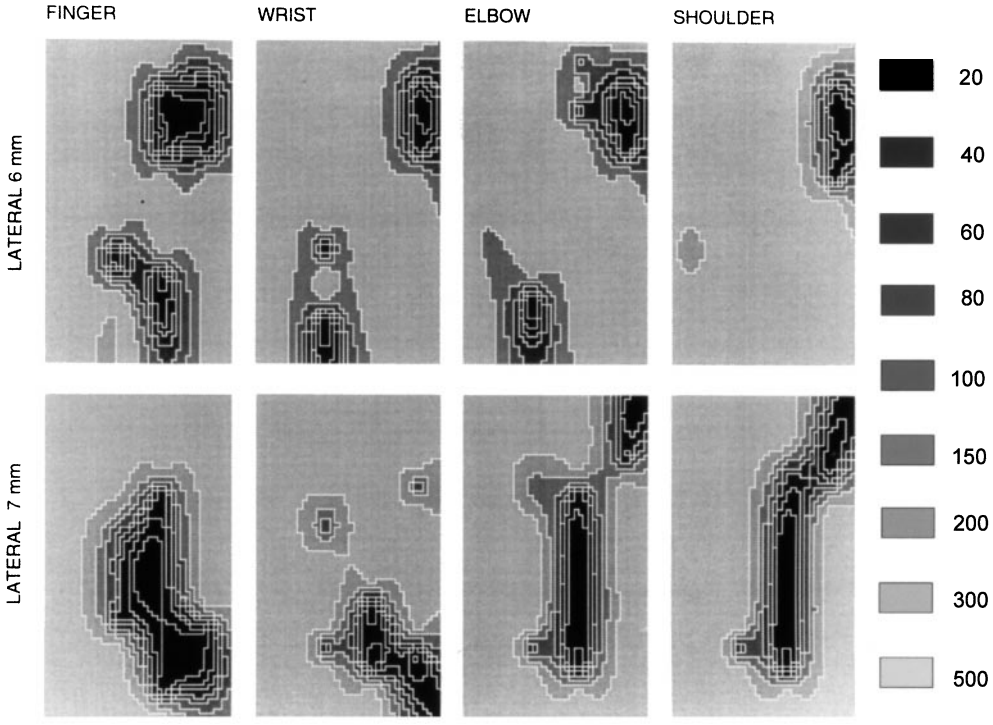

Fig. 6 Microstimulation maps for movement of different joints within the arm at two parasagittal slices in monkey no. 1. The *top row* are 6 mm lateral to the mid-line, the *bottom row* are 7 mm lateral. Contour levels are as in Fig. 1; the area of each panel is equivalent to the *grey area* shown in Fig. 1. Note the overlap of joint representations even at the lowest current thresholds

Table 1 Comparison of stimulation parameters

Reference	Waveform	Stimulus rate (Hz)	Train length (ms)	No. pulses	Max. current (μA)	Detection of response
Strick (1976)	Cathodal 0.2 ms	370	27[a]	11	<25	Visual
Anner-Barrati et al. (1986)	Cathodal 0.2 ms	300	60	19[a]	30–40	Visual
Buford et al. (1996)	Biphasic (cathodal/ anodal) 0.2 ms/phase	333	33[a]; 33 or 69[a]	12[b]; 12 or 24[c]	50, 100[d], 200[e]	Visual and palpation
Vitek et al. (1996)	Biphasic (cathodal/ anodal) 0.2 ms/phase	400	100–200	40 – 80[a]	40	Visual
Miall et al. (this paper)	Cathodal 0.2 ms	100 or 200	300	30 or 60	300–500	Visual and palpation

[a] Where data were not given on, e.g. train length, these have been calculated; [b] first animal; [c] second animal; [d] 100 uA was applied in 30% of cases where stimulation was ineffective (83/277); [e] 100 uA was applied in 17% of cases where stimulation was ineffective (48/277)

movement would rest only on the stimulus parameters we used. For example, Buford et al. (1996) reported no difference in response speed between 12 or 24 pulse stimulus trains (33- or 69-ms duration). Instead, it is more likely that the variations in the excitability of anaesthetised animals might affect the speed of movements. Both Strick (1976) and Vitek et al. (1996) reported that the alertness and attention of the awake animal affected the current thresholds, although they did not report any obvious changes in movement speed. Vitek et al. (1996) reported that the limb posture and immediate history of muscle contraction also affected thresholds, but of course these were relatively constant in our anaesthetised animals.

