Distinct striatal regions support movement selection, preparation and execution

Emmanuel Gerardin,[1,4] Jean-Baptiste Pochon,[1,3] Jean-Baptiste Poline,[3] Léon Tremblay,[2] Pierre-François Van de Moortele,[5] Richard Levy,[1] Bruno Dubois,[1] Denis Le Bihan[3] and Stéphane Lehéricy[1,3,5,CA]

[1]Inserm U610; [2]Inserm U289, Hôpital de la Salpêtrière, Paris; [3]Department of Medical Research, Service Hospitalier Frédéric Joliot and IFR 49, CEA, Orsay; [4]Department of Neuroradiology, Hôpital Charles Nicolle, Rouen, France; [5]CMRR/University of Minnesota, Minneapolis, MN, USA

[CA]Corresponding Author and Address: lehericy@cmrr.umn.edu

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The aim of this study was to determine whether distinct striatal territories are specifically involved during the selection, preparation and execution of a movement. Nine volunteers were studied using fMRI at 3 T. Subjects were presented with visual stimuli instructing them to prepare during a variable delay and then execute a button press with either the left or the right hand. The side of the movement was either freely selected by the subject (free selection) or specified by the instruction cue (preparation). Movement selection, preparation and execution were associated with activation in the caudate nucleus, the anterior and the posterior parts of the putamen, respectively. These results suggest that these three aspects of movement are represented within distinct basal ganglia regions. *NeuroReport* 15:2327–2331 © 2004 Lippincott Williams & Wilkins.

Key words: Basal ganglia; Functional MRI; Motor system

INTRODUCTION

The striatum is organized in several compartments, which receive afferents from distinct cortical regions including associative, sensorimotor, and limbic areas [1]. Electrophysiological studies in primates have shown that these compartments are differentially involved in the control of movement [2–5], although no study has examined simultaneously the associative, premotor, and motor compartments of the striatum.

Imaging studies in humans have shown that movement selection, preparation, and execution, which are frequent components of human behavior, are subserved by distinct areas in the frontal lobes [6–14]. These studies mainly examined cortical areas, and little is known about basal ganglia activation. Similarly to the frontal lobe, it is expected that these movement components would be represented in different territories of the striatum. To test this hypothesis, healthy subjects were examined during performance of motor tasks requiring selection, preparation, and execution of a finger movement.

MATERIALS AND METHODS

Subjects: Nine right-handed healthy volunteers were studied (six males, age range: 24–33 years) at 3 T using Bruker whole-body magnetic resonance imaging system. Subjects had no history of neurological or psychiatric disease. They were paid for their participation and gave informed consent in line with the Declaration of Helsinki. The local ethics committee of the Salpêtrière Hospital approved the experiment. All subjects completed the Edinburgh Handedness Inventory and were strongly right-handed.

Data acquisition: Twenty-four 5 mm contiguous axial slices were obtained with a T2*-weighted gradient echo, echo planar imaging sequence, using blood oxygen level dependent contrast ($TR=2000$ ms, $TE=40$ ms, flip angle 90°, matrix 64×64, field of view $220 \times 220\,mm^2$). A total of 140 brain volumes were acquired for each run. The first five volumes of each run were discarded to reach signal equilibrium. High-resolution 3D anatomical images of the whole brain were also acquired (gradient echo, inversion recovery, $TR=1600$ ms, $TE=5$ ms, matrix 256×256, field of view $220 \times 220\,mm^2$, slice thickness 1 mm).

Cognitive tasks: Subjects were required to perform motor tasks depending on a visually presented cue appearing for 1 s (Fig. 1). In the prepare condition, subjects were told to prepare to press a button with their right (prepD instruction cue) or left thumb (prepG). This task included instructed selection and preparation components. In the select condition (prepC instruction cue), subjects were asked to mentally choose the side of the movement and then to prepare to execute this movement. This task included free selection and preparation components, and probably working memory components as subjects were asked not always to press the same button. After a variable delay during which subjects fixed a central cross on a blank screen, a trigger signal indicated the subject to press the button in the execute condition (clicD or clicG following the prepare condition, or

