Behavioral Neuroscience
2006, Vol. 120, No. 4, 761–786

0735-7044/06/$12.00 DOI: 10.1037/0735-7044.120.4.761

The Impact of Selective Amygdala, Orbital Frontal Cortex, or Hippocampal Formation Lesions on Established Social Relationships in Rhesus Monkeys (*Macaca mulatta*)

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Social dominance, personality ratings, and frequency, duration, and timing of social behaviors were measured pre- and postsurgically in 6 groups of rhesus monkeys (*Macaca mulatta*), each consisting of 1 sham-operated control and 1 monkey each with a selective amygdala, hippocampal, or orbital frontal cortex lesion. Unlike previous reports, none of the operated groups showed changes in social dominance postsurgery, although changes in other measures varied by lesion site. Although sham-operated monkeys displayed heightened avoidant, anxious, and aggressive behaviors, those with hippocampal lesions also showed increased exploration and excitability, along with reduced responses to affiliative signals. Amygdala lesions yielded several personality changes that precluded positive social interactions (increased exploration and excitability, decreased affiliation and popularity) and altered responses to threatening social signals. By contrast, monkeys with orbital frontal lesions were involved in more aggressive interactions and responded differently to both affiliative and threatening signals. Although several findings differ from earlier nonhuman primate studies, they are largely in agreement with human data and emphasize the context-specific nature of social behavior studies. Interpretation of results in relation to cognitive processes mediated by each structure is discussed.

Keywords: macaque, social behavior, amygdala, orbital frontal cortex, hippocampal formation

Social interactions are a key component of primate behavior and require the use of specific skills that combine to efficiently regulate behavioral selection toward achieving a social goal, for example, recruiting an ally or attracting a mate. Although the neural network that mediates such complex cognitive skills is not completely understood, two brain structures, the amygdala and orbital frontal cortex, appear to be critical for efficient social cognition in several species, including humans (Adolphs, 2001, 2003; Baron-Cohen et al., 1999; Brothers, 2002). In monkeys, evidence stems from electrophysiological recording studies (Brothers & Ring, 1993; Brothers, Ring, & Kling, 1990; Kling, Steklis, & Deutsch, 1979; Leonard, Rolls, Wilson, & Baylis, 1985; O'Scalaidhe, Wilson, & Goldman-Rakic, 1997, 1999; Rolls, 1984; Thorpe, Rolls, & Maddison, 1983) indicating that neurons in both structures modulate their activity in response to a wide array of social signals, especially facial expressions of fear or anger. Additional evidence has been provided by lesions studies, although the effects of damage to either the orbital frontal cortex or amygdala on social behavior in monkeys are still controversial and have been poorly studied until recently.

Large temporal lobe resections (Rosvold, Mirsky, & Pribram, 1954) or aspiration lesions of the amygdala (for review, see Kling & Brothers, 1992) result in severe social disturbances in monkeys. However, the magnitude and direction (increase or decrease) of the social changes depend on many factors, including sex, age at the time of surgery, level of positive social signals in a group, amount of preoperative social experience with conspecifics, and complexity of the social environment in which the monkeys are observed (for review, see Bachevalier, 2000; Kling & Brothers, 1992). An additional potential factor is the extent of lesions, which in many early studies included not only the amygdala but also the adjacent temporal cortical areas. With the recent discovery that these temporal cortical areas regulate emotional responses (Meunier & Bachevalier, 2002), respond to various kinds of social cues (Bruce, Desimone, & Gross, 1981; Perrett, Rolls, & Caan, 1982), and associate visual stimuli with their incentive value (Liu, Murray, &

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This work was supported by National Institute of Mental Health (NIMH) Grant MH-58846 and National Institute of Child Health and Human Development Grant HD-35471 to Jocelyne Bachevalier and by National Research Service Award Predoctoral Fellowship NIMH MH-63577 to Christopher J. Machado. The data described here served as partial fulfillment of the requirements for the doctoral degree from the University of Texas Graduate School of Biomedical Sciences at Houston for Christopher J. Machado. We thank the University of Texas Health Science Center at Houston veterinary and animal husbandry staff for expert animal care, Roger E. Price and Belinda Rivera for the care and handling of the monkeys during the magnetic resonance imaging procedures, Edward F. Jackson for expert assistance in neuroimaging techniques, David Lane for statistical advice and guidance in data analysis, and Jennifer Chlan-Fourney, Diana Lay, and Alyson Zeamer for scoring behavioral data as second observers.

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Richmond, 2000; Liu & Richmond, 2000), it remains unclear whether this cortical damage in addition to, or instead of, an amygdala lesion could be responsible for the profound social changes observed in the previous reports. This idea received some support from a recent study (Emery et al., 2001) that used a neurotoxin (ibotenic acid) to destroy amygdala neurons while sparing the adjacent cortical areas, as well as fibers of passage, in middle-ranked adult monkeys. During dyadic social interactions with unfamiliar stimulus monkeys, amygdalectomized monkeys displayed fewer tension-related behaviors (yawning, self-grooming, and repetitive motor behaviors) than unoperated control monkeys. In contrast to previous data, monkeys with amygdala lesions were neither hyperaggressive nor socially withdrawn. Instead, these operated monkeys displayed more social signals (groom and mount solicitations) and social behaviors (sitting in close proximity, mounting, and social contact) toward the stimulus monkeys than did control monkeys, especially during initial encounters. Furthermore, stimulus monkeys sought out operated monkeys more for social interactions (social contact, grooming, or sitting in close proximity) than unoperated controls, implying that operated monkeys were perceived as less threatening and more attractive social partners. The single result from this study consistent with previous findings is that operated monkeys showed increased oral and tactile exploration. Overall, these results suggest that the severe social changes observed in the earlier studies following large temporal lobe lesions could have been due to damage of cortical areas adjacent to the amygdala or to combined amygdala and temporal cortex damage. However, an alternative explanation could be that social interactions in this most recent study were investigated in a relatively less challenging (dyadic) social environment than that provided to amygdalectomized monkeys in several previous studies. Given that the complexity of social environment is a critical factor for the emergence of social deficits following amygdala lesions, it remains possible that the outcome of selective neurotoxic amygdala lesions might differ if the operated monkeys were placed in a more challenging social context.

Fewer studies have investigated the effects of orbital frontal cortex damage on social behavior in monkeys. Butter and colleagues (Butter, Mishkin, & Mirsky, 1968; Butter, Snyder, & McDonald, 1970) reported a decrease in aggressive behaviors coupled with a transient increase in avoidance responses in monkeys with lesions of the orbital frontal cortex. These behavioral disturbances appeared to be exacerbated in cases where cortical damage was localized to the posteromedial region of the orbital frontal cortex, which is highly interconnected to the amygdala (Amaral, Price, Pitkanen, & Carmichael, 1992). In a subsequent study, Butter and Snyder (1972) performed a resection of the orbital frontal cortex in monkeys that had acquired the highest dominance rank in a group of five. When the operated monkeys were recombined with their familiar peers after surgery, they initially displayed increased aggression and reacquired their dominant status over older and heavier monkeys in the group. However, after repeated interactions, these operated monkeys lost their dominant status. Similar changes in social behavior have been observed following frontal lobotomies, including the orbital frontal cortex, in monkeys living in a free-ranging colony on the island of Cayo Santiago in Puerto Rico (Franzen & Myers, 1973; Myers, Swett, & Miller, 1973). Upon reintroduction to their colony, the operated monkeys displayed an overall decrease in positive social behaviors (grooming, huddling, near-body contact) and socially communicative facial, vocal, and postural behaviors, as well as an increase in inappropriate social interactions. However, similar to previous studies of amygdala lesions, most of the orbital frontal lesions in these early studies included cortex on the medial and/or lateral surface of the frontal lobe. Therefore, it is not clear whether the behavioral effects observed were actually due to orbital frontal cortex damage, damage to other adjacent regions within the frontal lobe, or a combination thereof. Thus, further investigation of the effects of more selective damage to the orbital frontal cortex on social behavior is still needed.

Finally, although damage to the hippocampal formation (dentate gyrus, CA fields, and subicular complex) has repeatedly been implicated with memory disorders in many species, including humans (for review, see Cohen & Eichenbaum, 1995), social, emotional, and behavioral changes following such lesions have not been mentioned or formally measured (Mayes, Holdstock, Isaac, Hunkin, & Roberts, 2001; Stark, Bayley, & Squire, 2002; Vargha-Khadem et al., 1997; Zola, Squire, & Amaral, 1986). Nonetheless, there exists evidence in rodents indicating abnormal social interactions after damage to the hippocampus (Becker & Grecksch, 2000; Becker, Grecksch, Bernstein, Hollt, & Bogerts, 1999; Daenen, Wolterink, Gerrits, & van Ree, 2002; Ely, Greene, & Henry, 1976; Kolb & Nonneman, 1974; Michal, 1973; Maaswinkel, Baars, Gispen, & Spruijt, 1996; Sams-Dodd, Lipska, & Weinberger, 1997), and in humans, neurons within the hippocampal formation display differential activity during presentation of social cues, such as faces, relative to objects (Fischer et al., 2003; Fried, Cameron, Yashar, Fong, & Morrow, 2002; Fried, MacDonald, & Wilson, 1997; Gur et al., 2002; Williams et al., 2001), which persists even after the stimuli disappear (Fried et al., 2002). Finally, the negative symptoms in patients with schizophrenia, such as social withdrawal, have also been associated with neuropathology in the medial temporal region, including the hippocampal formation (for review, see Benes, 1999; Weinberger, 1999). Thus, it is plausible that the normal mediation of social skills also requires the hippocampal formation, which provides access to stored information about social experiences.

To gain further knowledge of the respective contribution of the amygdala, hippocampal formation, and orbital frontal cortex to social cognition, the present study used selective lesion techniques and a seminaturalistic social environment, as well as ethologically valid and detailed behavioral observations of macaque monkeys, to compare and contrast the effects of selective damage to these three neural structures on the maintenance of previously established social relationships, taking into account the presurgical social rank (dominant vs. subordinate) of the monkeys. Preliminary reports of this work have appeared elsewhere (Machado & Bachevalier, 2001, 2004).

Method

Subjects

Subjects were 24 adult male rhesus monkeys (*Macaca mulatta*), weighing 3–6 kg and ranging between 2.4 and 3.2 years old at the beginning of presurgical social interactions. The dominance hierarchy, as assessed by food competition and linear rankings during this presurgical testing phase,

was used to characterize each monkey's social rank (dominant or subordinate). Presurgical testing also included assessments of emotional reactivity (human intruder task; Kalin, Shelton, & Takahashi, 1991) and food preference, which will be reported elsewhere.

Monkeys were then randomly assigned to one of the following four experimental groups balanced with respect to presurgical dominance rank: sham lesion (C; $n = 6$), ibotenic acid hippocampal formation lesion (H-ibo; $n = 6$), ibotenic acid amygdala lesion (A-ibo; $n = 6$), and ibotenic acid orbital frontal cortex lesion (O-ibo; $n = 3$). Given that the neurotoxic orbital frontal lesions resulted in incomplete damage to this region (see below), the remaining 3 monkeys in this group received aspiration orbital frontal cortex lesions (O-asp; $n = 3$).

During all testing procedures, monkeys were housed individually at the University of Texas Medical School Animal Care Facility (an institution accredited by the Association for the Assessment and Accreditation of Laboratory Animal Care International), given water ad libitum, and fed fresh fruit, vegetables, and high-protein monkey biscuits (Lab Diet No. 5045, PMI Nutrition International, Brentwood, MO) daily. Monkey housing rooms were maintained on a 12-hr light–dark cycle. All procedures performed with these monkeys were approved by the Animal Care and Use Committee of the University of Texas Health Science Center, Houston, Texas.

Neuroimaging

Magnetic resonance imaging (MRI) procedures have been detailed in two previous studies (Nemanic, Alvarado, & Bachevalier, 2004; Nemanic, Alvarado, Price, Jackson, & Bachevalier, 2002). Each operated monkey was first immobilized in its home cage using a mixture of ketamine hydrochloride and xylazine (10 mg/kg of 7:3 ketamine hydrochloride, 100 mg/ml, and xylazine, 20 mg/ml, im), intubated with an endotracheal cannula to allow for constant isoflurane sedation (1.0%–3.0%, vol/vol, to effect), and transported to the MRI scanner. The monkey's head was then secured in a nonferromagnetic stereotaxic apparatus (Crist Instruments, Damascus, MD) and centered with respect to the magnet. The MRI protocol included two sessions performed with a GE Signa 1.5 Tesla Echo Speed Scanner (GE Medical Systems, Milwaukee, WI) and acquired using a 5-in. circular surface coil (GE Medical Systems, Milwaukee, WI). The first MRI session occurred 1–3 weeks prior to surgery and included two series of coronal images through the entire brain: one T1-weighted structural scan (1 mm thick) and three fluid attenuated inversion recovery (FLAIR; 3 mm thick, each offset by 1 mm posterior) scans. The second MRI scanning session was performed 7–10 days after surgery and included the same 2 MRI series as acquired presurgery.

Presurgical T1-weighted magnetic resonance (MR) images were used to precisely select and calculate stereotaxic coordinates for neurotoxin injections in each target area (Saunders, Aigner, & Frank, 1990) or to visualize the individual sulcal pattern that served as landmarks for orbital frontal cortex lesions. Postsurgical T1-weighted images were compared with matched presurgical T1-weighted images to identify the location and quantify the extent of orbital frontal cortex aspiration lesions (Group O-asp). Postsurgical FLAIR images were compared with matched presurgical FLAIR and T1-weighted images to accurately identify localized areas of edema caused by neurotoxin-induced cell death and were therefore used to quantify the extent of lesion for all monkeys in Groups H-ibo, A-ibo, and O-ibo (Málková, Lex, Mishkin, & Saunders, 2001; Nemanic et al., 2002).

Surgery

All surgical procedures were performed under deep anesthesia using aseptic techniques. The monkey was first sedated with ketamine hydrochloride (10 mg/kg, im), intubated, and maintained on isoflurane gas (1.0%–2.0%, vol/vol, to effect) for the duration of the surgery. Monkeys also received an intravenous drip solution containing 0.45% sodium chloride to maintain hydration. Heart rate, respiration rate, blood pressure, expired CO_2, and body temperature were monitored throughout the surgical procedure until the monkey recovered fully from anesthesia. The monkey was placed on a heating pad to prevent hypothermia, was treated with EMLA cream (AstraZeneca, Wilmington, DE) to reduce ear and eye pain caused by pressure from the head-restraint device, and received ophthalmic ointment to prevent ocular dryness.

Monkeys in Groups C, A-ibo, and H-ibo were repositioned in the same stereotaxic apparatus used for presurgical neuroimaging, whereas those in Groups O-ibo and O-asp were placed in a head-holder that permitted easy rotation of the monkey's head during surgery. The head was shaved, the skin disinfected with Nolvasan solution (Wyeth, Fort Dodge, IA), and a long-acting local anesthetic (Marcaine [Astra Zeneca, Wilmington, DE] 25%, 1.5 ml, sc) was injected along the intended incision line. After a midline longitudinal incision from a midpoint on the supra-orbital ridge to the occipital notch, the skin, connective tissue, and temporalis muscles were gently retracted.

Monkeys in Groups A-ibo and H-ibo received a drip of 30 ml of mannitol (20%, 1 ml per min, iv) before the last ibotenic acid injection to control brain swelling, and for all monkeys, the wound was closed in anatomical layers. The monkey was removed from isoflurane gas and recovered in the surgical facility until it could breathe on its own and maintain a spot oxygen saturation of $> 88\%$ for 1 hr.

