Defensive Movements Evoked by Air Puff in Monkeys

Dylan F. Cooke and Michael S. A. Graziano

Department of Psychology, Princeton University, Princeton, New Jersey 08544

Cooke, Dylan F. and Michael S. A. Graziano. Defensive movements evoked by air puff in monkeys. *J Neurophysiol* 90: 3317–3329, 2003. First published June 11, 2003; 10.1152/jn.00513.2003. Electrical stimulation of two connected cortical areas in the monkey brain, the ventral intraparietal area (VIP) in the intraparietal sulcus and the polysensory zone (PZ) in the precentral gyrus, evokes a specific set of movements. In one interpretation, these movements correspond to those typically used to defend the body from objects that are near, approaching, or touching the skin. The present study examined the movements evoked by a puff of air aimed at various locations on the face and body of fascicularis monkeys to compare them to the movements evoked by stimulation of VIP and PZ. The air-puff–evoked movements included a movement of the eyes from any initial position toward a central region and a variety of stereotyped facial, shoulder, head, and arm movements. These movements were similar to those reported on stimulation of VIP and PZ. One difference between the air-puff–evoked movements and those evoked by stimulation of VIP and PZ is that the air puff evoked an initial startle response (a bilaterally symmetric spike in muscle activity) followed by a more sustained, lateralized response, specific to the site of the air puff. In contrast, stimulation of VIP and PZ evoked mainly a sustained, lateralized response, specific to the site of the receptive fields of the stimulated neurons. We speculate that VIP and PZ may contribute to the control of defensive movements, but that they may emphasize the more spatially specific reactions that occur after startle.

INTRODUCTION

A basic function of the motor system of all animals is to protect the body from attack or collision (e.g., Dosey and Meisels 1969; Hediger 1955; Schiff 1965). One type of defensive reaction, a fast, stereotyped response that is usually bilaterally symmetric, is called the *startle reflex* (Landis et al. 1939; Yeomans et al. 2002). A set of subcortical structures has been implicated in the control of this reflex (Koch 1999; Yeomans et al. 2002). Another more diverse class of defensive movement is spatially directed and can involve ducking or withdrawing from the direction of the stimulus, navigational veering during locomotion, or blocking an impending object with one body part (e.g., the forelimb) to protect another body part (e.g., the face) (Hediger 1955; King and Cowey 1992; King et al. 1992; Landis et al. 1939; Schiff et al. 1962). Areas in the pigeon brain, locust brain, and fly brain have been implicated in the detection of looming visual stimuli and the possible control of avoidance (Rind 2002; Schuster et al. 2002; Sun and Frost 1998; Tammero and Dickinson 2002). Portions of the rat superior colliculus are also apparently involved in the control of avoidance (Dean and Redgrave 1989).

We proposed that in monkeys, defensive movements are represented at least partly at the cortical level, and that 2 interconnected areas play a specific role in this class of behavior (Graziano et al. 2002b). These 2 areas are the ventral intraparietal area (VIP) in the posterior parietal lobe and the polysensory zone (PZ) in the precentral gyrus. Area VIP receives convergent input from many sources including visual, somatosensory, and possibly vestibular and auditory areas (Bremmer et al. 2002; Lewis and Van Essen 2001; Maunsell and Van Essen 1983; Schlack et al. 2000). PZ, which receives input from VIP, projects to a variety of motor structures including the spinal cord (Dum and Strick 1991; Lewis and Van Essen 2001; Luppino et al. 1999). Our suggestion that these 2 areas are involved in the control of defensive movement is based on 2 types of data.

1) The single neuron properties of both VIP and PZ are consistent with the coding of nearby objects, with a relative emphasis on those objects approaching or touching the body. Most neurons in both areas are bimodal, responding to visual and tactile stimuli (Bremmer et al. 2002; Colby et al. 1993; Duhamel et al. 1998; Fogassi et al. 1996; Graziano and Gandhi 2000; Graziano et al. 1997; Rizzolatti et al. 1991; Schaafsma and Duysens 1996). The tactile receptive field is usually on the face or arm and the visual receptive field is usually adjacent to the tactile receptive field, extending outward typically anywhere from 5 to 30 cm into the space surrounding the body. Some receptive fields (about 50% in VIP, about 10% in PZ) extend out to greater distances (Colby et al. 1993; Graziano et al. 1997). Most neurons are directionally selective, and a high proportion prefer movement of the visual stimulus in depth toward the tactile receptive field (Colby et al. 1993; Schaafsma and Duysens 1996). At least some neurons in both areas respond to nearby auditory stimuli (Graziano et al. 1999; Schlack et al. 2000).

