Cortical Connections of Functional Zones in Posterior Parietal Cortex and Frontal Cortex Motor Regions in New World Monkeys

Omar A. Gharbawie, Iwona Stepniewska and Jon H. Kaas

Department of Psychology, Vanderbilt University, 301 Wilson Hall, 111 21st Avenue South, Nashville, TN 37203, USA

Address correspondence to Omar A. Gharbawie, Department of Psychology, Vanderbilt University, 301 Wilson Hall, 111 21st Avenue South, Nashville, TN 37203, USA. Email: omargharbawie@vanderbilt.edu.

We examined the connections of posterior parietal cortex (PPC) with motor/premotor cortex (M1/PM) and other cortical areas. Electrical stimulation (500 ms trains) delivered to microelectrode sites evoked movements of reach, defense, and grasp, from distinct zones in M1/PM and PPC, in squirrel and owl monkeys. Tracer injections into M1/PM reach, defense, and grasp zones showed dense connections with M1/PM hand/forelimb representations. The densest inputs outside of frontal cortex were from PPC zones. M1 zones were additionally connected with somatosensory hand/forelimb representations in areas 3a, 3b, and 1 and the somatosensory areas of the upper bank of the lateral sulcus (S2/PV). Injections into PPC zones showed primarily local connections and the densest inputs outside of PPC originated from M1/PM zones. The PPC reach zone also received dense inputs from cortex caudal to PPC, which likely relayed visual information. In contrast, the PPC grasp zone was densely connected with the hand/forelimb representations of areas 3a, 3b, 1, and S2/PV. Thus, the dorsal parietal–frontal network involved in reaching was preferentially connected to visual cortex, whereas the more ventral network involved in grasping received somatosensory inputs. Additional weak interlinks between dissimilar zones (e.g., PPC reach and PPC grasp) were apparent and may coordinate actions.

Keywords: intracortical electrical stimulation, motor cortex, parietal–frontal network, posterior parietal cortex, premotor cortex, reach and grasp

Introduction

Most of what is known about the functions of posterior parietal cortex (PPC) emerged from neuronal recordings and anatomical investigations in macaque monkeys (for review, see Mountcastle 1995; Matelli and Luppino 2001; Fogassi and Luppino 2005). Imaging PPC activation in human subjects and macaques (Graziano, Taylor, and Moore 2002), have also been shown to evoke defensive forelimb and face movements from the ventral intraparietal area (Cooke et al. 2003). Subsequent long train stimulation studies in prosimian galagos revealed more comprehensive PPC maps that included zones of reach, defense, and other movements as well as matching functional zones in M1/PM (Stepniewska et al. 2009). Those mapping results were instructive for characterizing the function of the connections that link PPC with M1/PM (Stepniewska et al. 2009).

We adopted a similar experimental approach in New World monkeys to answer 4 questions. First, what are the parietal–frontal connections that link PPC zones with M1/PM? Second, what are the sensory inputs into the PPC functional zones? Third, what are the spatial relationships and the extent of segregation and overlap between the different parietal–frontal networks? Fourth, are the parietal–frontal networks in New World monkeys organized in ways similar to those in galagos and macaques? We hypothesized that a distinct profile of sensory and motor connections characterizes each PPC functional zone. We also hypothesized that matching zones in PPC and M1/PM are more densely interconnected than dissimilar zones. Last, we hypothesized that the organization of parietal–frontal networks is conserved in the major branches of primate evolution (New World anthropoids, prosimians, and Old World anthropoids).

We addressed these questions by mapping functional zones in M1/PM and PPC using long train stimulation. Retrograde tracers were injected into M1/PM zones, and the location of the labeled cells in relation to the PPC zones revealed the functional significance of the respective connections. Similarly,
retrograde tracers were injected into PPC zones, and the location of the labeled cells in relation to M1/PM zones and architectonic borders aided in the characterization of the functional significance of the connections. We purposely injected more PPC zones than M1/PM zones because less is known about their connectivity. The focus of this report is the corticocortical connections, and some of the results were briefly presented in an abstract (Gharbawie et al. 2009). The thalamocortical connections were described in a previous report (Gharbawie et al. 2010), and they were instructive for further characterization of the PPC zones.

Materials and Methods

Animals

Three squirrel monkeys (Saimiri sciureus) and 2 owl monkeys (Aotus trivirgatus) were studied. Animals from both species were 3–6 years old. Squirrel monkeys weighed 800–900 g, whereas owl monkeys weighed 800–1300 g. All procedures were approved by Vanderbilt University Animal Care and Use Committee and followed the guidelines of the National Institutes of Health guide for the care and use of laboratory animals.

Intracortical Electrical Stimulation

Motor mapping was conducted with the objective of identifying functional zones in M1/PM and PPC. Standard microstimulation parameters (trains of cathodal pulses up to 50 ms in duration) that evoke muscle twitches from M1/PM have not been shown to evoke movements from PPC. However, longer durations of electrical stimulation (trains of biphasic pulses 100–500 ms in duration) have been shown to evoke complex, limb, and face movements, from both PPC and M1/PM (Graziano, Taylor, and Moore 2002; Cooke et al. 2003; Stepniewska et al. 2005). These movements were reminiscent of ethologically relevant behaviors and considered elaborations of the muscle twitches evoked from M1/PM with standard microstimulation (Graziano, Taylor, Moore, and Cooke 2002). Also, because long train stimulation revealed matching zones of forelimb movements in PPC and M1/PM, which were likely nodes of the parietal–frontal networks pertinent to this study, it was more appropriate than standard stimulation parameters for identifying zones in both PPC and M1/PM for injections.

Monkeys were preanesthetized with ketamine hydrochloride (10–30 mg/kg intramuscularly) and maintained on 2% isoflurane during surgical procedures. Animals were placed in a stereotaxic frame for aseptic surgery. The skull was opened to expose the parietal and frontal lobes of one hemisphere. The opening extended from the tip of the lateral sulcus to approximately 7 mm rostral to the central sulcus. In its caudal extent, the craniotomy was bound by the midline of the hemisphere and the lateral sulcus. The opening widened rostrally to ensure that the hand/forelimb representations of M1/PM were exposed. The more medial trunk representations of M1/PM were also exposed. The dura was dissected, and the cortex was covered with inert silicon fluid. The surface of the cortex was digitally photographed, and a printout was used to record microelectrode penetrations.

Anesthesia was switched at this time to a continuous perfusion of ketamine mixed in physiological saline (20–40 mg/kg/h) delivered through the tail vein. Small doses of xylazine (0.2–0.4 mg/kg) were occasionally administered to control excessive muscle tone. Vital signs (respiratory rate, expired CO2 levels, oxygen saturation in blood, and heart rate) were monitored and recorded every 10 min for the duration of anesthesia.

A tungsten microelectrode (1 MΩ impedance) was perpendicularly lowered with a micromanipulator into the cortex to depths 1600–1800 μm beneath the surface. Interpenetration distances were 0.5–1.0 mm, varying primarily to avoid vascular branches on the cortex. Stimulation trains consisted of 150 biphasic pulses delivered over 500 ms. The duration of each phase was 0.2 ms at 300 Hz. For M1/PM long train stimulation, current intensity was increased from low levels (20 μA) until a movement was reliably evoked (up to a maximum of 200 μA), whereas the starting point for PPC was 150 μA until a movement was reliably evoked (up to a maximum of 400 μA).

Because the organization of PPC in New World monkeys remains largely unknown as compared with M1/PM, the primary objective was to map as many functional zones in PPC as possible for tracer injections. In the interest of minimizing the duration of anesthesia, M1/PM was less comprehensively mapped. Current thresholds were therefore not consistently determined to identify the borders between M1 and PM, and the full extent of the map was not revealed. Nevertheless, several zones were consistently identified in M1/PM and injected so that parietal–frontal connections could be studied in each case with injections in both PPC and M1/PM. In a terminal procedure, cortical sites of interest were marked with microlesions for later identification in histological sections. A microelectrode delivered 5 μA DC as it was retracted through the depth of the cortex.

