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Motor Subcircuits Mediating the Control of Movement Extent and Speed

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Turner, Robert S., Michel Desmurget, Jeff Grethe, Michael D. Crutcher, and Scott T. Grafton. Motor subcircuits mediating the control of movement extent and speed. *J Neurophysiol* 90: 3958–3966, 2003. First published September 3, 2003; 10.1152/jn.00323.2003. The functional correlates of movement extent, speed, and covariates were investigated using PET mapping of regional cerebral blood flow (rCBF) in 13 healthy right-handed adults. A whole-arm smooth pursuit tracking task was used to strictly control potential confounds such as movement duration, error, and feedback control. During each of four scans, images of relative rCBF were obtained while subjects matched the constant velocity movements of a target using a joystick-controlled cursor. Between scans, subjects were completely adapted to one of four joystick-to-cursor gains, thereby allowing constant visual stimulation and eye movements across arm movements that ranged in extent from 6 to 24 cm. Subjects were unaware of the changes in visuomotor gain. Analyses of arm and eye movements indicated that the only significant difference in behavior across the four gain conditions was the extent and velocity of arm movements, which were closely correlated with each other. Parametric statistical methods identified brain areas where rCBF covaried with the mean movement extent of individual subjects during individual scans. Increasing movement extent was associated with parallel increases of rCBF in bilateral basal ganglia (BG; putamen and globus pallidus) and ipsilateral cerebellum. Modest extent effects were detected also in the sensorimotor cortices bilaterally. No significant inverse relations were found. We conclude that a small subcircuit within the motor control system contributes to the control of movement extent and covariates and that the BG and cerebellum play central roles in the operation of that circuit.

INTRODUCTION

An important step in the neural control of movement is the transformation of information about target position and initial state of the limb into motor commands for reaching the target. Many behavioral studies suggest that this transformation includes a stage at which information about movement extent and direction are represented independently, as vectorial parameters (i.e., the "vector coding" hypothesis) (Bock 1992; Favilla et al. 1989; Ghez et al. 1997; Gordon et al. 1994; Krakauer et al. 2000b; Pine et al. 1996; Rosenbaum 1980; Vindras and Viviani 2002; Vindras et al. 1998). Despite the strong behavioral evidence for this hypothesis, a potential corollary—that distinct neuronal networks contribute to the control of movement direction and extent—has seldom been investigated. Neuronal correlates of movement direction have been described repeatedly for the motor cortices, cerebellum, and the basal ganglia (BG) (Georgopoulos 1995; Kalaska and Crammond 1992). Correlates of movement extent, however, have been generally described as weak, late, or confounded with other parameters (Ashe and Georgopoulos 1994; Fu et al. 1995; Georgopoulos et al. 1983; Messier and Kalaska 2000; Riehle and Requin 1989; although see Fu et al. 1993; Kurata 1993). Identification of a distinct CNS substrate for movement extent would both advance the cause of the vector coding hypothesis and elucidate its functional neuroanatomic underpinnings.

Human brain mapping studies have identified motor control networks involved in parameters such as static and dynamic force and the rate of movement (Dettmers et al. 1995, 1996a,b; Fink et al. 1996; Sadato et al. 1996). Our previous work identified a small circuit including sensorimotor cortex (SMC), cerebellum, and BG within which activity correlated with the speed of visuomanual tracking (Turner et al. 1998). The BG correlation was of particular interest because evidence from nonhuman primate physiology (Georgopoulos et al. 1983; Horak and Anderson 1984a; Turner and Anderson 1997), functional imaging (Taniwaki et al. 2003), and clinical disorders associated with BG dysfunction (Berardelli et al. 2001; DeLong et al. 1984; Desmurget et al. 2003a; Turner et al. 2003) have implicated BG motor circuits in the control of movement speed or extent. [In most settings, tangential velocity (i.e., movement "speed") and a constellation of other parameters covary closely with the extent of movement.] The generality of those earlier results was diluted, however, by undesirable covariations between movement speed and *1*) the rate of reversals in movement direction (movement extent was held constant), *2*) the speed and rate of eye movements, and *3*) visual stimulation.

The goal of this study was to identify neuronal correlates of movement extent using PET mapping of regional cerebral blood flow (rCBF). We used continuous visuomanual tracking to strictly control for potential confounds such as movement duration and the prevalence of feedback control. Subjects were fully adapted to different visuomotor gains between scans, thereby allowing constant visual stimulation and eye movements across a wide range of movement extents and velocities. We used parametric statistical methods to identify brain areas

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where CBF changed in concert with the movement extents of subjects on individual scans. We predicted that control of movement extent would be closely linked to activity in the BG, cerebellum, and/or motor cortex, similar to results obtained previously when movement speed and rate were manipulated.