2) Electrical stimulation of VIP and PZ evokes short latency, complex movements that appear similar to those typically made during startle and avoidance (Cooke et al. 2003; Dearworth and Gamlin 2002; Graziano et al. 2002a; Thier and Andersen 1998). For example, for some cortical sites in PZ and VIP, the neurons respond to tactile stimuli on the side of the head and visual stimuli near and approaching the tactile receptive field. Stimulation of these sites evokes a constellation of movements including blinking, squinting, flattening the ear against the side of the head, shifting the head away from the sensory receptive fields, shrugging the shoulder, and rapidly lifting the hand into the space near the side of the head as if to block an impending impact (Cooke et

al. 2003; Graziano et al. 2002a). For some cortical sites in PZ, the neurons respond to tactile stimuli on the hand and forearm and to visual stimuli near and approaching the hand. Stimulation of these sites evokes a fast withdrawal of the hand to a guarding-like posture behind the back (Graziano et al. 2002a). At least in PZ, these defensive-like movements can be obtained even in monkeys anesthetized with barbiturates, and thus do not appear to be reactions to a fictive sensory experience (Graziano et al. 2002a).

The sensory features that drive neurons in VIP and PZ, and the motor consequences of electrically stimulating these 2 brain areas, are therefore consistent with at least some role in monitoring nearby objects and protecting the body from impending collisions. Several questions remain, however, about the similarity of the movements evoked by brain stimulation and normal defensive movements. In the present study, we investigated air-puff– evoked defensive movements in monkeys to compare them to the movements evoked by electrical stimulation of VIP and PZ. We focused on 3 main questions. First, does a puff of air evoke a qualitatively similar set of movements as electrical stimulation of VIP and PZ? Second, does a puff of air evoke a similar pattern of facial muscle activity as electrical stimulation of VIP and PZ? Third, in some experiments (Fujii et al. 1998; Thier and Andersen 1998), stimulation in or near VIP and PZ evoked goal-directed or centering movements of the eye; does air puff to the face evoke similar centering eye movements?

METHODS

All husbandry, surgical, and behavioral procedures were approved by the Princeton University Institutional Animal Care and Use Committee and the attendant veterinarian and were in accordance with N.I.H. and U.S.D.A. guidelines. Behavioral responses were studied in 2 adult male *Macaca fascicularis* (3.5–4.5 kg). Behavior was measured in 3 ways: on video at 30 frames/s, with electromyographic (EMG) electrodes in facial and shoulder muscles, and with an eye coil to measure eye position. In monkey 1, eye position data and EMG data were collected on separate blocks. In monkey 2, all 3 types of data were collected simultaneously.

Surgery

For each monkey, an initial surgical operation was performed under isoflurane anesthesia and strict aseptic conditions, during which an acrylic skullcap was fixed to the skull with bone screws. A steel bolt for holding the head was also embedded in the acrylic. A scleral eye coil was implanted in one eye (left eye for monkey 1, right eye for monkey 2). Each animal recovered from the surgery within 1 wk, but was given an additional 2 wk to allow the skull to grow tightly around the skull screws. During testing the monkey sat in a Lexan primate chair. For most experiments, the head was restrained by the head bolt. In some tests, to study movements of the head, the head bolt was unfastened.

Air-puff stimulus

An air nozzle directed a stream of air at the monkey's skin from a distance of 5 cm. An electrically actuated valve was connected to the base of the nozzle. In most tests the air stream was 0.5 s in duration. In some tests the duration was varied between 0.2 and 1.0 s. The pressure of the air stream was controlled by a pressure regulator mounted to a tank of compressed air. Pressures were typically set between 5 and 30 psi (pounds per square inch). For most experiments, the pressure was set to 15 psi. In addition to the tactile stimulus, the air stream produced a sound that was measured to be 80 dB at a distance of 5 cm from the nozzle. In pilot experiments, when the air puff was directed near but not touching the monkey's face, little or no defensive reaction was observed. In contrast, when the air puff was directed at the face, even when the ears were plugged with wax thus reducing the sound, a robust defensive movement was observed. Thus the defensive movements were evoked mainly by the tactile stimulus and not the sound of the puff. The video record confirmed that the monkeys remained alert and calm during the air-puff trials. The defensive movements involved a brief blink, squint, or other movement as described in the RESULTS, and did not appear to agitate or distress the monkey.

In initial experiments, only one air nozzle was used. The nozzle was directed at different parts of the face, torso, and arms as shown in Figs. 1 and 2A. In other experiments, 10 air nozzles were used. The nozzles were aimed at different parts of the head as shown in Fig. 2A.

Eye position measurement

Eye position was sampled every 2 ms for monkey 1 and every 4 ms for monkey 2. Monkey 1 was trained to fixate on a small blinking light for 1 s for a juice reward. The fixation light was placed in 12 different positions 40 cm in front of the monkey to calibrate the eye position measurements. For monkey 2, calibration was performed by inducing smooth pursuit eye movements with small moving visual targets, such as pieces of fruit on the end of a stick. The trajectories included horizontal movement at -20, 0, and $20°$ elevation, and vertical movement at -20, 0, and $20°$ along the azimuth. Once the calibration measurements were complete, the monkey was then tested with the air-puff stimulus during free viewing in the light, to determine the effect of air puff on eye position. No task was used during data collection. The interpuff interval was variable between 3 and 30 s. On a small proportion of trials, the eye was in the process of executing a spontaneous saccade when the air puff was delivered. These trials, identified on the basis of eye speed at trial onset, were eliminated from the analysis. For almost all trials, the eye was stationary when the air puff was delivered, apparently fixating some feature in the room in front of the monkey. The video record indicated that the monkey was awake with its eyes open during the trials.

