Grasping in the Dark Activates Early Visual Cortices

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We have previously demonstrated that the primary motor and somatosensory cortices of monkeys are somatotopically activated for action-observation as are for action-generation, indicating that the recruitment of learned somatosensory-motor representations underlies the perception of others’ actions. Here we examined the effects of seen and unseen actions on the early visual cortices, to determine whether stored visual representations are employed in addition to the somatosensory-motor ones. We used the quantitative 14C-deoxyglucose method to map the activity throughout the cortex of the occipital operculum, lunate, and inferior occipital sulci of “rhesus monkeys” who reached to grasp a 3D object either in the light or in the dark or who observed the same action executed by another subject. In all cases, the extrastriate areas V3d and V3A displayed marked activation. We suggest that these activations reflect processing of visuospatial information useful for the reaching component of action, and 3D object-related information useful for the grasping part. We suggest that a memorized visual representation of the action supports action-recognition, as well as action-execution in complete darkness when the object and its environment are invisible. Accordingly, the internal representation that serves action-cognition is not purely somatosensory-motor but also includes a visual component.

Keywords: action in the dark, action-observation, action-simulation, reaching to grasp, visual cortex

Introduction

Observing other subjects in order to understand their behavior and to learn from their actions is crucial for social interaction. In the past, we demonstrated that the neural system that supports both the generation of an action and the perception of the same action performed by another subject encompasses widespread areas in a parietofrontal cortical network. It involves several premotor and cingulate areas as well as the primary motor and somatosensory cortices, which are somatotopically activated when subjects observe object-related hand actions, as they are for execution of the same actions (Raos et al. 2004, 2007). Our findings, so far, indicate that we perceive the actions of others by recruiting virtually the same parietofrontal cortical circuits that are responsible for generation of the same actions. In other words, observation of an action stimulates the motor controller used to execute the same action. These findings support the notion that we understand others’ actions by mentally simulating, not only the motor component of the observed action but also its somatosensory/kinesthetic consequence (Raos et al. 2007; Evangeliou et al. 2009). When we use the term “mental simulation of action,” we do not wish to imply that a conscious process is in operation. Action-execution, action-observation, and action-recognition share cerebral and physiological correlates with the so called “mental practice” or “mental simulation of action,” that is, the faculty whereby we mentally rehearse voluntary movements without bodily executing them (Decety et al. 1994; Lang et al. 1994; Jeannerod 1995; Stephan et al. 1995; Porro et al. 1996; Roth et al. 1996; Sirigu et al. 1996; Deiber et al. 1998; Gallese and Goldman 1998; Jeannerod et al. 2001; Jacob and Jeannerod 2005; Munzert et al. 2008). Accordingly, mental simulation of an action involves an off-line (decoupled from actual movement) process and is viewed as a window to motor control and cognitive motor processes (Annet 1995; Jeannerod 2001).

In the present study, we explored whether the proposed neural substrate of mental simulation of an action extends beyond the parietofrontal motor/kinesthetic network, to the striate and extrastriate occipital cortical visual areas representing the object to be reached and manipulated and its spatial location, information useful for guiding the arm and shaping the hand to interact with the object. We used the [14C]-deoxyglucose (14C-DG) quantitative autoradiographic method (Sokoloff et al. 1977) to obtain high-resolution functional images of the monkey occipital visual cortical areas activated for grasping small 3D objects in the light and in the dark, as well as for observation of the same grasping movements executed by another subject. The 14C-DG method is the only imaging approach to offer: 1) direct assessment of local cerebral metabolic activity, 2) quantitative measurement of glucose utilization, 3) spatial resolution of 20 μm, and 4) histological identification of the affected cortical areas. We reconstructed 2D maps of metabolic activity of the striate area V1 and the extrastriate cortices V2, V3, and V4, which occupy the occipital operculum and both banks of the lunate sulcus (Ls) and the inferior occipital sulcus (Ios). We revealed that specific early visual cortical areas are activated 1) for grasping in the dark, that is, for the voluntary manipulation of an invisible/memorized object and 2) for observation of grasping performed by another subject, involving mental simulation of the action. For memory-guided reaching in the dark, it has been suggested that the source of target information available to support the
control of movements is a stored visual representation residing in the ventral visual pathway (Goodale et al. 1994; Hu et al. 1999; Westwood et al. 2000; Lemay and Proteau 2002; Heath and Westwood 2003; Goodale et al. 2004; Heath 2005). Our findings suggest that during a memory-guided reaching-to-grasp action in the dark, as well as during its observation, visual representations of the action components stored in the dorsal visual stream are recalled from memory. We suggest that not only motor and kinesthetic but also visual representations of the action contribute to action control and cognition.

Materials and Methods

Subjects

Twelve adult female monkeys (Macaca mulatta) weighing between 3 and 6 kg were used in the present study. Experimental protocols were approved by the Animal Use Committee of the Foundation for Research and Technology-Hellas, in accordance with European Council Directive 86/609/EEC. A detailed description of the surgical procedures, the recording of electromyographic activity and eye position was reported previously (Raos et al. 2004, 2007). In brief, for immobilization of the head, a metal bolt was surgically implanted with the use of mandibular plates secured by titanium screws (Synthes). Surgical procedures took place under general anesthesia using aseptic techniques. Antibiotics and analgesics were administered systemically before and after surgery, and the monkeys were allowed to recover for 4 weeks before training started. Monkeys were trained to perform their tasks continuously for at least 1 h per day for several months before the 14C-DG experiment, until they perfected their performance displaying a 95% success rate. Monkeys received water as reward for each successfully completed trial, delivered through a tube placed close to their mouth. On the day of the 14C-DG experiment, monkeys performed their tasks continuously during the entire experimental period of 45 min. Digitized electromyograms, recorded with the use of Ag-AgCl surface electrodes from the biceps and wrist extensor muscles (gain × 2000, band-pass filter 0.3-3000 kHz), were previously reported (Raos et al. 2004). Eye position, recorded with an infrared oculometer (Dr Bouis), is illustrated in 3D histograms of the dwell time of the line of sight (Fig. 1).