METHODS

Subjects

Thirteen normal adults [53 ± 8 (SD) yr; range, 40–68 yr; 7 females, 6 males) were recruited from the general population. Subjects in this age range were chosen to serve as age-matched controls for a population of patients with Parkinson's disease. Exclusion criteria were history of neurologic or psychiatric disease, hypertension, or the use of any prescription medication. All subjects were strongly right handed by self-report. Informed consent was provided in accordance with the Emory University Institutional Review Board.

Apparatus and tasks

Subjects were positioned supine on the scanner bed, with the right upper arm placed on a level surface at the subject's side, the shoulder abducted 30°, and the elbow flexed 90° (Fig. 1). The right hand was bound within a padded plastic splint attached to a gimbal-mounted joystick. The joystick allowed medial and lateral longitudinal rotations of the shoulder with the hand and forearm musculature fully relaxed. The arm and joystick were hidden from the subject's view.

A 19-in computer monitor was suspended over the scanner bed and tilted to face the subject. During task performance, a "target" (solid white circle, 1.5 cm diam) moved horizontally across the monitor at a constant speed (10 cm/s) between endpoints 20 cm apart (Fig. 1). The target reversed direction of movement instantaneously on reaching left and right endpoints (2 s between each reversal). Subjects were instructed to match the position and movement of the target as closely as possible with an on-screen cursor (a hollow red 1.5-cm square) controlled by the hand-held joystick. On different scans, the gain of the relationship between joystick movement and cursor displacement was set to one of four levels in which joystick displacements of 6, 12, 18, and 24 cm produced cursor displacements of 20 cm. The number of leftward and rightward movements was held constant during a 100-s epoch of task performance (25 movements). To ensure that subjects were fully adapted to a new joystick-to-cursor gain before a scan, subjects performed an adaptation/practice session for 100 s starting 5 min before each scan. Because of trial-to-trial randomization and the presence of other scans types (see *Imaging*), a variable number of scans was preceded by a practice session in which the subject actually adapted to a new visuomotor gain, while prior to the remaining scans, subjects merely practiced tracking at a previously learned gain. Post hoc analysis confirmed that task performance was stable throughout scans, showing (as expected) that adaptation to a new gain setting was completed during the practice session prior to scanning. Silver/silver chloride surface electrodes were placed periorbitally to allow electro-oculographic (EOG) recording of horizontal movements of the eyes (gain = 1,000; band-pass filtering, 0.1–100 Hz). Joystick position and EOG signals were digitized at 250 Hz.

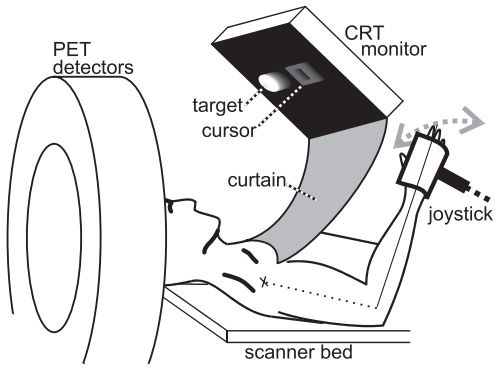

FIG. 1. Behavioral apparatus. The subject lay prone on the PET scanner bed with the right hand fixed to a joystick. A curtain blocked the subject's vision of the hand and joystick. During task performance, a computer monitor suspended over the bed displayed a computer-driven target (white circle) and a joystick-driven cursor (red square). Medial/lateral longitudinal rotations of the shoulder (axis of rotation, × and dotted line) resulted in horizontal displacements of the cursor.

Imaging

Four PET scans were acquired, one for each of the four gain settings, as part of a 10-scan series that included conditions not relevant to the current presentation. The 10 scan conditions (4 gain settings plus 6 other conditions) were presented in a different randomized order for each subject. To address concerns about the potential influence of preceding adaptation experience on activations during the four scan conditions reported here, the other conditions included visuomanual tracking of discrete step movements of the target and tracking with the eyes only. Step tracking was performed at the same four joystick-to-cursor gains as used for continuous tracking. Depending on the randomized order in which the 10 scan types were presented, the continuous tracking scans discussed here could be preceded by the following scan types: *1*) continuous tracking at a different gain, *2*) step tracking at the same gain, *3*) step tracking at a different gain, *4*) tracking with the eyes alone, and *5*) the first scan had no previous scan. Task performance began 10 s prior to the onset of scanning and continued for 100 s.

