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Somatotopic organization in the internal segment of the globus pallidus in Parkinson's disease

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Abstract

Ablation or deep brain stimulation in the internal segment of the globus pallidus (GPi) is an effective therapy for the treatment of Parkinson's disease (PD). Yet many patients receive only partial benefit, including varying levels of improvement across different body regions, which may relate to a differential effect of GPi surgery on the different body regions. Unfortunately, our understanding of the somatotopic organization of human GPi is based on a small number of studies with limited sample sizes, including several based upon only a single recording track or plane. To fully address the three-dimensional somatotopic organization of GPi, we examined the receptive field properties of pallidal neurons in a large cohort of patients undergoing stereotactic surgery. The response of neurons to active and passive movements of the limbs and orofacial structures was determined, using a minimum of three tracks across at least two medial-lateral planes. Neurons (3183) were evaluated from 299 patients, of which 1972 (62%) were modulated by sensorimotor manipulation. Of these, 1767 responded to a single, contralateral body region, with the remaining 205 responding to multiple and/or ipsilateral body regions. Leg-related neurons were found dorsal, medial and anterior to arm-related neurons, while arm-related neurons were dorsal and lateral to orofacial-related neurons. This study provides a more detailed map of individual body regions as well as specific joints within each region and provides a potential explanation for the differential effect of lesions or DBS of the GPi on different body parts in patients undergoing surgical treatment of movement disorders.

Keywords

Basal ganglia; Parkinson's disease; Microelectrode; Pallidotomy; Deep brain stimulation; Somatotopic organization

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Introduction

As one of two primary output structures of the basal ganglia, the internal segment of the globus pallidus (GPi) serves as a critical nodal point for both the direct and indirect pathways of the basal ganglia thalamocortical circuit. It has been demonstrated to play a role in normal motor behavior (DeLong, 1971) in the development of movement disorders (Alexander et al., 1986; DeLong, 1990; Filion and Tremblay, 1991; Filion et al., 1991) and serves as a surgical target for patients with Parkinson's disease (PD) (Kumar et al., 2000; Rodriguez-Oroz et al., 2005) or dystonia (Diamond et al., 2006; Mueller et al., 2008; Pretto et al., 2008). In monkeys rendered parkinsonian with the neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), it has been demonstrated that changes in motor behavior are associated with increased discharge rates in GPi (Filion and Tremblay, 1991; Filion et al., 1991). More recently, altered patterns of neuronal activity in the form of increased bursting and greater synchronization (Brown et al., 2004; Brown and Williams, 2005; Gatev et al., 2006; Maurer et al., 2004; Nini et al., 1995; Raz et al., 2000; Wichmann et al., 1994b; Wichmann et al., 2002) as well as a widening of receptive fields to proprioceptive input (Filion et al., 1988; Leblois et al., 2006; Vitek et al., 1998) have been reported to occur in GPi in the parkinsonian state. And while a causal relationship between these changes and the cardinal features of PD has yet to be determined, it is clear that therapeutic benefit can be achieved for patients with PD through exogenous modulation of pallidal activity (Baron et al., 2002; Bergman et al., 1990; Burchiel et al., 1999; Nakamura et al., 2007; Rodriguez-Oroz et al., 2005; Vitek et al., 2003; Weaver et al., 2005). As currently performed, such procedures involve the targeting and, in most centers, the identification of the sensorimotor region of the GPi, followed by either radiofrequency ablation or the implantation of a deep brain stimulation (DBS) lead for chronic electrical stimulation.

Studies of the sensory and motor systems of the central nervous system have revealed a high degree of topographic organization in both humans and non-human animal models. Within the GPi, studies using the non-human primate model have revealed that movement-related neurons tend to be located posterolateraly (DeLong, 1971; DeLong et al., 1985). Within that region, a gross somatotopic organization has been demonstrated such that units related to upper limb movement tend to be located inferior, lateral and to a lesser extent caudal to more centrally located lower limb-related units, with orofacial-related units concentrated within the caudal extend of the nucleus ventral to upper limb-related units (DeLong et al., 1985). Studies performed during intra-operative mapping of human patients with either PD (Guridi et al., 1999; Sterio et al., 1994; Taha et al., 1996; Vitek et al., 1998) or dystonia (Chang et al., 2007) have largely supported the presence of a somatotopic arrangement of the GPi in humans. However, most of these studies suffer from limited sample sizes or methodological shortcomings, including acquiring data from only a single trajectory (Taha et al., 1996) or mapping each patient only along a single parasagittal plane (Sterio et al., 1994; Taha et al., 1996). We report here the somatotopic characteristics of the GPi based on the collection of over 3000 neurons from 299 patients with PD obtained during microelectrode mapping of the GPi over a period of ten years.

