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Noninvasive functional MRI in alert monkeys

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ABSTRACT

Functional magnetic resonance imaging (fMRI) is now widely used to study human brain function. Alert monkey fMRI experiments have been used to localize functions and to compare the workings of the human and monkey brains. Monkey fMRI poses considerable challenges because of the monkey's small brain and naturally uncooperative disposition. While training can encourage monkeys to be more obliging during scanning, the usual procedure is to hold the monkey's head motionless by means of a surgically implanted head post. Such implants are invasive and require regular maintenance. In order to overcome these problems we developed a technique for holding monkeys' heads motionless during scanning using a custom-fitted plastic helmet, a chin strap, and a mild suction supplied by a vacuum blower. This vacuum helmet method is totally noninvasive and has shown no adverse effects after repeated use for several months. The motion of a trained monkey's head in the helmet during scanning was comparable to that of a trained monkey implanted with a conventional head post.

Introduction

Decades of work using invasive neurophysiological recording techniques in macaques have provided us with extensive knowledge about the functional organization of the primate brain. Indeed, the macaque monkey model is the basis for much of our understanding of sensory, motor, and cognitive processing in humans. Noninvasive imaging techniques, such as positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and magnetoencephalography (MEG), now provide a wealth of information on the workings of the human brain. To compare monkey and human brain data and to take advantage of the localizing power of fMRI, several laboratories have started doing functional MRI on monkeys. Some early monkey fMRI studies were done on anesthetized animals and proved its usefulness in localizing early sensory processes (Logothetis et al., 1999). Using anesthetized monkeys has the advantage that it does not require restraint or extensive training, but it cannot be used to map higher cognitive functions, therefore most laboratories have worked out ways to scan alert behaving monkeys (Dubowitz et al., 1998; Stefanacci et al., 1998; Logothetis et al., 1999; Vanduffel et al., 2001; Andersen et al., 2002; Tsao et al., 2003a, 2003b; Gamlin et al., 2006; Keliris et al., 2007; Hadj-Bouziane et al., 2008; Maier et al., 2008; Durand et al., 2009; Goense et al., 2009; Peeters et al., 2009).

Scanning awake monkeys is uniquely challenging. The main difficulty is that computing a reliable activation map requires a stationary brain—the activity-driven signal changes are small, and movement of the brain inside the magnetic field produces inconsistencies in phase and amplitude, which can generate blurring and ghosting motion artifacts larger than the activation signals. In most laboratories a head post that is surgically implanted onto the skull is used to keep the monkey's head stationary during the scan session. Metal head posts have been used for decades in neurophysiological recording, and plastic versions are now used for fMRI. The acrylic used to cement the post to the skull can cause scanning artifacts, can damage the underlying skull, and requires regular maintenance.

Several laboratories have tackled the challenge of noninvasive imaging of alert monkeys. Howell et al. developed a plastic helmet filled with expandable foam that fits snugly to the subject's head. This method allows PET scanning of alert monkeys (Howell et al., 2001), but the encompassing foam does not allow visual stimulation. Others have scanned alert marmosets in restraint chairs (Ferris et al., 2001, 2004), but putting the animal in this restraint requires anesthesia, which must then be reversed for scanning. Another fMRI approach used with macaques (Andersen et al., 2002; Joseph et al., 2006) still requires ear bars and skull pins.

In order to circumvent the problems of surgery, chronic acrylic implants, and susceptibility artifacts from the acrylic, we developed a noninvasive method for stabilizing monkeys' heads in a scanner. We found that head motion in our method is comparable to that of a head-post-fixed monkey.

Methods

Four rhesus macaque monkeys participated in these experiments: three males, 3, 3.5, and 10 years old weighing, respectively, 5.5, 6, and 10 kg, and one 6. 5 kg female. The oldest male monkey has a delrin head post affixed to his skull with ceramic screws and dental acrylic (Vanduffel et al., 2001) and has had several years of experience being scanned repeatedly (Tsao et al., 2003a, 2006). The two smaller male

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Fig. 1. (Left) The vacuum helmet and (right) an alert monkey sitting calmly, in the helmet, ready to be scanned.

monkeys had no head post implants and had 3 months biweekly training restrained by the vacuum helmet in a mock scanner before being scanned in a real scanner.

The female monkey had a delrin head post affixed to the skull with ceramic screws and dental acrylic and was scanned several times with the head post, then, during a routine cage transfer, she leaped through the door of her cage and knocked the head post off. The scalp skin was immediately sutured closed over the head post site, and after 5 months of rest she was trained to use the helmet in a mock scanner and later scanned using the helmet. We used this female monkey to directly compare movement during scanning with a head post vs. the helmet.