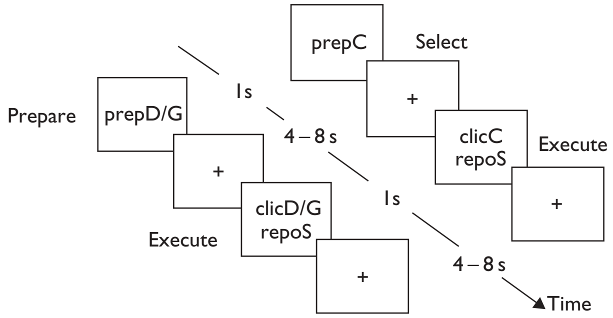

Fig. 1. Schematic description of the tasks. In the prepare condition, the subject was required to prepare a button press during a variable delay (4–8 s) on the side indicated by the instruction cue (right: prepD or left: prepG) and then to execute (clicD or clicG) or not (repoS) the movement after the trigger signal. In the select condition (prepC), the subject had to choose the side and to prepare the forthcoming movement during a variable delay (4 to 8-s), and then to execute (clicC) or not (repoS) the movement after the trigger signal. Execution (clicD or clicG) and rest (repoS) signals not preceded by preparation signals also occurred randomly.

clicC following the select condition) or a no-go signal indicated not to press the button (repoS). In both tasks, subjects were also told to respond as quickly as possible after the trigger signal. The pseudorandom inter-stimuli intervals (4, 6 or 8 s duration) were used to avoid habituation and anticipation during the tasks. Execution (clicD or clicG) and rest (repoS) signals not preceded by preparation signals (rest condition) also occurred at varying intervals. Instruction cues and trigger-signals were composed of five letters and were back-projected on a screen that subjects viewed through mirror glasses. Stimuli were randomized across six runs. Each run was composed of 27 pairs of conditions and lasted 4 min 40 s. Response times and response sides were recorded during image acquisition. All subjects were trained immediately before scanning with a different trial run.

Statistical analysis: Data analysis was performed with SPM99 (Wellcome Department of Cognitive Neuroscience, London). For each subject, anatomical images were transformed stereotactically to Talairach coordinates. The functional scans, corrected for subject motion, were then normalized using the same transformation and smoothed with a Gaussian spatial filter to a final smoothness of 5 mm. Data were analyzed across subjects (group analysis using fixed effect). Data from each voxel were modeled using the general linear model with separate hemodynamic response functions and their time derivatives modeling each period of the tasks. Overall signal differences between runs were also modeled. A 270 s temporal cut-off was applied to filter subject-specific low frequency drift of the signal. An SPMF map was obtained, reflecting significant activated voxels according to the model used ($p<0.001$). The estimates associated with the select, prepare and execute conditions and for both hands were respectively compared with the rest signals which were not preceded by preparation signals (rest condition). The rest signals which were preceded by a preparation cue corresponded to no-go signals and were not used for this comparison. To show activation specifically related to the free selection, estimates of select and prepare were also compared using linear contrasts. The resulting set of voxel values for each contrast were thresholded at $p<0.05$ ($Z>4.78$) corrected for multiple comparisons inside the volume of the whole brain (extent threshold=4 voxels).

For basal ganglia and thalamus, activated clusters were considered significant at $p<0.05$ corrected for multiple comparisons inside the volume of the striatum created for each controls using semiautomatic segmentation based on region growing (small volume correction) [15] (extent threshold=4 voxels).

RESULTS

Task performance: Mean reaction times during the execute condition were significantly shorter when the trigger signals were preceded by an instruction cue (select 617 ± 80 ms, prepare 571 ± 63 ms) than when they were not (787 ± 80 ms; $p<10^{-4}$). Mean reaction times were significantly longer in the select than the prepare conditions ($p=9\ 10^{-4}$). Mean reaction times were not significantly different between movements of the right and the left hands (execute 769 ± 76 ms and 803 ± 73 ms; prepare 552 ± 54 ms and 588 ± 74 ms; select 603 ± 82 ms and 632 ± 78 ms, for the right and left hands, respectively, $p<0.05$). Error range varied from 0% to 2.22% (mean ± s.d. 1.11 ± 0.7%). Errors consisted in execution of a button press after instruction cues (30%) or rest signals (18%), and errors in the side of the button press (52%). Errors were specified in the model as non-interest variables. Overall, percentages of button press in the select condition were 53 ± 0.1% with the right hand and 47 ± 0.1% with the left hand. Group and individual between hands differences were not significant. There was no significant interaction between task-side ($p=0.65$), task-subject ($p=0.24$), side-subject ($p=0.33$) and task-side-subject ($p=0.31$). There was no systematic effect of run position on response times. These results were similarly observed in each subject.

fMRI data: When subjects selected and prepared a right hand movement, significant signal changes were found in the left dorsolateral (DLPFC, BA 9/46) and ventrolateral prefrontal cortex (VLFPC, BA 44/45/47), preSMA, SMA, sensorimotor cortex (SMC), superior and inferior parietal cortex, putamen and thalamus, and in the caudate nucleus bilaterally (Table 1).