Electromyographic recordings

EMG activity was measured bilaterally in the orbicularis muscle (related to blinking and squinting), the nasolabialis muscle (related to lifting of the upper lip), and the trapezius muscle (related to shrugging). Fine insulated stainless steel wires were threaded into a 22-gauge syringe needle and inserted into the muscle. The wires had an exposed tip of 1–2 mm. Three wires were inserted in each muscle, spaced about 5 mm apart, to provide input to a differential amplifier and its ground (single-neuron amplifier model 1800; A-M Systems, Sequim, WA). The amplifier filters were set with a low cutoff at 300 Hz and a high cutoff at 1,000 Hz. Placement of the wires was confirmed by observing EMG activity during spontaneous movements such as blinking to an air puff on the face (orbicularis muscle), lifting of the lip during eating (nasolabialis muscle), and lifting of the shoulder during spontaneous arm movements (trapezius muscle). The EMG signal was sampled every 2 ms for monkey 1 and 4 ms for monkey 2. Each *EMG trace* shown represents the rectified EMG activity (in SDs above baseline) over time (ms) averaged over multiple trials as indicated in the figure captions.

Muscle activity was measured during air puff at 10 locations on the head. Air puffs were presented at the 10 locations on a pseudo-random schedule with an interpuff interval that varied between 2 and 30 s. Figure 2A shows the arrangement of puff locations, which included a 3×3 grid of locations on the front of the face and one location on the back of the head. The results from the muscles on the right side of the body were averaged with a mirror-reversal of the results from the muscles on the left side of the body. The histograms in Fig. 2B therefore show the results from puffer locations ipsilateral to the recorded muscles (positions 1, 4,
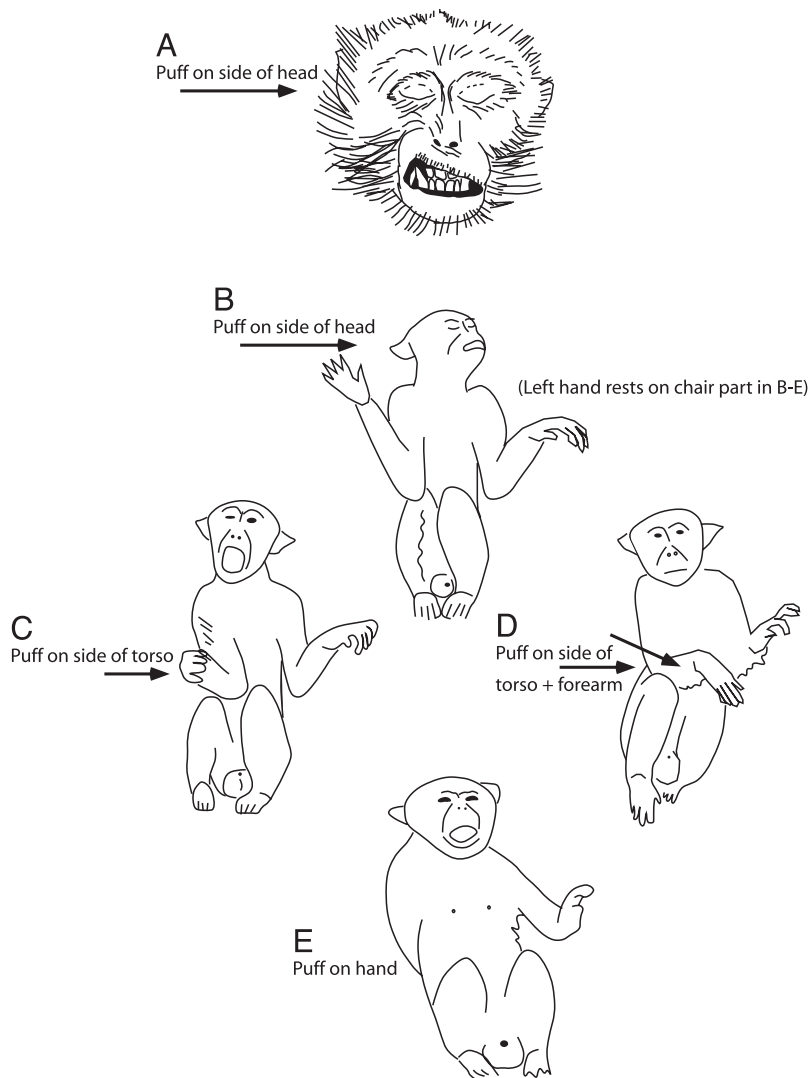
FIG. 1. Tracings of video frames showing behavioral response to air puff. *A*: air puff to side of face evokes blink and lifting of upper lip. *B–E*: air puff to different parts of right side of body evokes movement of right arm to different postures. *B*: puff to side of face evokes lifting of hand toward upper lateral space. *C*: puff to side of torso evokes retraction of elbow against side of torso and movement of hand to lateral position. *D*: puff to side of torso and forearm evokes retraction of elbow against side of torso and withdrawal of hand to opposite side of body. *E*: puff to hand evokes withdrawal of hand behind back. Of 15 video frames recorded within first 500 ms after onset of air puff, frame that showed peak effect was selected and traced.