Beginning 12 hr prior to surgery and continuing until 1 week after surgery, all monkeys were treated with dexamethazone sodium phosphate (0.4 mg/kg, im) and cephazolin (25 mg/kg, im) to prevent excessive immunoreactivity and protect against infection, respectively. For 3 days following surgery, monkeys also received an analgesic (acetaminophen, 10 mg/kg, p.o.) to minimize pain.

During recovery from surgical procedures, none of the monkeys displayed any changes in food and water consumption or arousal state. However, reduced locomotor behaviors and weakness of the limbs were observed in the two cases that sustained additional damage to the ventral putamen (i.e., Cases C-1-inj and H-ibo-1). All fur on the monkeys' scalps had regrown by the start of the postsurgery testing phase such that scars from surgery were not visible.

Neurotoxic Hippocampal Formation Lesions

Neurotoxic hippocampal formation lesions were intended to damage all ammonic fields, the dentate gyrus, and the prosubiculum and subiculum (see Figure 1, left column). The number of injection sites and their positions in the anterior–posterior, medial–lateral, and dorsal–ventral planes were determined from each monkey's presurgical T1-weighted MR images. For the posterior two thirds of the hippocampal formation, one injection site was selected every 1.5 mm and was centered within the body of the hippocampal formation. For the most anterior portion, where the uncus was clearly visible, two injection sites were selected every 1.5 mm. One was situated laterally, again within the body of the hippocampal formation, and the other located more medially within the uncus. Injection coordinates were then transformed into three-dimensional stereotaxic coordinates prior to surgery.

Small bilateral craniotomies were created above the injection sites, and small slits were cut in the dura bilaterally to allow the needle of the 10-μl Hamilton syringe, held by a Kopf electrode manipulator (David Kopf Instruments, Tujunga, CA), to be lowered to the appropriate injection coordinates. Two Hamilton syringes were filled with ibotenic acid (Biosearch Technologies, Novato, CA; 10 mg/ml in phosphate-buffered saline, pH 7.4) and used to inject 1.5 or 2.4 μl ibotenic acid (0.4 μl/min) at each of the 11 sites selected for each hemisphere. After each injection, a 3-min delay ensued to permit diffusion of the neurotoxin and minimize its spread along the needle track during retraction of the needles.

Neurotoxic Amygdala Lesions

Neurotoxic amygdala lesions were intended to damage all amygdaloid nuclei (see Figure 2, left column) and were also guided by presurgical

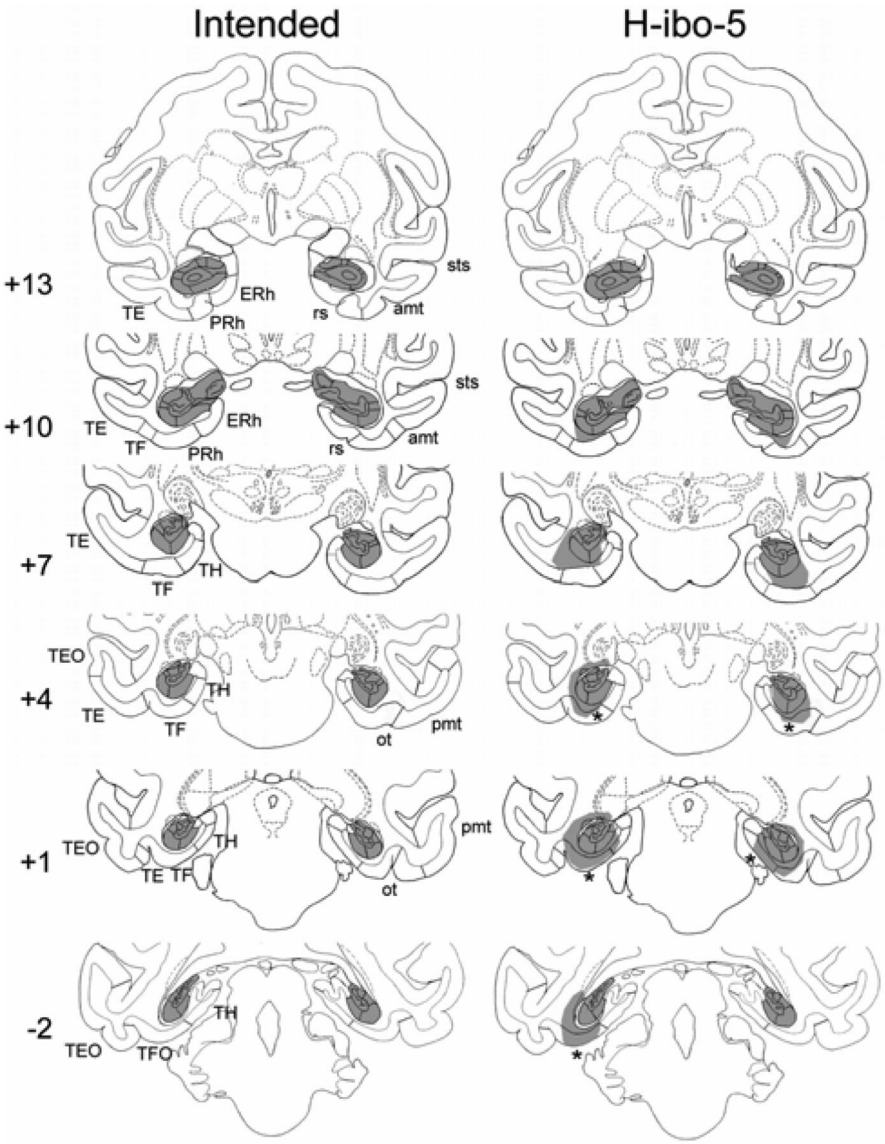


Figure 1. Coronal sections through the hippocampal formation depicting the intended damage (left column), shown in gray, and the estimated damage (right column), also shown in gray, from magnetic resonance images for a representative case with neurotoxic lesion of the hippocampal formation (Case H-ibo-5; see Nemanic & Bachevalier, 2006). The numerals on the left of each coronal drawing of the intended lesions indicate the distance in millimeters from the interaural plane. The asterisks indicate unintended damage to adjacent structures. amt = anterior middle temporal sulcus; ERh = entorhinal cortex; ot = occipitotemporal sulcus; PRh = perirhinal cortex; pmt = posterior middle temporal sulcus; rs = rhinal sulcus; sts = superior temporal sulcus; TE, TEO, TF, TFO, and TH = cytoarchitectonic fields described by von Bonin and Bailey (1947); H-ibo = monkeys with neurotoxic lesions of the hippocampal formation.

T1-weighted MR images. The coronal image through the midportion of the amygdala, usually including a complete view of the anterior commissure, was identified. On this image, 11 injection sites were selected and spaced 2 mm apart in the medial–lateral and dorsal–ventral directions. Two additional coronal images located 2 mm anterior and 2 mm posterior to this central image were also selected. For these two additional images, two injection sites were placed 1 mm lateral and medial to the center of the amygdala. During surgery, small bilateral craniotomies were created above the injection sites, and small slits were cut in the dura bilaterally to allow for a total of 15 injections per amygdala. Similar to hippocampal lesions (above), a 10-μl Hamilton syringe was used to deliver 0.2–0.6 μl ibotenic acid to each site at a rate of 0.4 μl/min.

Orbital Frontal Cortex Lesions

Orbital frontal cortex lesions (both ibotenic and aspiration) were intended to damage those areas of the ventral frontal cortex that are heavily interconnected with the amygdala (Amaral et al., 1992; see Figure 3, left column), namely, Areas 11 and 13 (as defined by Carmichael & Price, 1994). Because the shape and length of the orbital sulci vary between

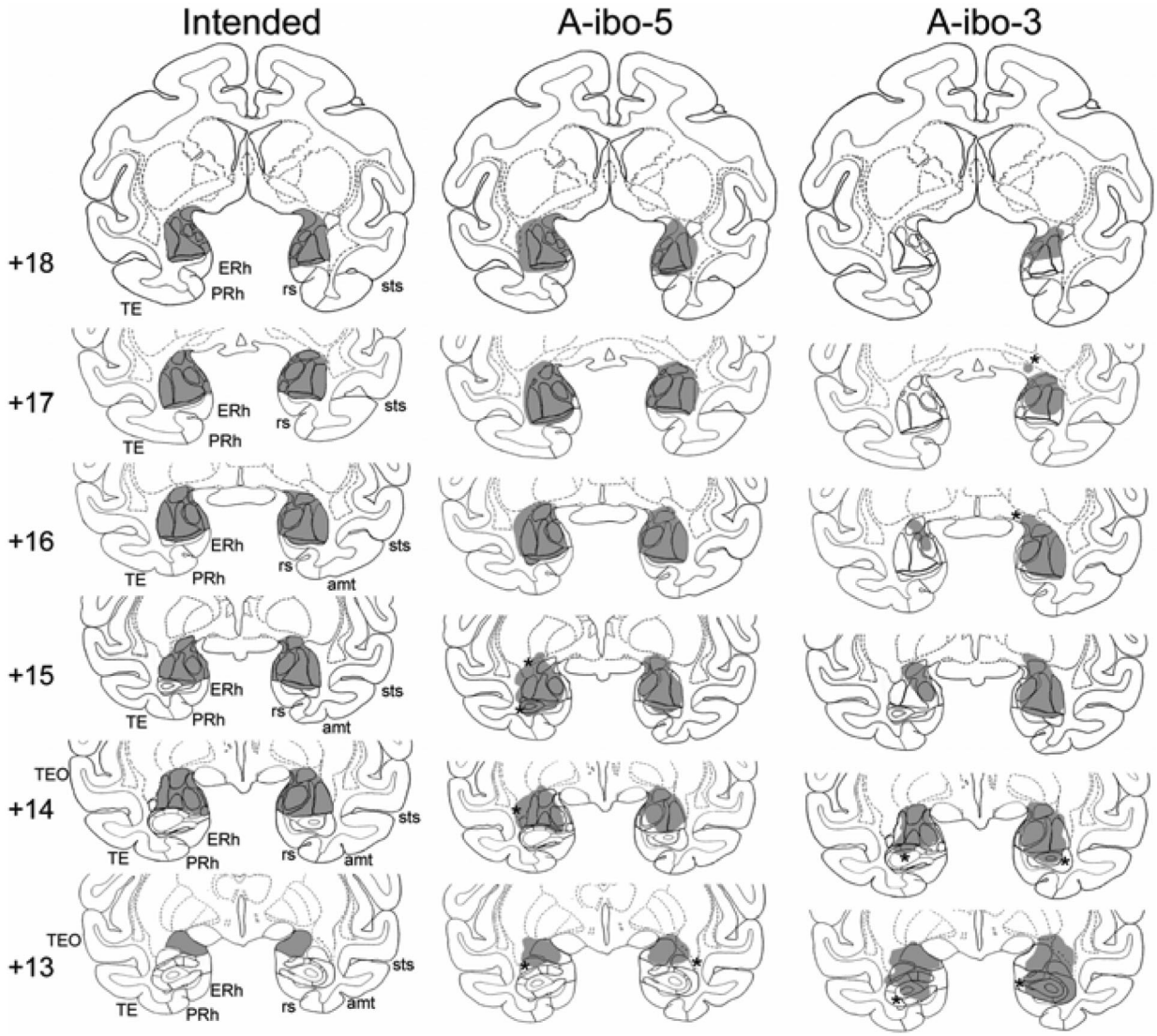


Figure 2. Coronal sections through the amygdala depicting the intended damage (left column), shown in gray, and estimated damage, also shown in gray, from magnetic resonance images in two cases that represent the largest (Case A-ibo-5, middle column) and smallest (Case A-ibo-3, right column) lesions in the group. The numerals on the left of each coronal drawing of the intended lesions indicate the distance in millimeters from the interaural plane. The asterisks indicate unintended damage to adjacent structures. amt = anterior middle temporal sulcus; ERh = entorhinal cortex; PRh = perirhinal cortex; rs = rhinal sulcus; sts = superior temporal sulcus; TE = cytoarchitectonic field described by von Bonin and Bailey (1947); A-ibo = monkeys with neurotoxic lesions of the amygdala.

monkeys, presurgical T1-weighted MR images were used to reconstruct the ventral surface of the frontal lobe for each monkey and approximate locations for 17–36 injection sites (all spaced ~2 mm apart) through Areas 11 and 13 for each hemisphere.

To access the orbital surface, a large craniotomy was created just above each orbit, and the bone of the supra-orbital ridge was gently eroded with the drill to gain a full view of the orbital frontal surface. The dura was cut and retracted, followed by gentle elevation of the frontal lobe using Neuro Patties (Allegiance Healthcare, McGaw Park, IL; 0.5 in. × 3.0 in. size) moistened with saline. With the aid of a surgical microscope, the lateral and medial orbital sulci and the olfactory stria were visualized. The boundaries of Areas 11 and 13 on the ventral surface of the frontal lobe were defined as follows. The anterior border was set as a line joining the anterior tips of the medial and lateral orbital sulci. The posterior border was a line joining the medial bank of the lateral orbital sulcus to the olfactory stria just anterior to its division into the medial and lateral olfactory tracts. The medial border followed the olfactory stria, and the lateral border followed the medial bank of the lateral orbital sulcus from its anterior tip to the posterior border of the lesion (see Figure 3, left column). These borders approximate the extent of Areas 11 and 13 in the macaque monkey.

For monkeys in Group O-ibo, a 2 mm × 2 mm grid of injections was then placed in the cortex within these borders. A 30-gauge needle attached to a 10-μl Hamilton syringe by polyethylene tubing was used to manually inject 0.4–0.8 μl ibotenic acid (0.4 μl/min) at each site.