Images of rCBF were obtained with a modified autoradiographic method. A bolus of $H_2{}^{15}O$ was injected intravenously into a left antecubital vein simultaneous with the onset of the task and 10 s prior to the collection of a 90-s scan. Images of radioactive counts were used to estimate rCBF. Images were acquired with a Siemens EXACT 921 scanner. The device collects 47 contiguous slices of 3.375 thickness and a nominal intrinsic resolution of approximately 5 mm full width at half-maximum (FWHM). Images were collected parallel to the canthomeatal line, reconstructed with a calculated attenuation and a 0.3-cm ramp filter, and smoothed with a Gaussian filter to an isotropic resolution of 11.8 mm FWHM.

Kinematic analysis

The mean extent of movement for a scan was computed as the mean of the difference between movement extremes for each movement cycle. Joystick velocity was derived from the position signal by digital low-pass filtering (5-Hz cutoff) and differentiation (Hamming 1983). The mean absolute velocity (i.e., speed) for a scan was computed from the velocity record after excluding periods during which absolute velocity fell below a threshold 1 cm/s. The mean temporal error was found by computing the mean difference between the times of reversals in the direction of arm movement and the times of reversals in target movement. The intermittency of tracking velocity was computed as the number of zero crossings in the acceleration record. In continuous visuomotor tasks, on-line corrections are reflected by changes in acceleration that can be detected as zero crossings (Eichhorn et al. 1996; Meyer et al. 1988; Siebner et al. 2001). A higher rate of zero crossings is considered evidence that continuous tracking is dominated by closed-loop as opposed to open-loop processes.

EOG records of horizontal eye movements (HEOG) were corrected for drift, low-pass filtered (5-Hz cutoff), and calibrated to gaze position by finding for each subject global offset and gain factors that best fit (i.e., minimized mean squared error) all of the subject's HEOG

records to target position. Mean temporal error (phase lead or lag) was computed by finding the temporal shift between gaze position and target position that minimized summed squared positional error across a record. Positional error was computed for each HEOG record as the root mean squared error between gaze position and target position after correcting for temporal error.

rCBF image analysis

Image processing was performed on SUN Ultra 1 and Dell Linux workstations. Within subject alignment of consecutive PET scans was performed using an automated registration algorithm (Woods et al. 1998a). A mean image of the co-registered PET scans was spatially normalized to a PET reference atlas generated from 18 normal subjects, centered in Talairach coordinates using an affine transformation with 12 df (Woods et al. 1998b). Spatially normalized PET images were smoothed to a final isotropic resolution of 15 mm FWHM.

Changes of brain activity as a function of movement amplitude were assessed using statistical parametric mapping (SPM99; Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK). Images were normalized to each other to a global CBF of 50 ml/dl/min using a common volume mask. Significant changes in rCBF were detected by ANCOVA in voxel-by-voxel comparisons using the mean extent of movement of individual subjects during individual scans as the covariate of interest. Separate comparisons were performed for positive and negative correlations between rCBF and movement extent across the four tracking conditions. The resulting voxel maps of the t statistic [SPM(T)] were evaluated at two statistical levels. *1*) Based on results of our prior study of movement speed and rate, there was a strong a priori prediction for amplitude/speed effects within the BG, SMC (pre- and postcentral gyri), and anterior cerebellum (Turner et al. 1998). Within these areas, as defined by a mask derived from Tzourio-Mazoyer et al. (2002), we used a threshold of $P < 0.001$ (>50 voxels) uncorrected for multiple comparisons. *2*) For the remainder of the brain, a threshold of $P < 0.05$ corrected for multiple pixel-wise comparisons was used (Friston et al. 1994; Genovese et al. 2002). Resultant t-maps were superimposed on a structural MRI scan derived from the average of the spatially normalized scans of all subjects in the study. Specific BG nuclei were identified from two cross-sectional atlases (Schaltenbrand and Warren 1977; Talairach and Tournoux 1988). For post hoc data analysis and display, rCBF values were extracted for individual subjects and scans from the coordinates of maximal activation within each significant activation.

RESULTS

Awareness and gain modification

Before presenting results in detail, it is worth noting that subjects showed no awareness that the joystick-to-cursor relation (gain) changed from scan to scan. This unexpected observation was consistent across all subjects. When a change in gain caused temporary inaccuracy at the beginning of an inter-scan training session, some subjects expressed mild surprise, but they never questioned the coherence of the joystick-to-cursor relationship from session to session. When questioned formally following the last scan, none of the subjects expressed awareness that the extent or speed of movement varied between scans. This result rules out the possibility that subjects adopted different conscious strategies for the different gain conditions.