and 7), contralateral to the recorded muscles (positions 3, 6, and 9), and on the midline (positions 2, 5, 8, and 10). In this fashion, any unintended asymmetry, such as in puffer placement or in the impedance of the EMG wires, was counterbalanced in the analysis.

RESULTS

We first give a qualitative description of the main types of movements evoked by an air puff presented to various locations on the face and body of monkeys. We then describe the time course and laterality of the EMG activity evoked by the air puff. Finally, we consider whether the eye moves toward a central location during air-puff–evoked defensive movements.

Qualitative description of video record

We observed 6 movements that occurred reliably in reaction to a puff of air on the face. These movements are *1*) a blink and a contraction of the musculature around the eye causing a squint (Fig. 1*A*, traced from video frame); *2*) a contraction of the musculature of the snout causing the upper lip to lift and the skin on the snout to wrinkle upward toward the eye (Fig. 1*A*); *3*) movements of the ear in which the pinna flattened back against the side of the head and rotated downward; *4*) a shoulder shrug; *5*) movements of the head, observed when the monkey's head was released from the holder; [the head retracted from the direction of the air puff (Fig. 1*B*)]; and *6*) movements of the arm. Typically the arm moved toward different postures depending on the location of the puff (Fig. 1, *B–E*). These movements included those bringing the hand into upper space when the puff was directed at the head; bringing the elbow against the side of the torso when the puff was directed at the side of the torso; or withdrawing the hand behind the back when the puff was directed at the hand.