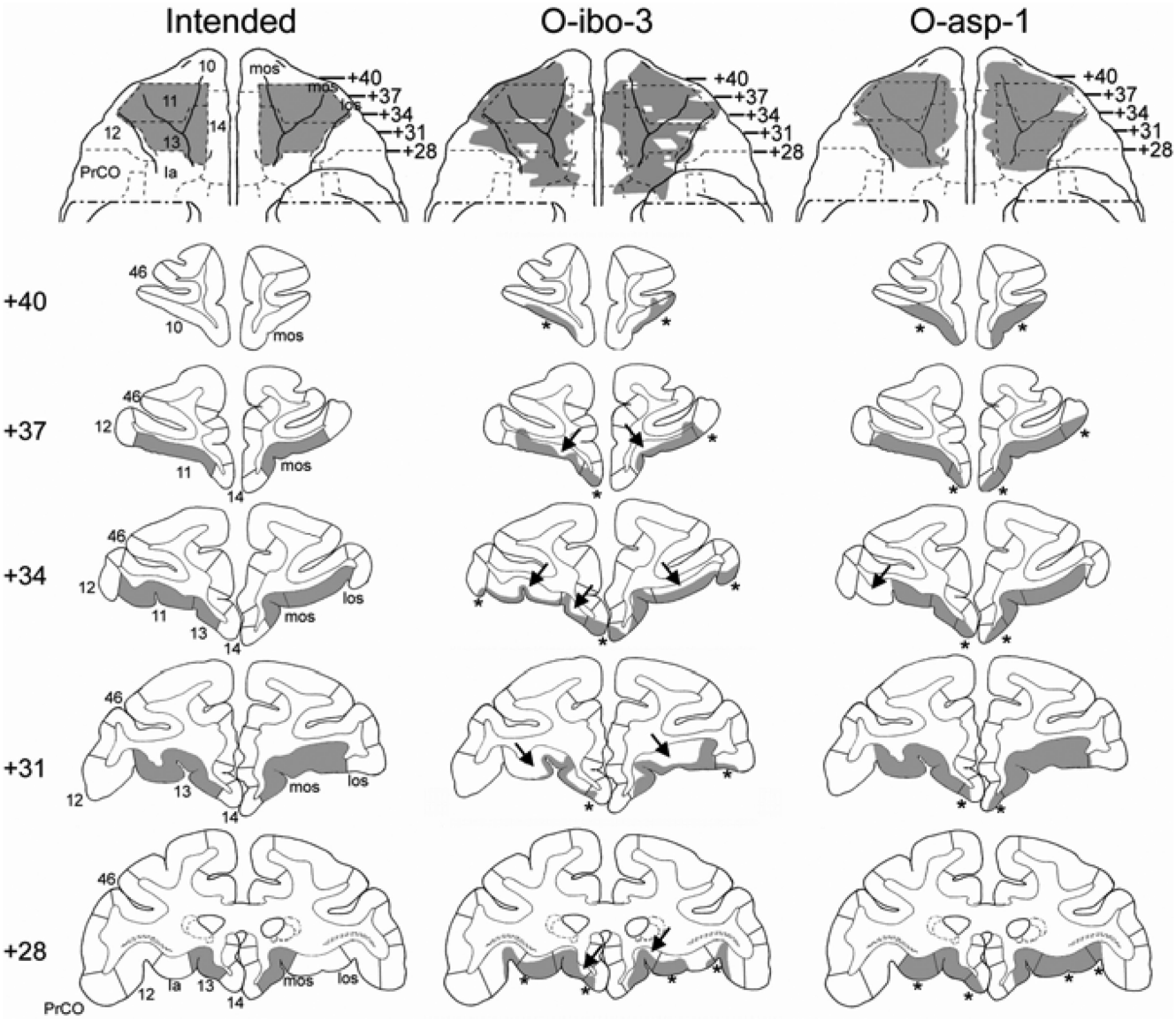


Figure 3. Ventral surface reconstruction and coronal sections through the orbital frontal cortex depicting the intended damage (left column), shown in gray, and estimated damage, also shown in gray, from magnetic resonance images for one representative case with a neurotoxic lesion of the orbital frontal cortex (Case O-ibo-3, middle column) and one representative case with an aspiration lesion of the orbital frontal cortex (Case O-asp-1, right column). Note that, for direct comparisons between coronal sections and ventral surface reconstructions, left hemisphere damage in the coronal views is reconstructed on the left half of the ventral view. The numerals to the right of each ventral reconstruction indicate the distance in millimeters from the interaural plane and correspond to the numerals given below on the left of each coronal section of the intended lesions. The asterisks indicate unintended damage to adjacent structures, whereas arrows point to areas of spared tissue. Dashed lines on the ventral surface of the brain represent borders that define cytoarchitectonic fields (Areas 10, 11, 12, 13, 14, and 46) as described by Carmichael and Price (1994). Ia = agranular insular area; mos = medial orbital sulcus; los = lateral orbital sulcus; PrCO = precentral opercular cortex; O-ibo = monkeys with neurotoxic lesions of the orbital frontal cortex; O-asp = monkeys with aspiration lesions of the orbital frontal cortex.

For monkeys in Group O-asp, 21- and 23-gauge suckers were used first to coagulate the pia matter along the defined borders of the lesion and then to gently aspirate the cortical tissue contained within these limits. Care was taken to not sever the white matter beneath the cortical mantle in all cases.

Sham Lesions

After opening the skin, bilateral craniotomies (similar to those used for hippocampal formation or amygdala lesions) were made as described above. For five of the six cases, the dura was cut bilaterally, but no needle

penetrations occurred. The remaining sham-operated monkey (case C-1-inj) was prepared to serve as a control monkey for one of the hippocampal formation–lesion monkeys that sustained inadvertent damage to the putamen (Case H-ibo-1; see Results, below). Case C-1-inj received ibotenic acid injections into the section of the putamen that lies dorsal to the posterior third of the amygdala and the anterior third of the hippocampal formation. A total of 17 injections were made per hemisphere, and 0.4–0.6 μl ibotenic acid were injected at each site at a rate of 0.4 μl/min.

MRI-Based Lesion Evaluation

All monkeys died in the flooding of Tropical Storm Allison in June 2001. Therefore, no histological evaluations of lesion location and extent were possible. However, all lesions were evaluated using MRI techniques that have been recently shown to provide an accurate estimate of actual cell loss following neurotoxic hippocampal lesions in monkeys (Málková et al., 2001; Nemanic et al., 2002). Because these neuroimaging techniques have been validated for neurotoxic lesions of the hippocampus, but not for those of the amygdala and orbital frontal cortex, hypersignals observed after ibotenic injections in the amygdala and orbital frontal cortex are used only as an approximation of actual damage.

For Case C-1-inj and all monkeys of Groups H-ibo, A-ibo, and O-ibo, presurgical T1-weighted images (1-mm slice thickness) were used as an aid to match the lower resolution pre- and postsurgical FLAIR images (3-mm slice thickness) to digital drawings of coronal sections from a normalized rhesus monkey template brain at 1-mm intervals. Hypersignals on postsurgical FLAIR MR images were then identified and, using the presurgical T1-weighted images to maximize accuracy, plotted onto corresponding coronal drawings from the template brain using Adobe Photoshop software (Version 6). These drawings were imported into a Java-based image analysis program (ImageJ; Rasband, 1997) to measure the surface area (in pixels squared) of damage for intended targets, as well as all areas sustaining unintended damage. For any given region of interest, the measured surface area of damage on each section through each hemisphere was summed and then multiplied by image thickness to calculate a total volume of damage (Gundersen & Jensen, 1987). The volume of damage was then divided by the normal volume of the region of interest (obtained from the template brain in a similar manner) to estimate a percentage of the total volume damaged.

For each monkey in Group O-asp, pre- and postsurgical T1-weighted images were used to measure the total volume of orbital frontal cortex (Areas 11 and 13) and adjacent cortical regions damaged. Pre- and postsurgical T1-weighted images were again matched to corresponding coronal drawings from the normal rhesus monkey template brain. Within each hemisphere, the total volume of aspirated tissue from the orbital frontal cortex and adjacent regions was measured as above and expressed as a percentage of the normal volume for that region.

Behavioral Procedures

Apparatus

Monkeys were tested in a social behavior enclosure (3.1 m long × 1.6 m wide × 1.9–2.3 m tall; see Figure 4), which was constructed from galvanized steel bars (0.6 cm in diameter, spaced 4.7 cm apart vertically and 14 cm horizontally), except for one side, which was constructed of clear lexan Plexiglas (2 cm thick) to permit optimal video recording of monkeys. This enclosure also contained two galvanized steel perches (75 cm long × 25 cm wide × 4 cm thick), two rope swings of differing heights, and a single horizontal PVC pole perch (4 cm in diameter, 1.6 m long) that spanned the width of the cage near its center. Three PVC tubes (4 cm in diameter) were also affixed to one side of the enclosure to allow delivery of preferred foods to stainless steel bins mounted at three distinct locations within the enclosure during the food competition condition (described below). This enclosure was located in a separate room adjacent to the monkey housing quarters.

Figure 4. Photograph of the social behavior enclosure taken in front of the clear lexan side to display the food delivery tubes (arrows) and food bins (circled) attached to the left side of the cage for delivering food pellets during the food competition condition.

Pre- and Postsurgical Social Behavior Testing

Six social groups of 4 monkeys each (tetrads) were formed randomly prior to surgeries. Each tetrad was allowed to freely interact in the social behavior enclosure for 1 hr on 15 days (5 days per week) approximately 1 month prior to surgery. To ensure that all social interactions between members of a given tetrad were captured on videotape and available for later analysis, monkeys were housed such that they had no direct visual contact with other members of their own tetrad but could see and hear members of other tetrads. To control for circadian effects on social behavior, time of day and the order in which tetrads were observed each day were counterbalanced across all tetrads.

At the beginning of each interaction session, the experimenter placed the 4 members of a tetrad into individual primate transport boxes (Prima-Carrier, Primate Products, Woodside, CA), transported them to the testing room, and released each monkey into the social behavior enclosure in reverse dominance order (lowest ranked monkeys entered first). The experimenter remained within the room during the entire interaction session but was concealed within an observation blind located in the corner of the room. The experimenter controlled the videotaping (Sony Handycam, Model CCD-FX710) of five 10-min social interaction episodes through the clear lexan side of the enclosure, which allowed for behaviors conducted in all areas of the cage to be captured. The experimenter also performed the following behavioral assessments during live interactions.

Dominance hierarchy assessments. The dominance hierarchy was measured in each tetrad using two methods. At the end of every 1-hr social interaction session, the experimenter subjectively ranked the monkeys in a linear dominance hierarchy with regard to the preceding interactions. Dominant monkeys (coded as Rank 1 or 2) typically moved around the enclosure freely, easily controlled preferred locations (high perches and swings), received high levels of positive social interactions (contact, grooming, etc.), and displayed disciplinary forms of aggression to lower ranked monkeys. Subordinate monkeys (coded as Rank 3 or 4) typically showed the opposite behavioral patterns. Dominance rank was also measured in a more empirical manner, using a food competition condition (Mirsky, 1960) on Test Days 7–9. During the five videotaped episodes on these days, the experimenter, concealed within the observation blind, delivered three different preferred foods, namely, unsalted peanuts, banana-flavored pellets (P. J. Noyes, Lancaster, NH; 1-g size), and M&M chocolate candies (Mars Candies, Hackettstown, NJ), into the food wells attached to the social behavior enclosure via the three PVC tubes. Food types and PVC tubes were selected pseudorandomly on each trial, and

foods were delivered at 1-min intervals (see Figure 4). The experimenter recorded the number of foods obtained by each monkey in the tetrad, assuming that the highest ranked monkeys would collect the majority of these preferred foods. Although the monkeys were not food restricted on days when the food competition condition was performed, they were tested more than 12 hr after their last feed, which had occurred the day before.

Personality ratings. At the end of every social interaction session, the experimenter subjectively rated each individual monkey and all possible dyads on 18 adjectives describing various aspects of macaque social and nonsocial personality, using a 5-point Likert-type scale (Capitanio, 1999; Stevenson-Hinde & Zunz, 1980). Table 1 displays the personality categories measured, along with a brief definition for each. The definitions for each Likert-scale level were as follows: 1 = *definition not at all descriptive,* 2 = *definition slightly descriptive,* 3 = *definition moderately descriptive,* 4 = *definition mostly descriptive,* and 5 = *definition completely descriptive.* All ratings were made solely on the basis of the interactions observed on a given day. Observers were explicitly instructed not to use prior knowledge of the monkeys to influence how each was scored.

Social and nonsocial behavior assessment. Episodes 1, 3, and 5 (10 min each) from Test Days 1–4 and 12–15 (early and late testing blocks, respectively) were converted into digital media files using an MPEG-1 capture board (Broadway Pro, Version 6.0, PCI interface, http://www.b-way.com) installed on a PC. From these digital files, the cumulative frequency and duration of social and nonsocial behaviors were coded using the Observer Video-Pro software package (Noldus, Trienes, Hendriksen, Jansen, & Jansen, 2000) and a focal sampling technique (Altmann, 1974). Each social interaction episode was viewed four separate times, each time with a different monkey of a tetrad as the focal monkey. The Observer Video-Pro software allowed the observer to record all social and nonsocial behaviors initiated and received by the focal monkey, as well as to specify the identity of the focal monkey's social partner (where applicable). Table 2 displays the ethogram of specific behaviors scored and gives a brief definition for each. Individual behaviors were also grouped into more general behavioral categories (also shown in Table 2) for statistical analyses.

One month following surgery, all monkeys were tested in the visual paired comparison task to assess their ability to recognize pictures of objects (these data will be reported elsewhere), and approximately 6 months after surgery, the same tetrads were allowed to interact again in the large enclosure to evaluate changes in dominance hierarchy, personality ratings, and social and nonsocial behaviors. Testing procedures and data collection occurred exactly as described for the presurgery testing phase above.

Data Analysis

For data sets that were normally distributed, general linear model analyses of variance (ANOVAs) were conducted with group (4) as the between-subjects factor and phase (2; pre- and postsurgery) as a within-subjects factor with repeated measures, using the SPSS 12.0 statistical analyses package. A Huynh-Feldt correction was used to adjust the degrees of freedom if sphericity could not be assumed. Significant main effects of group were investigated further using two-sided Dunnett's tests to investigate differences between Group C and the three operated groups and Tukey tests when comparing the three operated groups with each other. Significant main effects of phase were subjected to post hoc Bonferroni tests, and significant Group × Phase interactions were investigated with paired-sample *t* tests that were Bonferroni corrected for multiple comparisons if the number of these comparisons was greater than five. If zero occurrences of a particular behavior existed for one or more operated groups, these data were analyzed using nonparametric statistical tests, such as the Wilcoxon signed-rank test (for variables measured at two intervals)

Table 1
Personality Categories Rated for Each Monkey and Each Dyad Within a Tetrad

General category & adjective	Brief definition
	Individual personality categories
Nonsocial	
Active	Ambulates about the cage for the majority of the session.
Exploratory	Readily investigates the test setting orally or manually.
Sociable	
Confident	Behaves in a positive, assured manner, not restrained or tentative in any way.
Playful	Actively and freely initiates or joins in play behavior with many partners.
Affiliative	Sociable, seeks out the companionship of several different partners.
Popular	The monkey's companionship is actively sought out by several different partners.
Interaction inhibiting	
Avoidant	Refrains from interacting with others by repeatedly exhibiting evasive behavior or physically repelling others.
Solitary	Actively chooses to spend time alone.
Manipulative	Tries to control the behavior of others for individual gain.
Aggressive	Attempts to cause or actually causes physical harm to several other group members.
Anxious	Tense, extremely vigilant, exhibits stereotypic behaviors.
Excitable	Extremely reactive or overreacts to events in the group.
Fearful	Readily fear grimaces and retreats from others, readily shows submissive postures.
	Dyad personality categories
Sociable	
Playful	Dyad actively and freely engages in many instances of reciprocal play behavior.
Affiliative	Dyad displays friendly, free, and calm interactions for the majority of the session.
Interaction inhibiting	
Agonistic	Dyad engages in dominance/subordinate interactions (chases, physical aggression, displacements) for the majority of the session.
Tense	Dyad's interactions appear strained, unresolved, or nervous.
Avoidant	Monkeys actively avoid or repel each other for the majority of the session.

Table 2
Social and Nonsocial Behavior Ethogram

Behavior category & specific behavior	Brief definition
Affiliative social behaviors	
Proximity[a,b]	Within arm's reach of partner.
Contact[a,b]	Physical contact with partner.
Groom[a,b]	Picking through partner's fur.
Play[a,b]	Rough-and-tumble play or grappling.
Follow[a,b]	One monkey moves, and the other follows.
Mount[a,b]	Hands on partner's hips and double foot clasp.
Incomplete mount[a,b]	Hands on partner's hips or double foot clasp.
Affiliative social signals	
Lipsmack[b]	Rapid, submissive lip movements.
Groom solicitation[b]	Rigid posture with presentation of body part.
Mount solicitation[b]	Hind quarters oriented toward partner with tail up.
Anogenital explore[b]	Tactile, oral, or olfactory inspection of other's genitals.
Accept approach[b]	Subject approached and remains.
Dominance-related behaviors	
Cage aggression	Rapid shaking of cage bars.
Crooktail	Tail held up in "?" shape.
Aggressive behaviors	
Chase[a,b]	Aggressive, rapid movement after another subject.
Aggression[a,b]	Physical contact with intent to harm.
Threat[b]	Open-mouthed facial expression, head bobbing, or lunges.
Displace[b]	Take over another subject's position.
Bark vocalization	High-intensity, low-pitch vocalization.
Self-directed behaviors	
Self-clasp	Abnormal clasping of body part.
Self-groom	Picking through or licking of own fur.
Self-sex	Manipulation of own genitals.
Coprophagia	Ingestion of feces.
Urine drinking	Ingestion of urine.
Anxious behaviors	
Tooth grind	Audible rubbing together of teeth.
Scratch	Use of hands or feet to scratch oneself.
Fear grimace[b]	Exaggerated grin, exposing teeth.
Yawn	Exaggerated opening of mouth to expose teeth.
Motor stereotypy[a]	Abnormal and repetitive motor behaviors.
Scream vocalization	High-pitched, high-intensity vocalization.
Refuse approach[b]	Subject approached but moves away.
Exploratory behaviors	
Tactile explore[a]	Tactile manipulation of the test enclosure.
Oral explore[a]	Oral manipulation of the test enclosure.
Avoidant/solitary behaviors	
Withdrawal[a]	Moves out of proximity.
Locomotion[a]	Ambulating about the enclosure.
Stationary[a]	Subject remains in the same spatial location.
Other behaviors	
Coo vocalization	High-pitched "oooo" vocalization.
Walk by[b]	Movement into and out of arm's reach.