Anatomical Tracer Injections

Once long train stimulation mapping was complete, ketamine was withdrawn and anesthesia was maintained with isoflurane. Retrograde tracers (2–4) were injected into zones in M1/PM and PPC of each animal. Sixteen injections into 5 hemispheres of 5 monkeys labeled sufficient numbers of cells to be included in the present analysis. Tracers were pressure injected from a 1 or 2 μL Hamilton syringe fitted with a glass pipette beveled to a sharp tip. Tracers included Cholera toxin b-subunit (CTB; Molecular Probes; 1% in distilled water), and the fluorescent tracers Diamidino Yellow (DY; Sigma, 2% in distilled water), Fluoro Ruby (FR; Molecular Probes, 10% in distilled water), and Fast Blue (FB; Polysciences; 2% in distilled water). Two depths beneath the surface of the cortex (800 μm and 400 μm) were targeted at each injection site. Total volume for each injection site was 0.4 μL for DY, FB, and CTB and 0.6 μL for FR. A protective layer of gelfilm was placed over the exposed cortex. A skull cap prepared from dental acrylic was secured over the craniotomy, and the scalp was then sutured and covered with a topical antibacterial.

Histology

Approximately, 8 days were allowed for tracer transport. After a brief terminal procedure conducted primarily to induce cortical microlesions, animals were injected with a lethal dose of sodium pentobarbital (80 mg/kg) and perfused intracardially with phosphate-buffered saline (PBS; pH 7.4). For fixation, 2% paraformaldehyde in PBS and 2% paraformaldehyde in PBS with 10% sucrose solution were delivered in succession. The brain was removed from the skull, and the cortex was sectioned in a nonsuccessive series. One series was not processed and mounted onto glass slides for analysis of the distribution of fluorochrome-labeled cells. A second series was reacted for CTB immunohistochemistry and then labeled with multicolor fluorescent tracers Alexa Fluor 488 (A488; Molecular Probes; 5% in distilled water) and Alexa Fluor 568 (A568; Molecular Probes; 5% in distilled water). Two depths beneath the surface of the cortex (800 μm and 400 μm) were targeted at each injection site. Total volume for each injection site was 0.4 μL for DY, FB, and CTB and 0.6 μL for FR. A protective layer of gelfilm was placed over the exposed cortex. A skull cap prepared from dental acrylic was secured over the craniotomy, and the scalp was then sutured and covered with a topical antibacterial.

Data Analysis

Distributions of labeled cells in the cortex were plotted with a Leitz microscope (Leica Microsystems) connected to an X-Y encoder. An experimenter manually marked the positions of labeled cells on a computer system running Neurolucida software (V. 5.05.4, Microbrightfield). Cells labeled with DY and FB were visualized with fluorescence illumination passed through a 360-nm wavelength filter. FR-labeled cells were visualized with a 530- to 560-nm wavelength filter. CTB-labeled cells were visualized under bright field illumination. Cells labeled from each injection were plotted from 5 or 6 sections.
Architectonic borders, microlesions, and tissue artifact were traced on paper using a projection microscope from sections stained for CO and myelinated fibers. Tracings were digitized with a scanner, and architectonic borders were retraced using Adobe Illustrator software (v. CS4). Plots generated in Neurolucida were aligned to the digitized tracings of cortical borders using Adobe Illustrator. Microlesions, sulci, and tissue artifacts guided alignment. Symbols marking the location of labeled cells were adjusted for shape and color and digitally merged onto the retraced borders.

The distribution of labeled cells for each injection is presented as a composite from the 5 to 6 sections plotted. To assess the spatial overlap and segregation of 2 populations of labeled cells in the same case, composites of cells labeled from 2 injections were superimposed in the same illustration. Outlines were drawn around clusters of cells labeled from each injection. Multiple outlines were drawn for each population of labeled cells to conservatively estimate its spatial extent. Borders for each population were shaded and resembled islands of varying shapes and sizes. Regions of overlap between the 2 populations of labeled cells were inferred from overlapping aspects of the shaded islands. Intermingling between the 2 populations of labeled was inferred from the close proximity and partial overlap of the shaded islands. Segregation between the 2 populations of labeled cells was inferred from the separation of the shaded islands.

Results

Long train stimulation delivered to M1/PM and PPC evoked contralateral forelimb and face movements reminiscent of ethologically relevant behaviors. Although several classes of movements were evoked, only those pertinent to tracer injections are briefly described here. Detailed mapping results will be presented in a future report.

Reaching Movements

The shoulder flexed and the elbow extended. Concurrent digits extension was observed for most penetration sites. Forelimb trajectories were consistent for repeated electrical stimulation of a penetration site. Nevertheless, trajectories varied across sites to include end points in upper space, lower space, or level with the animal’s horizontal body.

Defensive Movements

Two constellations of movements were characterized as defensive. First, the shoulder extended and the forelimb concurrently abducted while the digits extended. The end point of the open palm was either near the face or lateral to the body presumably for protection. Second, the forelimb was withdrawn directly toward the body by a shoulder extension and a slight elbow adduction. The utility of the actions was presumed to remove the forelimb from a threatening stimulus. Aggressive face gestures typically involved a combination of ear pinna retraction against the neck, eye blinking, and exposure of the teeth in a grimace posture.

Grasping Movements

The digits flexed and the wrist concurrently dorsiflexed or supinated toward the mouth.

Concurrent Forelimb and Face Movements

In some sites, wrist supination toward the mouth was accompanied by mouth opening. Other sites evoked reaching and concurrent mouth opening. Islands of sites that evoked concurrent defensive forelimb movements in conjunction with aggressive face gestures were near other defensive zones.

Similar reaching, defensive, and grasping movements have been illustrated for galagos (Stepniewska et al. 2005) and macaques (Graziano, Taylor, and Moore 2002; Cooke et al. 2003).

Figure 1. Owl monkey cortex separated from thalamus and brainstem. Panels show progressive stages of flattening the cortex. Major landmarks include, central sulcus (CS), cingulate sulcus (CgS), superior temporal sulcus (STS), and primary visual cortex (V1).
Reach, defense, and grasp zones were organized in PPC in a caudomedial to rostralateral progression. Defense, grasp, and less consistently reach zones characterized M1. The border between M1 and PM cortex was estimated from the movements evoked with stimulation and architectonics, but it was not always certain. Favorable sections showed myelin light cortex rostral to M1. Reaching and other proximal forelimb movements were evoked from this cortex, which was presumed to be dorsal premotor (PMd) cortex. Ventral premotor (PMv) cortex was not as readily distinguishable from myelin sections. Microstimulation sites that evoked forelimb movements and simultaneous forelimb and face movements from cortex rostral to the orofacial zone of M1 were presumed to be in PMv (Preuss et al. 1996; Dancause, Barbay, Frost, Plautz, Stowe, et al. 2006). The border separating PMd and PMv was estimated according to previous work (Preuss et al. 1996) showing that it was lateral to the face representation of PMd. Maps from the present cases are presented in Figure 2.

**Figure 2.** Maps of movements evoked with long train stimulation (0.2 ms biphasic current trains delivered at 300 Hz for 500 ms) aligned to the respective outlines of flattened cortex. Illustrations are cropped to focus on stimulation targets in M1/PM and PPC. Microelectrode penetration sites are color coded to reflect evoked movements, and dual movements are represented in 2 colors. Major functional zones are highlighted. Each case received 2-4 tracer injections: Cholera toxin b-subunit (CTB), Fluoro Ruby (FR), Fast blue (FB), and Diamidino Yellow (DY). Each Hamilton syringe represents the location of an injection into a functional zone. Scale bar (5 mm) applies to all panels.
Injections were limited to zones of reach, grasp, defense, and concurrent forelimb and face movements, in both M1/PM and PPC. Injection locations are depicted on the maps in Figure 2, and examples of tracer injection sites were presented in Figure 2 of Gharbawie et al. (2010). The densest connections of M1/PM and PPC zones were respectively within frontal and parietal cortex. Parietal–frontal connections were the second order of connection density for the M1/PM and PPC zones. The distributions of cells labeled from each injection are presented in Tables 1 and 2. At least 2 distinct networks were revealed. A dorsal network linked the reach zone in caudomedial PPC with PMd, whereas a ventral connection linked the rostralateral grasp zone in PPC with M1 and PMv. The dorsal connection received dense input from cortex caudal to the PPC zones, whereas the ventral connection was more densely connected to the anterior parietal cortex.