Helmet and vacuum details

The helmet was fabricated by first making a 3D digital model of the monkey's head, based on a plaster cast and an anatomical MRI. We then constructed a 3D digital model of a helmet that would fit around the head model using SolidWorks 3D CAD software (Concord, MA). The design incorporated a post for attaching the

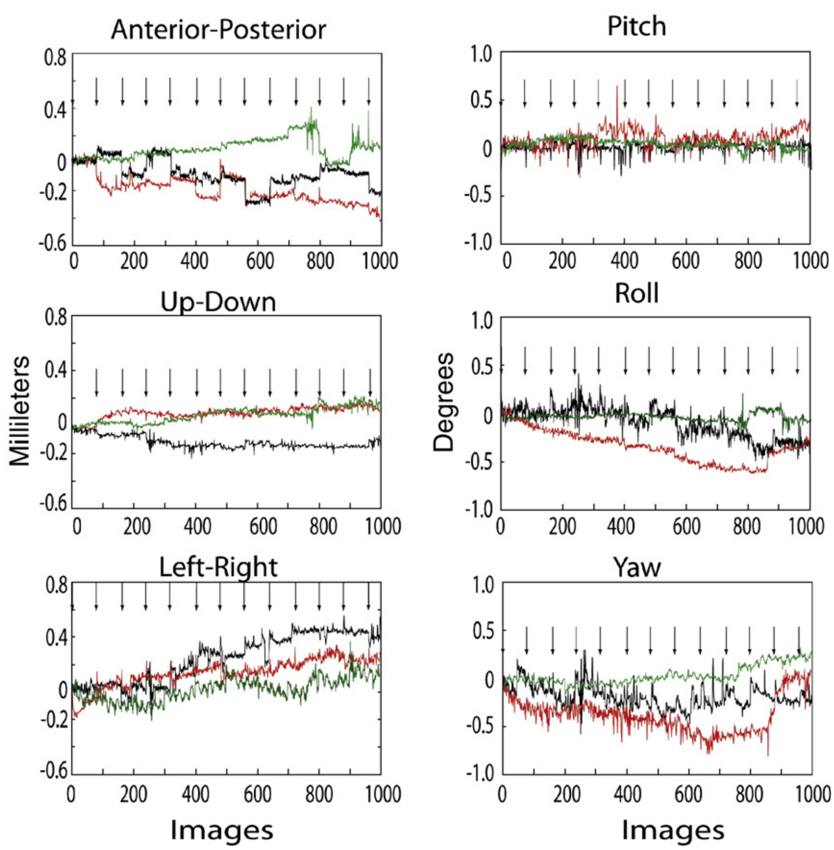

Fig. 2. (Left) Translation in millimeters and (right) rotation in degrees, normalized to the position at the beginning of each scan, during a single, typical, scan session for two vacuum-helmeted alert male monkeys (red and green traces) and a head-post-restrained alert male monkey (black traces). *X*-axis is image number; one image was taken every 2 s. Most of the large position shifts occurred between scans; each scan onset is indicated by an arrow.

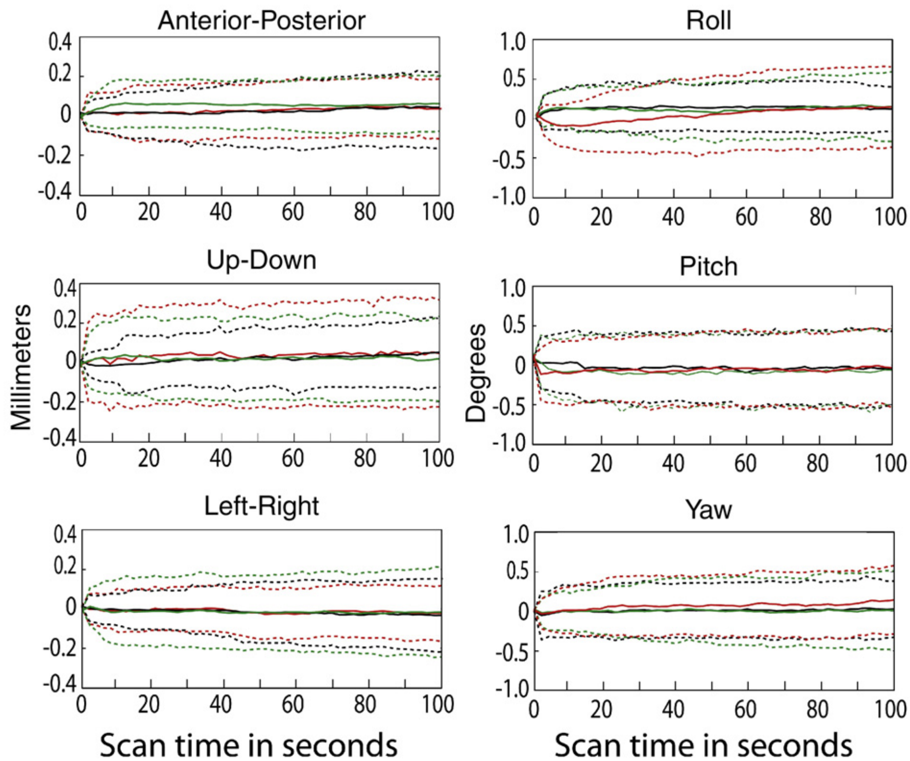

Fig. 3. Average brain movement, normalized to the position at the beginning of each scan, over the first 100 s of each scan for three alert monkeys ± standard deviation, averaged over 200 scans; for the two helmeted male monkeys in red and green and the head-post-restrained male monkey in black.

helmet to the scanning chair, grooves for silicon tubing, and two ports for vacuum. The helmet was then manufactured directly from the digital model by stereo-lithography from a UV-polymerized resin (Vaupell, Agawam, MA). Two rings of soft silicon tubing were bonded into concentric shallow grooves inside the helmet and served to partially seal and cushion the monkey's head inside the