Note. List of all social and nonsocial behaviors coded. All behaviors were coded for frequency (total number of occurrences).
[a] Behavior for which total duration was also measured. [b] Behavior for which a specific partner could be coded.

or a Mann–Whitney *U* test (when comparing groups for a nonrepeated variable).

In addition to analyzing changes in the total frequency and duration of social and nonsocial behaviors from data files generated with the Observer Video-Pro software, we also subjected these files to a lag-sequential analysis (Bakeman & Gottman, 1997) to examine how each monkey in a tetrad typically responded to both affiliative and aggressive social signals initiated by the other monkeys both prior to and following the lesion surgery. For these analyses, the Observer Video-Pro software was used to count the number of times each monkey gave an appropriate response (or target behavior) within 10 s after receiving one of three criterion behaviors (*mount solicitation, groom solicitation,* or *threat*). For mount solicitation and groom solicitation, the appropriate target behavior is quite specific, either a mount or a groom, respectively, so only transitions between *mount solicitation receive* and *mount initiate* or *groom solicitation receive* and *groom initiate* were counted. For threat, because responses to threatening gestures can vary greatly depending on the dominance rank of the threatening individual and recipient, transitions between *threat receive* and five general categories of target behaviors were counted: (a) *affiliative social behaviors initiate,* (b) *affiliative social signals initiate,* (c) *dominance-related behaviors initiate,* (d) *aggressive behaviors initiate,* and (e) *anxious behaviors initiate.* These tallies were then adjusted by the total number of other, nontarget behaviors that occurred within 10 s after a mount solicitation, groom solicitation, or threat was received to calculate an estimated

log odds ratio (Bakeman & Gottman, 1997). This estimated ratio indicates the likelihood of producing a particular response to each individual partner in the social group, as well as to all partners in general (mean across all partners). Pre- versus postsurgery changes in log odds ratio were compared for each group individually using a variant of the paired-sample t test (Bakeman & Gottman, 1997), again Bonferroni corrected for multiple comparisons.

Given that social dominance status significantly dictates the type and magnitude of social behaviors initiated and received by nonhuman primates, especially male macaques (Cheney & Seyfarth, 1990), statistical analyses were conducted on each behavioral variable using either each group as a whole ($n = 6$) or considering social hierarchical status (dominant and subordinate; each $n = 3$) as an additional factor. Each monkey's social status assignment (dominant or subordinate) was based on dominance rankings and food competition condition data collected during the presurgery phase.

For Groups O-asp and O-ibo, to investigate if lesion method itself impacted differentially on social behavior, behavioral measures collected from these two experimental orbital frontal groups were examined before comparing the four lesion groups. Differences between these two subgroups were analyzed using the statistical analyses outlined in the previous paragraphs. No significant main effects of group or interactions between group and phase were found. Therefore, in the results sections below, these two subgroups are pooled into a single Group O.

Initial analysis of frequency, duration, and estimated log odds ratios for the behavioral variables included groups, testing block (Test Days 1–4 vs. Test Days 12–15), and phase (pre- and postsurgery) as main factors. Repeated-measures ANOVAs (4 Groups $\times$ 2 Phases $\times$ 2 Blocks) did not reveal any significant Group $\times$ Phase $\times$ Block interactions regardless of whether or not dominance rank was considered in the analysis. Thus, cumulative frequencies, durations, and estimated log odds ratios were calculated across the two testing blocks (i.e., across a total of 4 hr of observation) and used for subsequent two-factor ANOVAs (4 Groups $\times$ 2 Phases).

Finally, for all experimental groups, Pearson product–moment correlation matrices were generated to determine if the extent of damage to any brain region (intended or unintended) might have significantly influenced the behavioral parameters measured. Only those regions displaying greater than 5% mean damage across hemispheres were included in this final analysis. For these correlation analyses, the social status assignment was not included in the analyses because of the small number of monkeys in the categories dominant and subordinate. Thus, the correlation analyses were performed on the six monkeys of each experimental group.

Interobserver Reliability Assessments

Because behavioral data collection and coding for the experiment described here were performed by a single, previously trained observer (Christopher J. Machado) who was also aware of the lesion condition for each monkey, it was necessary to perform interobserver reliability assessments to ensure data were coded without biases. To measure the interobserver reliability for the two dominance assessments and personality ratings, a second trained observer unaware of each monkey's lesion group also recorded these same measurements during a subset of live social interaction sessions along with the principal observer. The two dominance assessment data sets were then compared between the two observers, and a percentage agreement was calculated as follows: percentage agreement = [(number of exact agreements)/(number of total observations)] $\times$ 100. A percentage agreement was also calculated for the personality ratings in a similar fashion, with the exception that an agreement was counted if the two observers gave identical ratings or if the two observers' ratings were within 1 Likert-scale point of each other. Each of these behavioral measures was found to be highly reliable between observers (dominance assessments: 91.5% agreement; personality ratings: $\geq$ 95.0% agreement for all categories).

For social and nonsocial behaviors coded from digital media files, interobserver reliability was obtained from a subset of all possible episodes (balanced across lesion group), which were scored by both the principal observer and a second trained observer who was unaware of each monkey's lesion condition. Total frequency and duration of each individual behavior from the two observers were then compared using a Pearson product–moment correlation. This data set was also found to be highly reliable, with a correlation coefficient $\geq$ .80 for each individual behavior.

Results

Lesion Extent

Details of lesion extent for Group H-ibo have been recently described (Nemanic & Bachevalier, 2006), so only a brief description is provided here. For Groups A-ibo, O-ibo, and O-asp, a more extended description of the intended and unintended damage measured from postsurgical FLAIR or T1-weighted MR images is given using the following adjectives: *extensive* ($>$ 60.0%), *moderate* (25.0%–59.9%), *mild* (2.0%–24.9%), and *negligible* ($<$ 2.0%). The weighted average (W; Hodos & Bobko, 1984) was calculated to determine whether damage was highly unilateral (W% $<$ 25.0%) or particularly extensive and bilaterally symmetrical (W% $>$ 50.0%).

Case C-1-inj

The control lesion produced in this monkey was largely as intended but asymmetrical. Damage to the putamen was situated dorsal to the posterior amygdala–anterior hippocampal formation and was moderate on the right (40.3%) and mild on the left (5.7%).

Group H-ibo

The percentage damage for the hippocampal formation and adjacent regions (unintended damage) in both the left and right hemispheres is shown for all cases in Group H-ibo in Table 3. Five of the six monkeys in Group H-ibo (Cases H-ibo-1–3, -5, and -6) had bilaterally symmetrical lesions, ranging from 78.5%–99.1% average damage and extending throughout the entire anterior–posterior length of the hippocampal formation (see Figure 1, right column, for Case H-ibo-5). The only significant sparing occurred typically at the rostralmost portion of the hippocampal formation bilaterally and medially at the level of the uncus. In the remaining case (H-ibo-4), the lesion was more asymmetrical, totaling 56.2% on the left and 76.2% on the right. Spared tissue for this case was mostly located bilaterally in the rostral third of the hippocampal formations, at the level of the uncus.

Unintended damage (see Table 3) was mild to moderate in all cases and included, bilaterally, the parahippocampal gyrus (Areas TH and TF) for Cases H-ibo-2–6; the entorhinal cortex for Cases H-ibo-3, -4, and -6; and the perirhinal cortex for Cases H-ibo-3, -5, and -6 bilaterally; and unilaterally, the posterior and ventral portions of the amygdala for Case H-ibo-2. Finally, Case H-ibo-1 received moderate damage to the ventral putamen (34.0% on the right, 41.0% on the left), which likely resulted from vascular infarct caused by the needle penetrations.

Group A-ibo

The percentage damage for the amygdala and adjacent regions (unintended damage) in both the left and right hemispheres is

Table 3
Intended and Unintended Damage for All Experimental Groups

Case	L	R	Avg	W	L	R	Avg	W	L	R	Avg	W	L	R	Avg	W
	Hippocampal formation				Amygdala				Area TH				Area TF			
H-ibo-1	76.3	97.9	87.1	74.7	0	0	0	0	0	0	0	0	0	0	0	0
H-ibo-2	75.7	81.3	78.5	61.6	0	5.9	2.9	0	53.1	20.1	36.6	10.7	60.3	27.6	43.9	16.6
H-ibo-3	67.5	74.1	70.8	50.0	0	0	0	0	26.7	15.3	21.0	4.1	29.9	44.0	37.0	13.2
H-ibo-4	56.2	76.2	66.2	42.9	0	0	0	0	13.6	27.8	20.7	3.8	18.5	19.4	18.9	3.6
H-ibo-5	98.8	99.3	99.1	98.1	0	0	0	0	15.2	15.9	15.6	2.4	38.8	8.5	23.7	3.3
H-ibo-6	88.8	94.8	91.8	84.3	0	0	0	0	29.6	45.6	37.6	13.5	21.2	17.2	19.2	3.6
Mean	77.2	87.3	82.3	68.6	0	1.0	0.5	0	23.0	20.8	21.9	5.8	28.1	19.5	23.8	6.7
	Amygdala				Hippocampal formation				ERh				PRh			
A-ibo-1	20.6	82.2	51.4	17.0	10.6	1.6	6.1	0.2	0	1.8	0.9	0	0	0	0	0
A-ibo-2	48.9	88.1	68.5	43.1	1.2	0	0.6	0	0	0	0	0	0	0	0	0
A-ibo-3	27.1	73.1	50.1	19.8	15.7	13.6	14.6	2.1	0	0	0	0	0	0	0	0
A-ibo-4	79.1	92.5	85.8	73.2	3.4	3.0	3.2	0.1	0	0	0	0	0	0	0	0
A-ibo-5	88.7	91.3	90.0	81.0	1.5	0.1	0.8	0	0	5.5	2.8	0	0	0	0	0
A-ibo-6	70.3	90.0	80.2	63.3	21.1	10.3	15.7	2.2	0.8	0	0.4	0	0.1	0	0.1	0
Mean	55.8	86.2	71.0	49.6	8.9	4.8	6.8	0.8	0.1	1.2	0.7	0	0	0	0	0
	Orbital frontal cortex (Areas 11 & 13)				Area 12				Area 14				Ia			
O-ibo-1	37.1	19.9	28.5	7.4	2.3	0.9	1.6	0	49.0	23.8	36.4	11.7	37.0	25.3	31.2	9.4
O-ibo-2	33.9	37.5	35.7	12.7	28.1	41.7	34.9	11.7	8.3	5.9	7.1	0.5	28.2	34.3	31.3	9.6
O-ibo-3	43.0	47.3	45.2	20.3	9.9	20.9	15.4	2.1	25.4	11.7	18.5	3.0	44.9	38.0	41.4	17.0
Mean	38.0	34.9	36.4	13.5	13.4	21.2	17.3	4.6	27.6	13.8	20.7	5.0	24.4	24.1	24.2	8.9
O-asp-1	88.4	95.3	91.8	84.2	3.9	28.9	16.4	1.1	15.2	21.7	18.5	3.3	20.6	21.1	20.9	4.3
O-asp-2	83.0	92.0	87.5	76.3	7.0	9.3	8.2	0.7	10.7	5.9	8.3	0.6	21.4	23.7	22.6	5.1
O-asp-3	90.3	87.6	88.9	79.1	4.5	10.2	7.4	0.5	0.7	0	0.3	0	5.5	5.9	5.7	0.3
Mean	87.2	91.6	89.4	79.9	5.1	16.1	10.7	0.8	8.9	9.2	9.0	1.3	15.8	16.9	16.4	3.2

Note. Data are the estimated percentage of normal volume as assessed from MR images. Areas 11, 12, 13, and 14 = cytoarchitectonic subregions of the macaque frontal lobe as defined by Carmichael and Price (1994); ERh = entorhinal cortex; Ia = agranular insular area as defined by Carmichael and Price (1994); PRh = perirhinal cortex; L = percentage of damage to the left hemisphere; R = percentage of damage to the right hemisphere; Avg = average of L and R; W = (L × R)/100 (weighted index as defined by Hodos & Bobko, 1984); H-ibo = monkeys with neurotoxic lesions of the hippocampal formation; A-ibo = monkeys with neurotoxic lesions of the amygdala; O-ibo = monkeys with neurotoxic lesions of the orbital frontal cortex; O-asp = monkeys with aspiration lesions of the orbital frontal cortex.

shown for all cases in Group A-ibo in Table 3. Figure 2 depicts 2 representative monkeys: Case A-ibo-5 (see Figure 2, center column), with the most extensive and bilaterally symmetrical lesion, and Case A-ibo-3 (see Figure 2, right column), with the least and most unilateral damage.

Damage to the amygdala in 3 of the 6 cases (Cases A-ibo-4–6) was largely as intended, ranging from 80.2%–90.0% on average. For the remaining 3 monkeys (Cases A-ibo-1–3), the amygdala damage was greater on the right (range: 73.1%–88.1%) than the left (range: 20.6%–48.9%). Sparing of tissue in the left hemisphere was located in the anterior portion of the amygdala and included almost all nuclei in Cases A-ibo-1 and -3 (see Figure 2, right column, Levels +18 to +15), whereas sparing of tissue in Case A-ibo-2 was located mostly in the lateral portion of the amygdala through its entire anterior–posterior extent.

Finally, unintended damage was mild (see Table 3) and limited to the anterior hippocampal formation bilaterally in 4 monkeys (Cases A-ibo-1, -3, -4, and -6; see Figure 2, right column, Levels +14 and +13), the subjacent entorhinal cortex unilaterally in 2 monkeys (Cases A-ibo-1 and -5; see Figure 2, center column, Level +18), and the ventral putamen and tail of the caudate unilaterally in 1 monkey (Case A-ibo-5) and bilaterally in 3 monkeys (Cases A-ibo-3, -4, and -6).

Groups O-ibo and O-asp

The estimated percentage damage for the orbital frontal cortex (Areas 11 and 13) and unintended damage to adjacent regions in both the left and right hemispheres is shown for all cases in Groups O-ibo and O-asp in Table 3. Figure 3 depicts cases for each lesion type (Cases O-ibo-3 and O-asp-1). Extent of damage to Areas 11 and 13 in the 3 cases with ibotenic acid injections (Cases O-ibo-1–3) ranged from only 28.5% to 45.2% across hemispheres. The majority of the orbital frontal cortex surface area appears to have received damage in each case, but extensive sparing was observed throughout the deep cortical layers within Areas 11 and 13 (see arrow in Figure 3, center column). By contrast, the orbital lesions in the 3 cases with aspiration lesions (Cases O-asp-1–3) were largely as intended and bilaterally symmetrical (range: 87.5%–91.8%). In these latter cases, spared tissue was minimal and generally located at the most lateral and medial extremes of Areas 11 and 13 bilaterally (see arrows in Figure 3, right column). Unintended damage was mild across all cases in Group O-asp and limited to the neighboring cortical regions (Areas 10, 12, and 14) and the anterior agranular insular area.