There may then be two explanations for the complex responses we observed: the duration of the stimulation trains we delivered or the use of ketamine anaesthesia. Mitz and Wise (1987) suggested that SMA stimulation was easier, with lower thresholds, if the stimulus trains were greater than 50 ms, and, thus, they used trains of 100-ms duration. In primary motor cortex, increasing the stimulus trains up to 30 ms increases stimulus efficacy, but beyond that no change in responses are observed (Kwan et al. 1978). In this study, we used trains longer than other authors (300 ms, Table 1). Thus, it is possible that our lower stimulus rate and longer train durations evoked more complex movements, either by selective stimulation of a distinct subset of thalamo-cortical fibres or by recruitment within cortical circuits during the stimulus train. Trains of repetitive stimuli tend to have a potentiating effect within motor cortex, such that the responses to later pulses in the train are larger than to the first pulse (Porter and Lemon 1993; Gu and Fortier 1996). This gradual potentiation could be more effective within one thalamo-cortical path than another. Hence, given the similarities of the responses we evoked and those observed by Mitz and Wise (1987), it may be that the responses we

saw were caused principally by projection fibres from VL to premotor cortical areas. There are projections from VL (VPLo and VLc) to SMA, and Matelli and Luppino (1996) reported that 25% of thalamic cells retrogradely labelled from injection in SMA-proper (F3) were within these two nuclei. There is also a significant projection from VPLo to PMd (F2; Matelli and Luppino 1996). So the effects we observed may have arisen from direct, but complex activation of primary motor cortex or from indirect activation through other premotor cortical areas.

Alternatively, the effects of ketamine on the cortical and thalamic circuitry may have altered the response characteristics. Ketamine anaesthesia was used in these experiments because it does not depress the motor system as drastically as other anaesthetic agents. However, it is an NMDA antagonist, and its effects on the neural responses to stimulation are difficult to assess. We have not found any reports that suggest that the motor responses to cortical microstimulation are more complex under ketamine (see Gu and Fortier 1996). It is known to enhance sensory and motor evoked potentials (Lee 1994); it is thought not to modify oligosynaptic spinal reflexes, but may affect polysynaptic processes (Headley and Grillner 1990). So the evoked responses to microstimulation would be more prominent – with lower thresholds and perhaps greater amplitudes – with ketamine than other anaesthetic agents, but we cannot tell if they would be more complex in form. Finally, Mitz and Wise (1987) used ketamine to minimise spontaneous movements in their awake monkeys during SMA micro-stimulation, but did not discuss whether there were any differences in responses with or without ketamine.

However, in some respects, it is not surprising that thalamic stimulation could evoke movement that is more complex than has been reported by others (i.e. Strick 1976; Buford et al. 1996; Vitek et al. 1994; and their colleagues). The thalamus has only indirect connection with the motor output pathways, via primary motor cortex, and motor cortical pyramidal cells appear to have quite complicated projections to multiple motorneuronal pools in the spinal column (for a review, see Porter and Lemon 1993). Strick (1976) showed that only about 34% of the cells recorded within VL showed directional specificity, which would be expected if their activity was closely tied to a single muscle; furthermore, many cells did not respond differentially for fast or slow movement, further separating their firing patterns from the pattern of muscle activation. It would therefore be counterintuitive if the thalamic sites we activated resulted in only single-joint movements. VL does carry sensory information and is responsive to passive limb manipulation or torque perturbations (Vitek et al. 1994). Hence the responses to brief, high frequency, activation observed by Strick (1976), Buford et al. (1996), Vitek and colleagues (1994, 1996) in their awake animals might reflect trans-cortical reflex responses to this brisk ‘sensory’ input. However, whether the normal (unstimulated) neural activity in the motor thalamus contributes to complex movements still remains to be demonstrated in awake animals.