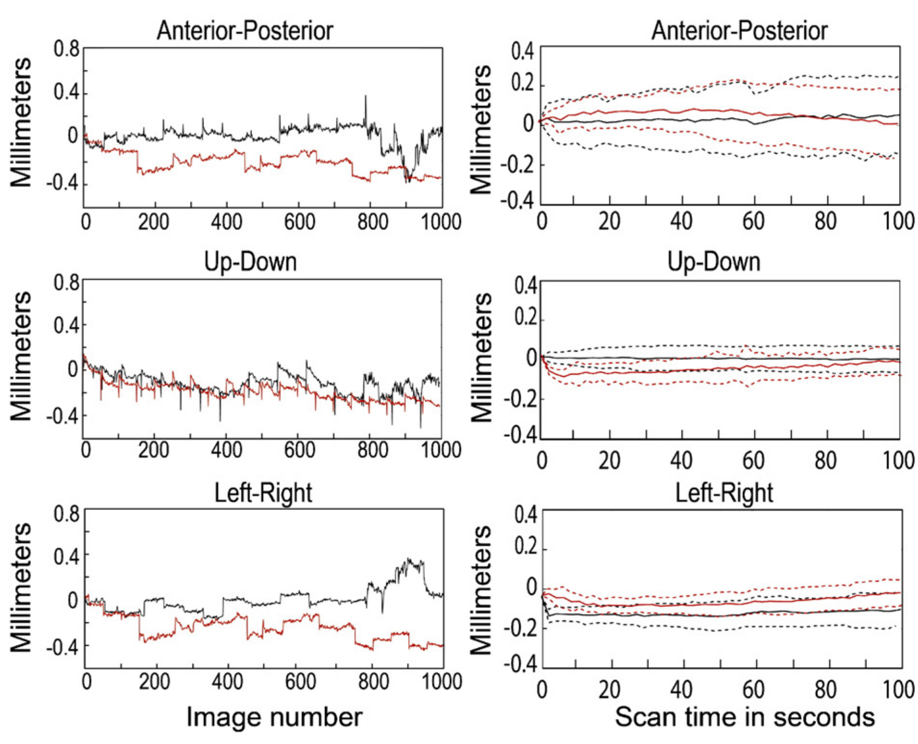

Fig. 4. Translational movements exhibited by one alert female monkey restrained using a helmet (red traces) or by a head post (black traces). (Left) Movements during 20 consecutive 100-s (50 images) scans each during two different scan sessions, normalized to the position at the beginning of the session. (Right) Average movement, normalized to the position at the beginning of each scan, ±standard deviation for all 20 scans under each restraint condition.

helmet. The monkey's fur was not shaved or trimmed. A Velcro chin strap and a vacuum of 2 psi held the monkey's head stationary in the helmet (Fig. 1). The chin strap and helmet alone allowed rotation of the head inside the helmet, but the gentle suction provided enough friction against the silicon rings that it inhibited the monkey from moving his head. We initially used a household canister vacuum, with a bleed valve to reduce the vacuum, and subsequently switched to a quieter industrial vacuum (Fuji regenerative blower model VFD3S, maximum vacuum 4.8 psi) fitted with a relief valve (Fuji VV5) to keep the vacuum under 2 psi. No adverse effects, such as bruising or swelling, have been observed after several months of use as long as the pressure is kept at or under −2 psi.

Training

Each monkey was trained to sit in a horizontal chair and was habituated to recorded sounds of MR scanning in a mock MR bore. It sat comfortably on its haunches, in a “sphinx” position. The monkeys' daily water access was delayed prior to each training or scanning session, and behavioral control was achieved using operant conditioning techniques. The monkeys were trained on a fixation task, and gaze direction was monitored using a pupil–corneal reflection tracking system (RK-726PCI, ISCAN, Cambridge, MA). The monkeys were rewarded with water or juice drops for maintaining fixation within a square fixation window (2° on a side). In order to encourage sustained periods of fixation, the interval between rewards was decreased systematically (from 2000 to 1000 ms) as the monkey maintained fixation within the window during the trials; as the scan progressed the intervals were further decreased to maintain motivation. After fixation performance reached asymptote in the mock scanner (after 20–50 training sessions), the monkeys were scanned in a 3-T horizontal GE Signa Excite scanner.

Scanning

A custom-made 4-channel receive coil (Resonance Innovations LLC, Omaha, NE) fitted around the helmet and covered the entire brain. In order to enhance contrast, before each scanning session each monkey was injected with microparticular iron oxide contrast agent (Leite et al., 2002; Leite and Mandeville, 2006). For one functional mapping session with a helmet-restrained monkey we injected i.v. 20 mg/kg of P904, a nanosized ultrasmall particle of iron oxide (USPIO) kindly supplied by Guerbet (Guerbet Research, Aulnay-Sous-Bois, France). For a second functional scan session in the same monkey (generating the results shown in Fig. 5) we used 12 mg/kg Feraheme (AMAG Pharmaceuticals, Cambridge, MA), which is an iron oxide nanoparticle with a polyglucose sorbitol coaboxymethylether coating. We obtained comparable contrast enhancement with the two agents, but the Feraheme had a much longer half-life (> 15 h compared to 1. 5 h for the P904). Each session consisted of 10–30 functional scans, each scan lasting 260 s (100 s for some of the earlier scan sessions). The raw movement data shown in Figs. 2 and 4 were taken during a single, typical, scan session for each monkey; the averaged data in Figs. 3 and 4 were averaged from 200 scans made during 8–10 scan sessions, and comprised 16,000 functional volumes. The scans that were averaged comprised all the scan sessions for that particular monkey over a