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Materials and methods

Data were collected from patients undergoing intra-operative physiological mapping prior to pallidotomy or DBS lead placement in the GPi for treatment of the motor symptoms of PD. All patients referred for surgery demonstrated a history compatible with the diagnosis of idiopathic PD, as confirmed by a movement disorders specialist. This included the presence of at least two cardinal motor signs of idiopathic PD (akinesia/bradykinesia, rest tremor and rigidity), a Hoehn and Yahr score of 3.0 or greater while off medication, intractable and disabling motor fluctuations or drug-induced dyskinesias and an established response to levodopa. Patients were excluded as surgical candidates if they presented with neurologic signs suggestive of a secondary form of Parkinsonism or with clinically significant medical disease that was considered to markedly increase surgical risk.

Physiological mapping for such procedures has been detailed previously (Vitek et al., 1998). Briefly, on the day of the procedure patients underwent placement of a stereotactic head frame followed by magnetic resonance (MRI) and computed tomographic (CT) imaging. Selection of the initial anatomical target coordinates was based on indirect targeting methods and defined relative to the mid-commissural point of the anterior commissure (AC)-posterior commissure (PC) line. Based on the Schaltenbrand and Bailey (1959) atlas, the typical coordinates for targeting the sensorimotor GPi are lateral 20–21 mm, anterior 3 mm and ventral 5 mm. Once identified, preoperative targeting was refined further based on direct visual inspection of the pallidal target and its relation to surrounding anatomical structures on high-resolution inversion recovery MRI. After the anatomical target was defined, an entry point was selected that allowed for physiological mapping to be performed along a parasagittal plane in an anterodorsal–posteroventral direction with an angle of approximately 30° from vertical.

Physiological mapping was performed in the awake patient using platinum-iridium microelectrodes with a typical impedance range of 0.6 to 1.0 MΩ. The signal was band-pass filtered and the amplified physiological tracings were monitored using a digital oscilloscope or computer display and a high-quality audio monitor. Sequential parallel trajectories were performed using an x–y stage to delineate the sensorimotor region of the GPi, which is marked by neurons whose spontaneous activity is modulated by passive manipulation and active movements of the extremities or orofacial structures. Neural activity was evaluated as the microelectrode traversed the striatum, the external segment of the pallidum (GPe) and the GPi, the internal and external medullary laminae, the nucleus basalis, the optic tract and the internal capsule. Each structure along the recording track has its own physiological signature (Vitek et al., 1998), which allows for delineation of the entry and exit points. Responses of neurons to passive manipulations of limbs were recorded and microstimulation was performed to aid in the identification of the internal capsule (i.e., muscle contractions) and optic tract (i.e., phosphenes). Identification of the optic tract was verified by the presence of audible neural responses to flashing a light at the eyes of the patient and/or the patient's report of phosphenes in response to microstimulation of the optic tract. The location, firing characteristics and receptive field properties were recorded for each neuron encountered along with the effects of microstimulation (e.g., muscle contraction, phosphenes). The three-dimensional coordinates of each neuron relative to the mid-

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commissural point were estimated by fitting the electrophysiological characteristics of the recording tracts to the Schaltenbrand and Bailey (1959) atlas. Confirmation of this method as an accurate depiction of the recording locations was determined histologically as reported previously (Vitek et al., 1998).

Data analysis

The receptive fields identified from intra-operative records were grouped into three primary body regions: upper limb, lower limb and orofacial. Responses related to manipulation of the cervical area, shoulder, elbow, wrist and hand or fingers were categorized as upper limb responses, while those involving the toes, ankle, knee, hip or trunk were classified as lower limb responses. In some cases, the individual joint or area of manipulation was not noted in terms of the specific joint and direction of movement, as this could not be determined precisely. In those cases, only the general body region was noted (i.e., “arm”, “leg”). Orofacial responses typically included active movements of the jaw or tongue, but responses to passive manipulation of the jaw also were observed by palpating the masseter or passively manipulating the jaw by applying gentle pressure to the chin.