Figure 1. The 3D histograms of the dwell time of the line of sight as a function of eye position. (Gl) Averaged oculomotor behavior from the 2 monkeys reaching to grasp in light. (O) Averaged behavior from the 3 grasping-observation monkeys. (Cm) Averaged behavior from the 2 motion-control monkeys. (Cf) Oculomotor behavior from the fixation-control monkey. (Gd) Averaged oculomotor behavior from the 2 monkeys reaching to grasp in the dark. (Cd) Averaged behavior from the 2 dark-control monkeys. Horizontal axis (H; x) and vertical axis (V; y) in degrees and z-axis in seconds. Grayscale bar indicates time in seconds.
Behavioral Tasks
A detailed description of the behavioral apparatus for grasping an object was reported previously (Raos et al. 2007). In brief, the apparatus was placed in front of the monkey at shoulder height, 25–45 cm away depending on whether the monkey or the experimenter had to perform the task. A sliding circular window of 8° diameter, at the front side of the behavioral apparatus, allowed the subject to grasp a horizontally oriented ring with the index finger inserted into it. In order to control for possible rate-related effects, the mean rate of movements was set to be similar for all tasks.

Two grasping-in-the-light (Gl) monkeys were trained to reach and grasp with the left forelimb, while the right forelimb was restricted. They were required to fixate the illuminated object behind the opened window (of 8° diameter) for 0.7–1 s, until a dimming of the light would signal reaching, grasping, and pulling the ring with the left forelimb while maintaining fixation. The maximum latency to grasp the object was set to 1 s, although the movement was usually completed within 500–600 ms. The Gl monkeys were allowed to move their eyes outside the window only during the intertrial intervals (ranging between 2 and 2.5 s).

Three grasping-observation (O) monkeys were first trained to perform the task with the Gl monkey (gaze- -reaching to grasp, hand to observe the same grasping movements executed by the experimenter (observation-training). In order to cancel any possible interhemispheric differences in the effects due to the earlier grasping-training, the first monkey was trained to grasp with its left hand, the second one with its right hand, and the third one with both hands consecutively. During the observation-training and during the 14C-DG experiment, both forelimbs of the O monkeys were restricted. The experimenter was always standing on the right side of the monkey and was using the right arm/hand for reaching/grasping. Both reaching and grasping components of the movement were visible to the monkey.

In order to disambiguate the effects of the purposely reaching/grasping action, that is, the components of reaching to grasp, hand preshaping, and object-hand interaction from 1) the non-goal-directed biological motion effect, elicited by a purposelessly moving forelimb in front of the monkey (arm-motion effect), and from 2) the visual stimulation effect induced by mere presentation of the 3D object to the monkey (object-presentation effect), we compared the effects on the Gl and O monkeys with those on 2 arm-motion control (Cm) monkeys. Each Cm monkey had both hands restricted, had no previous grasping training, and was trained to maintain its gaze straight ahead (within the 8° circular window) during the opening of the window of the apparatus, the presentation of the illuminated object behind the opened window, the closure of the window, and while the experimenter was reaching with extended hand toward the closed window (for a total period of 2.7–3 s per trial). The direction of motion and velocity of the experimenter’s arm were the same as in the observation task. At this point, it should be also noted that monkey and human movements share striking kinesiological similarities (Roy et al. 2000). The Cm monkeys were allowed to move their eyes outside the circular window only during the intertrial intervals (ranging between 2 and 2.5 s).

In order to remove the visual effect caused by plain fixation, the activations of the visual cortex of the Cm, Gl, and O groups of monkeys were compared with those of the 2 hemispheres of a fixation-control ( Cf) monkey. A detailed description of the behavioral apparatus for visual fixation was reported previously (Savaki et al. 2010). In brief, the behavioral apparatus was a video monitor placed 25 cm in front of the monkey. The visual target for fixation was a red circle, 1.5° in diameter, located straight ahead of the monkey. The Cf monkey had both its arms restricted and was required to hold eye position within a circular window, 2.5° in diameter, centered on the fixation target. This monkey had to maintain fixation for the duration of the trial (4 s). Interttrial intervals ranged between 0.2 and 0.3 s. The Cf monkey maintained fixation for 75% of the 14C-DG experimental time including intertrial intervals.

Two grasping-in-the-dark (Gd) monkeys were trained to reach and grasp with the left forelimb in complete darkness, while the right forelimb was restricted. To achieve complete darkness, the primate chair was enclosed within black curtains together with the behavioral apparatus, and an extra black drape was positioned in front of the monkey’s eyes. A speaker was placed 25 cm in front of the monkey, in the median sagittal plane, below the behavioral apparatus. Following a low-frequency auditory cue (90 Hz), each Gd monkey had to look straight ahead toward the memorized location of the object for 0.7–1 s, until a second high-frequency auditory cue (180 Hz) signaled the generation of the learned action (reaching, grasping, and pulling the memorized ring with the left forelimb) while maintaining its gaze straight ahead. The maximum latency to grasp the object was set to 1 s, although the movement was usually completed within 500–600 ms. The Gd monkeys were allowed to move their eyes outside the window only during the intertrial intervals (ranging between 2 and 2.5 s).

To reveal the effects induced by reaching to grasp in the dark, the metabolic maps of the 4 hemispheres from the 2 Gd monkeys were compared with those obtained from the 4 hemispheres of 2 control-in-the-dark monkeys (Cd). The Cd monkeys were presented with auditory stimuli similar to the acoustic cues presented to the Gd monkeys. Reward was delivered at random intervals to prevent association of the auditory stimuli with the reward expectancy. The total number of rewards that the Cd monkeys received matched that of the Gd monkeys. Figure 1Cd illustrates the 3D histogram of the dwell time of the line of sight as a function of eye position of the Cd monkeys. The roughly even distribution in much of the oculomotor space implies that the Cd monkeys were alert and actively exploring their environment during the 14C-DG experiment.