### M1/PM Connections

#### Reach

A reach zone was consistently identified in caudal PMd and encompassed into rostral M1. Connections were investigated in 2 cases. A DY injection into the center of the PMd reach zone (Fig. 2A; squirrel monkey 08-38) primarily labeled cells throughout the PMd forelimb zones (Fig. 3A). A contiguous and less densely concentrated population of labeled cells (referred to as “cells” for the remainder of the results) overlapped forelimb zones in rostral M1. The few cells in lateral M1 overlapped the face representation. A separate population of cells overlapped the grasp zone in rostroventral PMv. Another concentration of cells was in the supplementary motor area on the dorsolateral surface and on the medial wall. The adjacent concentration of cells in rostral cingulate cortex was less dense. The anterior parietal cortex was nearly devoid of cells except for a small concentration at the approximate level of the forelimb representation of area 3a. A few cells were labeled in S2/PV, but most cells in the upper bank of the lateral sulcus were at the level of the PPC zones and likely too caudal to overlap S2. The densest concentration of cells outside M1/PM was in PPC and overlapped the reach zone and its vicinity. A smaller proportion of cells was scattered in lateral aspects of the defense zone and immediately caudal to the grasp zone.

A FB injection in the center of the PMd reach zone (Fig. 2D; owl monkey 08-41) was larger and more medial than the DY injection (squirrel monkey 08-38). Although the FB injection labeled more cells, cell distributions were similar for both injections, except for the following differences. FB labeled a denser population of cells in rostral cingulate cortex and a sparser concentration in the supplementary motor area (Fig. 3B). However, this difference may be related to the identification of the border between the 2 regions. A dense concentration of FB cells was immediately medial to the PPC reach zone. This was likely related to incomplete mapping of the PPC reach zone that would have otherwise encompassed those cells. Also, a dense concentration of FB cells was in rostroventral PPC. Although a functional zone was not defined for those cells, a grasp zone was identified in the same vicinity in all other cases (Fig. 2) FB labeled more cells near the fundus of the lateral sulcus that likely overlapped the ventromedial somatosensory (VS) area.

### Defense

Multiple defense zones were identified in M1/PM in all monkeys except one, and the relative locations varied somewhat across cases. A large FB injection in rostral aspects of the M1 defense zone extended slightly into caudal aspects of the grasp zones (Fig. 2C; squirrel monkey 07-118). Cells were primarily in the M1 hand/forelimb representations (Fig. 4). A spatially segregated population of cells was in PMd and a denser one was in ventral PMv. Small concentrations of cells were on the medial wall distributed between the rostral cingulate cortex and supplementary motor area. Dense concentrations of cells were in the hand/forelimb representations of areas 3a, 3b, 1, and S2/PV. The densest concentrations of cells outside of frontal cortex were distributed in the ventromedial aspects of the defense zones.

---

**Table 1**

<table>
<thead>
<tr>
<th>Reach</th>
<th>Defense</th>
<th>Grasp</th>
<th>Face and forelimb</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td>41.19</td>
<td>47.53</td>
<td>Inj</td>
</tr>
<tr>
<td>PMd</td>
<td>6.59</td>
<td>9.13</td>
<td>Inj</td>
</tr>
<tr>
<td>PMv</td>
<td>19.10</td>
<td>5.26</td>
<td>3.53</td>
</tr>
<tr>
<td>Rostral cingulate</td>
<td>7.73</td>
<td>11.06</td>
<td>4.70</td>
</tr>
<tr>
<td>PFC</td>
<td>1.87</td>
<td>0.68</td>
<td>0.42</td>
</tr>
<tr>
<td>3a</td>
<td>2.89</td>
<td>17.41</td>
<td>8.08</td>
</tr>
<tr>
<td>3b</td>
<td>1.10</td>
<td>11.50</td>
<td>1.64</td>
</tr>
<tr>
<td>1</td>
<td>0.91</td>
<td>0.69</td>
<td>0.30</td>
</tr>
<tr>
<td>S2/PV</td>
<td>1.39</td>
<td>5.29</td>
<td>2.06</td>
</tr>
<tr>
<td>PR</td>
<td>—</td>
<td>—</td>
<td>1.20</td>
</tr>
<tr>
<td>Caudal upper bank</td>
<td>6.42</td>
<td>2.50</td>
<td>2.99</td>
</tr>
<tr>
<td>Insular</td>
<td>0.30</td>
<td>0.19</td>
<td>—</td>
</tr>
<tr>
<td>PFC</td>
<td>8.55</td>
<td>14.30</td>
<td>15.46</td>
</tr>
<tr>
<td>PFC caudal</td>
<td>1.17</td>
<td>1.69</td>
<td>—</td>
</tr>
</tbody>
</table>

**Note:** Rows sequentially list the M1/PM functional zones, case number of each monkey, tracer injected, and total numbers of labeled cells excluding cells labeled in the local cortical region of the injection. Cortical regions are listed in the first column, and successive columns contain the respective percentage of labeled cells. Cells labeled in the local injection location are listed as “Inj,” and concentrations less than 0.1% are listed as “—.”

**Table 2**

<table>
<thead>
<tr>
<th>Reach</th>
<th>Defense</th>
<th>Grasp</th>
<th>Face and forelimb</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td>2.14</td>
<td>3.19</td>
<td>4.39</td>
</tr>
<tr>
<td>PMd</td>
<td>16.24</td>
<td>8.58</td>
<td>15.89</td>
</tr>
<tr>
<td>PMv</td>
<td>5.56</td>
<td>0.93</td>
<td>1.83</td>
</tr>
<tr>
<td>SMA</td>
<td>6.84</td>
<td>1.54</td>
<td>1.57</td>
</tr>
<tr>
<td>Caudal cingulate</td>
<td>3.85</td>
<td>4.76</td>
<td>2.77</td>
</tr>
<tr>
<td>PFC</td>
<td>2.56</td>
<td>2.85</td>
<td>0.30</td>
</tr>
<tr>
<td>3a</td>
<td>—</td>
<td>—</td>
<td>0.43</td>
</tr>
<tr>
<td>3b</td>
<td>1.71</td>
<td>1.60</td>
<td>1.57</td>
</tr>
<tr>
<td>PR</td>
<td>—</td>
<td>—</td>
<td>1.20</td>
</tr>
<tr>
<td>Caudal upper bank</td>
<td>38.89</td>
<td>11.90</td>
<td>23.79</td>
</tr>
<tr>
<td>Insular</td>
<td>0.64</td>
<td>0.68</td>
<td>0.57</td>
</tr>
<tr>
<td>Caudal PFC</td>
<td>7.69</td>
<td>10.76</td>
<td>15.97</td>
</tr>
<tr>
<td>PFC medial wall</td>
<td>5.98</td>
<td>21.76</td>
<td>2.71</td>
</tr>
</tbody>
</table>

**Note:** Rows sequentially list the PPC functional zones, case number of each monkey, tracer injected, and total numbers of labeled cells excluding cells labeled in the local cortical region of the injection. Cortical regions are listed in the first column, and successive columns contain the respective percentage of labeled cells. Cells labeled in the local injection location are listed as “Inj,” and concentrations less than 0.1% are listed as “—.”
Figure 3. The distributions of cells labeled from injections into the PMd reach zone revealed with (A) DY and (B) FB, in a squirrel monkey and in an owl monkey, respectively. Each illustration is a composite of multiple flattened sections that were aligned according to the locations of blood vessels, tissue artifact, and microlesions (marked by stars). Architectonic borders were drawn from adjacent sections processed for cytochrome oxidase and myelin and aligned using the same strategy. Major functional zones identified in PPC with long train stimulation are highlighted PPC reach (transparent), PPC defense (light gray), PPC grasp (dark gray) and can be further cross referenced with Figure 1. Visual
and grasp zones in PPC. Small concentrations of cells were in caudal aspects of the upper bank of the lateral sulcus and more rostrally in area PR. A few cells were in insular cortex and possibly overlapped VS.