One possibility is that these defensive movements were distorted by testing the monkeys in a restrictive primate chair. We thus also placed the monkeys in a 1×1-m cage and videotaped their reactions to air puff from a handheld air nozzle directed through the bars of the cage. The video was analyzed off-line frame by frame to determine the facial and limb movements that occurred within the first 0.5 s after puff onset. The same constellation of movements described above was observed in the cage. Several other movements were also observed. A puff to one side typically caused the monkey to jump or climb to the opposite side of the cage. A threat to the hand, arm, or torso sometimes caused the monkey to thrust out its foot toward the direction of the threat.
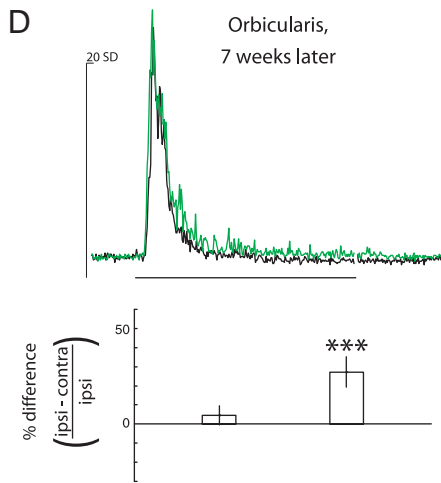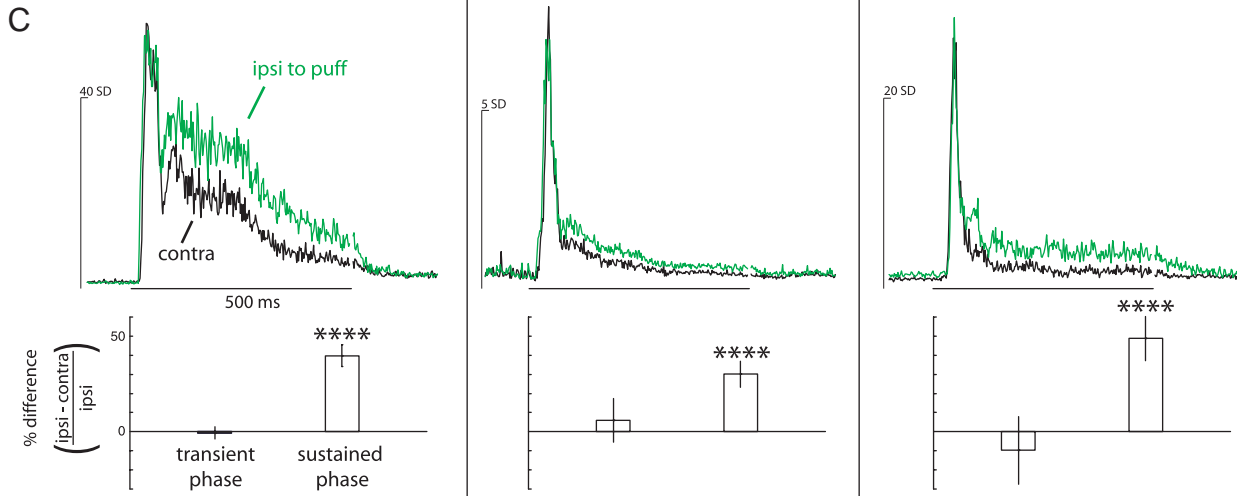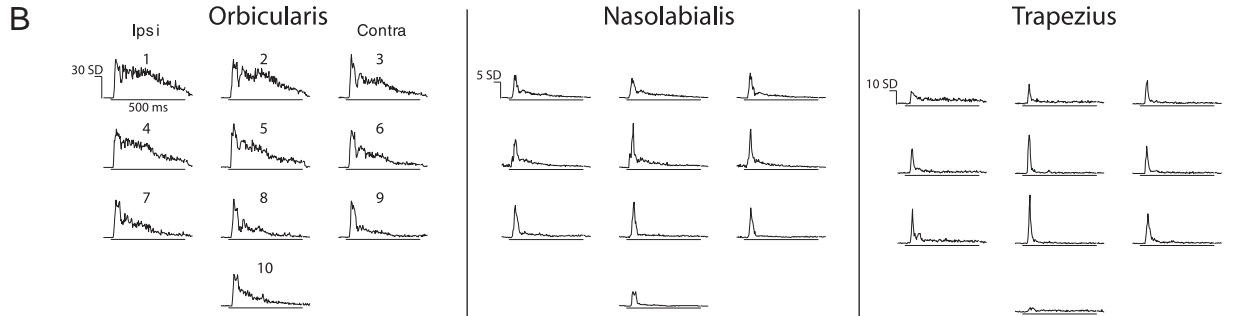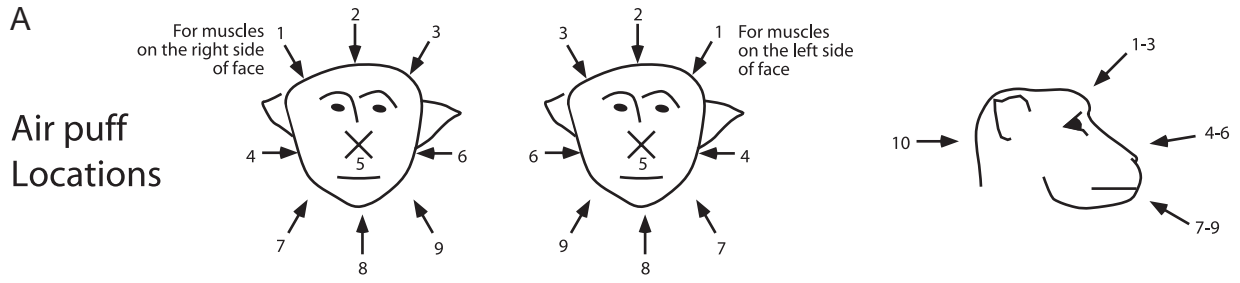
In the following sections we describe in greater detail some of the movements listed above. We begin with a description of activity recorded from facial and shoulder muscles, and then describe the movements of the eye evoked by air puff.

Muscle activity: startle response versus secondary, spatially specific response

To study muscle activity during air-puff–evoked defensive movements, we measured the EMG activity of 3 muscles: the orbicularis muscle (which participates in squinting and blinking); the nasolabialis muscle (lifting of the upper lip); and the trapezius muscle (elevation of the shoulders). Figure 2*B* shows the average EMG activity for each of the 3 muscles, evoked by each of the 10 puffer locations. For all 3 muscles, the air puff evoked an initial, sharp transient in the EMG. The latency (the time at which the mean activity exceeded 3 SD above baseline) was 18 ms for the orbicularis, 32 ms for the nasolabialis, and 34 ms for the trapezius. This initial, transient spike was evoked by all puffer locations. In particular, it was present whether the air puff was ipsilateral or contralateral to the studied muscle. It therefore appears to correspond to the previously described startle reflex, a transient, short latency, bilaterally symmetric response to intense stimuli (Landis et al. 1939; Yeomans et al. 2002).

After the initial, transient spike, we found a more sustained muscle activity that returned to baseline only after the air puff ended. Figure 2 shows this result for tests in which the air puff was 0.5 s in duration. In other tests, the air puff was presented for durations ranging from 0.2 to 1.0 s, and a similar result was obtained; that is, the sustained muscle activity was maintained during the stimulus and returned to baseline after stimulus offset. This more sustained muscle activity was clearly differentiable from the startle reflex in that it was not bilaterally symmetric; it was larger on the ipsilateral side, the side on which the air puff was presented, as further quantified below.