14C-DG Experiments
The 14C-DG experiment and the brain tissue processing for autoradiography were performed as previously described (Savaki et al. 1993; Gregoriou and Savaki 2001). In brief, during the day of the 14C-DG experiment, monkeys were subjected to femoral vein and artery catherization under general anesthesia and were allowed 4–5 h to recover. Five minutes after each monkey started performing its task, a pulse of 100 µCi/kg of 2-deoxy-D-[1-14C] glucose in saline (specific activity 55 mCi/mmol, American Radiolabeled Chemicals, Inc.) was iv delivered. Arterial samples were collected during the succeeding 45 min, and the plasma radioactivity and glucose concentrations were measured. Subsequently, the monkey was sacrificed by iv injections of 50 mg sodium thiopental in 5 ml saline and a saturated potassium chloride solution. The cerebral hemispheres were removed, frozen in isopentane at −50 °C, and stored at −80 °C. About 1300 serial horizontal sections of 20-µm thickness were cut in each hemisphere of each monkey, containing the visual areas of interest, using a cryostat at −10 °C. Autoradiographs were prepared by exposing these sections together with precalibrated 14C-standards with medical X-ray film (Kodak Biomax MR) in X-ray cassettes. One section every 500 µm was stained with thionine for identification of cytoarchitectonic borders. Our 20-µm thick sections of nonperfused tissue did not allow for cytochrome oxidase staining. However, we were able to cytoarchitectonically identify certain visual areas in the thionine-stained sections, based on characteristics described in early visual studies (von Bonin 1942; Rockland and Pandya 1981; Zilles and Clarke 1997; Luppino et al. 2005). Specifically, the primary visual cortical area V1 was easily distinguished from area V2 due to its well-developed and differentiated lamina granularis interna (layer IV). The third (III) layer of area V3 contained smaller pyramidal cells as compared with those in area V2. The fourth (IV) layer was more distinct and dense in area V2 as compared with that in area V3. Finally, the sixth layer (VI) in area V2 was sharply set off from the white matter, in contrast to that of area V3 that blended smoothly with the white matter. Reassuring is the fact that the surface of area V2 outlined by the cytoarchitectonically identified borders (between V1 and V2 and between V2 and V3) overlaps with the area characterized by stripes in our reconstructed maps of metabolic activity. Nevertheless, the cytoarchitectonic borders between areas V3 and V4 were not as clear and thus based on surface brain landmarks (see following section) according to the atlas of Saleem and Logothetis (2007).

Quantitative densitometric analysis of autoradiographs was performed with a computerized image processing system (Imaging Research), which allowed integration of the local cerebral glucose utilization (LCGU) values (in µmol/100 g/min) within each area of
interest, based on the original operational equation of the method (Sokoloff et al. 1977) and the appropriate kinetic constants for the monkey (Kennedy et al. 1978). Normalization of the measured LCGU values was based on the averaged unaltered gray matter value pooled across all monkeys (Bakola et al. 2007). Accordingly, LCGU values were multiplied with a factor that was separately determined for each hemisphere. This factor is equal to the ratio of the mean LCGU value found in the unaffected occipitotemporal cortex of the hemisphere in question over the mean LCGU value obtained from the same area after pooling all hemispheres from all monkeys. Very similar normalization factors were found when LCGU values from other unaffected cortical areas (such as the hind limb and body representations of the primary motor and somatosensory cortices in the central sulcus) were used instead (Raos et al. 2007). Because the ipsilateral to contralateral LCGU values of all the herein reported visual cortical areas did not differ for more than 7%, which is the maximum interhemispheric difference in normal monkeys (Kennedy et al. 1978), we averaged all hemispheres of all monkeys in each group for the final statistical comparisons. Percent LCGU differences between experimental and control subjects were calculated as follows: (experimental-control)/control × 100. To determine statistical significant differences (Table 1, bold values), we relied on Student’s unpaired t-test (Raos et al. 2007; Evangeliou et al. 2009; Savaki et al. 2010).

Reconstruction of Quantitative Cortical Maps and Their Geometrical Normalization

2D maps of the spatiointensive pattern of metabolic activity (LCGU values in μmol/100 g/min), within the rostrotocaudal and the dorsoventral extent of the occipital opercular stripate visual cortex between the calcarine sulcus and the Ls, and of the extrastriate visual cortex within the Ls and the IOs, was generated in each hemisphere from 20-μm thick horizontal sections (dorsoventral sampling resolution of 20 μm), as previously described (Daleziou et al. 1996; Savaki et al. 1997). Briefly, from each horizontal section, a data array was obtained by sampling the LCGU values along a rostrotocaudal line parallel to the surface of the cortex, including all cortical layers (anteroposterior sampling spatial resolution 50 μm/pixel). To avoid cutting artifacts, data arrays were averaged every 5 adjacent horizontal sections of 20 μm to produce one line in the reconstructed 2D maps of activity. Accordingly, each 2D-reconstructed map is made of 265 lines (1315 sections divided by 5 sections per line), and each line represents the average of 5 adjacent serial sections. Thus, the dorsoventral sampling resolution of our study equals 20 μm, whereas the dorsoventral plotting resolution of our 2D maps equals 100 μm.

The V1/V2 border, close to the posterior crown of the Ls, was used for the alignment of adjacent data arrays in the reconstructed maps. Tick marks (1-8 in Fig. 2b-d) in each horizontal section, which are labeling the surface landmarks of the brain such as crown, fundus, and intersection of sulci, were used for the geometrical normalization of maps, that is, to match the reconstructed 2D maps obtained from different hemispheres and animals. Explicitly, to allow for direct comparison of the cortical regions of activation, despite the inter- and intrahemispheric macroscopic anatomical variability, the individual functional 14C-DG/LCGU maps were further processed to match a reference map. The general procedure of the geometrical normalization of the LCGU maps, based on surface landmarks, was previously described (Evangeliou et al. 2009; Savaki et al. 2010). In specific, in each horizontal section, we measured the distances between the mediallymost point of the posterior crown of the calcarine sulcus (point 1, Fig. 2b-d) and the point of alignment, that is, the border between areas V1 and V2 close to the posterior crown of the Ls in the dorsal sections (point 2, Fig. 2b,c) or the posterior crown of the IOs in the ventromost sections (point 2, Fig. 2d). Also, for the dorsal sections in which the Ls appears, we measured the distances between V1/V2 border (point 2) and its fundus (point 3, Fig. 2b,c), its fundus and the mediallymost point of the posterior bank of the parieto-occipital sulcus (point 4, Fig. 2b) for the dorsalmost sections, and its fundus and its anterior crown (point 5, Fig. 2c) in the subsequent ventral sections. In the latter sections, we also measured the distance between the anterior crown of the Ls (point 5) and the posterior crown of the superior temporal sulcus (point 6, Fig. 2c). Finally, for the ventromost sections where the IOs is apparent, we measured the distances between its posterior crown (point 2, Fig. 2d) and its fundus (point 7, Fig. 2d) and also between its fundus and its anterior crown (point 8, Fig. 2d).