**Grasp**

Grasp zones were identified in M1 in all monkeys except one and the location varied somewhat across cases. A CTB injection in caudal aspects of the grasp zone (Fig. 2B; squirrel monkey 08-09) primarily labeled cells in the M1 hand/forelimb representations (Fig. 5). The concentration of cells extended rostrally into PMd forelimb zones. Two dense clusters of cells were identified in PMd. Although the vicinities of the ventral cluster of cells was not mapped in the present case, grasping movements were evoked from the same region of PMd in case 08-38. Cells rostral and lateral to PMd were presumed to be in prefrontal cortex. A separate concentration of cells was in the supplementary motor area on the dorsolateral surface and on the medial wall. A negligible focus of cells was located further ventrally on the medial wall in rostral cingulate cortex. Cells in the upper bank of the lateral sulcus were mostly in the region of S2/PV. Less dense concentrations of cells were likely in the parietal rostral somatosensory area (PR) and in caudal aspects of the upper bank of the lateral sulcus. Cells within the hand/forelimb representations of area 3a were contiguous with those in caudal M1. The small concentrations of cells in areas 3b and 1 were also confined to the hand/forelimb representations. The densest concentration of cells outside frontal cortex was in PPC and primarily overlapped the grasp zone. Fewer cells were in caudal aspects of the PPC defense zone and even fewer overlapped the PPC reach zone. Small concentrations of cells were caudal to the PPC zones.

**Concurrent Face and Forelimb**

A zone of concurrent forelimb and face movements was identified in PMv, near the M1/PM border, in all cases except one. Connections of this PMv zone were investigated in 2 cases with injections that labeled a limited number of cells. A FR injection near the M1/PMv border (Fig. 2B; squirrel monkey 08-09) mostly labeled cells in dorsal aspects of PMv and only a few

---

Figure 4. The distribution of cells labeled from a FB injection into the M1 defense zone in a squirrel monkey. Major functional zones identified in PPC with long train stimulation are highlighted for reference: PPC forelimb-to-body (transparent), PPC defense (light gray), PPC grasp (dark gray). The primary auditory area (Aud) and the visual medial temporal (MT) areas are also included for reference. All other conventions are the same as in Figure 3. Most labeled cells were in the M1 hand/forelimb representations. Separate concentrations of cells were in PMv, PMd, and motor areas of the medial wall. Dense concentrations of cells were also in the upper banks of the lateral sulcus and the anterior parietal cortex. Similar concentrations were in PPC near the vicinity of the defense and grasp zones.

---

areas of the medial temporal (MT) region are also included for reference but there were no attempts to identify its subdivisions. Illustrations were cropped to focus on the cortical regions that contained labeled cells. Each injection site is depicted in black and is surrounded by a gray halo of a dense concentration of labeled cells. Each filled circle denotes the location of a labeled cell. Black stars mark the locations of electrolytic lesions. Both cases show that most cells were labeled in M1/PM on the dorsolateral surface and the medial wall. Cells labeled in PPC were mostly concentrated in its caudomedial aspects near the vicinity of the reach zone. With the exception of some cells labeled in area 3a, most somatosensory inputs were with the upper bank of the lateral sulcus.
cells in ventral PMv. A contiguous population of cells in rostral M1 overlapped the grasp zone (Fig. 6). A less dense concentration of cells was in the adjacent PMd forelimb representations. An even sparser population of cells overlapped the forelimb representations in caudal M1. A few cells were in the supplementary motor area on the dorsolateral surface. Also, a few cells were in anterior parietal cortex and in the upper bank of the lateral sulcus. The densest concentration of cells outside frontal cortex was in PPC and mostly overlapped caudolateral aspects of the defense zone, which represented concurrent defensive forelimb movements and aggressive face gestures. Small concentrations of cells were caudal to the defense zone and in the vicinity of the grasp zone.

A DY injection (Fig. 2E; owl monkey 08-45) in the same PMv zone was caudal relative to the FR injection (case 08-09) and likely involved rostral M1. Nevertheless, both injections labeled similar distributions of cells in PMv and in rostral M1. The following differences were noted in other locations. DY labeled a denser concentration of cells in the supplementary motor area on the dorsolateral surface and medial wall (not illustrated). DY also labeled dense clusters of cells in areas 3a and S2/PV. A few DY cells were near the fundus of the lateral sulcus and were likely in VS.

**PPC Connections**

**Reach**

A reach zone was identified in caudomedial PPC in all monkeys except one. Connections were investigated in 3 cases. A small FR injection in the center of the PPC reach zone (Fig. 2A; squirrel monkey 08-38) mostly labeled cells within the PPC reach zone and its vicinity (Fig. 7A). A contiguous population of cells was medial to the PPC reach zone and extended to the cingulate sulcus on the medial wall. A separate population of cells was near the border of the PPC defense/grasp zones. A few cells were caudal to the PPC functional zones. A relatively dense concentration of cells in the upper bank of the lateral sulcus was too caudal to overlap S2. The anterior parietal cortex was nearly devoid of cells. The densest concentration of cells outside of PPC was in PMd and overlapping zones of proximal forelimb movements. A few cells were labeled near the PMv grasp zone, rostral cingulate cortex, and the presupplementary motor area.

A FB injection in the center of the PPC reach zone (Fig. 2B; squirrel monkey 08-09) was larger and more caudal than the FR injection. Although the FB injection labeled many more cells...
than the FR injection, cell distributions were similar in both cases with the following exceptions. A dense concentration of FB cells was in the PPC grasp zone and thinned as it extended into the lateral aspect of the PPC defense zone (Fig. 7B). The concentration of FB cells on the medial wall extended beyond the cingulate sulcus, and a denser concentration of cells was caudal to the PPC functional zones. The relatively large number of cells in middle and rostral M1 was probably the most distinguishing feature of the FB injection. Those cells were arranged in mediolateral clusters that overlapped reach, defense, and grasp zones.

A CTB injection into the center of the PPC reach zone (Fig. 2E; owl monkey 08-45) was at the approximate level of the injection in case 08-09. Similar cell distributions were apparent for both injections, with the exception of denser concentrations of CTB cells in PMd and the upper bank of the lateral sulcus (not illustrated). However, fewer CTB cells were in caudal PPC.

**Defense**

A defense zone was lateral and slightly rostral to the PPC reach zone in all monkeys. Connections were investigated in 3 cases. A CTB injection in lateral aspects of the defense zone (Fig. 2A; squirrel monkey 08-38), near sites that evoked concurrent defensive forelimb movements and aggressive face gestures, mostly labeled cells within the defense zone (Fig. 8A). A medial extension of this cell population partially overlapped the PPC reach zone and its vicinity and thinned toward the cingulate sulcus. A dense concentration of cells lateral to the grasp zone extended into the upper bank of the lateral sulcus, in a region too caudal to overlap S2. A dense concentration of cells in area 1 was mostly at the same mediolateral level as the injection, but it also extended medially beyond the forelimb representation. Two separate and dense clusters of cells were in area 3b at the approximate levels of the forelimb representation and the hand/face border. Fewer cells were in area 3a near the border with M1. The densest concentration of cells outside of parietal cortex was in M1 and mostly overlapped zones of defensive forelimb movements and to a lesser extent aggressive face gestures. A sparser concentration of cells was approximately distributed among rostral M1, PMd, and PMv. Those cells mostly overlapped proximal forelimb zones in M1 and PMd but were aligned with a trunk zone in PMv. A sparse concentration of cells was in the supplementary motor area on the dorsolateral surface and the medial wall. A comparable concentration of cells was in the rostral cingulate cortex.