When subjects selected and prepared a left hand movement, significant signal changes were found in the left DLPFC, preSMA, lateral premotor cortex (PMC) and insula, in the right SMC and caudate nucleus, and in bilateral VLPFC, inferior parietal cortex, thalamus and anterior parts of the putamen, the putamen being arbitrarily divided into an anterior and a posterior area using the anterior commissure as a landmark (Table 1).

The select minus prepare condition allowed isolating processes specifically related to the selection of movement side (Table 1). Selection of right hand movement was associated with significant signal changes in the left DLPFC, VLPFC, preSMA and anterior putamen, and in bilateral caudate nuclei. Selection of left hand movement was associated with significant signal changes in the left DLPFC, preSMA, inferior parietal and insular area, right VLPFC, anterior putamen, and in bilateral dorsomedial thalamus (Fig. 2, Table 1).

Table I. Coordinates of significant cluster maxima for the group analysis. Coordinates are given in millimeters of the Talairach's space. Data were thresholded at $p < 0.05$ corrected for multiple comparisons.

		Right hand										Left hand									
		Select *vs* Rest		Select *vs* Prepare		Prepare *vs* Rest		Execute with prep *vs* Rest		Execute without prep *vs* Rest		Select *vs* Rest		Select *vs* Prepare		Prepare *vs* Rest		Execute with prep *vs* Rest		Execute without prep *vs* Rest	
Brodmann's areas (BA)		(x, y, z)	T	(x, y, z)	T	(x, y, z)	T	(x, y, z)	T	(x, y, z)	T	(x, y, z)	T	(x, y, z)	T	(x, y, z)	T	(x, y, z)	T	(x, y, z)	T
DLPFC BA 9/46	L	(−42, 21, 30)	5.49	(−45, 15, 42)	6.16							(−45, 21, 33)	6.60	(−45, 27, 27)	6.09						
VLPFC BA 44/45/47	R											(39, 27, −3)	5.37	(45, 21, 0)	4.99						
	L	(−42, 18, 6)	5.99	(−39, 30, 0)	4.94							(−57, 9, 15)	5.60								
PreSMA	R															(6, 3, 54)	6.04				
	L	(−6, 12, 57)	6.11	(−3, 18, 57)	6.07							(−3, 18, 51)	6.59	(−3, 21, 48)	6.80						
SMA	R																			(0, −9, 51)	4.79
	L	(−6, −9, 54)	6.64			(−6, −9, 54)	7.26			(−6, −9, 57)	6.25										
Lateral PM BA 6/8	R															(36, −12, 60)	6.84				
	L					(−42, −15, 60)	5.54					(−30, 0, 60)	5.25								
SMC BA 1-3/4	R											(36, −18, 54)	5.66			(36, −15, 57)	10.44	(45, −30, 57)	5.20	(33, −21, 51)	5.94
	L	(−39, −27, 6)	7.37			(−42, −27, 57)	8.50	(−42, −30, 57)	5.40	(−42, −27, 60)	7.05										
SII BA 40/43	L							(−39, −3, 15)	7.79	(−39, −3, 15)	7.97									(−42, −3, 15)	5.03
Sup. Parietal BA 5/7	L	(−36, −57, 54)	6.74																		
Inf. Parietal	R							(42, −45, 42)	6.38	(54, −42, 42)	5.93	(42, −51, 45)	5.66					(51, −42, 42)	6.18	(51, −36, 30)	6.42
BA 39/40	L	(−48, −39, 42)	5.60			(−51, −21, 24)	6.07	(−54, −45, 42)	5.64			(−48, −42, 42)	6.64	(−48, −45, 45)	5.99						
Insula	L											(−30, 27, 0)	5.09	(−30, 24, 3)	5.22					(39, 12, 0)	5.50
	L																			(−36, 21, 9)	5.13
Occipital BA17	R																	(3, −75, 12)	5.04		
Caudate nucleus	R	(15, 6, 12)	4.38	(15, 6, 12)	4.24					(9, 18, 3)	3.47	(18, 18, 3)	4.78							(12, 12, 3)	4.67
	L	(−12, 6, 12)	5.43	(−12, 6, 12)	5.19					(−15, 3, 21)	4.70									(−9, 9, 9)	5.28
Ant. Putamen	R					(21, 15, 9)	4.25			(21, 9, 6)	4.36	(27, 12, 6)	5.14	(27, 12, 6)	3.87	(21, 15, 9)	4.52			(30, 3, −3)	4.27
	L	(−24, 6, 6)	4.11	(−18, 12, 6)	3.89	(−24, 9, 9)	4.18					(−27, 12, 6)	3.87			(−24, 9, 9)	3.58				
Post. Putamen	R																	(30, −15, 3)	4.42		
	L	(−24, −3, 12)	3.60					(−30, −3, 6)	4.87											(−33, 0, 0)	4.18
Thalamus	R											(9, −9, 6)	4.41	(9, −12, 9)	4.36					(6, −9, 0)	5.64
	L	(−12, −12, 6)	4.56					(−18, −15, 3)	3.13			(−9, −12, 3)	3.52	−9, −15, 12	3.53			(−12, −6, 15)	4.61		