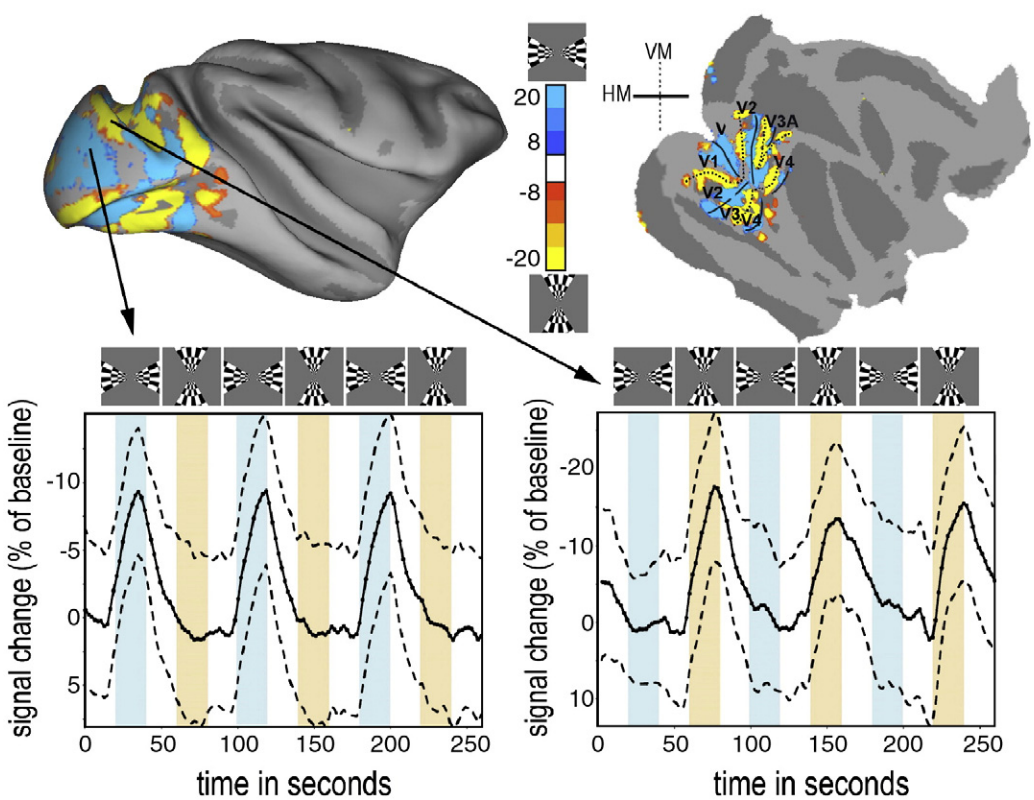

Fig. 5. (Top left) Semi-inflated and (top right) flattened brain maps showing significant activation in response to horizontal (red) and vertical (blue) meridian stimuli viewed by an alert monkey noninvasively restrained by a vacuum helmet. (Bottom) Time course of the mutually exclusive signal changes ± standard deviation in response to alternating horizontal (bottom left) and vertical (bottom right) meridians from two 4.5 × 4.5 × 4. 5 mm ROIs as indicated calculated from 20 scans obtained in a single scanning session. Activations are both large and negative, compared to BOLD signal, because the monkey was injected with the iron oxide contrast agent Feraheme prior to scanning; the agent causes a decrease in the baseline and an inversion of signal (Leite et al., 2002). The functional activation maps were overlaid on the F99 atlas in Caret (Van Essen, 2002); http://sumsdb.wustl.edu/sums/macaquemore.do. Areal borders were drawn by hand according to alternating meridians.

several-week period, with the only selection criterion being that the monkey fixated more than 80% of the duration of the scan (except for the female monkey who does not fixate as well, and for whom the criterion was 70%). The activation maps shown in Fig. 5 for the helmeted monkey were calculated from 20 scans from one scan session (260 functional volumes, 9100 slices), using the following scanning parameters: 2D Gradient-Echo Planar Imaging (GE-EPI); Repetition Time (TR) = 2 s, Echo Time (TE) = 20 ms; 64 × 64 matrix; 1.5 × 1.5 × 1. 5 mm voxels; 35 contiguous slices. Slices were horizontal and covered the entire brain. In a separate session, a higher resolution anatomical scan (1.0 × 1.0 × 1. 0 mm) was obtained using a small volume coil (a commercial GE "knee" coil) while the monkey was anesthetized with ketamine and xylazine. For the anatomical scan in Fig. 6 we used the same coil as for the functional scans and the following scan parameters: 3D Fast Spoiled Grass Sequence with Inversion Recovery Preparation (IR-FSPGR), Echo Time (TE) = 3. 4 ms; 128 × 128 matrix; 0.5 × 0.5 × 1 mm voxels; coronal slices.