A multivariate mixed model that accounted for repeated measurements within patients was created to determine whether there were differences between the coordinates of the body regions. The three coordinates were set as the dependent variables while body region was used as the explanatory variable. A compound symmetry assumption for the repeated neuron measurements was created for the multivariate model variance–covariance structure. In the case of significant multivariate findings, further exploration of the coordinates associated with body regions was conducted to identify those pairs that were significantly different. Mean estimates and tests for significant differences were reported from this model, which uses a restricted maximum likelihood estimation technique. Significance level was initially set to 5% (i.e. α=.05), with the Bonferroni correction for multiple comparisons applied to limit the probability of obtaining a significant result purely by chance. Based on the application of nine planned comparisons, this resulted in a significance level of 0.6% (i.e., p<0.006). All analyses were conducted using SAS® v9.1.

Results

Between 1993 and 2004, a total of 3183 neurons were examined from 299 patients (193 males) during 348 unilateral procedures (Table 1). Of those, 1972 (62.0%) responded with changes in firing pattern during passive manipulation, primarily rotation of the joints, or active movement of the limbs or face. The responsive neurons included 1767 neurons that were noted to modulate activity only during manipulation of a single, contralateral body region as follows: 940 (53.2%) for the upper limb, 769 (43.5%) for the lower limb and 58 (3.3%) for orofacial movements. The majority (85.8%) of neurons were specific to manipulation of a single joint, while the remaining 14.2% responded to manipulation of multiple joints within the same body region. There was also a greater representation of proximal versus distal joint movements (Table 2). Of the remaining neurons, 120 (6.1%) responded to movements of more than one contralateral body region (e.g., upper and lower limb), while 85 (4.3%) showed modulated activity in response to movements of the

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ipsilateral body, either alone (n = 61) or in combination with regions of the contralateral body (n = 24). Overall, approximately 23% (456/1972) of the neurons that responded to passive manipulation of the contralateral hemibody demonstrated a response to more than one joint, more than one limb and/or to the ipsilateral limb.

For the purpose of examining the three-dimensional somatotopic organization within the GPi, those neurons that responded to multiple body regions or to manipulation of ipsilateral body regions were excluded, leaving a total of 1767 responsive neurons for analysis. Fig. 1 depicts the locations of neuronal responses for all patients on a series of parasagittal planes of the GPi. The number shown above each section represents the lateral location, in millimeters from the midline, of each plane. A preponderance of orofacial responses is observed in the ventral and posterior regions of the area explored in addition to a tendency for lower limb responses to be encountered more anterior and dorsal within the sensorimotor GPi. Upper limb responses were, in contrast more widespread throughout the mapped region. These data are summarized further in Fig. 2, where a series of two-dimensional plots depict the mean coordinates, collapsed across the axial, sagittal and coronal planes, for both the overall body region (black symbols) as well as the individual joints that comprise each body region (gray symbols).

The multivariate analysis confirmed the observed trends, with at least one of the coordinates significantly different between body regions (p<.0001). Further exploration revealed that all pair-wise combinations of arm, leg/torso and face coordinates were significantly different except for the mediolateral dimension values between arms and face (Table 2). Fig. 3 depicts the response data collapsed across each of the three orthogonal dimensions. The percentage of neurons responsive to upper limb, lower limb or orofacial manipulation is displayed as a function of distance along each single dimension, with the zero point of each representing the mid-commissural point of the AC–PC line. The percentage of non-responsive units is also depicted in the figure; however, those units were not included in the statistical model. Along the dorsoventral dimension, leg-related neurons tended to be more dorsal than arm-related neurons, which in turn were more dorsal than neurons related to orofacial movements. There was a similar leg–arm–face progression in the anteroposterior dimension, with leg-related neurons more anterior than arm-related neurons, which in turn tended to be more anterior than head-related units. The results were mixed, however, for the mediolateral dimension, with both arm- and head-related neurons tending to be more lateral than leg-related neurons but with no significant difference in laterality between arm- and head-related neurons. In general, proximal limb regions tended to be dorsal to distal limb regions with distal arm cells (wrist, hand and finger) being found more lateral than proximal arm cells. This is best illustrated in the coronal section of Fig. 2. Summary statistics and a breakdown of each of the pair-wise mean comparisons are presented in the lower portion of Table 2.