Ant., anterior; Inf., inferior; L, left; R, right; sup., superior; T, T-score.

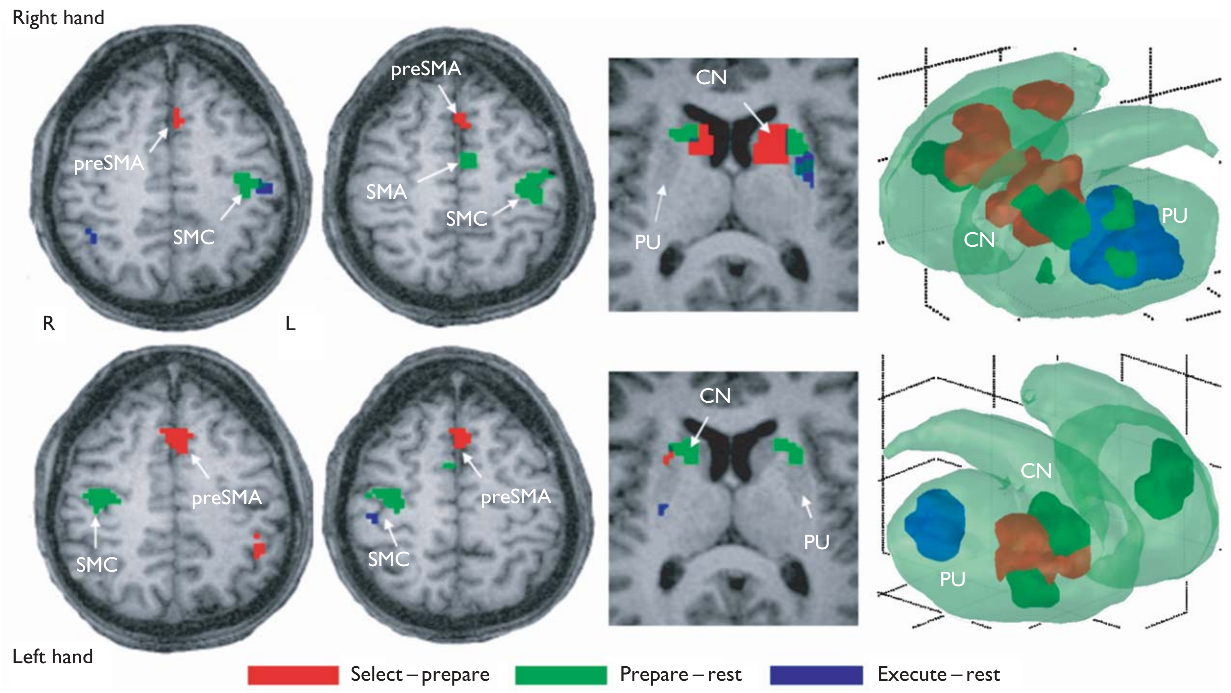

Fig. 2. Activation observed during the select minus prepare (red), prepare minus rest (green), and execute after select or prepare minus rest (blue) conditions for the right and left hand movement superimposed on axial images (left and middle) and a 3D reconstruction of the striatum (right; $p<0.05$ corrected). There was a rostrocaudal gradient in the frontal lobes, and the basal ganglia contralateral to the movement for selection, preparation and execution of movement, predominating for right hand movement. CN, caudate nucleus; L, left; preSMA, presupplementary motor area; PU, putamen; R, right; SMC, sensorimotor cortex.