Social Behavior Assessments

Dominance Hierarchy Assessments

Table 4 displays the pre- versus postsurgery data for both the dominance rankings and the food competition condition. None of the lesions consistently altered an experimental group's mean rank from pre- to postsurgery regardless of whether or not lesion groups were split into dominant and subordinate subgroups (Wilcoxon; ps $> .10$ with and without presurgical dominance rank considered). Likewise, for the food competition conditions, there were no significant main effects of group or phase and no Group $\times$ Phase interactions when all monkeys were pooled together, $F(3, 20) = 0.459$, $p = .71$, or when dominance rank was considered as a factor in the analysis, dominant: $F(3, 8) = 0.937$, $p = .47$; subordinate: $F(3, 8) = 1.97$, $p = .20$.

Personality Ratings

Ratings at the individual level. Table 5 displays the mean ratings for the three general personality categories (nonsocial, sociable, and interaction inhibiting) as well as for the specific personality labels within each general category. Personality labels such as active and exploratory were included in the general category of nonsocial because these adjectives relate more to how monkeys interact with the testing environment than with other group mates. Qualities such as confident, playful, affiliative, and popular tend to promote strong social bonds between adult male macaques and therefore were grouped into a general category of sociable. By contrast, qualities such as avoidant, solitary, manipulative, aggressive, anxious, excitable, and fearful inhibit strong positive social interactions and thus were categorized under the general label of interaction inhibiting. Repeated-measures ANOVAs (4 Groups $\times$ 2 Phases) were conducted separately for these three general personality categories, followed by similar analyses for each of the specific personality labels within each category, to determine if any general changes in personality were actually driven by more distinct alterations. Difference scores (postsurgery rating $-$ presurgery rating) for each operated group were also contrasted with all other operated groups.

Group C. From pre- to postsurgery, only interaction inhibiting qualities significantly increased ($p < .01$; see Table 5). This increase was mostly due to increased ratings for nearly all interaction inhibiting aspects of personality, such as solitary, avoidant, anxious, fearful, and aggressive (ps $< .05$; see Table 5).

Group H-ibo. Postsurgery, Group H-ibo also displayed significant increases in interaction inhibiting qualities ($p < .01$; see Table 5), as well as increases in nonsocial qualities and decreases in sociable traits that both fell just short of significance ($p = .08$ and $p = .09$, respectively). Like sham-operated controls, monkeys in Group H-ibo became more aggressive, solitary, avoidant, anxious, and fearful (ps $\leq .05$). However, Group H-ibo displayed additional changes not observed in Group C, such as decreases in affiliative ($p = .06$) and increases in excitable ($p < .05$) qualities. Furthermore, the difference score for nonsocial traits, particularly generalized activity, was greater in Group H-ibo than Group C ($p < .05$) but not significantly different from Groups A-ibo and O.

Group A-ibo. Postsurgery, Group A-ibo displayed an increase in both interaction inhibiting and nonsocial categories (both ps $<$ .05; see Table 5) associated with a decrease in the sociable category. Like monkeys in Groups C and H-ibo, those in Group A-ibo were rated as more aggressive, avoidant, and anxious (ps $< .05$) during the postsurgery phase relative to presurgery. Similar to Group H-ibo, Group A-ibo also exhibited robust increases in active and excitable (both ps $< .05$) and a decrease in affiliative ($p <$ .01) qualities. Finally, the changes in personality that were shown only by Group A-ibo included a significant increase in the exploratory quality ($p < .05$) and a decrease in the popular quality that fell just short of significance ($p = .09$). The difference scores for excitable, active, affiliative, and nonsocial qualities were all greater for Group A-ibo than Group C (ps $< .05$) but not significantly different from Groups H-ibo or O.

Group O. As compared with the other three groups, Group O displayed the fewest changes in personality between the pre- and postsurgery phases (see Table 5). This group showed only a significant increase in interaction inhibiting qualities ($p < .05$), which seems to have been due to increased ratings of avoidant ($p = .01$) and a nearly significant decrease in sociable ($p = .07$) qualities. Unlike the three other groups, Group O did not change

Table 4
Dominance Assessment Data

Measure & grouping of data	Group C		Group H-ibo		Group A-ibo		Group O	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Dominance rankings								
Overall ($n = 6$)	2.0 ± .42	2.2 ± .51	2.5 ± .40	2.4 ± .44	2.6 ± .57	2.7 ± .44	2.9 ± .42	2.6 ± .47
Dominant ($n = 3$)	1.1 ± .04	1.0 ± .04	1.7 ± .11	1.5 ± .18	1.4 ± .26	1.8 ± .08	2.0 ± .04	1.6 ± .22
Subordinate ($n = 3$)	2.9 ± .15	3.3 ± .31	3.3 ± .33	3.3 ± .33	3.8 ± .17	3.8 ± .25	3.8 ± .15	3.6 ± .26
Food competition								
Overall ($n = 6$)	32.5 ± 11.0	31.4 ± 11.0	23.8 ± 11.4	15.1 ± 9.5	27.5 ± 11.6	33.5 ± 15.6	15.6 ± 9.4	19.4 ± 9.3
Dominant ($n = 3$)	54.3 ± 11.0	51.6 ± 9.1	44.7 ± 14.4	28.1 ± 16.7	50.9 ± 11.2	64.9 ± 15.0	30.3 ± 14.8	38.8 ± 7.5
Subordinate ($n = 3$)	10.6 ± 1.6	11.1 ± 10.7	3.0 ± 2.6	2.0 ± 1.3	4.2 ± 2.4	2.0 ± 2.0	0.7 ± 0.4	0.0 ± 0.0

Note. Data are the presurgery (Pre) and postsurgery (Post) mean (± *SEM*) social ranking (dominance ranking: 1 = highest, 4 = lowest) and mean percentage (± *SEM*) of total preferred foods collected (food competition: 135 foods maximum) for each experimental group (overall) and for dominant and subordinate subgroups. C = monkeys with sham operations; H-ibo = monkeys with neurotoxic lesions of the hippocampal formation; A-ibo = monkeys with neurotoxic lesions of the amygdala; O = monkeys with neurotoxic or aspiration lesions of the orbital frontal cortex.

Table 5
Individual Personality Rating Data

	Group C			Group H-ibo			Group A-ibo			Group O		
General category	Pre	Post	Dif	Pre	Post	Dif	Pre	Post	Dif	Pre	Post	Dif
Nonsocial	2.9 ± .21	2.7 ± .13	−0.2 ± .16	2.8 ± .13	3.2 ± .08†	0.4 ± .16#	3.0 ± .13	3.5 ± .08*	0.5 ± .13##	3.0 ± .20	3.0 ± .23	0.0 ± .11
Active	3.2 ± .21	3.0 ± .13	−0.2 ± .14	3.1 ± .24	3.5 ± .14	0.4 ± .21#	3.4 ± .18	3.9 ± .15*	0.5 ± .15#	3.4 ± .20	3.5 ± .27	0.1 ± .10
Exploratory	2.6 ± .24	2.4 ± .15	−0.2 ± .21	2.6 ± .08	2.9 ± .24	0.3 ± .23	2.6 ± .15	3.2 ± .17*	0.6 ± .16	2.5 ± .13	2.5 ± .23	0.0 ± .18
Sociable	3.0 ± .25	2.7 ± .24	−0.3 ± .17	2.7 ± .35	2.4 ± .22†	−0.3 ± .14	2.6 ± .36	2.2 ± .25	−0.4 ± .19	2.6 ± .15	2.2 ± .18†	−0.4 ± .16
Confident	3.6 ± .29	3.2 ± .38	−0.3 ± .16	3.0 ± .46	2.8 ± .47	−0.2 ± .13	2.9 ± .54	3.0 ± .47	0.1 ± .23	2.7 ± .32	2.7 ± .38	0.0 ± .09
Popular	3.2 ± .36	3.1 ± .34	−0.1 ± .15	2.8 ± .43	2.5 ± .24	−0.3 ± .23	2.7 ± .46	2.1 ± .22†	−0.6 ± .32	2.7 ± .25	2.3 ± .28	−0.4 ± .20
Affiliative	3.3 ± .16	3.1 ± .13	−0.1 ± .18	3.1 ± .26	2.6 ± .16†	−0.5 ± .19	3.0 ± .30	2.4 ± .22**	−0.6 ± .12#	3.1 ± .11	2.6 ± .19*	−0.5 ± .19
Playful	2.0 ± .39	1.4 ± .23	−0.6 ± .29	1.8 ± .37	1.5 ± .32	−0.3 ± .20	1.7 ± .25	1.5 ± .32	−0.2 ± .23	1.8 ± .27	1.3 ± .15	−0.5 ± .29
Interaction inhibiting	1.9 ± .16	2.4 ± .11**	0.5 ± .10	1.9 ± .17	2.6 ± .12**	0.7 ± .13	2.3 ± .20	2.7 ± .22**	0.4 ± .12	2.2 ± .20	2.5 ± .16*	0.3 ± .12
Solitary	1.5 ± .24	2.1 ± .19**	0.6 ± .14	1.7 ± .29	2.5 ± .26**	0.8 ± .17	2.1 ± .41	2.6 ± .54	0.5 ± .26	2.0 ± .26	2.5 ± .43	0.5 ± .27
Avoidant	1.5 ± .28	2.3 ± .26*	0.8 ± .25	1.9 ± .44	2.7 ± .33**	0.8 ± .16	1.9 ± .48	2.5 ± .56**	0.6 ± .15	2.2 ± .41	2.6 ± .37**	0.4 ± .10
Anxious	2.0 ± .24	2.6 ± .27**	0.6 ± .12	2.2 ± .29	2.9 ± .33**	0.7 ± .10	2.7 ± .41	3.3 ± .38**	0.6 ± .16	2.7 ± .27	2.9 ± .27	0.2 ± .24
Fearful	1.5 ± .25	2.1 ± .27*	0.6 ± .21	1.8 ± .39	2.3 ± .41**	0.5 ± .10	2.1 ± .53	2.4 ± .54	0.3 ± .16	2.2 ± .43	2.6 ± .31	0.4 ± .31
Excitable	1.9 ± .26	2.1 ± .22	0.2 ± .18	1.8 ± .32	2.8 ± .17*	0.9 ± .33	2.4 ± .31	3.4 ± .33**	1.0 ± .23#	2.1 ± .26	2.6 ± .41	0.5 ± .33
Aggressive	2.4 ± .29	2.9 ± .18*	0.5 ± .15	2.0 ± .30	2.6 ± .38*	0.6 ± .17	2.2 ± .30	3.0 ± .43*	0.8 ± .32	2.4 ± .32	2.8 ± .30	0.4 ± .34
Manipulative	2.5 ± .44	2.8 ± .37	0.3 ± .46	2.2 ± .49	2.1 ± .36	−0.1 ± .34	2.6 ± .57	2.0 ± .40	−0.6 ± .40	1.6 ± .28	1.8 ± .32	0.2 ± .37

Note. Data are the mean presurgery (Pre), postsurgery (Post), and difference score (Dif = Post − Pre) personality rating (± *SEM*) for each experimental group. C = monkeys with sham operations; H-ibo = monkeys with neurotoxic lesions of the hippocampal formation; A-ibo = monkeys with neurotoxic lesions of the amygdala; O = monkeys with neurotoxic or aspiration lesions of the orbital frontal cortex.

† $.10 > p > .05$, within-group comparison (Pre vs. Post). * $p < .05$, within-group comparison (Pre vs. Post). ** $p \leq .01$, within-group comparison (Pre vs. Post). # $p < .05$, between-groups comparison of Dif for Group C versus each operated group. ## $p \leq .01$, between-groups comparison of Dif for Group C versus each operated group.

appreciably in qualities such as aggressive and anxious, although, like Groups H-ibo and A-ibo, Group O showed a decrease in affiliative ratings ($p < .05$). Difference scores for all personality categories did not differ appreciably between Group O and any other experimental group.

Ratings at the dyad level. The alterations in individual personality qualities described above for each lesion group likely influenced the social dynamic of each tetrad, but it is not clear whether these changes impacted relationships with all possible partners equally or only with specific ones. Thus, dyadic personality ratings were also analyzed to investigate this specific question (see Table 6).

All dyads displayed a decrease in sociable dyadic interactions between pre- and postsurgery. These decreased ratings of sociable reached significance only for A-ibo + H-ibo and A-ibo + O dyads (ps $< .05$) but approached significance for all other dyads except the C + O dyads. The decrease in sociable ratings mostly derived from a reduction in ratings of affiliative because ratings of playful from pre- to postsurgery did not change appreciably for any dyad.

Interaction inhibiting ratings, by contrast, increased significantly for all dyads (ps $< .01$) except the C + O dyads (see Table 6). This increase in interaction inhibiting ratings was mostly due to an increase in agonistic, tense, and avoidant interactions between monkeys with a hippocampal or amygdaloid lesion and all other partners (ps $\leq .07$).

Total Frequency and Duration of Behaviors

Because only the Group × Phase interactions specifically identify changes in behavior that occurred between the pre- and postsurgical phases, the main effects of group and phase have been omitted to simplify the description of the data below.

Nonsocial and self-directed behaviors. None of the experimental groups displayed any changes in behaviors listed in the categories of self-directed, anxious, or exploratory from pre- to postsurgery. However, for two of the specific behaviors in the avoidant–solitary category (e.g., withdrawal initiate and locomotion; see Figure 5), a significant Group × Phase interaction was found. Specifically, the Group × Phase interaction was significant for the frequency of withdrawal initiate in dominant monkeys only, $F(3, 8) = 6.61$, $p < .05$. Post hoc analyses revealed that high-ranking monkeys from Group H-ibo withdrew significantly less from social interactions after surgery relative to presurgery ($p < .05$; see Figure 5A). Furthermore, this change in behavior for Group H-ibo was uniform across all 3 partners in the social group.

The Group × Phase interaction for the duration of locomotion approached significance for subordinate monkeys only, $F(3, 8) = 3.82$, $p = .06$. Post hoc analyses showed that, relative to presurgery, low-ranking monkeys of both Groups O and H-ibo showed an increase in nonsocial locomotion that was more robust in Group O ($p < .05$; see Figure 5B) than in Group H-ibo ($p = .07$).

Social and dominance-related behaviors. None of the experimental groups displayed changes for the categories of affiliative social behaviors or affiliative social signals or for any of the specific behaviors within each of these two categories. However, a significant Group × Phase interaction was detected for the frequency of dominance-related behaviors initiate, $F(3, 20) = 5.63$, $p < .01$, which was due to an increase in dominance-related behaviors initiated by Group A-ibo only ($p < .01$; see Figure 6A).