The average of each one of these measures was separately estimated from all 24 hemispheres (of the 12 monkeys used in our study) to produce a reference map of surface landmarks (Fig. 2e). Subsequently, each individual cortical map with its own landmarks was linearly transformed (Moschovakis et al. 2004) with the help of custom-designed routines in the Matlab environment (Mathworks) to match the reference map. The geometrically normalized maps were combined 1) to obtain average LCGU maps out of control or experimental hemispheres and 2) to subtract control from experimental averaged maps. In specific, to generate average maps (glucograms), the LCGU value found in a certain pixel in one of the geometrically normalized maps was added to the value found in the pixel occupying the same position in one or more other similar maps, and the result was divided by the number of maps used. Similarly, to generate a difference map, the LCGU value found in a certain pixel of a geometrically normalized map of a control hemisphere was subtracted from the value found in the pixel occupying the same position in a similar map obtained from an experimental hemisphere. With this procedure, although the total

| Table 1 |
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| Metabolic effects in occipital cortical areas of the monkey brain |
| Cortical area | n | Ct (LCGU ± SD) | Cm (LCGU ± SD) | Gl (LCGU ± SD) | G/Cm (%) | Ct/Cm (%) | O (LCGU ± SD) | O/Cm (%) | Ct/O (%) | Cd (LCGU ± SD) | Gd (LCGU ± SD) | Gd/Cd (%) |
| V1-00 | 263 | 51 ± 2 | 61 ± 1 | 61 ± 2 | 0 | 20 | 64 ± 2 | 5 | 25 | 44 ± 1 | 48 ± 1 | 9 |
| V1-00 (central) | 172 | 59 ± 4 | 60 ± 2 | 60 ± 1 | 0 | 2 | 65 ± 2 | 8 | 10 | 42 ± 1 | 44 ± 1 | 5 |
| V1-00 (peripheral) | 263 | 50 ± 2 | 61 ± 1 | 61 ± 2 | 0 | 2 | 64 ± 2 | 5 | 28 | 45 ± 2 | 49 ± 1 | 9 |
| V2d-Ls (central) | 155 | 60 ± 3 | 52 ± 2 | 53 ± 2 | 2 | 12 | 53 ± 2 | 2 | 12 | 37 ± 1 | 38 ± 2 | 3 |
| V2d-Ls (peripheral) | 196 | 48 ± 4 | 54 ± 2 | 57 ± 3 | 6 | 19 | 54 ± 3 | 0 | 13 | 40 ± 5 | 50 ± 4 | 25 |
| V2v-Ios | 67 | 47 ± 2 | 52 ± 1 | 54 ± 1 | 4 | 15 | 51 ± 1 | -2 | 9 | 39 ± 1 | 43 ± 2 | 10 |
| V3d-at (central) | 81 | 57 ± 4 | 55 ± 3 | 65 ± 2 | 18 | 14 | 65 ± 2 | 18 | 14 | 48 ± 3 | 51 ± 6 | 6 |
| V3d-ap (peripheral) | 62 | 53 ± 4 | 55 ± 1 | 65 ± 4 | 18 | 20 | 61 ± 4 | 11 | 13 | 52 ± 3 | 68 ± 3 | 31 |
| V3v-Ios | 67 | 58 ± 4 | 54 ± 2 | 56 ± 1 | 4 | -3 | 54 ± 1 | 0 | -7 | 42 ± 2 | 46 ± 3 | 10 |
| V3A | 89 | 56 ± 3 | 53 ± 2 | 61 ± 4 | 15 | 9 | 59 ± 4 | 11 | 5 | 49 ± 3 | 55 ± 7 | 12 |
| V4-Ls | 81 | 65 ± 6 | 52 ± 2 | 60 ± 2 | 15 | -8 | 54 ± 1 | 4 | -17 | 46 ± 2 | 48 ± 4 | 4 |
| V4-Ios | 67 | 57 ± 4 | 53 ± 2 | 56 ± 3 | 6 | 0 | 54 ± 2 | 2 | -5 | 43 ± 2 | 45 ± 2 | 5 |

Note: n, number of sets of 5 adjacent horizontal sections used to obtain the mean LCGU values (in μmol/100 g/min) for each region; Ct, average LCGU values from the 2 hemispheres of the fixation-control monkey; Cm, average LCGU values from the 4 hemispheres of the 2 motion-control monkeys; Gl, average LCGU values from 4 hemispheres of 2 control-in-dark and 2 grasping-in-dark monkeys, respectively; SD, standard deviation of the mean; G/Cm and O/Cm, percent differences between Gl or O and Cm, respectively; G/Ct and O/Ct, percent differences between Gl or O and Ct, respectively; Gd/Cd, percent differences between Gd and Cd; O, occipital operculum; op, occipitoparietal; ot, occipitotemporal. Values in bold indicate statistically significant differences by the Student’s unpaired t-test at the level of P < 0.001.
surface of an area may change when it is geometrically normalized, the intensity and the spatial distribution of LCGU effects are preserved within it because these effects are proportionally shrunk or expanded within its borders.

To create geometrically normalized anatomical maps matching our metabolic ones, we used the combined magnetic resonance imaging (MRI) and histology monkey atlas of Saleem and Logothetis (2007). The horizontal sections of this atlas, including 1) the labeled surface landmarks and 2) the anatomical borders between visual cortical areas, were processed the same way as our autoradiographic sections, in order to match the same reference map. Thus, the so generated 2D reconstruction (Fig. 2f) contains the anatomical borders of the visual areas of interest in addition to the surface landmarks. A, anterior; As, arcuate sulcus; Cs, central sulcus; D, dorsal; IOs, inferior occipital sulcus; IPs, intraparietal sulcus; Ls, lunate sulcus; op and ot, occipitoparietal and occipitotemporal segments of area V3d, respectively; P, posterior; STs, superior temporal sulcus; V, ventral.