Task performance

The mean extent and speed of hand movement changed together in a linear fashion across the four gain settings, while eye movements and other aspects of hand movements did not vary systematically (Figs. 2 and 3, *top*). Temporal errors in hand movement (lead and lag relative to the target) were small and did not vary significantly across gain conditions (Fig. 3, *bottom left*; $F_{(2,48)} = 0.59$; $P > 0.5$, main effect of gain). The variability of tracking velocity (i.e., number of acceleration zero crossings), thought to reflect the degree to which continuous movement is feedback-controlled (Eichhorn et al. 1996; Siebner et al. 2001), also did not change across the four gain conditions (Fig. 3, *bottom right*; $F_{(2,48)} = 0.58$; $P > 0.5$, main effect of gain). Finally, horizontal eye movements were very similar across the four gain conditions with respect to their mean relative extents, positional errors, and temporal errors ($F_{(2,48)} = 1.1$, 0.1, and 1.3, respectively; all $P > 0.2$, main effects of gain).

PET results

As predicted, rCBF within bilateral BG and ipsilateral cerebellum exhibited significant positive parametric relationships with mean movement extent (Figs. 4 and 5). Contralateral to the moving hand, extent-related CBF changes were observed primarily within the postcommissural dorsal putamen (Talairach coordinates: −24, −2, 12; $t_{38} = 3.8$, $P < 4.7\text{e-}4$). Ipsilateral to the moving hand, rCBF increased with extent within the postcommissural right putamen and globus pallidus (24, −3, 6; $t_{38} = 3.6$, $P < 8.8\text{e-}4$). A restricted focus of extent-related activity was also found in lobule 6 of the cerebellum, ipsilateral to the moving arm (15, −64, −20; $t_{38} = 3.6$, $P < 8.3\text{e-}4$). Figure 5 shows the near linear increase of CBF in these areas for increasing movement extent. No significant effects of movement extent were observed in pre- or postcentral gyri [i.e., the primary sensory and motor cortices (SMC); threshold $P < 0.001$, uncorrected for multiple comparisons]. Exploratory analysis at a relaxed statistical threshold ($P < 0.01$) found significant, modest increasing activation of left and right dorsal SMC with increasing movement extent (*left:* coordinates −30, −34, 69; $t_{38} = 2.85$, $P < 7\text{e-}3$; *right:* coordinates 36, −30, 54; $t_{38} = 3.15$, $P < 3.2\text{e-}3$). No significant inverse relationships were found (i.e., rCBF decrease with increasing extent) nor were additional effects of movement extent found outside of the predefined search region (threshold $P < 0.05$, corrected for multiple comparisons).

Regional blood flow at the loci identified above was not influenced by subjects' experience of a gain adaptation during the preceding inter-scan interval. Adaptations to a new gain preceded only 37 of the 52 total scans, because the four scan types of interest here were interleaved randomly with six other scan types (see METHODS). Individual post hoc analyses for each of the five loci identified above found that mean rCBF did not differ between scans that were preceded by adaptation during the inter-scan practice session and scans that were preceded by practice alone ($t_{51} < 1.0$, $P > 0.3$ for all 5 comparisons).

DISCUSSION

The results are consistent with our prediction that activity in the BG, cerebellum, and/or SMC would be modulated as a function of the speed or extent of movement. With increasing movement scale (i.e., speed, extent, and covariates), there was a parallel increase of CBF in bilateral putamen and ipsilateral