Discussion

A three-dimensional somatotopic organization was identified in the GPi of patients with idiopathic PD with leg- to arm- to face-related neurons found in both an anterior-to-posterior and a dorsal-to-ventral progression. Leg-related neurons were additionally noted to be situated medially relative to arm- and face-related units, with no significant difference in the

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mediolateral location of arm- versus face-related cells. This relative organization of the major body regions is consistent with prior work in humans that involved a three-dimensional mapping of the GPi (Guridi et al., 1999; Vitek et al., 1998), with the current data extending those findings to provide a more detailed mapping of the individual joints within the sensorimotor GPi. The findings are also consistent with electrophysiological data derived from the MPTP primate model (DeLong et al., 1985) and retrograde transport work done in the normal monkey (Hoover and Strick, 1999), suggesting that the sensorimotor area in the GPi of the non-human primate reflects that found in humans with idiopathic PD.

The present study represents the largest sampling of kinesthetic cells in the GPi to date and provides statistical confirmation for the three-dimensional organization observed. While several prior studies have addressed the issue of pallidal somatotopy in humans (Dogali et al., 1994, 1995; Guridi et al., 1999; Sterio et al., 1994; Taha et al., 1996; Vitek et al., 1998), most were limited with respect to the number of kinesthetic cells identified (Guridi et al., 1999; Sterio et al., 1994; Taha et al., 1996) or by methodological considerations (Sterio et al., 1994; Taha et al., 1996) and three represent the same data set (Dogali et al., 1994, 1995; Sterio et al., 1994). Two of the earliest reports (Sterio et al., 1994; Taha et al., 1996) were based on data sets of less than 60 cells overall and provide only subjective assessments of the relative clustering and location of these cells within the GPi. Moreover, the data were derived using either only a single microelectrode trajectory per patient (Taha et al., 1996) or using an approach that focused on only changes in the anteroposterior dimension, providing only a two-dimensional map for each patient (Sterio et al., 1994). The work by Guridi et al. (1999) addressed the three-dimensional mapping for each patient, although the data set was still comprised of only 18 patients and 145 kinesthetic units the relative location of which were again addressed only semi-quantitatively. Even our previous study had a relatively limited number of neurons ($n = 424$), with the somatotopic organization described semi-quantitatively (Vitek et al., 1998).

The somatotopic distribution of cells within the GPi, as determined using only those neurons with contralateral, single limb responses, appears less organized than what has been found throughout several other nodal points in the basal ganglia thalamocortical circuit, in particular that for the motor and sensory thalamus (Asanuma et al., 1983; Thach and Jones, 1979) and motor cortical areas (Penfield and Rasmussen, 1950).While it is possible that the GPi simply does not have as finely tuned, or concentrated, of a somatotopic arrangement as other nodal points within the circuit, one reason for this disparity may be that the results represent the effect of our limited ability, in the clinical setting, to thoroughly sample an otherwise complex, multi-circuit organization within the GPi where multiple somatotopic representations reflect the different precentral motor fields that project to this region (Hamada et al., 1990; Hoover and Strick, 1993). This would be similar to the multiple, input-based, subdivisions of the motor thalamus and consistent with the dual-homunculus organization reported in the STN of the untreated non-human primate (Nambu et al., 1996). The somatotopic picture of any such system is likely to be obscured further by the need to combine small amounts of data from a relatively large cohort of patients, particularly when combined with the inability to derive histological confirmation of the locations of the recording tracts. The pooling and collapse of data across multiple patients leads to a blurring of the discrete representations in individual patients or animals. Non-human primate studies,

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in contrast, have allowed for intensive and closely spaced microelectrode mapping of a single nucleus, enabling the investigators to discern the degree of separation of such representations (Bergman et al., 1994; DeLong et al., 1985; Wichmann et al., 1994a). Such separation has been reinforced by retrograde labeling approaches (Hoover and Strick, 1993), where there is clear evidence as to the degree of separation of individual limb representations from the different precentral motor fields in the monkey. Finally, the preponderance of proximal limb cells relative to distal ones is consistent with prior reports in both human (Taha et al., 1996) and non-human studies (DeLong et al., 1985; Filion et al., 1988).