Results
The behavioral performance, such as the number of executed or observed grasping movements per minute and the oculomotor activity of some of the monkeys used in the present study was reported previously (Raos et al. 2007; Evangeliou et al. 2009). However, because more monkeys per group and more groups are included here, we presently report both the oculomotor and skeletonmotor performance. The dwell time of the line of sight as a function of eye position averaged over the monkeys belonging to each one group, during the first 10 min of the 14C-DG experiment, is illustrated in 3D histograms in Figure 1. This period of time is critical because more than 85% of the radiolabeled DG is taken up before it ends (Sokoloff et al. 1977). As required, all the monkeys performing their tasks in...
the light spent most of the critical time fixating straight ahead (Fig. 1Gl, O, Cm, Cf). The same is true of the Gd monkeys, except that in this case the distribution is shallow and more spread out because they were fixating in the absence of a visible target (Fig. 1Gd). As expected, the Cd monkeys display a roughly even distribution in much of the oculomotor space (Fig. 1Cd).

Figure 2 demonstrates the way we reconstructed the 2D metabolic and the anatomical maps (see Materials and Methods). Figure 3 illustrates quantitative 2D maps of the spatiointensive distribution of metabolic activity (in \( \mu \text{mol}/100 \text{g/min} \) of glucose consumption) within the reconstructed occipital operculum, the Ls and the IOs of the monkeys generating reaching-to-grasp movements in the light (Gl), the monkeys observing the same movements performed by the experimenter (O), and the motion-control (Cm) monkeys. The surface landmarks (black lines) and the anatomical borders (white lines) are also included (see Materials and Methods). In this and the following figures, reconstructions from the left hemisphere are reflected to match those from the right, whereas anterior is right and posterior is left. Each map of Figure 3 is from a separate group of monkeys and illustrates the spatial distribution of activity, in a geometrically normalized map, of the reconstructed maps averaged across all members of the group. As explained in the methods, the lack of interhemispheric differences allowed us to average both hemispheres of each monkey. Thus, the Gl map is the average LCGU map (glucogram) from the 4 hemispheres of 2 monkeys (Fig. 3a), the O map represents the averaged glucogram from 6 hemispheres of 3 monkeys (Fig. 3b), and the Cm map is the average from 4 hemispheres of 2 monkeys (Fig. 3c). These glucograms were used for measurement of the LCGU values in the striate V1 and extrastriate V2-V4 visual cortical areas based on the borders of Figure 2f and subsequently for their statistical comparisons and the estimation of the percent differences from the corresponding values of the Cm monkey (Table 1).

The Gl monkeys, which executed an average of 10 grasping movements per minute and fixated within the window of the behavioral apparatus \((8 \times 8^\circ)\) for an average of 7 min (Fig. 1Gl) during the critical 10 first minutes of the \(^{14}\text{C-DG} \) experiment,

![Figure 3](image-url)

**Figure 3.** Quantitative 2D maps of metabolic activity in the occipital cortex of viewing monkeys. (a) Averaged map from the 4 hemispheres of the 2 monkeys reaching to grasp in the light (Gl). (b) Averaged map from the 6 hemispheres of the 3 monkeys observing another subject performing the same reaching-to-grasp movements (O). (c) Averaged map from the 4 hemispheres of the 2 motion-control monkeys (Cm). Black lines correspond to surface landmarks and white lines to anatomical borders of cortical areas, as illustrated and labeled in Figure 2. Grayscale bar indicates LCGU values in micromoles per 100 g per minute.
display significant activations when compared with the Cm in areas V3d, V3A, and V4 (Table 1, Gl/Cm, bold values). The 2 segments of area V3d, the occipitoparietal reflecting peripheral vision and the occipitotemporal reflecting central vision (Baizer et al. 1991), were equally activated for grasping in the light. The O monkeys, which observed an average of 12 grasping movements per minute and fixated for an average of 7 min (Fig. 1O) during the critical 10 first minutes of the 14C-DG experiment, display significant activations as compared with the Cm in areas V1 (representation of central vision), V3d (with the region of representation of central vision more activated than that of peripheral vision), and V3A (Table 1, O/Cm, bold values). Finally, during the critical 10 first minutes of the 14C-DG experiment, the Cm monkeys observed 12 movements of the experimenter’s arm per minute and fixated within the window of the behavioral apparatus for 7 min (Fig. 1Cm). To illustrate the tabulated percent LCGU differences between the experimental monkeys and the Cm, we generated images using the formula \( \frac{Gd - Cm}{Cm} \times 100 \) and \( \frac{O - Cm}{Cm} \times 100 \) (Fig. 4). When the averaged maps of the Gl or those of the O monkeys are compared with the averaged map of the Cm monkeys (Fig. 4a,b, respectively) increased metabolic activity is indeed apparent in the areas which appear significantly affected in Table 1, with area V3d displaying the highest activations in both cases. It should be mentioned that when we subtract the Cm from the Gl and O groups, we actually subtract all visual information related to the presentation of the object and the purposeless (non-goal directed) movement of a forelimb. Thus, the remaining “net activation” specifically represents the visual information that is required by the motor system to guide the forelimb to reach accurately and grasp properly. Accordingly, areas V3d and V3A activated for both Gl and O groups after subtraction of the Cm should encode visual information useful for motor control. Of course, activations are different if we use the Cf monkey as a reference instead of the Cm. In the latter case, we subtract the effect due to spot fixation, instead of subtracting the effects due to the object–presentation and arm–motion. When we used the Cf as control case, the striate area V1 of the occipital operculum as well as the extrastriate area V2 of the Ls and the IOs were found to be activated in both Gl and O groups as compared with the Cf, in addition to area V3 which was also activated as compared with the Cm (Table 1, Gl/Cf and O/Cf, bold values).

The Gd monkeys, which executed an average of 11 grasping movements per minute and kept their gaze straight ahead within a window of \( 10 \times 10^3/10 \) \( \times 10^3 \) for an average of 7 min during the critical 10 first minutes of the 14C-DG experiment (Fig. 1Gd), display significant activations when compared with their corresponding control monkeys, Cd, in areas V1, V2, V3A, V3v, and the occipitoparietal segment of V3d (Table 1, Gd/Cd, bold values). These effects are demonstrated in Figure 5, which illustrates the quantitative 2D maps of the spatiointensive distribution of metabolic activity (in \( \mu \)mol/\( 100 \) g/min of LCGU) within the reconstructed occipital operculum, Ls and IOs, of the monkeys generating reaching-to-grasp movements in the dark (Gd) and of the control in the dark (Cd) monkeys, as well as their comparison. Each one of the Gd (Fig. 5a) and the Cd (Fig. 5b) glucograms represent the averaged maps from 4 hemispheres of 2 monkeys. To pictorially represent the LCGU differences between the Gd and the Cd groups of monkeys, we generated an image using the formula \( \frac{Gd - Cd}{Cd} \times 100 \) (Fig. 5c). This image illustrates the increased metabolic activity.