Table 6
Dyadic Personality Rating Data

	C + H-ibo dyads		C + A-ibo dyads		C + O dyads		H-ibo + A-ibo dyads		H-ibo + O dyads		A-ibo + O dyads	
General category	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Sociable	2.4 ± .23	2.1 ± .20†	2.0 ± .31	1.7 ± .20†	2.3 ± .25	1.8 ± .20	2.0 ± .30	1.7 ± .22*	2.0 ± .22	1.6 ± .13†	2.0 ± .24	1.5 ± .15*
Affiliative	3.3 ± .26	2.8 ± .33†	2.5 ± .36	2.0 ± .23†	3.0 ± .35	2.5 ± .38	2.6 ± .46	1.9 ± .37*	2.6 ± .35	2.0 ± .26†	2.6 ± .33	1.8 ± .21**
Playful	1.6 ± .30	1.3 ± .17	1.5 ± .28	1.3 ± .19	1.6 ± .31	1.1 ± .06	1.4 ± .19	1.4 ± .27	1.4 ± .19	1.1 ± .09†	1.5 ± .18	1.2 ± .16
Interaction inhibiting	1.8 ± .28	2.6 ± .22**	2.3 ± .31	3.1 ± .22**	2.3 ± .28	2.7 ± .28	2.0 ± .35	3.3 ± .32**	2.3 ± .21	3.1 ± .17**	2.5 ± .27	3.3 ± .12**
Agonistic	1.7 ± .26	2.6 ± .20**	2.0 ± .20	2.8 ± .25†	2.3 ± .33	2.7 ± .37	1.9 ± .37	2.8 ± .31*	2.2 ± .12	2.8 ± .28†	2.2 ± .23	2.9 ± .33
Tense	2.0 ± .32	2.8 ± .25**	2.6 ± .32	3.4 ± .27**	2.5 ± .29	2.9 ± .32	2.0 ± .36	3.4 ± .31**	2.5 ± .22	3.2 ± .15*	2.7 ± .28	3.5 ± .18*
Avoidant	1.6 ± .31	2.4 ± .25*	2.4 ± .48	3.2 ± .40**	2.1 ± .36	2.5 ± .31	2.0 ± .43	3.6 ± .52**	2.3 ± .35	3.2 ± .26**	2.5 ± .40	3.5 ± .43**

Note. Data are mean (± *SEM*) personality ratings for all possible dyads within a tetrad during presurgery (Pre) and postsurgery (Post) interactions. C = monkeys with sham operations; H-ibo = monkeys with neurotoxic lesions of the hippocampal formation; A-ibo. = monkeys with neurotoxic lesions of the amygdala; O = monkeys with neurotoxic or aspiration lesions of the orbital frontal cortex.
† $.10 > p > .05$, Pre versus Post comparison. * $p < .05$, Pre versus Post comparison. ** $p \leq .01$, Pre versus Post comparison.

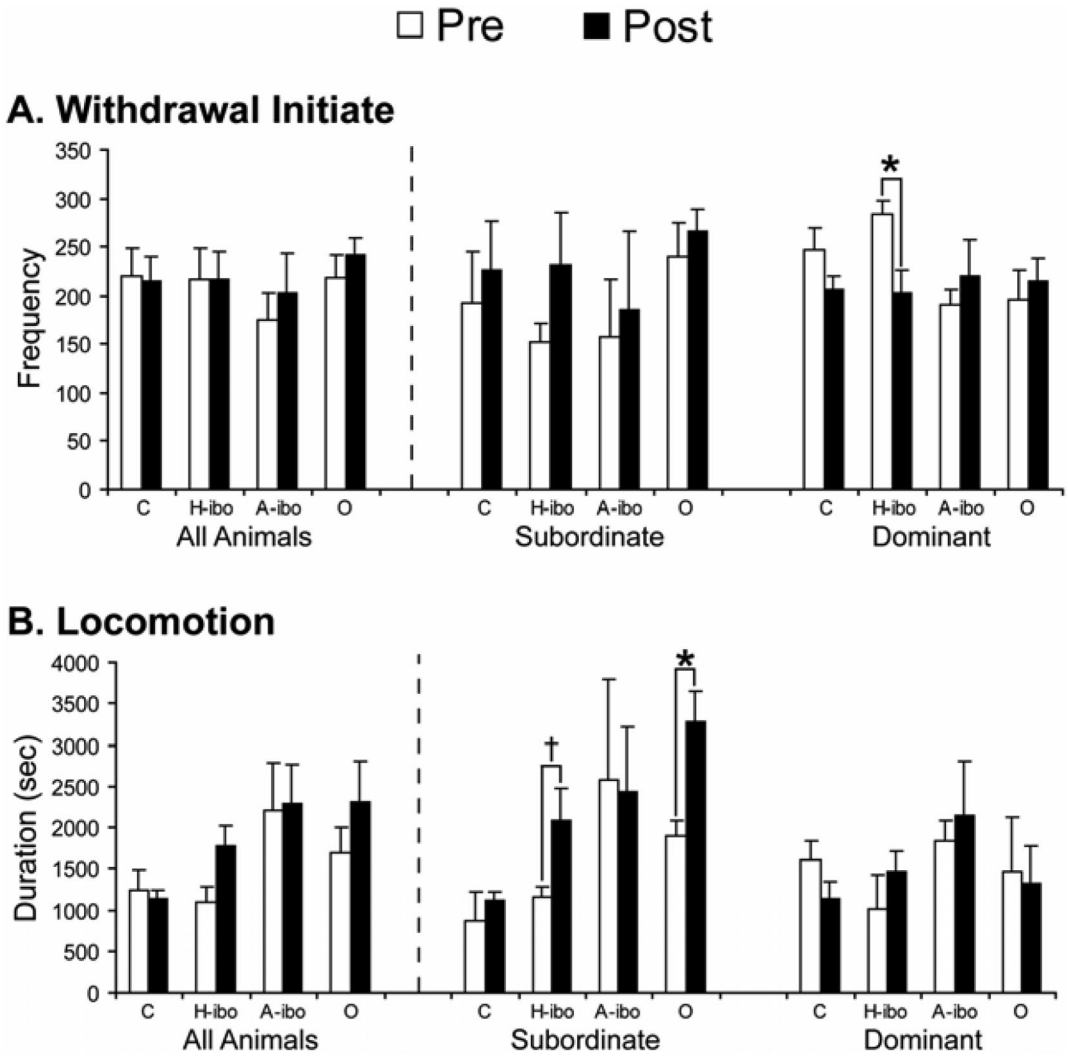


Figure 5. Cumulative frequency of withdrawal initiate (A) and cumulative duration of locomotion (in seconds; B) averaged across all monkeys in each group (left panel) and for the dominant and subordinate monkeys in each group separately (right panels) before surgery (Pre; white bars) and after surgery (Post; black bars). Error bars indicate the standard error of the mean. C = monkeys with sham operations; H-ibo = monkeys with neurotoxic lesions of the hippocampal formation; A-ibo = monkeys with neurotoxic lesions of the amygdala; O = monkeys with neurotoxic or aspiration lesions of the orbital frontal cortex. †$.05 < p < .10$. *$p < .05$.

This increase occurred mostly for one particular behavior, the crooktail (Wilcoxon; $p < .05$).

Similarly, there was a Group × Phase interaction for the frequency of threat initiate, $F(3, 8) = 4.735$, $p < .05$, for dominant monkeys only. Post hoc tests showed that, relative to the presurgery phase, high-ranking monkeys in Group O initiated more threatening gestures in the postsurgery phase ($p < .05$; see Figure 6B) to all other partners.

Finally, there was a Group × Phase interaction for the frequency of aggressive behaviors receive for dominant monkeys only, $F(3, 8) = 4.735$, $p < .05$. Post hoc tests revealed that high-ranking Group O monkeys received more aggressive behaviors from all other partners in the postsurgery phase ($p < .05$; see Figure 6C).

Lag-Sequential Analysis

Responses to threatening gestures. Figure 7 depicts the estimated log odds ratio (or probability) of initiating a particular type of behavioral response within 10 s after receiving a threatening gesture from any partner in the social group (mean across all possible partners; see Figure 7A) or from a specific partner within the group (see Figures 7B–7D). Groups C and H-ibo did not show any changes in how they responded to threatening gestures between the pre- and postsurgery phases. However, as shown in Figure 7A, after receiving a threat gesture from any partner in the tetrad, all monkeys in Group A-ibo showed a decreased tendency to initiate affiliative social signals ($p < .05$). Furthermore, after receiving a threat from sham-operated controls, Group A-ibo was

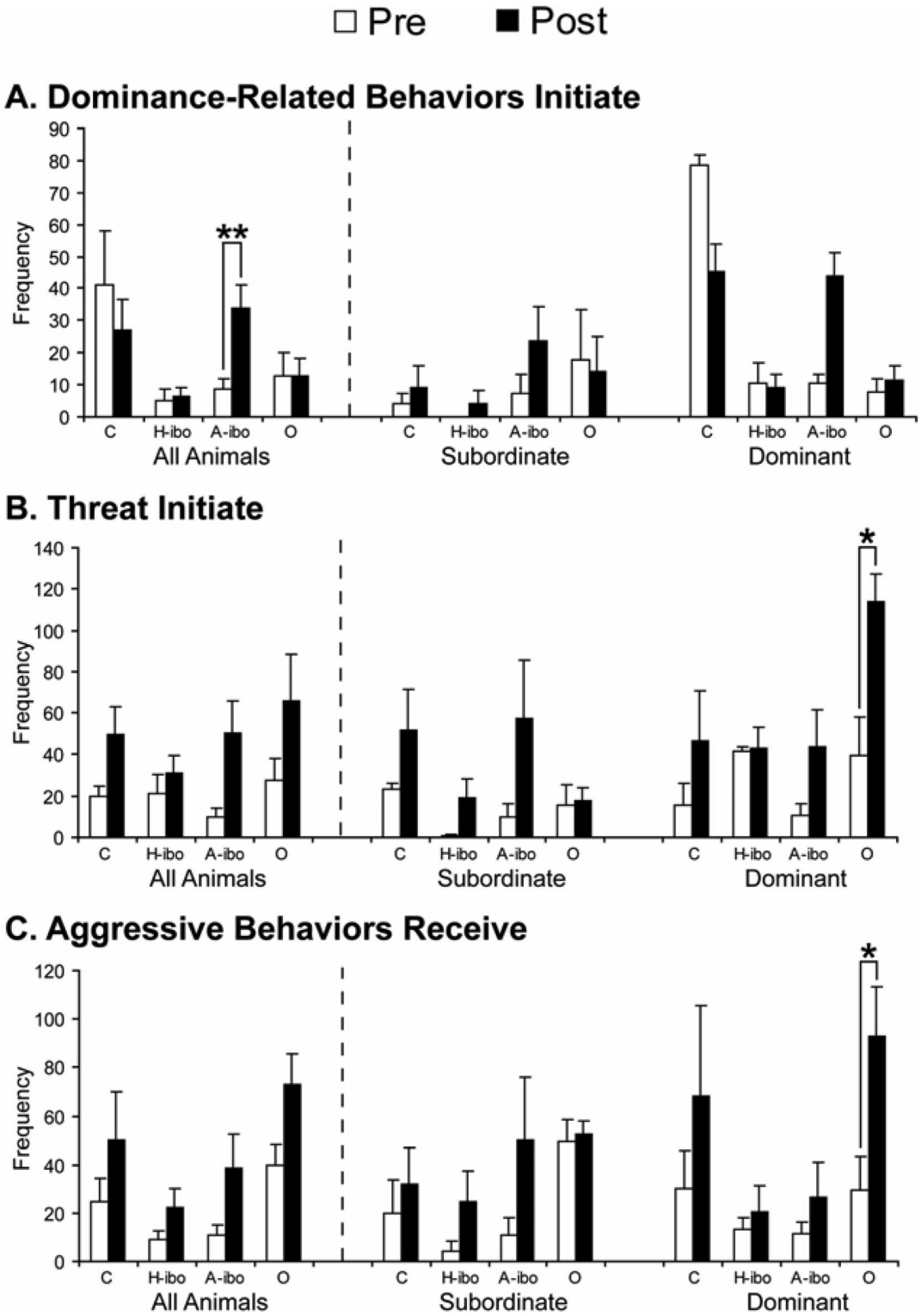


Figure 6. Cumulative frequency of dominance-related behaviors initiate (A), threat initiate (B), and aggressive behaviors receive (C) averaged across all monkeys in each group (left panel) and for the dominant and subordinate monkeys in each group separately (right panels) before surgery (Pre; white bars) and after surgery (Post; black bars). Error bars indicate the standard error of the mean. C = monkeys with sham operations; H-ibo = monkeys with neurotoxic lesions of the hippocampal formation; A-ibo = monkeys with neurotoxic lesions of the amygdala; O = monkeys with neurotoxic or aspiration lesions of the orbital frontal cortex. *$p < .05$. **$p \leq .01$.

also less prone to initiate dominance-related behaviors ($p < .05$; see Figure 7B), although this change was significant only for the subordinate monkeys in this group ($p < .05$).

Finally, when threatened by monkeys in Group C, subordinate members of Group O initiated more affiliative social signals ($p = .06$; see Figure 7C). By contrast, when threatened by monkeys in Group H-ibo, dominant members of Group O initiated fewer aggressive behaviors ($p < .01$; see Figure 7D).

Responses to mount solicitations. Figure 8 depicts the probability of initiating a mount following a mount solicitation from any partner in general (see Figure 8A) or from monkeys in Group C (see Figure 8B). When solicited by any partner in general, Group C showed a greater tendency to initiate a mount ($p < .01$). This change was especially true for the subordinate members of Group C ($p = .01$). When solicited by monkeys in Group C, dominant members of Group H-ibo and all monkeys of Group O showed a decreased tendency to initiate a mount ($p < .01$ and $p < .05$, respectively).

Responses to groom solicitations. Analysis of each group's tendency to initiate a groom when solicited indicated that none of the groups altered their tendency to respond appropriately. This was true for all lesion groups whether considering dominance rank or not and whether considering specific partners or not.

Correlations Between Lesion Damage and Behavioral Measures

There were few significant correlations between intended or unintended damage and behavioral measures, and all were for Group O. First, a significant negative correlation was found between intended damage to Areas 11 and 13 and the frequency of threat initiate ($r = -.95$, $p < .01$) and of aggression receive ($r = -.846$, $p < .05$) behaviors during the postsurgery testing phase, indicating that the increases in these behaviors were seen predominantly in cases with less extended lesions, especially those with the smallest ibotenic acid lesions (Cases O-ibo-1 and -2). Interestingly, these 2 O-ibo cases not only showed the highest levels of threat initiate and aggression receive behaviors in the postsurgery phase but were also 2 of the 3 monkeys in Group O categorized as dominant by the presurgery testing. Therefore, a complex interplay between social dominance and lesion extent appears to be driving this negative correlation. Second, unintended damage to agranular insular area correlated positively with the frequency of threat initiate behavior ($r = .825$, $p < .05$), indicating that inadvertent damage to this area may have amplified this behavioral change, especially for Cases O-ibo-1, -2, and -3.

Summary

None of the lesions studied here appreciably disrupted a tetrad's established dominance hierarchy either when measured subjectively (experimenter rankings) or more empirically (food competition). However, changes in personality ratings (individual and dyadic) as well as frequency, duration, and timing of social behaviors were found in all groups, including control monkeys, but the specific pattern of behavioral changes differed between groups.

Sham-operated control monkeys displayed increases in several personality categories that do not promote prolonged positive social interactions, such as avoidance, fear, aggression, and anxiety. Furthermore, established relationships between control monkeys and those with hippocampal or amygdala lesions were rated as more agonistic, avoidant, and tense, as well as less affiliative, after surgery but did not change appreciably between control monkeys and those with orbital frontal lesions. Finally, control monkeys tended to respond more often to mount solicitations with mounts in the postsurgery phase.

Degradation of social bonds between familiar control and hippocampal-operated monkeys may have been fostered by similar, but even more severe, changes in personality for monkeys in Group H-ibo (i.e., increases in generalized activity and excitability not observed for Group C). Furthermore, hippocampal-operated monkeys also displayed an important change in how they responded to social signals. Dominant monkeys with hippocampal lesions became less likely to mount when solicited by control monkeys after surgery, whereas control monkeys became more likely to mount when solicited by any partner in general.