At 62%, the relative proportion of kinesthetic versus non-kinesthetic neurons identified in the present study is outside of the 19–46% range that has been reported previously in humans with PD (Favre et al., 1999; Guridi et al., 1999; Lozano et al., 1998; Sterio et al., 1994; Taha et al., 1996; Vitek et al., 1998). However, our findings are in line with the 64% ratio reported for normal primates by Delong et al (DeLong et al., 1985) and the 52–67% range reported for the MPTP-intoxicated monkey (Baron et al., 2002; Filion et al., 1988; Leblois et al., 2006). While the nature of the variability in human studies is not clear, it may be contributed to by variations in sampling technique, patient selection and sample size as well as by the constraints imposed by any effort to acquire research data in a clinical environment during an awake surgical procedure. For what are likely similar reasons, the reported figures for ipsilateral or bilateral receptive fields within the GPi are also rather variable in human studies, ranging from 2% to 42% (Favre et al., 1999; Guridi et al., 1999; Sterio et al., 1994; Taha et al., 1996; Vitek et al., 1998), with the 64% value reported by Filion et al. (1988) in the MPTP model again well outside the upper limit of that range. We found approximately 4% (85/1972) of neurons with ipsilateral responses to passive manipulation; however, this is certain to be an underestimate of the true incidence as the ipsilateral body regions were not always systematically explored.

Although there is no normal human data for comparison, the finding of broadened receptive fields in 23% of neurons in GPi in humans with idiopathic PD likely represents an abnormal response to movement as it has not been reported in normal monkeys. This may reflect the defocusing effect of striatal input in the dopamine depleted state and is consistent with previous descriptions in PD patients and observations in the MPTP treated non-human primate (Leblois et al., 2006). The contribution of these changes in receptive fields to the development of PD motor signs remains speculative; however, previous studies have reported increased and less specific responses of GPi neurons to passive movement that are also present in the thalamus, suggesting these changes may permeate throughout the pallido-thalamocortical circuit (Pessiglione et al., 2005; Vitek et al., 1990, 1998). The enhanced response of these neurons and the apparent increased gain and loss of specificity of sensory information transmitted to the cortex during movement have led some to speculate that these changes in receptive field properties contribute to the reduction of associated movements and development of the bradykinetic state (Leblois et al., 2006). This is hypothesized to occur secondary to a perceived excessive increase in movement in the depleted dopaminergic state that leads to a down-regulation of the motor output command. In support of this theory is the previous data by A. P. Moore where an asymmetric PD patient was asked to flex the “affected” upper limb at the elbow to match the degree of movement

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perceived in the unaffected limb which was passively flexed by the examiner (Moore, 1987). The patient consistently moved the affected limb less than the unaffected limb. Although compelling these data do not directly implicate a causal role for sensory changes in the development of motor signs in PD and their relationship to the development of motor signs in PD remains to be determined.

Relevance to stereotaxic surgery for movement disorders

Electrophysiological confirmation or refinement of stereotaxic targeting continues to be the gold standard for surgical identification of the sensorimotor subregion of the GPi. Lesions that do not include or only partially include the sensorimotor portion of GPi are likely to result in partial and/or transient improvement, alone or in conjunction with side effects (Lombardi et al., 2000; Vitek et al., 1998). Identifying the receptive field of neurons during electrophysiological mapping is clearly helpful in identifying the sensorimotor GPi; however, the utility of defining a somatotopic pattern in the individual patient for placing a lead or lesion has not been determined. And while there are instances where receptive field data can provide clinical direction, these data are not adequate in and of themselves to allow a determination for placing a lead without identifying the boundaries of the structure to be implanted or lesioned. If indeed the somatotopic pattern of the GPi is highly complex and comprised of multiple, parallel homunculi (Hoover and Strick, 1993, 1999), development of a method by which to identify these subcircuits could be useful as a localizing tool. Even with the present data however, one can make some assumptions to help to localize the recording location within the GPi. For example, while identification of neurons with responses to passive or active movement without regard for somatotopy can indicate that one is in the sensorimotor region, a trajectory that involves the identification of multiple, robust lower limb-related units to the exclusion of all other body regions could be taken as suggestive of a more medial trajectory, just as the identification of predominately arm or distal arm-related units would imply a more lateral location within GPi. These data can be very helpful in defining the somatotopic plane but should be taken alongside data concerning the relative locations of the pallidal borders, including capsule, GPe and optic tract, as identified through recordings and microstimulation to develop a complete map of the pallidum and surrounding structures prior to placing a lead or lesion.