**Figure 4.** Percent LCGU differences from the motion control. (a) Map of net activations induced by reaching to grasp in the light, averaged from the 4 hemispheres of the 2 Gl monkeys as compared with the 4 hemispheres of the 2 Cm monkeys. (b) Map of net activations induced by grasping–observation, averaged from the 6 hemispheres of the 3 O monkeys as compared with the 4 hemispheres of the 2 Cm monkeys. White lines correspond to surface landmarks and anatomical borders labeled in Figure 2. Color bar indicates percentage of LCGU differences from the Cm.
net activation) in the areas that appear significantly affected in Table 1, that is, in areas V1, V2, V3d, and V3A. It should be emphasized that the occipitoparietal segment of area V3d, representing peripheral vision, displayed a pronounced activation for action-generation in the dark in contrast to its occipitotemporal division reflecting central vision which remained inactive. At this point, it should be mentioned that, although the activation of specific areas in our study reflects their explicit involvement in the generation and the observation of a reaching-to-grasp action, the overlapping activations for execution in the light or in the dark and for observation do not necessarily indicate involvement of the same cell populations in all conditions.

Figure 6a illustrates the quantitative 2D map of metabolic activity (in \( \mu \text{mol}/100 \text{g/min} \)) in the reconstructed occipital operculum, Ls and IOs, averaged from the corresponding maps of the 2 hemispheres of a monkey fixating a spot of light 1.5° in diameter, in the dark (Cd). To pictorially represent the “net effect of fixation,” we generated an image of LCGU differences between the Cf and the Cd monkeys, using the formula (Cf – Cd)/Cd \( \times 100 \) (Fig. 6b). The early visual cortical regions that are illustrated in this figure to be involved in fixation (central vision) are in close agreement with those of a previous meticulous functional magnetic resonance imaging (fMRI) study (Brewer et al. 2002). Indeed, Figure 6b illustrates 1) increased metabolic activity within the foveal representation of the visual field (central 1.5°, corresponding to the used target of fixation) which covers about 10 mm of cortex in the striate area V1 and about 7 mm in the extrastriate area V2, and 2) a continuous zone of activation occupying areas V2, V3, and V4 which corresponds to their central vision, which is adjacent to the V1 foveal activation. To illustrate the net effects of

Figure 5. Quantitative maps of activity in the occipital cortex of monkeys in the dark. (a) Averaged map from the 4 hemispheres of the 2 monkeys reaching to grasp in the dark (Gd). (b) Averaged map from the 4 hemispheres of the 2 control monkeys in the dark (Cd). Black lines correspond to surface landmarks and white lines to anatomical borders of cortical areas, as illustrated in Figure 2. Grayscale bar indicates LCGU values in micromoles per 100 g per minute. (c) Map of net activations induced by reaching to grasp in the dark, averaged from the 4 hemispheres of the 2 Gd monkeys as compared with the 4 hemispheres of the 2 Cd monkeys. White lines correspond to surface landmarks and anatomical borders labeled in Figure 2. Color bar indicates percent LCGU differences from the Cd.
arm-motion and object-presentation, we generated an image of LCGU differences between the Cm and Cf monkeys, using the formula \[(Cm - Cf)/Cf \times 100\] (Fig. 6c). The image of Figure 6c is nearly complementary to that of Figure 6b, verifying the zone of foveal vision in areas V1, V2, V3, and V4 of the occipital cortex (Brewer et al. 2002). Moreover, the fact that the Cm group displays activations in extrafoveal regions of areas V1, V2, and V3 (Fig. 6c) explains the reason why more visual areas are activated when the Gl and the O groups are compared with the Cf (Table 1, Gl/Cf, O/Cf) than to the Cm (Table 1, Gl/Cm, O/Cm). In fact, when the Gl is compared with the Cf, similar activations are found with those observed when the Gd is compared with the Cd.

The plots in Figure 7 represent percent LCGU differences between experimental groups and their corresponding controls, that is, between the Gl or O and the Cm, and between the Gd and the Cd, in the different subdivisions of areas V3d and V4. The LCGU differences trace a path that traverses 1) the V3d cortex from its ventralmost posterior occipitotemporal point (0 mm) to its dorsalmost posterior occipitoparietal point (12.5 mm) and then to its dorsalmost anterior occipitoparietal point (35.4 mm), and finally 2) the V4 occipitotemporal cortex from its dorsal to its ventralmost point (49.2 mm), as indicated in the diagrammatic representation of the reconstructed map above the plots. The length of this path in the diagrammatic representation corresponds to the length of the abscissa in the graph (Fig. 7). The Gl monkeys (red line) demonstrate a peak of activity in the ventral occipitotemporal part of area V3d representing central vision (which extends between 0 and 10 mm) and another peak in its dorsal occipitoparietal segment representing peripheral vision (which extends between 10 and 35 mm), while area V4 is steadily activated throughout its
The O monkeys (green line) display also 2 peaks of activity, one in the occipitotemporal and another one in the occipitoparietal segment of V3d, and no activation in area V4. Finally, the Gd monkeys (blue line) demonstrate pronounced activity only in the occipitoparietal segment of area V3d.