Figure 6. The distribution of cells labeled from a FR injection into the face/forelimb zone near the border of M1 and PMv in a squirrel monkey. All conventions are the same as in Figure 3. A border is drawn in the PPC defense zone around sites that evoked concurrent aggressive face gestures and defensive forelimb movements to separate them from the more rostral sites in the same zone that evoked only defensive forelimb movements. The injection labeled a relatively small number of cells, which were mostly concentrated in M1/PM. Most cells labeled in PPC were in caudal aspects of the PPC defense zone.
Figure 7. The distributions of cells labeled from injections into the PPC reach zone revealed with (A) FR and (B) FB, in 2 squirrel monkeys. All conventions are the same as in Figure 3. The patterns were similar despite the relatively small number of cells labeled in case 08-38. Cells were mostly labeled in the PPC reach zone and its vicinity. A separate concentration of cells was near the vicinity of the PPC grasp zone. Cells were also labeled in the upper bank of the lateral sulcus. Cells labeled in frontal cortex were mostly concentrated in PMd. Fewer cells were labeled in PMv and motor areas of the medial wall.
Figure 8. The distributions of cells labeled from injections into the PPC defense zone revealed with (A) CTB and (B) FB, in a squirrel monkey and in an owl monkey, respectively. All conventions are the same as in Figure 3. Most cells were labeled in the PPC defense zone and extended into other PPC zones. Cells labeled in frontal cortex were mostly concentrated in rostral M1, PMd, and to a lesser extent PMv. Cells were also labeled in motor areas of the medial wall. Cells labeled in the upper bank of the lateral sulcus were most concentrated in its caudal aspects.
A CTB injection in caudal aspects of the PPC defense zone (Fig. 2D; owl monkey 08-41) was more medial and caudal than the CTB injection in case 08-38. The injection in case 08-41 labeled more cells, and the following differences in cell distributions were noted for this injection. Denser concentrations of cells were in medial PPC caudal to the tip of the cingulate sulcus (Fig. 8B). Denser concentrations of cells were also in the upper bank of the lateral sulcus. Cells in M1 were concentrated near the center. A denser concentration of cells was in the supplementary motor area on the dorsolateral surface and the medial wall. A small concentration of cells was in prefrontal cortex.

A small FB injection in caudal aspects of the PPC defense zone (Fig. 2E; owl monkey 08-45) was at the approximate location of the CTB injection in case 08-41. Although the FB injection labeled fewer cells (not illustrated), the distributions of cells were similar for both injections. However, FB labeled more cells in insular cortex and fewer cells in the supplementary motor area.

**Grasp**

A grasp zone was lateral and slightly rostral to the PPC defense zone and immediately caudal to area 1. A grasp zone was found in all monkeys except one. Connections were investigated in 4 cases.

A FB injection into the center of the PPC grasp zone (Fig. 2A; squirrel monkey 08-38) primarily labeled cells within the PPC grasp zone. This dense concentration of cells extended rostrally into the hand representation of area 1 and to a lesser extent into area 3b (Fig. 9A). Cells were in lateral aspects of the PPC defense zone and a separate cluster overlapped the PPC reach zone and its vicinity. A dense population of cells was in the hand representation of area 3a. The densest concentration of cells outside of parietal cortex was in the hand/forelimb representations of M1. Cells were more concentrated caudally and thinned toward rostral M1. The few cells in PMd overlapped zones of proximal forelimb movements. A denser concentration of cells in rostroventral PMv primarily overlapped the grasp zone. It is not clear if cells rostral and lateral to PMv were part of PMv, additional motor-related field (Dancauce et al. 2008), or prefrontal cortex. Two clusters of cells were in the supplementary motor area on the dorsolateral surface and in the rostral cingulate cortex. The dense population of cells in the upper bank of the lateral sulcus was primarily in S2/PV. Two sparser concentrations were caudal to S2 and rostral to PV. A FR injection into the PPC grasp zone (case 08-45, not illustrated) labeled fewer cells, but they were distributed in a similar pattern.

A DY injection into the rostrolateral aspect of the PPC grasp zone (Fig. 2B; case 08-09) was at the approximate location of the FB injection (case 08-38). Although DY labeled fewer cells, distributions were comparable for the 2 cases. However, the following differences were noted for the DY injection. Cells were not labeled in the PPC reach zone (Fig. 9B), possibly due to tissue damage from a large FB injection into the reach zone. Only a small proportion of cells was in ventral PMv, which might have been due to insufficient tracer transport.

A CTB injection in the center of the PPC grasp zone (Fig. 2C; 07-118) also labeled a similar distribution of cells (not illustrated) as the FB injection in case 08-38. However, the CTB injection labeled a denser concentration of cells in rostral aspects of the upper bank of the lateral sulcus, possibly in PR as well as a few cells in V5. Also, more cells were in lateral prefrontal cortex.

**Topography of M1/PM and PPC Connections**

Injecting multiple functional zones in each case facilitated direct comparisons of the topographical organization of the connections of several functional zones. Three comparisons were particularly pertinent. 1) Injections into the PMd and PPC reach zones in case 08-38 revealed considerable overlap in the 2 populations of cells (Fig. 10). The extent of overlap was largest in PPC, but overlap between the 2 populations was also apparent in caudal PMd, caudal aspects of the upper bank of the lateral sulcus, the supplementary motor area, and the rostral cingulate cortex. The 2 populations intermingled in rostral PMd. However, cells labeled from the PMd injection did not extend as far caudally in PPC as the population labeled from the PPC injection. 2) Injections into the M1 and PPC grasp zones in case 08-09 revealed considerable spatial overlap between the 2 cell populations (Fig. 11). The extent of overlap was largest in the grasp zones of PPC and M1 and also in caudal M1. Overlap was also apparent in the hand/forelimb representations of the anterior parietal cortex (areas 3a, 3b, and 1), S2/PV, and in caudal aspects of the upper bank of the lateral sulcus. The 2 cell populations intermingled in PMv, PMd, supplementary motor area, and the rostral parietal area (PR) but were spatially segregated in rostral cingulate cortex. 3) Comparisons between the connections of the PPC reach and grasp zones were possible in 2 cases. Case 08-38 revealed largely segregated populations of cells (Fig. 12A). Nevertheless, the 2 populations overlapped in the vicinities of the respective injections and in caudal aspects of the upper bank of the lateral sulcus. The 2 populations also intermingled in PMd, PMv, and the presupplementary area. Segregation between the cells labeled from PPC reach and grasp injections was also apparent in case 08-09 (Fig. 12B). However, the 2 populations of cells overlapped in the PPC grasp zone and in the upper bank of the lateral sulcus. The 2 populations also intermingled in PMd but were segregated in PMv.