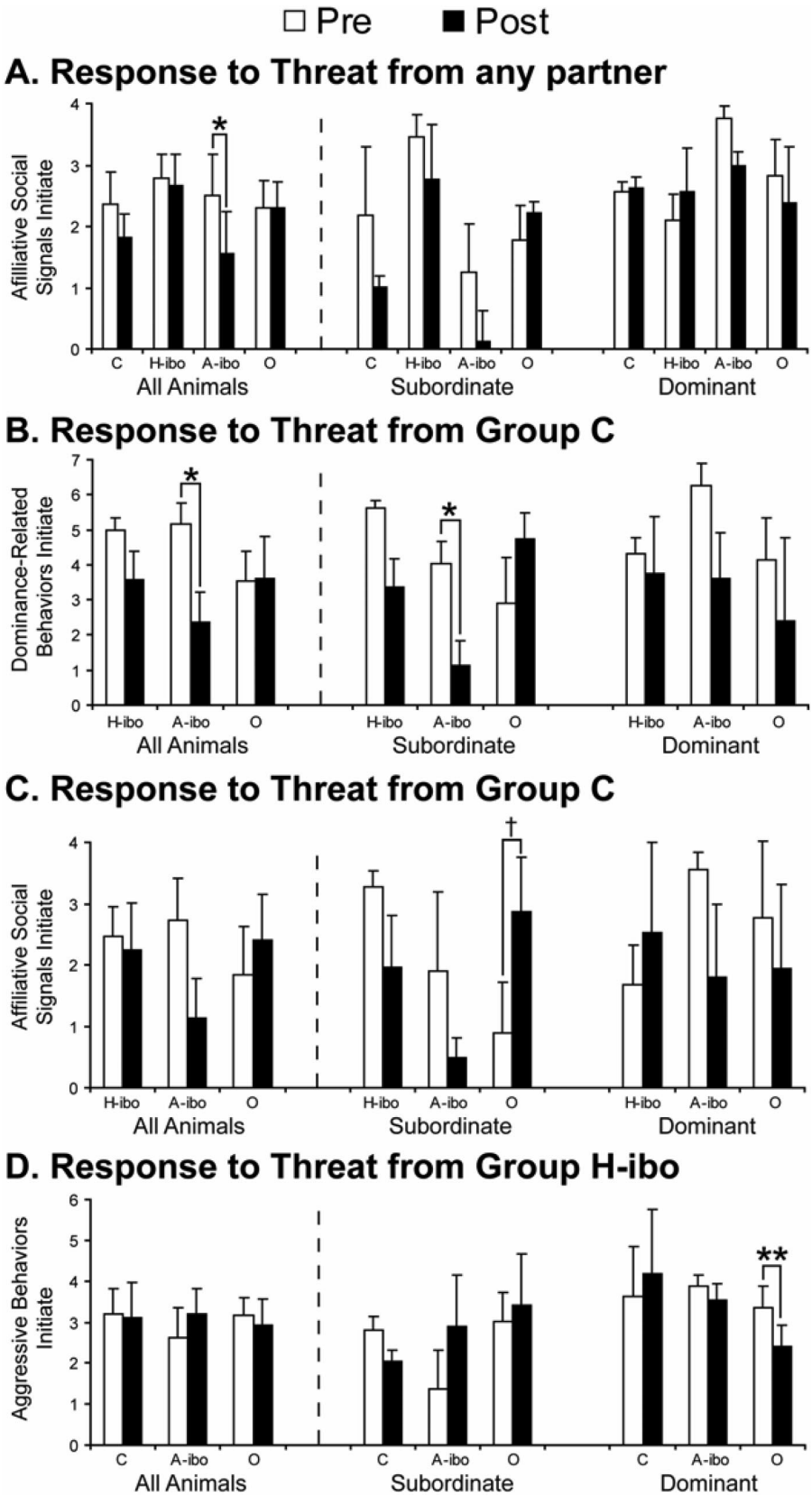
Like Group H-ibo, the degradation of social bonds observed for Group A-ibo could also be attributed to this group's increase in personality qualities (beyond that observed for Group C) that do not promote strong, positive social interactions (i.e., excitability, generalized activity, and nonsocial cage exploration). Group A-ibo also displayed notable decreases in ratings for more positive personality qualities such as affiliation with others and popularity within the social group. Furthermore, Group A-ibo showed an overall increased frequency of dominance-related signals from pre- to postsurgery, a change not exhibited by any other experimental group. Finally, Group A-ibo was the only group that became less likely to respond to threatening gestures with dominance-related gestures or affiliative social signals.

By contrast, monkeys with orbital frontal lesions differed from all other experimental groups in that they did not show commensurate increases in fearful, anxious, excitable, or exploratory personality ratings in the postsurgery phase. Furthermore, dyadic social relationships (both affiliative and aggressive) between familiar control monkeys and monkeys with orbital frontal lesions did not change appreciably between the two testing phases. However, orbital frontal lesions increased the monkeys' tendency to participate in aggressive encounters with all familiar partners after surgery, in the form of both more threatening gestures initiated and more contact aggression received. Finally, monkeys with orbital frontal cortex lesions were the only group to display significant changes in how they responded to both threatening and affiliative social signals.

Discussion

Social Rank

A key component in social cognition is the ability to predict what others will do at any given moment or across various contexts. Several factors can aid in these predictions, such as recognizing the meaning of communicative displays and knowing how animals of various dominance ranks typically act (Cheney & Seyfarth, 1990; Tomasello & Call, 1997). Dominance rank heavily dictates the behavioral options available to an individual. Dominant monkeys typically gain access to resources (food, shelter, mates, etc.) more readily, initiate more disciplinary forms of aggression, and receive more submissive or affiliative behaviors than


Pre
Post
A. Response to Threat from any partner
Affiliative Social Signals Initiate
C
H-ibo
A-ibo
O
All Animals
Subordinate
Dominant
B. Response to Threat from Group C
Dominance-Related Behaviors Initiate
C. Response to Threat from Group C
Affiliative Social Signals Initiate
D. Response to Threat from Group H-ibo
Aggressive Behaviors Initiate

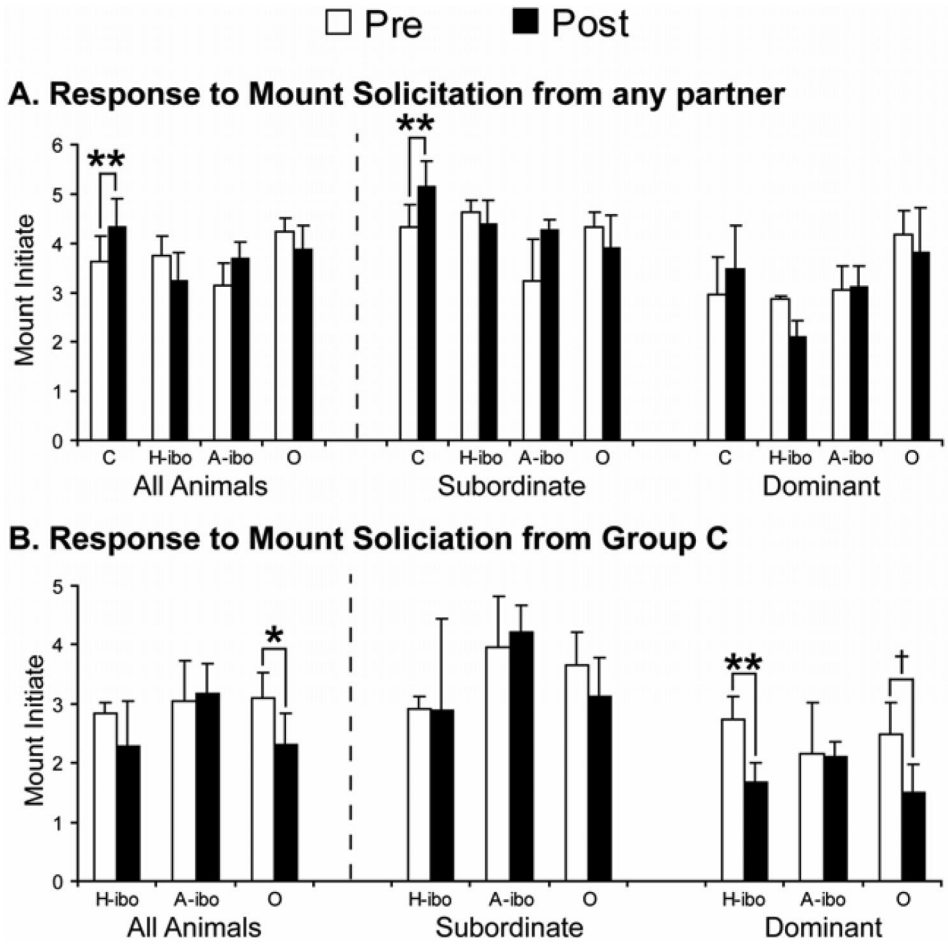


Figure 8. Estimated log odds ratio (or probability) of initiating a mount when solicited by any partner in general (A) or by monkeys in Group C (B) averaged across all monkeys in each group (left panel) and for the dominant and subordinate monkeys in each group separately (right panels) before surgery (Pre; white bars) and after surgery (Post; black bars). Error bars indicate the standard error of the mean. C = monkeys with sham operations; H-ibo = monkeys with neurotoxic lesions of the hippocampal formation; A-ibo = monkeys with neurotoxic lesions of the amygdala; O = monkeys with neurotoxic or aspiration lesions of the orbital frontal cortex. †$.05 < p < .10$. *$p < .05$. **$p \leq .01$.

their subordinate counterparts. By contrast, the behavior of subordinate monkeys is under the constant scrutiny of dominant group mates, and accordingly, subordinate monkeys typically show higher levels of generalized anxiety or fear of higher ranked conspecifics, as well as receiving fewer affiliative interactions and less access to resources (Chase, 1984; Cheney & Seyfarth, 1990). Dominance rank in macaque monkeys is acquired early in life (for review, see Machado & Bachevalier, 2003), and asymmetries in agonistic interactions indicate that dominance rank is recognized and used by members of the troop to guide behavior (Cheney &

Figure 7 (opposite). Estimated log odds ratio (or probability) of initiating affiliative social signals after receiving a threat from any partner in general (A), probability of initiating dominance-related behaviors (B) or affiliative social signals (C) after receiving a threat from Group C, and probability of initiating aggressive behaviors after receiving a threat from Group H-ibo (D), averaged across all monkeys in each group (left panel) and for the dominant and subordinate monkeys in each group separately (right panels) before surgery (Pre; white bars) and after surgery (Post; black bars). Error bars indicate the standard error of the mean. C = monkeys with sham operations; H-ibo = monkeys with neurotoxic lesions of the hippocampal formation; A-ibo = monkeys with neurotoxic lesions of the amygdala; O = monkeys with neurotoxic or aspiration lesions of the orbital frontal cortex. †$.05 < p < .10$. *$p < .05$.

Seyfarth, 1990). Furthermore, the formation of dominance hierarchies within groups of unfamiliar macaques occurs after only a few minutes of interaction and remains extremely stable over time regardless of the outcome of subsequent social interactions (Barchas & Mendoza, 1984). Given several previous reports suggesting that presurgical dominance rank can significantly influence the behavioral changes resulting from frontal and temporal lobe damage (for review, see Kling & Brothers, 1992), the present study was specifically designed such that each experimental group was balanced with respect to presurgical dominance rank, and the behavioral data were analyzed both with and without dominance included as a main factor. In addition, we used more empirical methods of dominance assessment than those used in previous reports.

One of the most surprising results of the present study is the lack of changes in preestablished dominance rank following damage to either the amygdala or the orbital frontal cortex. These findings seem to contradict earlier reports demonstrating significant alterations in dominance rank following lesions of the amygdaloid complex and ventral frontal cortex (Brody & Rosvold, 1952; Rosvold et al., 1954). There are several factors that could account for these discrepant results. First, in the present study, the lesions were more confined to the amygdaloid nuclei or Areas 11 and 13 of the orbital frontal cortex than those in earlier studies, thus avoiding damage to adjacent cortical fields (i.e., the ento- and perirhinal cortices adjacent to the amygdala and Areas 12 and 14 on the ventral frontal cortex) that could by itself or in combination with the amygdala or orbital frontal cortex damage have resulted in the decreases in dominance rank observed previously. Another potential factor relates to the social context in which the monkeys were tested. Previous studies indicating changes in dominance status after amygdala or ventral frontal lesions placed operated monkeys into larger social groups than the tetrads studied here, and those monkeys interacted with several unoperated peers (for review, see Bachevalier & Meunier, 2005; Kling & Brothers, 1992). Thus, the lack of changes in dominance status in the present study could have arisen from the amygdala- and orbital frontal–operated monkeys being placed in a comparatively less challenging social context. Finally, another factor relates to the number of reunions operated monkeys have with other members of their social group. Interestingly, Butter and Snyder (1972) observed monkeys' agonistic behavior prior to and after receiving orbital frontal lesions when these monkeys were introduced singly into an established group of 4 normal monkeys. Prior to surgery, the to-be-operated monkeys were older and heavier than the other 4 normal members of the group and therefore rapidly acquired a dominant status. Following the orbital lesions, when the operated monkeys were reintroduced in the group, these monkeys exhibited a higher degree of aggression and initially achieved the top dominance position again. However, because this reintroduction procedure was repeated every 2 months, Butter and Snyder were also able to observe that over time, the operated monkeys eventually lost their ability to reclaim their dominant status. It is therefore possible that changes in dominance status could have occurred in the present study if the operated monkeys had been replaced in their social groups at more staggered time points following the surgical intervention. Thus, additional studies investigating the effects of amygdala and orbital frontal lesions need to assess the effects of each lesion in even larger, more challenging social groups and over longer periods of time.

Although lesions of the amygdala, orbital frontal cortex, and hippocampal formation did not drastically affect social rank, all three lesions resulted in altered social behavior. Interestingly enough, the nature of behavioral deficits observed in preestablished social groups differed between the three types of lesions.

The Amygdala, Behavioral Restraint, and Response to Threat

In the present study, monkeys with amygdala lesions displayed profound changes in overall personality, such as increased ratings of excitability, activity, cage exploration, aggression, anxiety, and social avoidance, as well as decreased ratings of affiliation and popularity within the group, as compared with presurgical assessments. Dyadic personality rating data indicated that these changes in personality may have severely degraded social relationships with all other members of their social group. The increases in excitability, activity, and cage exploration are consistent with several earlier reports indicating hypermetamorphosis (monkeys' compulsory impulse to attend and react to all stimuli) after large temporal lobe lesions, including the amygdala and surrounding cortex (for review, see Bachevalier & Meunier, 2005). Although decreases in aggression have typically been reported following amygdala damage (for review, see Kling & Brothers, 1992), increased aggression has also been reported in certain social contexts following damage to the medial temporal lobe, which includes the amygdala (Rosvold et al., 1954). These consistencies between the results generated here and several previous reports add weight to the idea that the amygdala is a critical neural structure for restraining inappropriate or potentially dangerous behavior.

However, the increases in anxiety observed here following amygdala damage would seem to be at odds with several recent studies that showed a consistent lack of fear and avoidance of dangerous stimuli (such as a rubber snake) following bilateral neurotoxic amygdala lesions (Izquierdo, Suda, & Murray, 2005; Kalin, Shelton, Davidson, & Kelley, 2001; Meunier, Bachevalier, Murray, Málková, & Mishkin, 1999) or combined unilateral lesions of the amygdala and orbital frontal cortex (Izquierdo & Murray, 2004). Furthermore, our observation that monkeys with amygdala lesions displayed increased social avoidance and decreased affiliative interactions also seems to conflict with results generated recently by Emery and colleagues (2001), who found a lack of wariness of unfamiliar conspecifics and heightened affiliative social behaviors initiated by monkeys with neurotoxic amygdala lesions relative to controls. Although the lesion method and extent of amygdala damage are quite similar between the present report and these earlier studies, the discrepancies in results could again be due to the context under which the amygdala-lesion monkeys were observed in each study. As mentioned briefly above, Rosvold and colleagues (1954) found that the effect of amygdala damage varied from increased submissive behavior and a drastic decrease in social rank to hyperaggression and increase in rank depending upon the specific social context in which the operated monkeys were observed. The four-member social groups used here certainly provided the amygdala-operated monkeys with a very different environment in which to act than the constrained and unconstrained dyadic social groups (Emery et al., 2001) or

Wisconsin General Testing Apparatus (Izquierdo & Murray, 2004; Izquierdo et al., 2005; Kalin et al., 2001; Meunier et al., 1999) used in the previous reports. Furthermore, given the increased tendency of monkeys with amygdala lesions to explore the environment, the use of completely unfamiliar partners for social interactions by Emery and colleagues (2001) as compared with familiar partners in the present study may explain the enhanced affiliative behaviors observed in the earlier study. Therefore, the role of the amygdala in social avoidance, anxiety, and affiliation appears to be quite complex and certainly warrants further study in multiple social contexts.