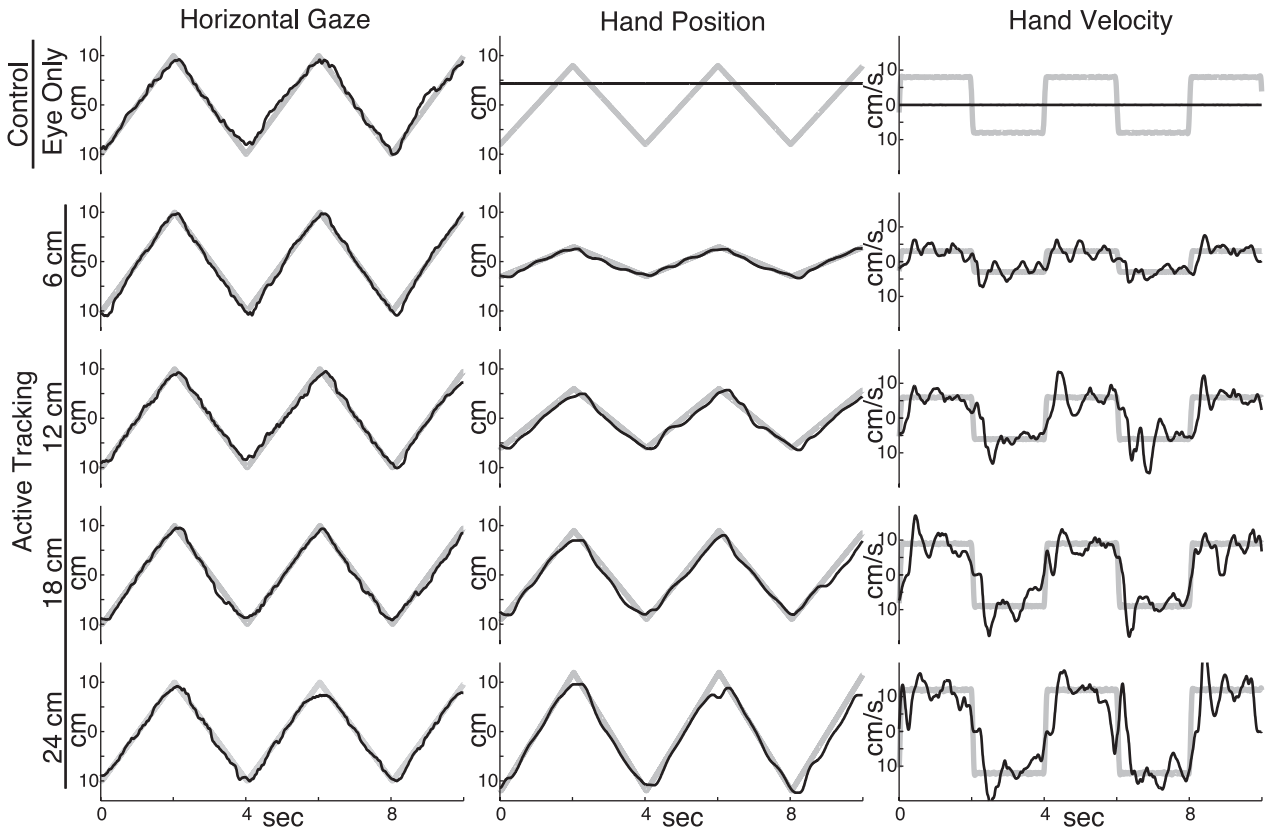

FIG. 2. Behavior during continuous tracking. Representative 10 s of behavioral data from an individual subject under 4 gain conditions (smallest/slowest to largest/fastest movements ordered in rows from *top* to *bottom*). Eye movements [horizontal electro-oculographic (EOG), normalized across conditions to yield approximate horizontal gaze, *left*] were very similar across gain conditions. Hand displacement (*middle*) and velocity (*right*) increased as functions of desired movement extent and velocity. Thick gray lines plot time/displacement trajectories of the on-screen target (*left*), desired time/displacement trajectory for hand movement (*middle*), and desired velocity profile for hand movement (*right*).

cerebellum. Weak effects of movement speed and extent were detected in bilateral SMC. It is remarkable that a fourfold change in movement scale results in activation of a small fraction of the CNS territory normally activated by visuomotor tasks (e.g., Winstein et al. 1997). These results are consistent with a model in which a discrete subcircuit of brain regions including BG, cerebellum, and SMC is involved in setting global scaling parameters to match motor output with task or workspace demands (Sainburg et al. 2003; Vindras and Viviani 2002).

Potential confounds were well controlled in the continuous tracking task. Changes in visual input or the number of reversals in movement direction cannot account for our findings because these were held constant across the four gain conditions. It is unlikely the effects are due to differences in eye movements, temporal error or movement continuity, because these did not vary significantly across gain conditions. It is also unlikely the results are related to differences in conscious strategy, because subjects were unable to see the moving limb and subjects were unaware that the joystick-to-cursor gain changed between scans. Finally, it is unlikely the results are attributable to gain adaptation itself because rCBF at the activated sites did not differ between scans that were preceded by gain adaptation and those that were not. Thus the only significant difference in behavior across the four conditions was the extent and velocity of arm movements.

The present results differ from those of our earlier study (Turner et al. 1998) in two important respects. In the earlier study, strong rate/speed effects were found contralateral to the moving arm in primary SMC and in the posterior globus pallidus (i.e., "skeletomotor" territory of pallidum; Alexander et al. 1990; Middleton and Strick 1997). Here, effects of extent and/or speed were barely detectable in SMC, and the BG was activated bilaterally in middle dorsal putamen (i.e., premotor or associative territories of the striatum). The origin(s) of these differences is a matter of speculation due to multiple differences between the two studies and the indirect relationship between neuronal activity and PET results (Jueptner and Weiller 1995). Potential explanations worthy of note can be found in the general discussion below.