Visual stimuli

Visual stimuli were projected onto a screen at the end of the bore, 57 cm from the monkey's eyes. The stimuli consisted of pairs of black and white checkerboard 45° wedges flickering in counterphase at 2 Hz, with a central fixation spot, on a black background, one pair centered on the horizontal meridian and the other on the vertical meridian. The vertical wedges extended 10° above and below the fixation spot; the horizontal wedges extended 10° to the left and right of fixation. The checks subtended 0.2° of visual angle in the center of the display and increased exponentially in size to 5° in the periphery. Each scan lasted 160 s and consisted of 20-s blocks of vertical or horizontal meridian stimuli, presented alternately, separated by 20-s blocks of fixation spot alone.

Data analysis

Data were analyzed using FS-FAST and Freesurfer (http://surfer.nmr.mgh.harvard.edu). Only scans in which the monkey fixated within 1° of the fixation spot for >80% of the duration of the scan were used for statistical analysis. To generate the significance maps, the data were motion-corrected, quadratically detrended, and smoothed with a Gaussian kernel of 2-mm full-width-at-half-magnitude. We then calculated the mean and variance of the response in each voxel to each condition across the entire scan session. Then *t*-tests were used to compare activity during blocks of horizontal stimulation to blocks of vertical stimulation.

Movement estimation

We used the motion correction algorithm in FS-FAST to estimate the movement of the monkeys' heads during each scan. The scanner computes images from the Fourier spectra of the RF signals. FS-FAST aligns each calculated image in a series with the first image in that series and determines the difference in position of the two images; this is the "movement" we report. Since body movements can distort the magnetic field and thereby distort the images of the brain, both body and head movements can contribute to the calculated position, so the estimated movement is actually an upper estimate of the head movement.

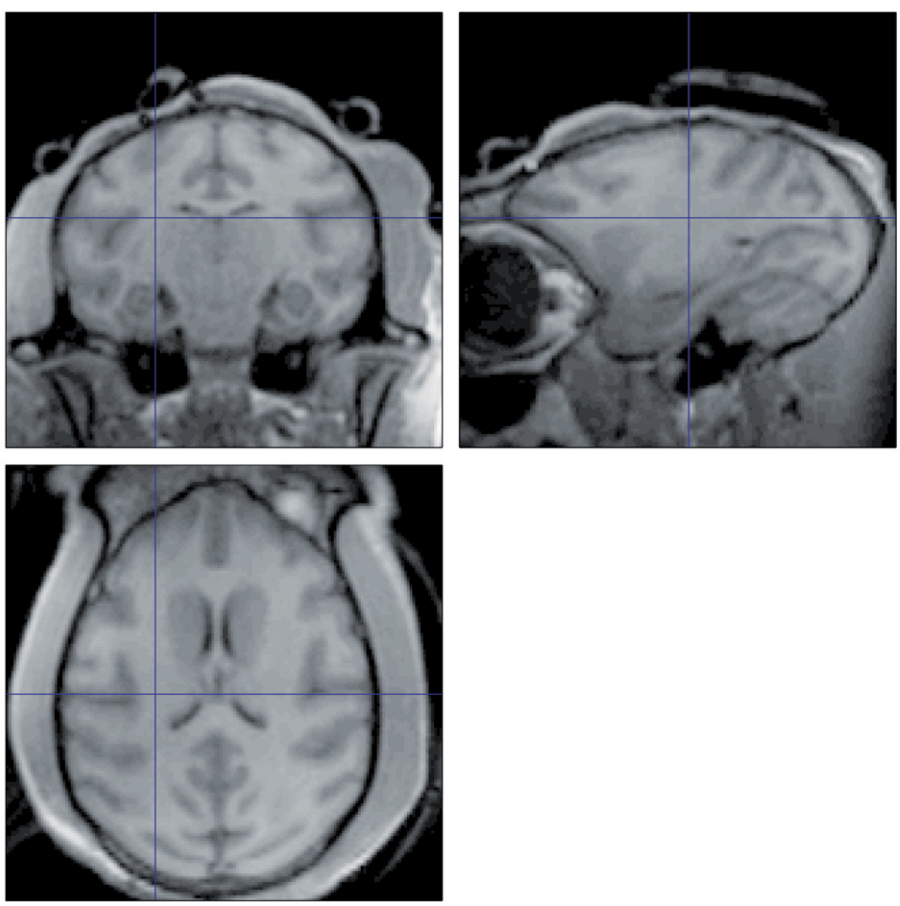

Fig. 6. Anatomical scans for monkey F1 obtained during one 4-min anatomical scan using the same helmet and coil as was used for the functional imaging. The section plane was coronal, so any changes in position during the scan should result in blurring or shifts in position between anterior and posterior sections, yet no difference in resolution is apparent between the coronal and the horizontal or sagittal reconstructions.

All experiments were done in accordance with procedures approved by the Harvard Medical School Standing Committee on Animals.