Discussion

In the past, we demonstrated that the motor cognitive process involved in both action–observation and action-in-the-dark has a somatosensory character, indicated by the somatotopic activation of the SI cortex (Gregoriou and Savaki 2003; Raos et al. 2004). Here, we examine whether this process has also a visual character. Therefore, we provide quantitative maps of activity in the early visual occipital cortical areas of monkeys, while they are processing information useful for the generation (in the light and in the dark) and the observation of the same reaching-to-grasp action. In comparison with the motion-control monkeys which were exposed to the presentation of the object and the aimless arm-motion, V1 and V2 cortical regions of both the central and peripheral visual representations in the occipital operculum, as well as V3v and V4 regions within the IOs were not affected either by action–execution in the light or by action–observation. The lack of any effect within areas V1 and V2 indicates that the motion-control group provided us with the means to correct for object–vision and arm–motion. The absence of any activation in the ventral regions of V3 and V4 is explained by the fact that our behavioral tasks involved activities in the lower rather than in the upper visual field of the monkeys (e.g., arm reaching to grasp). Area V4, which is a component of the ventral visual stream, was activated only for action-generation in the light, indicating that the attentive visual processing of detailed color- and form-related information about the object and the grasping hand is important for the generation but not for the observation/recognition of the action (Pasupathy and Connor 2001; Buffalo et al. 2010). In contrast, areas V3d and V3A, which are part of the dorsal visual stream, were activated for both execution in the light and observation. The activation of area V3 cannot be attributed to differences in oculomotor behavior because the motion-control monkeys kept their eye position within the same window and for the same period of time as the experimental subjects in the light (Gl and O). Consequently, our results indicate that area V3 is processing visual information predominantly related to the requirements of the motor system to control the action. For example, area V3 may be receiving efferent feedback signals from the motor system enabling the visual system to focus on elements useful for the

Figure 7. Plots of percent LCGU differences along areas V3d and V4. The striped region in the schematic representation of the reconstructed cortex above the plots traces the path of measurement of the percent LCGU differences in the reconstructed cortical fields. This path traverses the V3d cortex from the ventralmost (0 mm) to its dorsalmost extent (12.5 mm) and then from the caudalmost (12.5 mm) to its rostralmost coverage (35.4 mm), as well as area V4 dorsoventrally (between 35.4 and 49.2 mm). Colored lines illustrate the percent LCGU differences between control and experimental groups as indicated in the insert. Red, green, and blue shaded areas, around the corresponding lines, indicate 95% confidence intervals. Baseline (zero on the ordinate axis) corresponds to 0% LCGU difference from the corresponding control. The distances (mm) in the abscissa of the graph correspond to those marked in the schematic representation of the reconstructed cortex, op and ot, occipitoparietal and occipitotemporal segments of area V3d, representing peripheral and central vision, respectively.
successful completion of the action. We wish to emphasize that this motor-related visual information is processed not only during action-generation but also during action-observation.

Based on our findings and in agreement with its known functional role, we suggest that area V3 may relay to the motor system, via the parietofrontal visuomotor stream, visuospatial information required for the reaching component of the action, and 3D object-related information useful for the grasping component. Indeed, there are several reports supporting the above-mentioned suggestion. First, it is known that V3 cells have strong binocular interactions (Zeki 1978a, 1978b) and are disparity selective (Felleman and Van Essen 1987; Poggio et al. 1988; Adams and Zeki 2001), thus contributing to stereopsis. Moreover, area V3A (Van Essen and Zeki 1978) may construct an objective map of the visual field by combining visual and eye position information (Galletti and Battaglini 1989) and may play a role in cognitive functions, such as attention, anticipation, and memory (Nakayama and Colby 2000). Furthermore, areas V3d and V3A are considered to process the 3D shape of an object and the global 3D layout (Tsao et al. 2003). Second, although the only direct projections of area V3 to the frontal cortex are those to frontal eye fields (Barbas and Mesulam 1981), V3 is an important link between early visual areas and the parietal sensory–motor integration areas (Andersen et al. 1990; Baizer et al. 1991; Felleman and Van Essen 1991). It projects to posterior parietal areas (Felleman et al. 1997) which are involved in visuomotor transformation for prehensile hand movements (Nakamura et al. 2001) and also to parieto-occipital areas (Shipp et al. 1998) which are engaged in encoding the extrapersonal visual space (Galletti et al. 1995) and in sensory–motor integration of reaching arm movements (Galletti et al. 1997).

Thus, on the basis of the cellular properties, the functional organization, and the intercortical connections, we suggest that the activation of areas V3d and V3A for action–generation in the light reflects the processing of stereoscopic depth information, useful for the analysis of forelimb position, object depth, and 3D form for the appropriate reaching to grasp. Because mental simulation of action has already been demonstrated during action–observation in monkeys (Jeannerod 2001; Raos et al. 2004), here we suggest that the activation of areas V3d and V3A for action–observation reflects the processing of visual information related to the mental simulation of the observed action. This information is relayed via the parietal projections of areas V3d and V3A (Andersen et al. 1990; Baizer et al. 1991; Felleman and Van Essen 1991), which were activated for grasping–observation (Evangelioiu et al. 2009), to the premotor/motor cortices (Petrides and Pandya 1984; Matelli et al. 1998; Petrides and Pandya 1999) which were also activated for observation of grasping movements (Raos et al. 2007).

The monkeys that were reaching to grasp in complete darkness displayed activations in the peripheral, but not in the central, regions of visual representation of areas V1, V2, and V3, and also displayed no effect in area V4. The activation of the early visual cortices of our blindfolded monkeys may reflect the top-down feedback from frontoparietal dorsal stream areas and their cross talk with the early visual cortices, concerning memorized visual information required for action in the dark. We suggest that this information represents the spatial location and the 3D form of the object, required for motor control, that is, for the estimation of the required reaching distance and the appropriate shaping of the hand for grasping in the dark. In our previous study, the somatotopic activation of the primary somatosensory cortex for action–observation was attributed to the predicted/recalled somatosensory consequence of the mental simulation of the observed action (Raos et al. 2004). Similarly, the presently demonstrated activation of the early visual cortices during action–generation in complete darkness may reflect the recalled visual representation of the invisible/memorized object to be reached and grasped within its unseen spatial surrounding.

Based on psychophysics, it has been reported that memory-guided actions (by introducing brief delays between the stimulus presentation and the action onset) are based on perceptual mechanisms and not on visuomotor coordinates and that stored information regarding the target is used for offline control of the action mediated by the ventral visual stream (Goodale et al. 1994; Hu et al. 1999; Westwood et al. 2000; Westwood et al. 2001; Lemay and Proteau 2002; Heath and Westwood 2003; Westwood et al. 2003; Goodale et al. 2004; Heath 2005). However, other psychophysical studies indicate the participation of the dorsal visual stream in the motor control of memory-guided reaching and grasping (Himmelbach and Karnath 2005; Franz et al. 2009; Hesse and Franz 2009). Moreover, participation of the dorsal visual stream in the execution of memorized delayed movements has been indicated by transcranial magnetic stimulation (TMS) (Cohen et al. 2009) and fMRI (Singhal et al. 2006; Fiehler et al. 2008; Himmelbach et al. 2009) studies. Our finding that the occipitoparietal V3d segment, which is part of the dorsal visual stream, is activated for action in the dark is compatible with the results of the latter psychophysical, inactivation, and imaging studies. At this point, we wish to emphasize that all the above cited studies concern brief target-recall delays (up to 18 s), whereas in our case the monkeys grasping in the dark did not see the object to be grasped for months before the 18C-DG experiment. Therefore, our study demonstrates that the motor system can use stored visual information for the control of memory-guided actions not only for short delays between visual occlusion and movement onset but also for much longer periods of time. Furthermore, our results illustrate that visual representation of the memory-guided action is stored in early components of the dorsal visual stream.