For each muscle, we first averaged the results for puffer locations 1, 4, and 7. This average represents the activity of the muscle during puff on the ipsilateral side of the face. This result is shown by the green line in Fig. 2*C*. We also averaged the results for puffer locations 3, 6, and 9; this average represents the activity of the muscle during puff on the contralateral side of the face and is shown by the black line in Fig. 2*C*. As can be seen in the figure, the initial spike in muscle activity was similar in magnitude regardless of whether the air puff was ipsilateral or contralateral to the muscle. As the trial proceeded,

the muscle activity fell from its initial peak to a more sustained level, and this level was greater for puff on the ipsilateral side than for puff on the contralateral side. Thus the initial startle response was not sensitive to the lateral position of the air puff, whereas the second, more sustained phase of the response was more spatially specific: it was stronger on the side of the face where the air puff was presented.

The bar graphs in Fig. 2*C* show the percentage difference between the activity evoked by ipsilateral air puff and the activity evoked by contralateral air puff. The first bar (labeled "transient phase") is based on the 24 ms of muscle activity during the highest portion of the peak response. This bar is not significantly different from zero, indicating that ipsilateral and contralateral air puff evoked a similar level of activity, with a percentage difference near zero (see figure caption for significance levels). The second bar (labeled "sustained phase") is based on the activity during the sustained portion of the response, with an analysis window that began 100 ms after stimulus onset and ended at stimulus offset. This bar is significantly above zero, indicating that during this part of the trial the ipsilateral air puff evoked greater activity than the contralateral air puff. A similar result was obtained for all 3 muscles studied.

Monkey 1 was tested a second time at a later date. Perhaps because of adaptation, the monkey's defensive reaction to the air puff was reduced in this second test. In particular, the second, sustained phase of muscle activity was reduced. However, even in this attenuated response, the pattern was similar, as shown in Fig. 2*D*. We obtained an initial spike in activity that was relatively bilaterally symmetric, followed by a more sustained activity that was greater for ipsilateral air puff than for contralateral air puff.

These results show that air puff evoked an initial, bilateral startle response that then gave way to a more spatially specific, lateralized response. The lateralized response was sustained throughout the remainder of the air puff and for 50 to 100 ms beyond the end of the puff. As described in greater detail in the DISCUSSION section, it is this second component of the response that resembles the movements evoked by electrical stimulation of areas VIP and PZ.

Eye movements evoked by air puff

Figure 3*A* shows the movement of the eye evoked by an air puff to the center of the chin. Each green line shows the movement of the eye on one air-puff trial, beginning at puff

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FIG. 2. Muscle activity evoked by air puff to face. EMG activity was recorded from 3 muscles bilaterally: orbicularis (involved in blinking and squinting), nasolabialis (involved in lifting of upper lip), and trapezius (involved in shrugging). *A*: 10 locations on head stimulated by air puff. Puff locations were numbered relative to side of recorded muscle. *B*: histograms showing EMG activity from 3 muscles at 10 puffer locations, for monkey 1. Data were rectified and integrated in 4-ms bins. Each histogram is average of 40 trials; *y*-axis shows magnitude of EMG signal normalized to SD obtained in 100-ms prestimulus period. Tick mark on *y*-axis indicates signal level in units of SD above baseline. Horizontal line under each histogram shows 500-ms stimulus period. An electrical artifact occurred within 2 ms after closure of air puff valve; this artifact was removed (gap in *EMG trace* at end of stimulus period). Each histogram shows mean of muscles from both sides of body; e.g., histogram labeled Orbicularis, Ipsi, 1, is average of right orbicularis activity during air puff at upper right position and of left orbicularis activity during air puff at upper left position. *C*: effect of ipsilateral vs. contralateral air puff. Green line shows average EMG activity during ipsilateral puff (positions 1, 4, 7; average of 120 trials); black line shows average activity during contralateral puff (positions 3, 6, 9; average of 120 trials). Bar graphs under histograms show percentage difference in EMG signal between ipsilateral puff and contralateral puff; error bars are SE. First bar (transient phase) = percentage difference during 24 ms of peak response. Second bar (sustained phase) = percentage difference during period from 100 to 500 ms after stimulus onset. Results of *t*-test: orbicularis, transient phase, $t = -0.23$, $P = 0.82$; sustained phase, $t = 6.87$, $P < 0.0001$. Nasolabialis, transient phase, $t = 0.53$, $P = 0.59$; sustained phase, $t = 4.40$, $P < 0.0001$. Trapezius, transient phase, $t = -0.55$, $P = 0.58$; sustained phase, $t = 4.20$, $P < 0.0001$. *D*: result of retesting monkey 1 at a later date with similar stimulus apparatus and EMG wires in same muscles. Each histogram is mean of 90 trials. Results of *t*-test: transient phase, $t = 0.93$, $P = 0.35$; sustained phase, $t = 3.47$, $P < 0.0006$.