**Summary of Corticocortical Connections**

Six injections revealed the connections of 4 M1/PM zones. 1) The PMd reach zone was primarily connected with the rest of PMd and with the forelimb/hand representations in rostral M1 (Fig. 13A). Weaker connections with the supplementary motor area, rostral cingulate cortex, and PMv overlapped the hand/forelimb representations. Connections with somatosensory cortex were limited to minimal inputs from the hand/forelimb representations of area 3a. Connections with the upper bank of the lateral sulcus originated caudal to S2. The densest connections outside of frontal cortex were with the PPC reach zone and its vicinity. 2) The M1 defense zone was primarily connected within the hand/forelimb representations of M1 (Fig. 13B). Weaker connections with the supplementary motor area, rostral cingulate cortex, PMv, and PMd were also with the hand/forelimb representations. Dense somatosensory connections were with areas 3a, 3b, 1, and S2/PV. Connections with PPC were dense and nearly equally distributed between the defense and grasp zones. 3) The M1 grasp zone was most densely connected within the hand/forelimb representations of M1 (Fig. 13C). Connections with PMd and PMv were
Figure 9. The distributions of cells labeled from injections into the PPC grasp zone revealed with injections of (A) FB and (B) DY, in 2 squirrel monkeys. All conventions are the same as in Figure 3. Cells were mostly labeled in the PPC grasp zone and its vicinity. In one case (08-38), a separate concentration of cells overlapped the PPC reach zone. In both cases, a dense concentration of cells was labeled in the anterior parietal cortex and extended into M1. Separate concentrations of cells were also labeled in ventral PMv, S2/PV, caudal aspects of the upper bank of the lateral sulcus, and to a lesser extent the motor area in the medial wall.
confined to the hand/forelimb representations and were less dense than the local M1 connections. Connections with the supplementary motor area and rostral cingulate cortex were even less dense than those with PMd and PMv. Dense inputs originated from areas 3a, S2/PV, and to a lesser extent area 3b and 1. The densest connections outside of frontal cortex originated from the PPC grasp zone. Connections from other PPC zones were relatively minimal. 4) The zone of concurrent forelimb and face movements on the M1/PMv border was primarily connected within dorsal aspects of PMv. The densest connections were with M1 followed by PMd. The density of the connections with the supplementary motor area varied between cases. Connections with the upper bank of the lateral sulcus were primarily from S2. At least some of the inputs from PPC originated from the face representation of the defense zone.

Ten injections revealed the connections of 3 PPC zones. 1) The PPC reach zone was densely connected within its immediate vicinity. Less dense connections originated from the vicinity of the PPC grasp zone (Fig. 13D). Connections from caudal PPC, which likely relay visual information from the medial temporal and the dorsal medial areas, were present in all cases albeit with varying densities. Somatosensory connections were primarily from the upper bank of the lateral sulcus and to a much weaker extent areas 3a and 1. The densest connections outside of PPC were with the PMd forelimb zones. Connections with PMv and the supplementary motor area were less dense. Relatively weak inputs originated from M1 and rostral cingulate cortex. 2) The PPC defense zone was densely connected within its vicinity and to a lesser extent with other PPC zones (Fig. 13E). Sparse inputs originated from caudal PPC. Connections with the hand/forelimb representations in the anterior parietal cortex were denser for the defense zone than for the reach zone. The density of connections with the upper bank of the lateral sulcus varied among cases, but they were mostly with its caudal aspects. Unlike the PPC reach zone, the PPC defense zone received dense inputs from M1. Connections with PMd forelimb zones were consistent, whereas the density of inputs from the supplementary motor area and rostral cingulate cortex varied among cases. Also, the PPC defense zone was more densely connected with the anterior parietal cortex and S2/PV than the PPC reach zone. 3) The PPC grasp zone was primarily connected within its vicinity. Connections with the lateral aspect of the PPC defense zone were relatively sparse, whereas connections with the vicinity of the reach zone were more apparent (Fig. 13F). Dense connections with the hand/forelimb representations of the anterior parietal cortex and S2/PV distinguished the connection patterns of the PPC grasp zone. Dense connections with caudal M1 also distinguished the PPC grasp zone. Separate and less dense connections were with ventral aspects of PMv. Sparser connections were with the PMd forelimb zones. Connections with the supplementary motor area and rostral cingulate cortex were even sparser.
Discussion

Parietal–frontal networks that support actions were studied in squirrel and owl monkeys. Tracers were injected into M1/PM and PPC zones that were defined with long train stimulation. The same mapping results and architectonics aided in the functional characterization of connected regions in M1/PM and PPC and also in the identification of sensory inputs. In addition, injecting multiple functional zones in each monkey revealed the spatial relationships of different parietal–frontal networks. This direct characterization of the origins and terminations of various parietal–frontal networks with attention to spatial relationships is arguably a departure from the approach used in investigations of parietal–frontal networks to date.

The novelty of our experimental approach complicates comparisons with previous work. With the exception of some preliminary results (Stepniewska, Collins, et al. 2006), M1/PM and PPC of New World monkeys have not been mapped with long train electrical stimulation. Moreover, pertinent connection studies in New World monkeys have been limited to injections into M1/PM (Stepniewska et al. 1993; Dum and Strick 2005; Dancause, Barbay, Frost, Plautz, Popescu, et al. 2006; Dancause, Barbay, Frost, Plautz, Stowe, et al. 2006; Stepniewska, Preuss, and Kaas 2006). Results from galagos are more comparable because of previous mapping of M1/PM and PPC with long train stimulation and concurrent PPC injections (Stepniewska et al. 2005, 2009). Although M1/PM was comprehensively mapped in macaques with long train stimulation (Graziano, Taylor, and Moore 2002), only a defensive movement zone has been identified in PPC with the same stimulation parameters (Cooke et al. 2003). The relationships of the present PPC zones to PPC zones defined in macaques by single unit recordings can only be inferred. Similar limitations apply to previous descriptions of parietal–frontal connections in macaques that did not directly reveal the functional roles of the respective connections (Petrides and Pandya 1984; Cavada and Goldman-Rakic 1989a, 1989b; Caminiti et al. 1999; Luppino et al. 1999; Lewis and Van Essen 2000; Tanne-Gariepy et al. 2002; Rozzi et al. 2006; Borra et al. 2008).

Reach Zones in PMd and PPC

Long train stimulation evoked proximal forelimb movements from a large territory of PMd, and a reach zone was consistently...
Figure 12. Comparisons of the distributions of cells labeled from (A) injections into the PPC reach zone (FR-labeled cells represented in red) and the PPC grasp zone (FB-labeled cells represented in blue), in the same squirrel monkey (case 08-38). The 2 populations of labeled cells were largely segregated except for overlap near the 2 injection sites and in caudal aspects of the upper bank of the lateral sulcus. The 2 populations also intermingled in rostral PMd, PMv, and in the presupplementary motor area. The relative distributions of the 2 populations of labeled cells was confirmed in (B) a second squirrel monkey (case 08-09) with injections into the PPC reach zone (FB-labeled cells represented in red) and the PPC grasp zone (DY-labeled cells represented in blue).
Figure 13. Summary of the main sensory and motor connections for (A) PMd reach zone, (B) M1 defense zone, (C) M1 grasp zone, (D) PPC reach zone, (E) PPC defense zone, and (F) PPC grasp zone. The thickness of each connecting arrow and the size of the arrowhead are proportional to the mean density of the connection, which was calculated from the values presented in Tables 1 and 2. Major functional zones identified in M1/PM and PPC with long train stimulation are highlighted where appropriate for reference: PPC reach (green), PPC defense (red), and PPC grasp (gray).
identified within it. Previous M1/PM mapping in New World monkeys has been limited to short train stimulation, which evoked proximal forelimb movements from PMd (Preuss et al. 1996). Similar results have been shown in galagos (Fogassi et al. 1994) and macaques (Godschalk et al. 1995). However, long train stimulation identified reach zones in galagos (Stepniewska et al. 2009) and macaques (Graziano, Taylor, and Moore 2002) in M1/PM locations similar to the present PMd reach zone. In addition, neuronal activity recorded in caudal PMd in macaques was shown to be strongly correlated with forelimb reaching (Caminiti et al. 1991; Grammond and Kalaska 1994). Thus, the present PMd reach zone is in cortex where short train stimulation evoked proximal forelimb movements in New World monkeys, galagos, and macaques; and long train stimulation evoked reaching movements in galagos and macaques.

The caudomedial location of the present PPC reach zone is consistent with previous results in owl monkeys (Stepniewska, Collins, et al. 2006), and the location of the PPC reach zone defined by long train stimulation in galagos (Stepniewska et al. 2005, 2009). Although reaching movements have not been evoked from macaque PPC, a “parietal reach region” has been identified from correlations of neuronal activity in the MIP and the adjacent cortical field (PEc) with the kinematics of reaching (Kalaska et al. 1990; Johnson et al. 1996; Battaglia-Mayer et al. 2000; Cohen and Andersen 2002). Thus, there is evidence for a PPC reach zone in New World monkeys, galagos, and Old World monkeys.