The minimal activation of SMC is an issue of importance because many studies have shown that SMC neurons encode information about movement extent/speed (Ashe and Georgopoulos 1994; Fu et al. 1993, 1995; Messier and Kalaska 2000; Moran and Schwartz 1999) or muscle force (Cheney and Fetz 1980; Evarts 1968; Kalaska et al. 1989), and that SMC activity, measured by functional imaging, is strongly influenced by the rate or speed of movement (Blinkenberg et al. 1996; Rao et al. 1996; Sadato et al. 1997; Schluag et al. 1996; VanMeter et al. 1995; Wexler et al. 1997). Several factors could account for the divergent results. First, use of continuous tracking may account for some of the differences. Unlike what is commonly reported for extent and/or speed coding during discrete movement tasks, neuronal correlates of speed are reported to be rare during

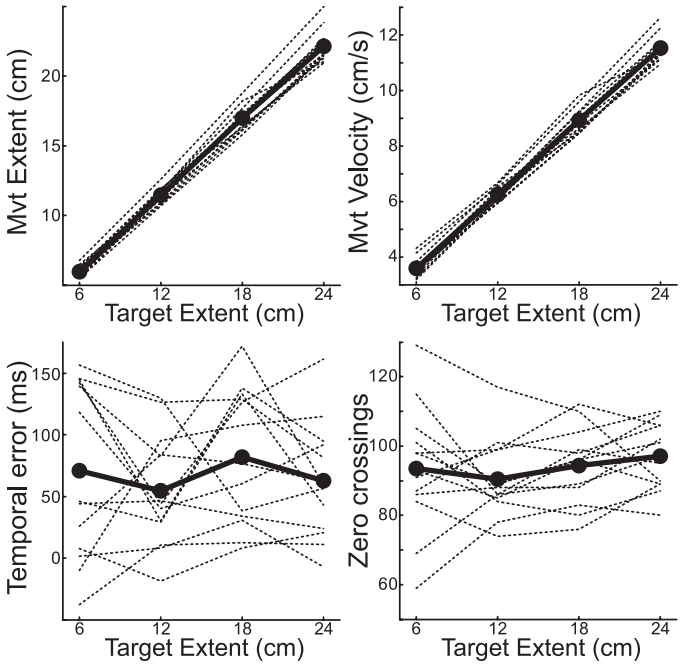

FIG. 3. Mean continuous tracking performance for all 13 subjects. Movement extent (*top left*) and speed (*top right*) increased as close linear functions of desired movement extent (Target extent) both for the mean across subjects (●) and for all subjects individually (. . . .). On average, subjects tended to reverse direction of movement in advance of the time when the target reversed directions (Temporal error, *bottom left*). Temporal errors were highly variable across subjects and conditions such that there was no systematic change across gain conditions. Number of zero crossings in the acceleration record (a measure of tracking intermittency, *bottom right*) was also variable across subjects and conditions and, on average, remained constant across gain conditions.

periods of continuous visuomanual tracking (Johnson and Ebner 2000; Schwartz 1992). Second, any activations attributable to a relationship of SMC activity with movement rate or with the dynamics and muscle forces associated with large changes in acceleration were held constant in the present experiment because the rate of movement (i.e., reversals per second) was constant across conditions. Third, it is unlikely, but possible, that effects in SMC of extent or speed were attenuated by a countervailing effect of movement precision. Through our manipulation of joystick-to-cursor gain, smaller movement extents were associated with higher visuomotor gains, and potentially, an increased requirement for movement precision. Although such an effect would be consistent with the long recognized sensitivity of neurons in SMC to movement precision requirements (Evarts et al. 1983), our failure to find any independent effects of precision on brain activity (detectable here as inverse correlations with movement extent) argues against precision having an important influence on brain activity in this study. Despite the minimal activation, it remains likely that SMC contributes to the control of movement scale, if for no other reason, because the motor cortices are on the principal pathways by which cerebellar and BG outflow influence the spinal motor apparatus (Alexander et al. 1990; Middleton and Strick 2000). The small SMC activations found here were located bilaterally within cortical regions identified as rate-related in our previous work (Turner et al. 1998) and established as the proximal arm representation in other imaging studies (Colebatch et al. 1991; Grafton et al. 1993). We conclude that SMC is less sensitive to parameters associated with movement scale than are regions within the BG and cerebellum.