Results

The monkeys adapted to sitting still in a helmet in a horizontal chair in a mock scanner about as well as monkeys adapt to the same procedure using a conventional head post. At first they pulled out of the suction and shifted their head position frequently, but after several days they settled down and sat quite still for up to an hour; after 2 months of training they would sit still for 2 or even 3 h. Monkeys with head posts also require training to learn to sit calmly with their heads fixed. The monkeys could overcome the suction using much less force than would be required to break off a head post: The vacuum exerts at most 15 lb of force total (2 psi × 7 sq. in.). Using a strain gauge to pull on a ceramic screw (Thomas Recording, Giessen, Germany) threaded into an autopsy skull we determined that a single screw can be pulled out of a skull by 20 lb of force. Therefore we would expect a head post held on with 10 ceramic screws to be more than 10 times stronger than the vacuum helmet. However if the monkey pulls out of the helmet we lose one scan, which is significantly less of a problem than losing a head post.

Comparison of calculated motion for head-post- and helmet-restrained monkeys

We first compare the head movements during scanning between two small male monkeys held by the vacuum helmet and a large male monkey fixed with a head post. Fig. 2 compares the rotation and translation movements for the vacuum-helmeted monkeys (red and green traces) and the head-post-fixed monkey (black traces) during 12 consecutive scans in one typical scan session for each monkey. The figure plots the calculated position for 960 consecutive functional volumes, compared to the first volume in the session, for each monkey. The relative position was estimated from differences between corresponding slice images in consecutive volumes. Most of the movements occurred between scans (scan starts indicated by arrows) when we often paused and the monkey was not fixating and was not rewarded. The movements in all directions were comparable between the head-posted animal and the helmeted animals.

Fig. 3 compares the average movements during scanning for the same three monkeys, averaged over two hundred 160-s scans (9 sessions each) for the helmeted monkeys (red and green) and over 200 scans (10 sessions) for the head-posted monkey; these averaged sessions represent all the sessions for these 3 monkeys over a continuous period of several weeks for each monkey except that only scans in which the monkey fixated for more than 80% of the time were used to compute this average. None of the rotation or translation parameters were significantly different between the helmeted and the head-posted monkeys (two-tailed t-test; Table 1); thus the head motion using the helmet method is comparable to the head movements of monkeys restrained using a conventional head post.

Direct comparison of head post vs. helmet in a single monkey

The female monkey had a head post and was scanned several times before the head post broke off. After recovery she was trained to use the helmet and scanned using the helmet. Fig. 4 shows a comparison of her translational head movements during one scan session with the head post (black traces) compared to one session with the helmet (red traces). The graphs on the left of Fig. 4 show the brain positions relative to the position at the beginning of the session for 20 consecutive 100-s scans, and the graphs on the right show the average movement during one scan, relative to the position at the beginning of each scan, averaged over all 20 scans. Thus the translational movements (and rotational movements, not shown) of this one monkey using the helmet are comparable to the same monkey's movement when restrained using a head post.

Visual topographic maps for a vacuum-helmet-fixed monkey

Since our goal was to hold a monkey's head stable enough to do functional MRI, we did a simple visual mapping experiment using the helmet with one of the small male monkeys. We used flickering checkerboard wedges to map the cortical representations of the horizontal and vertical meridians. The two stimuli evoked strong activation in mutually exclusive regions of visual cortex (Fig. 5). Fig. 5 (top left) shows significant activations ($p < 10^{-8}$) for horizontal meridian activity (blue) and vertical meridian activity (yellow) on a semi-inflated brain. Fig. 5 (top right) shows the same activations on a flattened map. The time courses of the signal changes for horizontal (bottom left) and vertical (bottom right) meridians from the two $3 \times 3 \times 3$ voxel ROIs ($4.5 \times 4.5 \times 4.5$ mm) indicated are shown at the bottom. The maps are comparable with earlier published maps of visual cortex (Fize et al., 2003).

Lastly we did anatomical scans of the alert female monkey restrained by the helmet while she fixated on the screen. The images were obtained at $0.5 \times 0.5 \times 1$ mm resolution, and the 1-mm sections were in the coronal plane. Because the scan lasted 4 min any head motion would produce shifts in position of the coronal slices between the front and the back of the brain. We did not, however, observe any evidence in the horizontal or sagittal reconstructions of any such artifacts (Fig. 6).

Discussion

Monkey fMRI has already proven to be a profoundly useful tool for comparing and enriching human brain imaging studies with the extensive nonhuman primate brain data. However, functional imaging requires minimal subject motion, which poses a major problem for animal imaging. Usually a plastic head post must be affixed to the skull using ceramic screws and dental acrylic. Head posts must be regularly cleaned to prevent infection and are difficult to implant and maintain in young monkeys who have very thin skulls. Our vacuum helmet method involves no invasive procedures and can be used even on quite young monkeys. The helmet technique works

Table 1
Mean ± S.D. of all movement parameters for the 3 male monkeys averaged over the first 100 s of each of 200 scans obtained during 9 sessions for M1 and M2 and 10 sessions for M3.