The identification of kinesthetic neurons is re-assuring that one is in the sensorimotor region of the GPi and the presence of a somatotopic arrangement provides, at least in part, a rationale for the partial benefit that may be seen in patients with small lesions or with DBS leads that are placed such that the volume of tissue affected by stimulation does not encompass the majority of the somatotopic region of GPi. Improvement predominately in the arm may reflect a lead that is placed more lateral to or with pallidotomy a lesion that does not encompass medial portions of the sensorimotor GPi. In support of this hypothesis is the report by Vasques et al. (2009) that benefit in patients with dystonia is related to the volume of sensorimotor GPi affected by stimulation. Another factor that may influence the outcome of surgical interventions is the course of pallidal efferents. Recent studies have suggested that neurons in the caudal (sensorimotor) portions of the GPi do not travel in the ansa lenticularis as previously believed but rather in the lenticular fasiculus, i.e., the axons of neurons in the sensorimotor portion of GPi travel directly through the nucleus and traverse

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the internal capsule to reach the thalamus (Baron et al., 2001). Thus, lesions or stimulation of the lateral portions of the GPi would not influence more medial regions of the sensorimotor area and, conversely, lesions or DBS in medial portions of the GPi would also influence lateral areas by affecting fibers of passage from these lateral areas. These findings suggest that medial lesions and DBS would perhaps be more effective in altering pallidal output and relieving clinical features.

In summary, while not providing the precise tool to identify the exact location within GPi, these data, together with anatomical and physiologic data, help to provide a better understanding of the functional organization of GPi in a way that allows us to translate these information to current surgical procedures with the goal of improving clinical outcomes.

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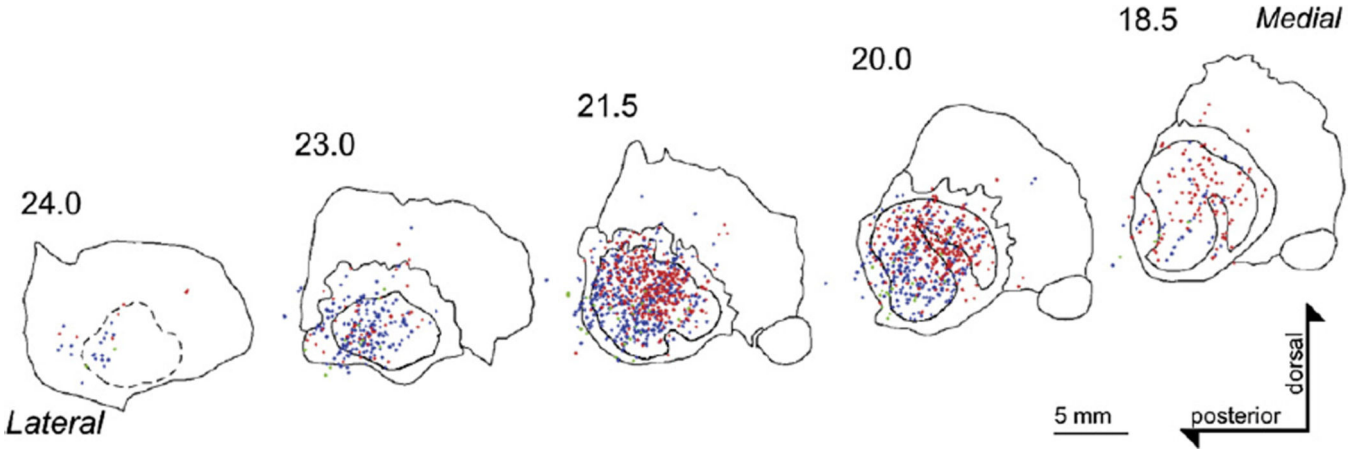

Fig. 1.

Illustrative depiction of the relative distribution of neuronal responses observed within the GPi. Data are shown only for those neurons responsive to a single body region (red = lower limb; blue = upper limb; green = orofacial). The numbers above each section reflect its mediolateral position relative to midline. The data for neurons identified 0.5 mm medial or lateral to the indicated section have been collapsed onto the closest section (e.g., data for neurons determined to be between mediolateral 20.0 and 22.0 are represented on plane section 21.5).