The differential activation of the occipitoparietal segment of area V3d that represents peripheral vision and projects to the dorsal visual stream, and the occipitotemporal segment that represents central vision and projects to the ventral visual stream (Baizer et al. 1991), in our experimental groups, is compatible with previous reports. When vision is removed and concurrent visual feedback is not available, participants rely on an internal representation to guide their movements, as if there is imaging of the self in action (Fourkas et al. 2003). Motor imagery may involve the retrieval of memorized somatosensory and/or visual representations of the imaginary stimulus/event (Annet 1995). There is evidence in the literature that early visual cortical areas are activated for visual imagery, the faculty whereby we can visualize a visual item from memory (Kosslyn and Ochsner 1994; Roland and Gulyas 1994; Slotnick et al. 2005), and focal TMS over the occipital cortex interferes with the internal generation of mental visual images (Kosslyn et al. 1990). Moreover, cross-modal interaction between vision and touch, such as visual imagery during tactile perception, is supported by the activation of early visual cortices during Braille
reading in the blind (Sadato et al. 1996; Busch et al. 1998) and is expected if the brain holds an inner inclusive representation of the body based on the integration of corresponding visual and somatosensory information (Haggard et al. 2007; Berlucchi and Aglioti 2010). There is also evidence (Levine et al. 1985; Farah et al. 1988) that mental imagery for object features involves mainly the ventral, occipitotemporal stream of visual processing, whereas spatial or movement-related imagery involves primarily the dorsal, occipitoparietal stream of processing (Mishkin et al. 1983; Milner and Goodale 1995). Accordingly, the occipitoparietal segment of area V3d activated for reaching to grasp in the dark, in our study, suggests a major involvement of visuospatial movement-related representations during action-generation in the dark. The activation of both the occipitotemporal and occipitoparietal segments of area V3d for action-generation in the light and for action-observation supports the assumption that visual perception and mental simulation of action, respectively, involve both object-feature and visuospatial-related components (Kosslyn and Thompson 2003). Moreover, the stronger activation of the occipitoparietal portion of V3d for grasping in the dark than for grasping in the light is reminiscent of the stronger somatosensory activation for reaching in the dark than for reaching in the light, in previous studies (Savaki et al. 1993; Gregoriou and Savaki 2003). It appears that, both the somatosensory and visual consequences of an action are more heavily represented when the action is executed without visual guidance.

We suggest that the occipitoparietal segment of area V3d, which was markedly activated for action in the dark, may be specifically involved in spatial or movement-related mental imagery. When we use the term "mental imagery," we do not wish to imply that a conscious process is in operation. This is particularly true of nonhuman primates, in which the involvement of mental imagery is speculative as it cannot be assessed directly. Instead, we use it to refer to the retrieval of internal representations of an act that were memorized months before the experiment. Our suggestion that the occipitoparietal segment of area V3d is specifically involved in mental imagery is in accordance with the following 2 reports. First, an extrastriate visual area near the parieto-occipital fissure is associated with the visual imagery implicated in tactile perception of unseen objects (Sathian and Zangaladze 2002). Second, the occipital visual cortex Brodmann area 19 is activated in blindfolded volunteers reaching to remembered targets, reflecting its involvement in the creation of mental visual images of the target locations (Darling et al. 2007). Therefore, we suggest that visual imagery may take place during reaching to grasp in the dark, recruiting stored visual representations to support action-execution in blindfolded subjects. Accordingly, stored visual representations of the unseen forelimb in the environment for reaching and of the invisible 3D object to be grasped are recalled for the accomplishment of an appropriate action in the absence of visual input. Indeed, "visual control representation" has been suggested to sustain feedback-based control when visual information about the target and limb is removed (Glover 2004). Also, the control of memory-dependent reaching was suggested to rely on the use of stored visual representation of the target (Heath and Westwood 2003). Presumably, as a visual representation of an action (action-observation) may restore its motor correlate (activates somatotopically the primary motor cortex (Raos et al. 2004), the motor representation of an action (action-generation in the dark) may restore its visual correlate (activates the early visual cortices).

Overall, our suggestion that the activation of areas V3d and V3A reflects handling of visual features of action representations is in agreement with several fMRI studies which have demonstrated an extrastriate occipital area associated with motor imagery of walking (Bakker et al. 2008), visual and motor imagery tasks (de Lange et al. 2005), and the imagery pre-shot routine of expert golfers (Milton et al. 2007). Actually, this area in monkeys may correspond to the human extrastriate body area (EBA) which is associated with functions similar to those ascribed to monkey V3 in our and others' studies. In fact, EBA is reported to be involved in visual perception of the human body, in limb movements to visual targets even when the eyes are shut, and in mental imagination of goal-directed movements (Astafiev et al. 2004). Also, EBA has been implicated in distinguishing between self and others (Jeannerod 2004; Saxe et al. 2006), a faculty inevitably involved in discriminating between the actor and the observer.

In synopsis, we suggest that the same sensory (somatosensory and visual) effects of the action may be triggered "bottom-up" as consequences of the overtly performed action and "top-down" as predictions of the memorized consequences of the mentally simulated action, with the top-down mechanism presumably generated by a forward model (Wolpert and Ghahramani 2000). Here we propose that the single neural substrate used "bottom-up" (sensory driven) or "top-down" (mentally driven) to represent physical or mental practice extends beyond the parietofrontal somatosensory–motor circuit described in the past (Raos et al. 2004, 2007; Evangeliou et al. 2009) to also include early occipital cortices which reflect the physical or mental visuospatial representations of the motor act.

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