**Connections of Reach Zones in PMd and PPC**

The long train stimulation results ensured that our PMd injections were in the reach zone. The densest connections were with the hand/forelimb representations of M1/PM, which is similar to previous descriptions in New World monkeys (Dum and Strick 2005; Stepniewska, Preuss, and Kaas 2006), galagos (Fang et al. 2005), and macaques (Matelli et al. 1998). Somatosensory inputs were primarily from higher order somatosensory areas on the upper bank of the lateral sulcus (Coq et al. 2004), which have also been reported for owl monkeys, galagos, and macaques. The densest connections to the PMd reach zone outside frontal cortex originated from caudomedial PPC, a location of PMd inputs in owl monkeys (Stepniewska, Preuss, and Kaas 2006), galagos (Fang et al. 2005), and macaques (Petrides and Pandya 1984; Johnson et al. 1996; Matelli et al. 1998; Tanne-Gariepy et al. 2002). The novel contribution here is directly showing that these connections originated from a physiologically defined PPC reach zone and its vicinity.

The long train stimulation results also ensured that our injections into caudomedial PPC were in the reach zone. Connections were primarily within the reach zone but also included inputs from the PPC grasp zone and its vicinity and to a lesser extent the PPC defense zone and its vicinity. Connections between dissimilar zones may be central to coordinating actions. For example, the connections between the PPC reach and grasp zones may be important for executing the appropriate successive order of reaching and grasping. In addition, the connections may mediate the conflicting kinematics of reaching that include extensions of the forelimb and digits, and the kinematics of grasping that include digits flexion and wrist supination. Connections of the PPC reach zone with caudal and medial PPC were present in all cases, albeit to varying degrees. These inputs likely relay visual information from MT, DM, and other visual areas (Wagor et al. 1975; Weller et al. 1984; Krubitzer and Kaas 1990; Kaas and Morel 1993; Rosa et al. 2009). The proximity of the PPC reach zone to extrastriate visual areas is apparent from a previous study that showed that injections into the PPC reach zone that were relatively caudal, such as the injection in Figure 7b of the present study, labeled a small proportion of cells in the lateral pulvinar (Gharabawie et al. 2010). Somatosensory inputs were limited to connections with the upper bank of the lateral sulcus, and their origins spatially overlapped those that projected to the PMd reach zone. The densest connections outside PPC were with PMd. Mapping results showed that most of those connections overlapped zones for proximal forelimb movements in PMd, and some were localized in the PMd reach zone. There are no relevant previous results from PPC injections in New World monkeys for comparison. The single study of PPC connections in titi monkeys (Padberg et al. 2005) focused on a part of PPC distant from the PPC reach zone. Nevertheless, in galagos, the PPC reach zone was found to be densely connected with PMd (Stepniewska et al. 2009). Similarly in macaques, MIP and PEc, parts of a “reach region” (Cohen and Andersen 2002), were found to be densely connected with PMd (Petrides and Pandya 1984; Caminiti et al. 1999). Both MIP and PEc also receive inputs from the lateral posterior nucleus of the thalamus (Jones et al. 1979; Pons and Kaas 1995; Schmahmann and Pandya 1990; Cappe et al. 2007; Padberg et al. 2009), which is a defining feature of the present PPC reach zone (Gharabawie et al. 2010). The comparable connections of MIP and PEc in macaques and the PPC reach zone in New World monkeys suggests further functional similarities.

Thus, the concurrent mapping of M1/PM and PPC and injections into the reach zones in PMd and PPC revealed a parietal-frontal network specifically involved in reaching. Both of the 2 main nodes (PMd and PPC) in this network receive somatosensory inputs from the upper bank of the lateral sulcus. Additional motor-related inputs from frontal cortex are primarily focused on the PMd node, whereas visual inputs from caudal and medial PPC are largely directed at the PPC node. Inputs to the PMd and PPC reach zones from overlapping regions of the supplementary motor area, rostral cingulate cortex, and the upper bank of the lateral sulcus provide further support for the conclusion that they are nodes within the same parietal-frontal network.

**Defense Zones in M1 and PPC**

Defensive forelimb and face movements were evoked from 1 to 3 zones in M1. Similar defensive movements were evoked from 1 to 2 M1 zones in galagos (Stepniewska et al. 2009) and macaques (Graziano, Taylor, and Moore 2002), but they have not been previously investigated in New World monkeys. In the present study, the same types of defensive movements were evoked from a PPC location similar to that reported in galagos (Stepniewska et al. 2005, 2009). Similar defensive movements were also evoked from the ventral intraparietal (VIP) area in macaques (Cooke et al. 2003). Thus, previous and present studies have demonstrated a PPC defense zone, which is located in between the PPC reach and grasp zones.
Connections of Defense Zones in M1 and PPC

The dense connections of the M1 defense zone with the hand/forelimb representations of M1/PM, the supplementary motor area, and the cingulate motor areas are similar to the connection patterns of other M1/PM hand/forelimb zones. The M1 defense zone injection was the most caudal of the present M1/PM injections and revealed denser connections with the hand/forelimb representations of the anterior parietal cortex than any of the other M1/PM injections. Although it is not clear if the PPC inputs more closely overlapped the defense or the grasp zones of PPC, connections with caudomedial PPC were sparse. Similar PPC connections have been reported for the proximal forelimb representation in caudal M1 in owl monkeys (Stepniewska et al. 1993).

Although rostral aspects of the PPC defense may have encroached into the anterior parietal cortex, the pertinent injections were too caudal to overlap the anterior parietal cortex. The PPC defense zone connections shared features with the PPC reach and grasp zones. This is perhaps related to the location of the PPC defense zone in between the PPC reach and grasp zones. Similarities to the PPC reach and grasp zones were further dependent on the injection location within the PPC defense zone. Connections with M1 were denser than those observed for the PPC reach zone but less dense than those for the PPC grasp zone. Connections were only slightly denser with PMd than with PMv, which is unlike the PPC reach and PPC grasp zones that were more heavily connected with PMd and PMv, respectively. Connections with the supplementary motor area and cingulate motor areas were similar to those of the other PPC zones. The PPC defense zone was more densely connected with the other 2 PPC zones than either PPC zone was connected with the remainder of PPC. Connections with dissimilar zones are likely important for coordinating actions. Results from comparable PPC injections in New World monkeys have not been reported. In general, the connections of the PPC defense zone are similar to those reported in galagos (Stepniewska et al. 2009). If the present PPC defense zone is physiologically comparable with macaque VIP, then similarities in connections are expected. Indeed, the present results are consistent with previously reported connections of VIP with M1/PM in macaques (Luppino et al. 1999). Strong inputs from MT have been emphasized as a defining feature of VIP (Maunsell and Van Essen 1983; Lewis and Van Essen 2000), but we did not find MT inputs in our study and Luppino et al. (1999) did not evaluate them. It should be noted that VIP was not physiologically defined in macaques for most connection studies and that different parts of VIP may have distinctive connections.

Grasp Zones in M1/PM and PPC

Long train stimulation evoked grasping movements and concurrent grasping and wrist supination from a large zone in M1. Previous M1/PM mapping in New World monkeys has been limited to short train stimulation, which evoked hand (thumb, fingers, and wrist) movements from the same region (Strick and Peterson 1978; Gould et al. 1986; Donoghue et al. 1992; Nudo et al. 1992; Stepniewska et al. 1993). Grasping movements have not been shown in M1/PM in galagos. In macaques, long train stimulation of caudal M1 evoked grasping with the forefinger and the thumb as well as other hand manipulations (Graziano, Taylor, and Moore 2002). This grasping zone overlapped the representation of the fingers revealed with short train stimulation (Sessle and Wiesendanger 1982) in the rostral bank of the central sulcus, which has the densest concentration of corticospinal cells with monosynaptic contacts onto spinal motoneurons (Rathelot and Strick 2009). An additional grasping and concurrent grasping and wrist supination zone was identified in PMv in 2 of the present squirrel monkeys that were mapped more extensively. Short train microstimulation evoked hand movements from the same approximate location of PMv in New World monkeys (Preuss et al. 1996; Dancause et al. 2006). In macaques, long train stimulation evoked grasping and hand-to-mouth movements from the same aspect of PMv (Graziano, Taylor, and Moore 2002).