The observation of activity in the BG related to extent and/or speed is consistent with our previous results (Turner et al. 1998) and other studies showing that activity in the BG is correlated with the speed of arm movement (Hanakawa et al. 2002; Taniwaki et al. 2003) or speech volume (Liotti et al. 2003). We have also found recently that BG activity is increased when early information about movement extent allows preplanning of that parameter compared with conditions in which movement direction is preplanned or no early information is provided (M. Desmurget, S. T. Grafton, P. Vindras, H. Grea, and R. S. Turner, unpublished observations). These functional imaging results, along with data from nonhuman primates studies using neuronal recording (Georgopoulos et al. 1983; Turner and Anderson 1997), inactivation (Alamy et al. 1996; Horak and Anderson 1984a; Hore and Vilis 1980; Inase et al. 1996; Kato and Kimura 1992; Mink and Thach 1991) and electrical stimulation (Horak and Anderson 1984b), are all consistent with the hypothesis that BG outflow contributes preferentially to the control of movement scale independent of movement direction control. Additional evidence for this hypothesis comes from the selective impairments in control of movement scale commonly observed in BG disorders such as Parkinson's disease (Berardelli et al. 2001; Desmurget et al.

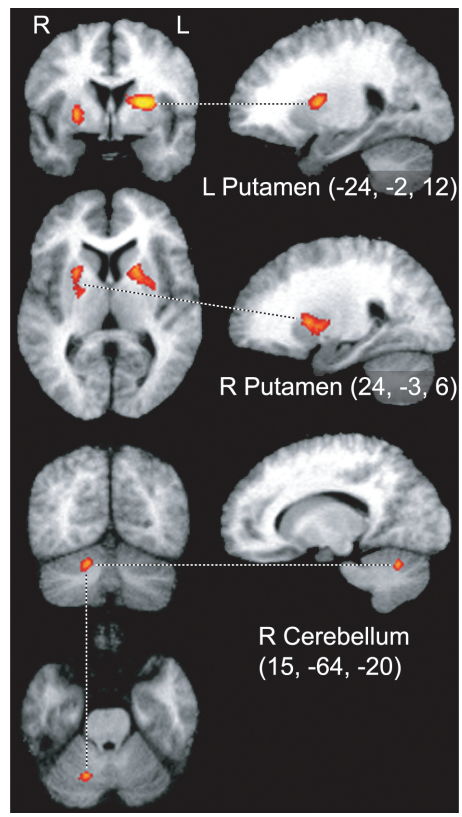

FIG. 4. Brain correlates of visuomotor gain. Areas of increasing cerebral blood flow (CBF) with increasing movement speed and extent are shown in orange-yellow (threshold for illustration, $P < 0.005$; all locations, $P < 0.001$ uncorrected). Significant changes were identified in left (*top*) and right dorsal putamen (*middle*) and right cerebellum (*bottom*), superimposed on the mean MRI derived from the study population. No other changes, positive or negative, reached significance.

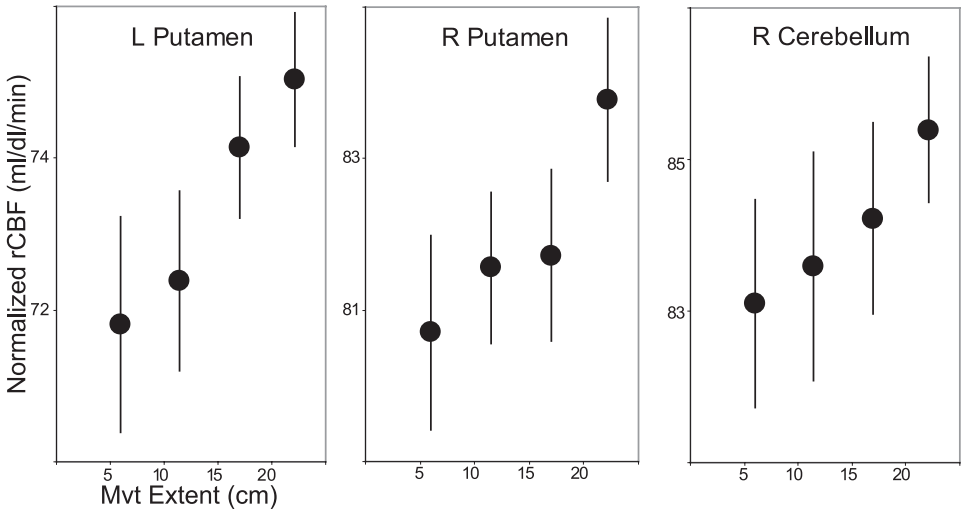

FIG. 5. Mean CBF at 3 cerebral locations during visuomotor tracking. At the 3 sites identified as gain-related (L putamen, R putamen, and R cerebellum), CBF increased as a monotonic function of desired movement extent (Target extent). Error bars = SE.

2003a; Godaux et al. 1992) and Huntington's disease (Berardelli et al. 1999; Thompson et al. 1988). Topics for further investigation include the actual mechanism by which BG output influences movement extent or speed and how this function meshes with hypothesized roles for the BG in movement selection and reward-based learning (Graybiel et al. 1994; Hikosaka et al. 2002; Mink 1996).