onset (black dot). The black oval indicates the *x* and *y* SD of eye position at the start of the air puff. On almost all trials, the eye moved roughly toward a central location. As described in more detail below, the eye position reached its tightest cluster 166 ms after puff onset for monkey 1 and 228 ms after puff onset for monkey 2. The red dot on each trace indicates the position of the eye at this time of tightest clustering, and the red oval indicates the *x* and *y* SD of eye position at this time. This location to which the eyes moved did not match the lower-field location of the air nozzle or the location on the face touched by
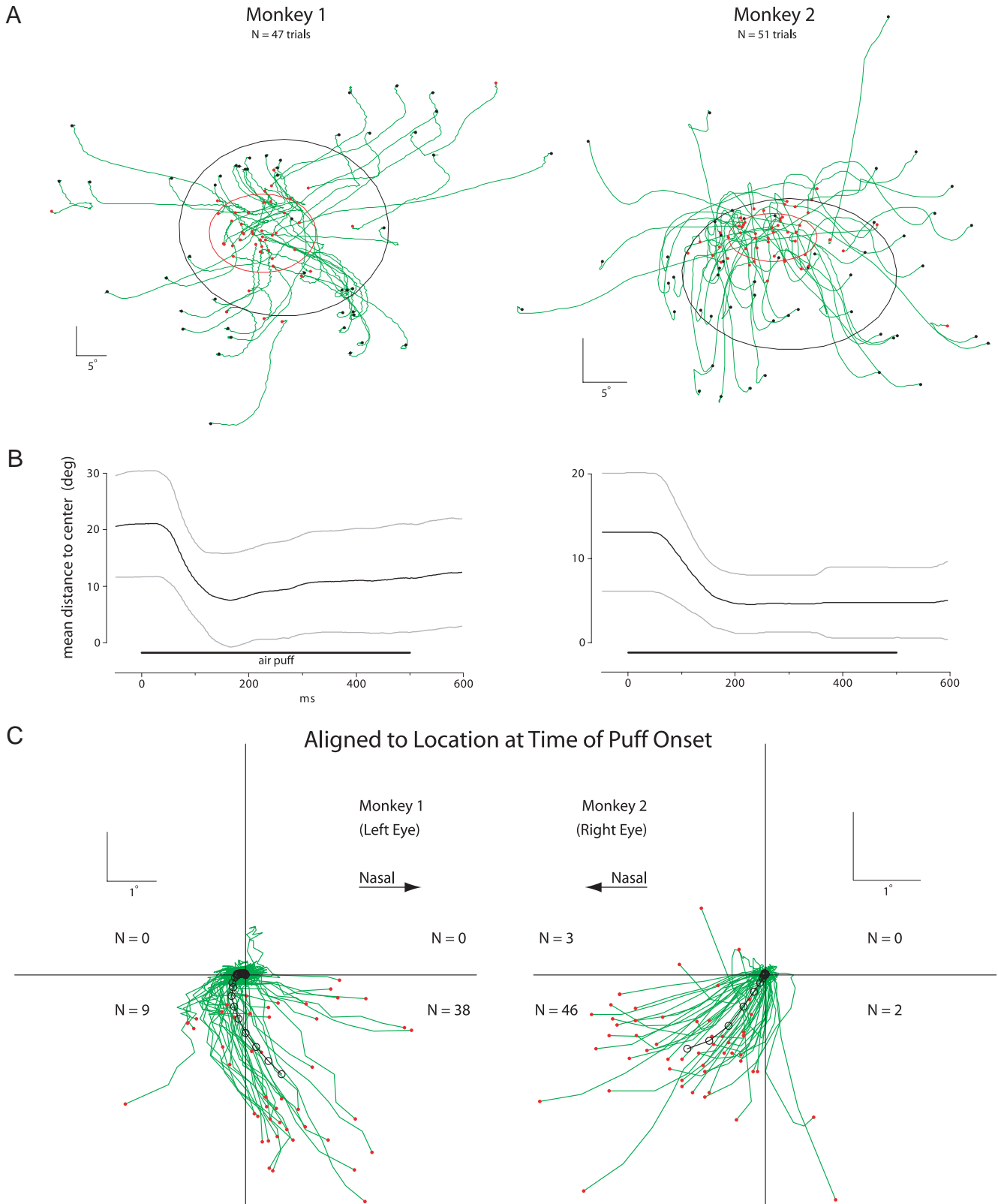
the air; that is, the monkey was not saccading to the stimulus. Rather, the movement was to a central orbital position. As described in a later section (*Effect of air puff location*), the eye converged to a similar central position regardless of the location of the air-puff stimulus. Even an air puff on the back of the head elicited a movement of the eyes to a central orbital position.