No significant voxel was detected when the prepare condition was compared to the select condition.

When subjects had only to prepare but not select the side of the movement, signal changes were strongly lateralized in the hemisphere contralateral to the prepared movement (Table 1). For preparation of a right hand movement, activation was observed in the left SMA, lateral PMC, SMC, inferior parietal cortex, and in bilateral anterior putamen. Activation trends was found in the preSMA at a lower statistical threshold (−3/9/60; T-score=4.05 at $p<0.001$ not corrected for multiple comparisons). For preparation of a left hand movement, activation was observed in the right preSMA, SMC and adjacent lateral PMC, and in bilateral anterior putamen. SMA activation was located more caudally during the prepare than the select conditions (Fig. 2). Activation located in the anterior part of the putamen extended into the posterior part of the caudate nucleus (Fig. 2).

During execution after preparation or selection, for each hand movement, significant signal changes were found in the SMC and posterior putamen contralateral to the moving hand, in the right inferior parietal cortex and left thalamus (Fig. 2, Table 1). During right movement, additional activation was found in the left secondary sensory area (SII) and inferior parietal cortex. During left hand movement, additional activation was found in the right occipital cortex.

During execution without preparation, for each hand movement, significant signal changes were found in the SMC and SMA contralateral to the moving hand, in the right inferior parietal cortex and anterior putamen, the left SII, and bilateral caudate nuclei (Table 1). During left movement, additional activation was found in the insula bilaterally, in the left posterior putamen and the right ventro-lateral nucleus of the thalamus.

DISCUSSION

Movement selection, preparation and execution of a visually-guided limb movement were associated with activation in the caudate nucleus, the putamen rostral to the anterior commissure, and the posterior putamen, respectively. A similar rostro-caudal gradient was observed in the frontal lobes, as already reported [6–14].

Anatomically, studies in primates have shown that these three striatal compartments receive mainly afferents from prefrontal [16,17], premotor [18], and primary sensorimotor cortices [19], respectively. A rostrocaudal distribution of preSMA *vs* SMA projections to the striatum was also evidenced [18]. This rostrocaudal topography of pre-SMA and SMA projections to the putamen is in agreement with our functional results, e.g. the preSMA was activated along with the anterior striatum.

These results are in line with electrophysiological studies in primates, which showed that neurons in rostral parts of the striatum including the caudate nucleus were activated during tasks which required higher order motor processes, such as working memory, early learning of complex movement sequences, or reward components [3,4,20,21]. In the putamen, neurons with set-related activity were located rostral to neurons with movement-related activity, although partially overlapping with preparatory activities [2,5,22].

In humans, the caudate nucleus was activated in tasks requiring preparation and selection of a sequence of movements based on information stored in working memory [7], new learning [23], and planning [24]. Functional imaging studies of movement preparation focused on cortical areas reporting activity located rostral to activation associated with movement execution [6,10–14]. In humans, PET [23] or fMRI reports [9,25] have shown activation in the posterior putamen and ventrolateral areas of the thalamus during execution of simple hand movement. In contrast to prepared movements, unprepared hand movements resulted in additional activation of the anterior striatum including the caudate nucleus. Caudate nucleus activation was usually not reported during simple hand movements [6,9,25]. Caudate nucleus activity may thus be related to additional cognitive processes necessary to execute movement when it was not preceded by a preparation cue. A possibility was that activation was associated with signal- or instruction-related activity, coding the forthcoming behavioral reaction [20].

CONCLUSION

These results suggest that the representation of the different motor components related to the selection, preparation, and execution of a simple movement are represented in distinct basal ganglia areas organized along a rostrocaudal axis. These results are in agreement with the concept of parallel cortico–basal ganglia motor circuits [1].

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