The complexity of the topographic maps we have observed has features in common with the findings of Vitek et al. (1996), in that there is a suggestion of the shell-like somatotopy they reported. Our maps generally positioned the distal joints more rostral than the proximal joints. In our case, this caudal region also included leg and truck movement, whereas Vitek et al. (1994) reported the leg region to lie as a shell around the anterior margin of the forelimb regions. The anterior border of the VL regions at which movement could be evoked was very close to (and overlapped in some cases) the border with VA. This corresponds to recording data from Vitek et al. (1994) and to micro-stimulation results from Buford et al. (1996). Vitek et al. (1996) found that the majority of micro-excitable sites in VAdc or within Olszewski’s VPLc and VLc all lay close to the borders with VPLo. However, the micro-excitable zones we found seem to overlap the nuclear boundaries within VL (especially those between VLpc, VLc and VPLo), and, therefore, the complex map may reflect three or more separate somatotopic maps in VL.

Like Vitek et al. (1994; 1996), we found a significant volume represented by the proximal arm (shoulder and elbow), in relationship to the distal wrist and finger representations. We also confirmed their finding that the majority of sites evoked arm or face movements, with relatively few sites evoking movements of the trunk and leg. They suggested that their result might be due to a more thorough sampling of the arm areas. We sought to sample the volume as uniformly as possible and so would not have expected the same sampling bias.

Finally, Buford et al. (1996) raised the possibility that their observed differences in excitability between pallidal-receiving and cerebellar-receiving nuclei could be due either to a sampling bias, to differences in projection sites from the thalamus to primary motor cortex or to differences in the laminar projections to primary motor cortex (M1). They suggested that there were more secure connections between VL (VPLo or VLc) and the pyramidal cells of M1 via deeper cortical laminae, whereas the inputs from VA (VApc or VAdc) have access to M1 only via lamina 1 (Nakano et al. 1992). The high currents we used would confirm Buford et al.’s (1996) suggestion that it was unlikely that sampling error could be blamed. With currents of 300 or 500 μ A, we would expect sufficient current spread, so that small sites missed by the electrode tip would still be activated (Ranck 1975).

So, the correspondence of our stimulation maps with the thalamic nuclear boundaries within the volume we tested suggests that the cerebellar-receiving nuclei do have a different role within the complete motor system from the basal ganglia-receiving regions. The difficulty in evoking movement from basal ganglia territories suggests that this circuit is not closely tied to movement execution; whereas the ease with which movements were evoked from the cerebellar territories suggests that these circuits are much more closely tied to movement execution. Strick (1976) suggested that VL may play a part in initiating activity in muscle controlling body posture as well as discrete limb movement. However, many VL cells are not obviously di-

rectionally tuned (Strick 1976), and the rather slow movements evoked in our study by electrical stimulation argue against a relatively direct influence on muscle activity. There may also be task-specific differences within the cerebellar territories of the thalamus. We have seen that the cells in VPLo and area X differ in their selectivity for visually guided or internally triggered movements (van Donkelaar et al. 1997a), and inactivation of these two thalamic sites had differential effects on each task (van Donkelaar et al. 1997b). This task specificity further argues against a thalamic role tied closely with motor execution. Mink and Thach (1991a,b,c) suggested that the basal ganglia might be particularly important in allowing movement to occur by silencing inappropriate muscle activity, and they proposed that the pallidal output focally disinhibits selected cells in the thalamus while inhibiting others (Mink 1996). Inase et al. (1996) have found that pallidal inactivation led to behavioural deficits consistent with this hypothesis, and that at least a proportion of pallidal-receiving cells in the thalamus were disinhibited, consistent with that interpretation. However, because of their increased baseline firing, the cells' modulation of firing rates was reduced or unchanged, and this might translate to a reduced functional signal. But, if thalamic activation is expected to correlate with voluntary movement, then it is still not clear why the microstimulation of thalamic cells does not generate any motor output. Our failure to evoke any significant movement activity by microstimulation of these sites is inconsistent with this model. It may be that the normal pattern of activation of VA includes spatially distributed disinhibition and inhibition (Mink 1996). This pattern of thalamic activity projected onto the motor cortical areas may then match or combine with ongoing cortical activity and result in facilitated motor responses. A volley of synchronous discharge evoked by microstimulation around a focal point within the pallidal-receiving thalamus may not provide a pattern of activity appropriate for activating the motor cortex.

It therefore seems that the cerebellar projections to motor regions of the cortex, which pass through the VL thalamic territory, have a different relationship to movement than the projections from basal ganglia via the VA territory. It is now necessary to continue to explore these differences in more detail. In particular, we think that comparisons of VA and VL with single-unit recording and by reversible inactivation will be useful ways forward (van Donkelaar et al. 1997a,b).

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