Long train stimulation identified a grasp zone in rostrolateral PPC that included some sites with concurrent wrist supination. This is consistent with preliminary results in owl monkeys (Stepniewska, Collins, et al. 2006). A grasp zone was also reported in PPC in one studied galago (Stepniewska et al. 2009) in a relatively similar location to the present grasp zone. Comparisons with macaques are limited by the lack of PPC long train stimulation results. However, the involvement of at least one PPC zone in grasping has been suggested from neuronal activity recorded in AIP, which was strongly correlated with grasping and hand manipulation movements (Sakata et al. 1995; Murata et al. 2000).

Connections of Grasp Zones in M1 and PPC

The long train stimulation results ensured that one M1 injection was in the grasp zone. The M1 grasp zone was most densely connected with the hand/forelimb representations of M1/PM and the cingulate motor areas. Similar connections have been reported for the M1 hand representations in New World monkeys (Stepniewska et al. 1993; Dum and Strick 2005), galagos (Fang et al. 2005), and macaques (Matelli et al. 1986). The M1 grasp zone was weakly connected to the somatosensory hand/forelimb representations of the anterior parietal cortex. Additional somatosensory inputs were from higher order regions of the upper bank of the lateral sulcus. The densest connections outside M1/PM originated from rostrolateral PPC where they mostly overlapped the grasp zone. Although a similar connection pattern was previously reported in owl monkeys (Stepniewska et al. 1993) and galagos (Fang et al. 2005), the novel contribution here is showing that this connection is involved in grasping. In macaques, M1 connections with the inferior parietal lobe have been shown to originate from the areas currently known as AIP and 7b (Petrides and Pandya 1984; Matelli et al. 1986). Although the relationship between AIP in macaques and the present PPC grasp zone in New World monkeys remains uncertain, the high levels of neuronal activity that occur in AIP during grasping suggests similarities between it and the present PPC grasp zone.

The long train stimulation results also ensured that our injections into rostrolateral PPC were in the grasp zone. Connections were primarily within the PPC grasp zone but also included caudomedial PPC and the reach zone. Reciprocal connections revealed with injections into the PPC reach zone may confirm that connections between the 2 zones are indeed important for coordinating reaching and grasping. Unlike the PPC reach zone, the grasp zone received dense somatosensory inputs from the hand/forelimb representations of the anterior parietal cortex and from higher order representations of the
upper bank of the lateral sulcus. The densest connections outside of PPC originated in the hand/forelimb representation of M1 and some overlapped the M1 grasp zone. Dense inputs from ventral PMs were also apparent and cases that were mapped more comprehensively showed that those connections overlapped grasping zones.

Comparing the connections of the PPC grasp zone to results from other primate species is complicated by the lack of relevant connection studies and the challenge of identifying the PPC grasp zone architectonically. The present PPC grasp zone injections were caudal to area 1, and the pattern of connections shares features with that previously revealed for several cortical areas. For example, the present PPC grasp zone shares important features with the macaque AIP such as the aforementioned neurophysiological parallels and dense connections with the hand representation of PMv (Clower et al. 2005; Borra et al. 2008). Also, area 2 in macaques is distinguishable by neurophysiological, connectional, and architectonic criteria as a strip of cortex caudal to area 1 (Pons et al. 1985; Pons and Kaas 1986; Lewis et al. 1999). The location of area 2 in macaques and its connections with areas 3a, 3b, and 1 support the possibility that injections into the present PPC grasp zone, included area 2. However, the identity of cortex caudal to area 1 has been uncertain in New World monkeys. In owl monkeys, the representation of the body identified in a strip caudal to area 1 using multunit recordings was proposed to be area 2 (Merzenich et al. 1978). In titi monkeys, recordings caudal to area 1 revealed weakly responsive neurons with large receptive fields (Padberg et al. 2005), which were considered uncharacteristic of area 2 and presumed to be in PPC. The same study identified 2 connection patterns for cortex caudal to area 1. First, injections that were considered in area 5 labeled dense inputs from M1/PM, area 3a, S2/PV, AIP/7b, and more limited inputs from areas 1 and 3b. Second, injections that were considered in AIP/7b showed dense inputs from PM, S2, medial aspects of PPC, the medial bank of the intraparietal sulcus, insular cortex, and less consistent inputs from area 3b. The present PPC grasp zone shares some of the connection patterns described for AIP/7b, but patterns are more similar to those described for area 5. Thus, the present pattern of cortical connections and previously reported connections with anterior pulvinar and ventral lateral and ventral posterior nuclei of the thalamus (Gharbawie et al. 2010) raise the possibility that the present PPC grasp zone includes parts of areas 2, 5, and AIP/7b.

Regardless of the precise characterization of the PPC grasp zone, the concurrent mapping and injections into M1 and PPC grasp zones revealed a specific parietal–frontal network for grasping. PMv connections with the M1 and PPC grasp zones suggest that this parietal–frontal network includes 3 main nodes (PPC, M1, and PMv). Additional motor-related inputs from frontal cortex are primarily focused on the M1 node, whereas somatosensory inputs from anterior parietal cortex are largely directed at the PPC node. Inputs from overlapping regions of caudal M1, supplementary motor area, and the upper bank of the lateral sulcus to the M1 and PPC grasp zones, further support the premise that they are nodes within the same parietal–frontal network.

Concurrent Forelimb and Face Parietal–Frontal Network
Connections the PMv forelimb and face zone with PPC were weak, but the patterns were readily distinguishable from those of PMd and M1. Distinctly different connection patterns for PMv and PMd have been reported for owl monkeys (Stepniewska, Preuss, and Kaas 2006) and macaques (Tanne-Gariety et al. 2002). The relatively ventral connections of PMv in the present cases were similar to those reported for caudal and rostral PMv in macaques (Matelli et al. 1986; Luppino et al. 1999).

Conclusions
Injecting multiple functional zones in M1/PM and PPC that were identified with long train stimulation provided novel observations about the organization of parietal–frontal networks in New World monkeys. A dorsal parietal–frontal network connecting caudomedial PPC with PMd is involved in reaching. Visual inputs from caudal PPC and additional motor inputs from M1/PM further characterize this network. Nodes in PMd and PPC receive somatosensory inputs from overlapping regions of the upper bank of the lateral sulcus and receive motor inputs from overlapping regions of the supplementary motor area and cingulate motor areas. The more ventral parietal–frontal network interconnecting rostrolateral PPC, M1, and PMv is involved in grasping. Somatosensory inputs from overlapping regions of the anterior parietal cortex to the M1/PM and PPC nodes as well as additional motor inputs to the M1 node are distinctive features of this network. Interlinks between the reach and grasp networks, for example, connections between the PPC reach and grasp zones and connections between the PMd reach and M1 and PMv grasp zones may represent channels for coordinating reaching and grasping. Thus, the parietal–frontal networks and their sensory inputs may be envisioned as sensory-effector modules specialized for actions. Evidence for the existence of these parietal–frontal networks in 2 species of New World monkeys, prosimian galagos, and Old World monkeys suggests that these networks have been retained from a common ancestor and that they likely exist in all primates, including humans.

Funding
National Institutes of Health (NS16446 to J.H.K. and NS055843 to L.S.); Postdoctoral fellowship from the Natural Sciences and Engineering Research Council of Canada and subsequently a fellowship from the Canadian Institutes for Health Research (to O.A.G.).

Notes
We are grateful to Mark Burish for assistance with intracortical stimulation mapping, Laura Trice for assistance with histology, and Mary Feurtado for preoperative and postoperative animal care. Conflict of Interest: None declared.

References