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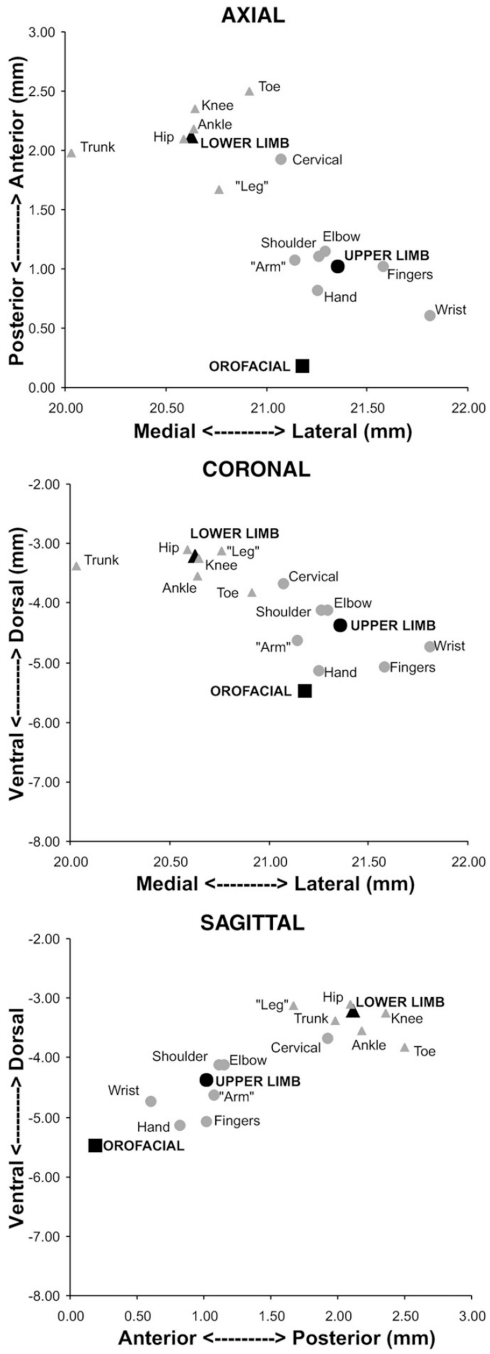

Fig. 2.

A series of two-dimensional plots depicting the mean coordinates for each body region (bold, dark points), along with the mean coordinates for each specific joint (grey), collapsed across the axial, coronal and sagittal planes ("▲" = Lower limb, "●" = Upper limb, "■" = Orofacial). *X, Y* and *Z* represent the mediolateral, anteroposterior and dorsoventral planes, respectively, with the zero point of the *Y* and *Z* planes representing the mid-commissural point (positive values for *Y* and *Z* are anterior and dorsal, respectively).

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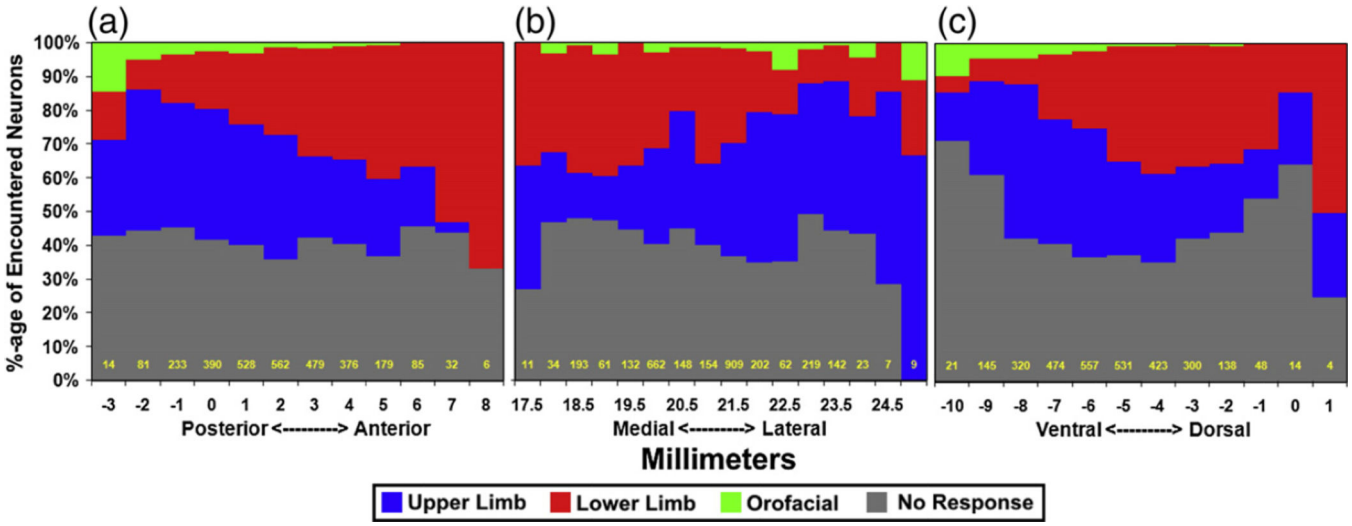