Despite these rather profound changes in personality, amygdala-operated monkeys showed very few changes in the actual frequency or duration of social and nonsocial behaviors measured from videotaped interactions. Only dominance-related behaviors, such as crooktails, increased significantly for this group as a whole between the pre- and postsurgery testing phases. This specific change in behavior following an amygdala lesion has not been previously reported. It is also interesting to note that although they displayed more signals related to social dominance, monkeys with amygdala lesions did not increase in social dominance rank on average. This would seem to indicate that although amygdalectomized monkeys were emitting more behaviors typically used to increase social status, these signals were not acknowledged by the other members of their social group. Again, these results contrast with the increase in social behaviors, such as mount solicitations, mounts, and proximity, reported by Emery and colleagues (2001). This discrepancy between these two studies could again be a result of several factors, such as the differing social context under which the operated monkeys were observed (groups of two for Emery et al., 2001; groups of four here) and the familiarity of social partners (unfamiliar for Emery et al., 2001; familiar here), as well as the average age of the monkeys (~6 years old for Emery et al., 2001; ~2.9 years old here). Age could be an important factor responsible for the differences in aggressive gestures given that in adolescence (i.e., 2–3 years of age), male macaques typically initiate and receive heightened levels of aggressive behaviors (for review, see Machado & Bachevalier, 2003).

One of the most interesting and novel findings generated by the current study is that monkeys with amygdala lesions displayed significant changes in the way they responded to threatening gestures from other monkeys of the group but did not display changes in how they responded to affiliative social signals, such as groom and mount solicitations. Similar to their decrease in affiliative personality ratings, monkeys with amygdala lesions displayed a decreased probability of initiating affiliative social signals after receiving a threatening gesture. It is also noteworthy that amygdala-operated monkeys showed decreased probabilities of responding to threats with dominance-related behaviors, although this group displayed an increased frequency of these behaviors overall. This again emphasizes that not only were these monkeys initiating more dominance-related behaviors but also the timing of these behaviors was different from that displayed prior to surgery.

Finally, the extent of intended damage to the amygdala did not significantly correlate with any behavioral measure, indicating that even moderate damage to the amygdala (such as in Cases A-ibo-1 and A-ibo-3; see Table 3) can produce the changes in social behavior observed. Partial neurotoxic lesions of the amygdala (Meunier et al., 1999) or of its central amygdaloid nucleus alone (Kalin, Shelton, & Davidson, 2004) are also sufficient to produce decreased fear reactivity and defensive behaviors, especially when confronted by a snake stimulus. Similarly, unilateral drug-induced transient dysfunction of the basolateral subdivision of the amygdala (using a $GABA_A$ antagonist) produces decreased social behavior, such as play and contact, and increased active withdrawal and passivity (Málková, Barrow, Lower, & Gale, 2003). Given these recent findings, further investigations are needed to assess whether some nuclei within the amygdala are more specifically responsible for the personality and social behavior changes.

Taken together, the recent findings in monkeys indicate that the amygdala may contribute to normal social behavior in at least two ways. First, although the amygdala does not appear to be critical for producing species-typical social behaviors, this structure appears essential for inhibiting inappropriate behaviors that do not promote the formation of strong social bonds (such as generalized activity, cage exploration, and aggression). Second, the amygdala may also be crucial for specifically detecting threatening or potentially dangerous social stimuli and/or mediating appropriate behavioral and physiological responses. Interestingly enough, the findings in monkeys are now in agreement with those found in humans. Thus, like the monkeys with amygdala lesions, patients with similar damage do not show striking changes in social behavior, although they have difficulty in detecting and rating the magnitude of threatening social signals, such as fearful and angry facial expressions, but not other facial expressions displaying basic emotions (for review, see Adolphs, 2002). Similarly, neuroimaging studies in humans have demonstrated that the human amygdala most reliably activates when subjects view fearful and angry social signals (such as facial expressions, vocalizations, or body postures) relative to other emotional social signals (for review, see Whalen, 1998). These results are interesting because fearful and angry facial expressions can be thought of as those social signals that specifically indicate the presence of external danger or threat in the vicinity and that behavior should be changed to avoid such danger (Whalen et al., 1998).

Orbital Frontal Cortex, Behavioral Adaptation, and Assessment of Social Signals

Damage to the orbital frontal cortex yielded changes in personality ratings, such as decreases in affiliative and increases in avoidant personality qualities. These results are consistent with those of previous reports showing that orbital frontal damage results in decreased positive social behavior and communicative facial expressions, along with an increase in avoidance (Butter et al., 1968, 1970; Franzen & Myers, 1973; Myers et al., 1973). Furthermore, orbital frontal damage resulted in very few changes in personality qualities between pre- and postsurgery assessments, as compared with the sham-operated as well as the two other operated groups. This lack of behavioral modulation when changes in context or changes in the behavior of familiar social partners occur suggests that the orbital frontal cortex may be critical for adapting general social interaction patterns, such as those measured by personality ratings. This interpretation is consistent with a large body of literature that has previously shown that the orbital frontal cortex is involved in flexibly modulating behavior depending on current reinforcement contingencies or the value/meaning of primary and secondary reinforcers (both objects and social

cues), thereby allowing advantageous social and nonsocial decisions to be made across various contexts (Baxter, Parker, Lindner, Izquierdo, & Murray, 2000; Izquierdo & Murray, 2004; Izquierdo, Suda, & Murray, 2004; Rolls, 2002). However, in the social context studied here, the lack of normal personality adaptation displayed by orbital frontal cortex–operated monkeys did not severely degrade these monkeys' social interactions with normal controls. Dyadic relationships (as assessed by personality ratings) did not change appreciably between Groups C and O between pre- and postsurgery, whereas relationships between nearly all other dyads became more agonistic, tense, and avoidant, as well as less affiliative. Therefore, control monkeys seemed to prefer interacting with orbital frontal cortex–operated monkeys over their two other operated (amygdala or hippocampal lesion) partners, perhaps because of the lack of drastic changes in personality exhibited by Group O across testing phases.

A second interesting change in behavior for the orbital frontal cortex–operated monkeys was derived from analysis of videotaped social interactions. These monkeys displayed an increase in the frequency of threatening gestures initiated and also received higher levels of aggression from their group mates after surgery. This result appears consistent with the decreases in affiliative and increases in avoidant personality traits measured for this group. These results are also consistent with two previous reports (Butter & Snyder, 1972; Izquierdo et al., 2005) showing that monkeys with orbital frontal cortex lesions displayed high levels of aggression. However, it is interesting to note that in different contexts (when confronted with a staring human, a humanlike doll, or a toy snake), monkeys with orbital frontal cortex lesions display reduced aggression (Butter et al., 1968, 1970). Therefore, as mentioned for the amygdala above, the role of the orbital frontal cortex in aggressive behavior seems to be quite complex and context specific, thus requiring future in-depth study of orbital frontal–lesion animals in both social and nonsocial contexts that elicit aggressive responses.

The increased aggression observed in the current study occurred only for the dominant members of Group O. This result seems appropriate from an ethological perspective because dominant male macaques typically initiate more threatening gestures and engage in more aggression than their subordinate counterparts. This significant finding for dominant but not subordinate individuals again underscores the importance of considering an animal's dominance rank when studying the effects of various brain lesions on social behavior because social dominance strongly constrains an individual's behavioral repertoire.

Like monkeys with amygdala lesions, those with orbital frontal cortex damage showed changes in how they typically responded to social signals received from their group mates. However, unlike the amygdala-operated monkeys, those with orbital lesions responded abnormally to both threatening and affiliative social cues. When receiving threatening gestures, subordinate monkeys with orbital frontal cortex damage displayed increased affiliative social signals, whereas dominant monkeys with such damage showed decreased aggressive behaviors. In addition, monkeys with orbital frontal cortex lesions were less likely to mount when solicited, although this change was more evident in the dominant monkeys of the group. Although these lag-sequential results would seem to directly contradict the decreased affiliative personality ratings and the increased frequency of threatening gestures initiated reported for this group, they in fact underscore the importance of analyzing both the frequency and duration of behaviors initiated and the use of these behaviors in response to social cues provided by other partners to characterize changes in social behaviors. Thus, although monkeys with orbital frontal cortex lesions showed fewer affiliative traits and more threatening gestures over a total of 4 hr of postsurgery observations (30 min per day across 8 test days), when the analysis focused more on specific social exchanges, these monkeys alone used more affiliative signals and fewer threatening gestures in response to threats from other partners, indicating inappropriate use of social gestures in response to both threatening and affiliative signals.

The present findings are also in line with those in humans indicating that the orbital frontal cortex, but not the amygdala or hippocampal formation, may play an important role in making judgments based on social cues. More specifically, the orbital frontal cortex displays heightened metabolic activity when subjects are required to make social judgments, such as rating the attractiveness of a face (O'Doherty et al., 2003), using the meaning of a facial expression to guide one's own behavior (Kringelbach & Rolls, 2003), choosing to cooperate with or deceive another individual (Rilling et al., 2002), or judging whether or not another individual's behavior is morally right or wrong (Moll, Oliveira-Souza, Bramati, & Grafman, 2002) or has violated social norms (Berthoz, Armony, Blair, & Dolan, 2002).

Therefore, the experimental and clinical data suggest that the orbital frontal cortex may also impact on primate social behavior in at least two ways. First, the orbital frontal cortex may be critical for normal modulation of aggression, affiliation, and avoidance when a change in social context occurs or when the behavior of familiar social partners changes. Second, the orbital frontal cortex may play a more global role in social cognition than the amygdala by flexibly representing the current value or meaning of both positive and negative social signals, thereby facilitating the selection of the most appropriate behavioral response.

Modulatory Role for the Hippocampal Formation in Social Behavior

Behavioral changes in monkeys with hippocampal lesions were observed mainly during personality ratings and included a general increase in nonsocial qualities (e.g., solitary, avoidant, anxious, and fearful) together with an increase in excitability and generalized activity. Although there exists little evidence of behavioral changes following hippocampal lesions in monkeys, decreased fear toward a human observer (Mirsky, 1960) and a mild reduction in social contacts (Chaudhuri, Málková, Bachevalier, Suomi, & Mishkin, 1996) have already been reported. Furthermore, in a detailed review of the rodent literature, Gray and McNaughton (1983) showed that hippocampal lesions increase activity, attenuate aggressive responses, and prevent the formation of social hierarchies (but see Becker et al., 1999)

Given the profound and well-documented loss of rich, context-dependent memory that follows hippocampal lesions (Alvarado & Bachevalier, 2005; Murray, 2000; Squire & Knowlton, 2000), the increases in general ambulatory activity, excitability, and social avoidance for hippocampal-operated monkeys observed in the current study and elsewhere (Beauregard & Bachevalier, 1996; Beauregard, Málková, & Bachevalier, 1995; Becker & Grecksch,

2000; Becker et al., 1999; Daenen et al., 2002; Sams-Dodd et al., 1997) could in part be due to a lack of memory for the testing context from day to day. Reintroduction to the testing enclosure each day could have triggered exploration and activity and thus taken these monkeys away from social interactions with their group mates. Similarly, memory impairments could have conceivably hampered the ability of hippocampal-lesion monkeys to modulate their behavior with regard to past experience and therefore resulted in heightened excitability, inappropriate responses to social signals, and diminished social relationships with familiar partners.

Behavioral Changes of Sham-Operated Monkeys

One final unexpected result generated from the present experiment is the significant behavioral changes displayed by the sham-operated control monkeys. Very few previous studies have described the behavior of control and operated animals both prior to and following lesions similar to those studied here. Two reports have observed an increase in agonistic displays and physical attacks initiated by unoperated rhesus macaques when interacting with familiar partners having sustained either frontal lobotomies (Brody & Rosvold, 1952) or orbital frontal cortex lesions alone (Butter & Snyder, 1972). A similar observation was also made by Rosvold and colleagues (1954) in an established group of rhesus monkeys containing 5 unoperated controls and 3 with anterior temporal lobe removals (including the amygdala). One could argue that these changes observed previously in unoperated monkeys and the changes in personality attributes, dyadic relationships (with Groups H-ibo and A-ibo only), and responses to affiliative social signals displayed by the control monkeys of the present study could be due simply to normal maturational changes in macaque social behavior between the pre- and postlesion testing phases. This argument seems to be unlikely, however, because the monkeys appear to have been young adults (according to reported weights) in the three previous reports and averaged 2.9 years old at the beginning of testing in the present study, indicating that the control monkeys were beyond the age where normal macaque social behavior displays significant maturational changes (for review, see Machado & Bachevalier, 2003). It is more likely that the behavioral changes displayed by the unoperated control monkeys were the result of interactions with operated social partners displaying abnormal behaviors. This conclusion is substantiated by several previous reports indicating differential social responses by control monkeys depending on the lesion status of their social partners (Bachevalier, Málková, & Mishkin, 2001; Bauman, Lavenex, Mason, Capitanio, & Amaral, 2004; Emery et al., 2001).

Concluding Comments

It is important to note that the experimental design used here (pre- vs. postsurgery comparisons with static group membership) limits the conclusions one can make about how the amygdala, orbital frontal cortex, and hippocampal formation contribute to primate social behavior. Given the argument made above regarding the significant impact of testing context on the study of lesion-induced behavioral impairments, conclusions drawn here apply only to how these three neural structures mediate social interactions within established or highly familiarized groups. Therefore, it would be difficult at this point to generalize these ideas to other contexts, such as the initial formation of new social relationships. This topic will be addressed in a future article.

A related point concerns the external validity of functions one can attribute to the amygdala, orbital frontal cortex, and hippocampal formation for all group-living primates on the basis of observations of only 6 monkeys per experimental group. Although this sample size is similar to several recent studies (Emery et al., 2001; Málková, Mishkin, Suomi, & Bachevalier, 1997) and although power of ANOVA tests (Zar, 1999) conducted prior to this experiment indicated sufficient statistical power, the conclusions generated here must be treated with caution considering the interindividual variance in behavior inherent to macaques and humans. However, it is this interindividual variability that makes macaques an excellent model for studying human social cognition. Furthermore, experimental groups were balanced with respect to presurgical dominance rank, and data were analyzed both with and without dominance rank as main factors to minimize the effects of intermonkey variability on the behavioral results and increase the external validity of the conclusions.

One final point for discussion is related to inferring neural function on the basis of behavioral testing in a social context. Although the conclusions drawn from the current experiment are compelling and largely complement the established literature in both nonhuman primates and humans, the analysis of monkey social behavior following specific brain lesions cannot provide precise knowledge regarding the cognitive processes by which changes in social behaviors occur. Therefore, additional investigations of these same monkeys in controlled nonsocial testing paradigms can help to identify the specific cognitive processes affected by amygdala, orbital frontal cortex, and hippocampal formation damage and to validate conclusions regarding the distinct functions of the primate amygdala, orbital frontal cortex, and hippocampal formation in social cognition offered by the present study.

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Received August 24, 2005
Revision received March 8, 2006
Accepted April 11, 2006 ■