It is important to consider the possibility that use of a gain adaptation procedure influenced the present results. The question is of particular relevance because Krakauer et al. (2000a) reported a nearly identical activation pattern (bilateral BG and ipsilateral cerebellum) during adaptation to a new visuomotor gain. There are multiple reasons to think the present results are not direct effects of gain adaptation. Scans were started approximately 4 min after practice sessions during which gain adaptation could occur. Measures of task performance indicated volunteers were adapted fully to a new gain during practice, so any rCBF changes related to adaptation itself would have to persist across the 4-min interval between adaptation and scanning. Although some forms of adaptation do induce changes in brain activity that persist well beyond the period of overt error reduction (e.g., Krakauer et al. 2000a; Shadmehr and Holcomb 1997), gain adaptation apparently does not cause long-lasting effects (Krakauer et al. 2000a). Consistent with this interpretation, our post hoc analysis found no evidence for lingering effects of gain adaptation on activity at the brain loci identified here. It is quite possible, nonetheless, that the circuits engaged to mediate movement scale depend on factors such as a subject's recent experience with the task environment. For instance, based on the abundant behavioral evidence that adaptation to a new visuomotor gain can be generalized across directions of movement (Krakauer et al. 2000b; Pine et al. 1996) and between arms (Bock 1992; Van Den Dobbelsteen et al. 2003; Vindras and Viviani 2002), Vindras et al. predicted that the CNS structures mediating movement scale under conditions of gain adaptation represent motor acts at an abstract level (i.e., independent of specific muscles or movements) and that the representation must be bilateral (Vindras and Viviani 2002). The bilateral activation of associative BG circuits observed here fits well with those predictions. Additional work is required to determine whether the BG circuit identified here is involved in both scaling movement in general and the regulation of visuomotor gain. It bears noting that the impairments in movement scaling observed in BG disorders are well explained as deficits in regulating visuomotor gain to match the metrics of the workspace (Berardelli et al. 2001).

An involvement of cerebellar structures in the control of scale-related parameters of movement is well established. Recording studies in the cerebellum of nonhuman primates have demonstrated relations of single unit discharge to motor parameters such as velocity (Coltz et al. 1999; Mano and Yamamoto 1980; Mano et al. 1986; van Kan et al. 1993) and extent (Fu et al. 1997). Single unit and modeling studies of oculomotor behaviors suggest the cerebellum is involved in compensating for extraneous loads that might otherwise interfere with movements of the eye (Krauzlis and Lisberger 1994; Mizukoshi et al. 2000). Functional imaging studies have implicated the cerebellum in regulating the level of dynamic force output (Dettmers et al. 1995) and processing motor error (Desmurget et al. 2001; Ebner et al. 1996; Imamizu et al. 2000; Jueptner et al. 1995). Studies in human cerebellar patients have suggested the cerebellum is involved in compensating for interaction torques generated during multijoint reaching movements (Bastian and Thach 1995; Bastian et al. 1996). The cerebellum receives strong proprioceptive input which may also contribute to speed/extent activations (Bower 1997). All of these factors (dynamic force, interaction torques, tissue loads, motor error, and proprioceptive inputs) are scaled with the speed and extent of movement. For this reason, it is not surprising that this study demonstrated an extent-related activation in the cerebellum. Unlike the BG, however, damage to the cerebellum leads to errors in specification of movement direction as well as movement scale. Thus it is likely the cerebellum contributes to the control of movement scale at the level of dynamics where extent, speed, and direction of movement are not controlled independently.

The effects observed here need not be interpreted exclusively as evidence for BG or cerebellar contribution to feedforward planning of movement extent or speed. For instance, the activations observed here could arise in part from sensory reafference that correlates closely with the speed or extent of movement. It is less likely, although possible, these results are attributable to feedback control processes engaged to varying degrees depending on movement speed/extent. Although a variety of studies have implicated both the BG (Brainard and

Doupe 2000; Siebner et al. 2001; Smith et al. 2000; Winstein et al. 1997) and cerebellum (Desmurget et al. 2001; Ebner et al. 1996; Imamizu et al. 2000; Jueptner et al. 1995) in feedback control, it remains unclear why feedback control would become more prevalent during larger, faster movements. Moreover, our analysis of tracking performance failed to produce evidence that feedback control (i.e., intermittency) changed across the four gain conditions.

In summary, the present results are consistent with the view that a small subcircuit within the motor control system contributes to the control of movement extent, speed, and covariates and that bilateral BG and ipsilateral cerebellum play central roles in the operation of that circuit.

DISCLOSURES

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