Fig. 3.

A series of unidimensional histograms depicting the percentage of neurons responsive to upper limb (blue), lower limb (red) or orofacial (green) manipulation as a function of distance along the anteroposterior (a), mediolateral (b) and ventrodorsal (c) dimension. For each dimension, the relative percentage of neurons responsive to manipulation of the upper, lower and orofacial regions of the body as well as non-responsive units (gray) are displayed across the length of the explored region, as displayed in millimeters. One millimeter bins were applied for the anteroposterior and dorsoventral dimensions, while half millimeter bins were used in the mediolateral dimension. The zero point along each dimension represents the mid-commissural point of the AC–PC line, while the numbers shown in yellow at the bottom of each column represent the number of units sampled at that level.

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Table 1

Response characteristics of neurons encountered during physiological mapping of the GPi.

Contralateral	1887		
Single body region		1767	
Single joint			1516
Multiple joints			251
Multiple body regions		120	
Upper limb and orofacial			1
Upper limb and lower limb			117
Lower limb and orofacial			2
Ipsilateral	61		
Mixed (contralateral/ipsilateral)	24		
Same body region		20	
Different body regions		4	
No receptive field identified	1211		
Total	3183		

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Table 2

Three-dimensional coordinates of kinesthetic neurons responsive to manipulation of a single body region.

	X		*Y*		*Z*		*n* (%)
Upper limb	**21.4**	(**1.8**)	**1.1**	(**2.8**)	**−4.4**	(**2.8**)	**940**
Finger/hand	21.4	(1.3)	0.9	(1.8)	−5.1	(1.5)	149 (15.9)
Wrist	21.8	(1.4)	0.6	(1.7)	−4.7	(1.7)	173 (18.4)
Elbow	21.3	(1.4)	1.2	(1.9)	−4.1	(1.7)	238 (25.3)
Shoulder	21.3	(1.4)	1.1	(1.9)	−4.1	(1.8)	500 (53.2)
Cervical	21.1	(0.8)	1.9	(1.3)	−3.7	(1.0)	7 (0.7)
“Arm”	21.1	(1.1)	1.1	(1.9)	−4.6	(1.9)	95 (10.1)
Lower limb	**20.8**	(**1.7**)	**2.0**	(**2.6**)	**−3.3**	(**2.7**)	**769**
Toe	20.9	(1.2)	2.5	(1.7)	−3.8	(0.9)	6 (0.8)
Ankle	20.6	(1.4)	2.2	(1.8)	−3.5	(1.8)	133 (17.3)
Knee	20.7	(1.2)	2.4	(2.0)	−3.3	(1.7)	213 (27.7)
Hip/trunk	20.6	(1.3)	2.1	(1.9)	−3.1	(1.6)	459 (59.7)
“Leg”	20.8	(1.5)	1.7	(2.1)	−3.1	(2.0)	102 (13.3)
Orofacial	**21.4**	(**1.2**)	**0.1**	(**1.8**)	**−5.7**	(**1.9**)	**58**
Scalar difference in coordinate means between body regions							
Upper vs. lower	0.59 *		−0.94 *		−1.13 *		
Orofacial vs. lower	0.52		−1.92 *		−2.38 *		
Orofacial vs. upper	0.07		−0.99 *		−1.25 *		

Coordinates are displayed as means (SD). Total for individual joints includes cells responsive to more than one joint. Bold values represent grand mean for specified body region. “(%)” values represent the percentage of cells responsive to the specific joint relative to the total number for that particular body region. In some instances, only the body region (i.e., “arm”, “leg”), and not the specific joint, was indicated on the operative notes (* $p<0.001$).