	Helmeted monkeys			Head-posted monkeys	
	M1	M2	F1	M3	F1
Left–right in millimeters	−0.042 ± 0.098	−0.016 ± 0.082	0.067 ± 0.037	−0.015 ± 0.067	−0.053 ± 0.038
Up–down in millimeters	0.020 ± 0.153	−0.016 ± 0.126	0.018 ± 0.038	0.041 ± 0.232	0.060 ± 0.046
Anterior–posterior in millimeters	0.053 ± 0.083	0.048 ± 0.089	0.050 ± 0.056	0.026 ± 0.105	−0.035 ± 0.133
Pitch in degrees	0.058 ± 0.489	0.060 ± 0.499	0.050 ± 0.240	0.020 ± 0.426	−0.054 ± 0.450
Yaw in degrees	0.021 ± 0.465	0.017 ± 0.42	−0.070 ± 0.300	0.002 ± 0.510	0.013 ± 0.190
Roll in degrees	0.067 ± 0.36	0.032 ± 0.414	0.046 ± 0.150	0.055 ± 0.354	0.020 ± 0.180

The mean ± S.D. of all movement parameters for the female monkey helmeted or head-posted were averaged over 20 scans each, each scan is 100 s long, obtained during 1 session with a head post and 1 session with the helmet. Movements were calculated for each TR as the change in position of the brain from the position at the beginning of each scan.

well for juvenile male macaques and for adult females. We have not tried the helmet on any large mature adult males. Most laboratories that do functional scanning on alert monkeys using the widely available horizontal bore MRI scanners prefer to use small animals who fit more easily in the bore. Laboratories that do scan large males usually use the less commonly available vertical-bore scanners, and in these laboratories the problems with acrylic (bone resorption and susceptibility artifacts) can be avoided by using custom-made PEEK implants held onto the skull with ceramic screws (Keliris et al., 2007). The long-term success of implants held in place with screws alone, without acrylic, is excellent for animals with thick skulls, like adult males (Adams et al., 2007) but, in our experience, is poor for younger animals who tend to have quite thin skulls.

The helmet technique allows us to scan monkeys without a surgically implanted head post. The helmets cost about $300 each to manufacture, and designs for different sizes with different types of attaching posts are easily adapted from our original 3D model, which is available on request. Because the helmet is lined with two rings of soft silicone tubing, the fit does not need to be precise, and we found that one helmet design fits all four of the young (2.5–3.5 years old) male monkeys in our colony and two adult females. The helmet would not benefit those laboratories who want to combine fMRI with single-unit electrophysiology using an implanted chamber but would be compatible with chronically implanted electrode arrays.

The overall movement of the head in the helmet-fixed monkeys was comparable to that of two head-post-fixed monkeys, and in one monkey both methods were equally effective. Even when the head is immobilized, however, there is the additional problem that the monkey's body movement can cause distortions in the magnetic field, which can cause artifacts and distortions in the reconstructed image (Goense et al., 2009); this problem is an issue no matter how the head is immobilized. The feasibility of our helmet approach to functional scanning was confirmed by a visual mapping experiment. We mapped the horizontal and vertical meridians in visual cortex and the maps were comparable to previously reported areal boundaries and representations of visual quadrants (Daniel and Whitteridge, 1961; Van Essen et al., 1984; Felleman and Van Essen, 1991; Fize et al., 2003).

In summary, we present a noninvasive method for holding a monkey's head still enough in a scanner to do functional MRI. The method requires extensive training, but the time required is not much greater than that necessary for training a head-posted monkey and the approach provides other benefits such as eliminating susceptibility artifacts from the acrylic and the surgery and maintenance required for chronic implants.

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References

Adams, D.L., Economides, J.R., Jocson, C.M., Horton, J.C., 2007. A biocompatible titanium headpost for stabilizing behaving monkeys. J. Neurophysiol. 98 (2), 993–1001.

Andersen, A.H., Zhang, Z., Barber, T., Rayens, W.S., Zhang, J., Grondin, R., Hardy, P., Gerhardt, G.A., Gash, D.M., 2002. Functional MRI studies in awake rhesus monkeys: methodological and analytical strategies. J. Neurosci. Methods 118 (2), 141–152.

Daniel, P., Whitteridge, D., 1961. The representation of the visual field on the cerebral cortex in monkeys. J. Physiol. J. Physiol. 159, 203–221.

Dubowitz, D.J., Chen, D.Y., Atkinson, D.J., Grieve, K.L., Gillikin, B., Bradley Jr., W.G., Andersen, R.A., 1998. Functional magnetic resonance imaging in macaque cortex. Neuroreport 9 (10), 2213–2218.

Durand, J.B., Peeters, R., Norman, J.F., Todd, J.T., Orban, G.A., 2009. Parietal regions processing visual 3D shape extracted from disparity. Neuroimage 46 (4), 1114–1126.

Felleman, D.J., Van Essen, D.C., 1991. Distributed hierarchical processing in the primate cerebral cortex. Cereb. Cortex 1 (1), 1–47.

Ferris, C.F., Snowdon, C.T., King, J.A., Duong, T.Q., Ziegler, T.E., Ugurbil, K., Ludwig, R., Schultz-Darken, N.J., Wu, Z., Olson, D.P., Sullivan, J.M., Tannenbaum, P.L., Vaughan, J. T., 2001. Functional imaging of brain activity in conscious monkeys responding to sexually arousing cues. Neuroreport 12 (10), 2231–2236.

Ferris, C.F., Snowdon, C.T., King, J.A., Sullivan Jr., J.M., Ziegler, T.E., Olson, D.P., Schultz-Darken, N.J., Tannenbaum, P.L., Ludwig, R., Wu, Z., Einspanier, A., Vaughan, J.T., Duong, T.Q., 2004. Activation of neural pathways associated with sexual arousal in non-human primates. J. Magn. Reson. Imaging 19 (2), 168–175.

Fize, D., Vanduffel, W., Nelissen, K., Denys, K., Chef d'Hotel, C., Faugeras, O., Orban, G.A., 2003. The retinotopic organization of primate dorsal V4 and surrounding areas: a functional magnetic resonance imaging study in awake monkeys. J. Neurosci. 23 (19), 7395–7406.

Gamlin, P.D., Ward, M.K., Bolding, M.S., Grossmann, J.K., Twieg, D.B., 2006. Developing functional magnetic resonance imaging techniques for alert macaque monkeys. Methods 38 (3), 210–220.

Goense, J.B., Whittingstall, K., Logothetis, N.K., 2009. Functional magnetic resonance imaging of awake behaving macaques. Methods DOI: S1046-2023(09)00198-4 [pii] 10.1016/j.ymeth.2009.08.003.

Hadj-Bouziane, F., Bell, A.H., Knusten, T.A., Ungerleider, L.G., Tootell, R.B., 2008. Perception of emotional expressions is independent of face selectivity in monkey inferior temporal cortex. Proc. Natl. Acad. Sci. U. S. A. 105 (14), 5591–5596.

Howell, L.L., Hoffman, J.M., Votaw, J.R., Landrum, A.M., Jordan, J.F., 2001. An apparatus and behavioral training protocol to conduct positron emission tomography (PET) neuroimaging in conscious rhesus monkeys. J. Neurosci. Methods 106 (2), 161–169.

Joseph, J.E., Powell, D.K., Andersen, A.H., Bhatt, R.S., Dunlap, M.K., Foldes, S.T., Forman, E., Hardy, P.A., Steinmetz, N.A., Zhang, Z., 2006. fMRI in alert, behaving monkeys: an adaptation of the human infant familiarization novelty preference procedure. J. Neurosci. Methods 157 (1), 10–24.

Keliris, G.A., Shmuel, A., Ku, S.P., Pfeuffer, J., Oeltermann, A., Steudel, T., Logothetis, N.K., 2007. Robust controlled functional MRI in alert monkeys at high magnetic field: effects of jaw and body movements. Neuroimage 36 (3), 550–570.

Leite, F.P., Mandeville, J.B., 2006. Characterization of event-related designs using BOLD and IRON fMRI. Neuroimage 29 (3), 901–909.

Leite, F.P., Tsao, D., Vanduffel, W., Fize, D., Sasaki, Y., Wald, L.L., Dale, A.M., Kwong, K.K., Orban, G.A., Rosen, B.R., Tootell, R.B., Mandeville, J.B., 2002. Repeated fMRI using iron oxide contrast agent in awake, behaving macaques at 3 Tesla. Neuroimage 16 (2), 283–294.

Logothetis, N.K., Guggenberger, H., Peled, S., Pauls, J., 1999. Functional imaging of the monkey brain. Nat. Neurosci. 2 (6), 555–562.

Maier, A., Wilke, M., Aura, C., Zhu, C., Ye, F.Q., Leopold, D.A., 2008. Divergence of fMRI and neural signals in V1 during perceptual suppression in the awake monkey. Nat. Neurosci. 11 (10), 1193–1200.

Peeters, R., Simone, L., Nelissen, K., Fabbri-Destro, M., Vanduffel, W., Rizzolatti, G., Orban, G.A., 2009. The representation of tool use in humans and monkeys: common and uniquely human features. J. Neurosci. 29 (37), 11523–11539.

Stefanacci, L., Reber, P., Costanza, J., Wong, E., Buxton, R., Zola, S., Squire, L., Albright, T., 1998. fMRI of monkey visual cortex. Neuron 20 (6), 1051–1057.

Tsao, D.Y., Freiwald, W.A., Knutsen, T.A., Mandeville, J.B., Tootell, R.B., 2003a. Faces and objects in macaque cerebral cortex. Nat. Neurosci. 6 (9), 989–995.

Tsao, D.Y., Vanduffel, W., Sasaki, Y., Fize, D., Knutsen, T.A., Mandeville, J.B., Wald, L.L., Dale, A.M., Rosen, B.R., Van Essen, D.C., Livingstone, M.S., Orban, G.A., Tootell, R.B., 2003b. Stereopsis activates V3A and caudal intraparietal areas in macaques and humans. Neuron 39 (3), 555–568.

Tsao, D.Y., Freiwald, W.A., Tootell, R.B.H., Livingstone, M.S., 2006. A cortical region consisting entirely of face-selective cells. Science 311, 670–674.

Van Essen, D.C., 2002. Windows on the brain: the emerging role of atlases and databases in neuroscience. Curr. Opin. Neurobiol. 12 (5), 574–579.

Van Essen, D.C., Newsome, W.T., Maunsell, J.H., 1984. The visual field representation in striate cortex of the macaque monkey: asymmetries, anisotropies, and individual variability. Vis. Res. 24 (5), 429–448.

Vanduffel, W., Fize, D., Mandeville, J.B., Nelissen, K., Van Hecke, P., Rosen, B.R., Tootell, R.B., Orban, G.A., 2001. Visual motion processing investigated using contrast agent-enhanced fMRI in awake behaving monkeys. Neuron 32 (4), 565–577.