To further quantify the amount of centering of eye position over time, we calculated a metric that we called the "mean distance to center." This metric was calculated separately for each time bin throughout the trial. For example, for *time 0* (onset of air puff), we first calculated the mean eye position across trials. Then, for each trial, we computed the distance from the eye to that mean position. Finally, we averaged across trials to arrive at the mean distance to center. A large mean distance to center indicates a large scatter in eye position; a small mean distance to center indicates a more clustered distribution of eye positions. This metric was calculated every 2 ms for monkey 1 and every 4 ms for monkey 2 (determined by the different data acquisition rates used for the 2 monkeys).

Figure 3*B* shows how the mean distance to center changed over time through the trial. The mean distance to center began to drop about 50 ms after the puff onset for monkey 1 and about 70 ms after puff onset for monkey 2. The mean distance to center reached a minimum at 166 ms after puff onset for monkey 1 and at 228 ms for monkey 2. This minimum represents the time at which the eye position was most tightly clustered. As discussed in a later section, the rate at which the eye moves to the center appears to be related to the magnitude of the defensive reaction. Thus the air puff may have evoked a greater defensive reaction in monkey 1 than in monkey 2. Indeed, the video record showed a strikingly more pronounced facial reaction in monkey 1 than in monkey 2.

To test whether the amount of centering was statistically significant, we compared the mean distance to center at puff onset, that is, before centering began, and 200 ms into the trial, that is, after the centering was mostly complete. These two means were significantly different by *t*-test (for monkey 1, $t = 8.0$, $P < 0.0001$; for monkey 2, $t = 9.6$, $P < 0.0001$). Thus the air puff evoked a significant reduction in the spread of the eye position distribution.

On each air-puff trial, the initial movement of the eye was not always directed toward the center. The centering movements of the eye began 50–70 ms after puff onset (as can be seen in Fig. 3*B*), but an earlier, noncentering movement of the eye can be seen at the start of most trials in Fig. 3*A*. In most trials this initial movement appears to curl in a downward and nasal direction. To further examine this initial component of the eye movement, we plotted the eye position data such that the starting eye position for all trials was aligned on a single

point. This plot is shown in Fig. 3*C*, in which the green lines show individual trials and the black circles show the average trajectory. The plot shows the data starting at puff onset and continuing until the approximate time at which the centering of the eye position began (0–50 ms for monkey 1, 0–68 ms for monkey 2). On most trials, the eye began movement in a downward and nasal direction. (Note that opposite eyes were measured in the 2 monkeys.) Fig. 3*C* shows the number of trials for which the initial eye movement was directed into the lower nasal, lower lateral, upper nasal, and upper lateral quadrants. The distribution was significantly skewed toward the lower nasal quadrant for both monkeys (monkey 1, $\chi^2 = 37.59$, $P < 0.0001$; monkey 2, $\chi^2 = 44.4$, $P < 0.0001$).

To determine the latency of the eye movement, we plotted the average speed of the eye over time during the air-puff trial (Fig. 4*A*). The latency of eye movement (the time at which the average eye speed exceeded 3 SD above baseline) was 30 ms for monkey 1 and 48 ms for monkey 2. The longer latency and lower average speed in monkey 2 may reflect the smaller defensive reaction in this monkey. The double peak in average speed for monkey 1 was caused by some trials in which the speed peaked relatively late. In general, the speed profile for each individual trial had a single peak and was relatively symmetric. This speed profile is shown more clearly in Fig. 4*B*. Here, the black line shows the average speed for puff-evoked movements, aligned on the time of peak speed. The gray line shows the result for spontaneous saccades measured in the interval between air puffs. The 2 types of eye movement had similar velocity profiles; that is, for both spontaneous and puff-evoked movements, the velocity profile was relatively symmetrical. However, the puff-evoked movements were on average slower than the spontaneous saccades.

Figure 4*C* shows the peak speed of each eye movement plotted against the amplitude of the movement (the "main sequence"). The red crosses show the data for puff-evoked movements and the blue dots show the data for spontaneous saccades. For both monkeys, puff-evoked movements were on average slower than spontaneous saccades (regression analysis: for monkey 1, $F = 85.0$, $P < 0.0001$; for monkey 2, $F = 33.2$, $P < 0.0001$). However, the populations overlapped; most puff-evoked movements were in the lower range for normal saccades. Note also that the 2 monkeys were different in that monkey 2 made fewer large amplitude spontaneous saccades. (Because large-amplitude saccades have greater peak speed, monkey 2 had a lower mean speed for saccades, as can be seen in Fig. 4*B*.) One possibility is that, because monkey 1 displayed more pronounced defensive reactions, this monkey may have been in a state of greater behavioral arousal and thus made more and larger spontaneous saccades. Despite these

FIG. 3. Eye movements evoked by air puff to chin. *A*: green lines show *eye movement traces* on individual trials during air puff for monkey 1 (*left*) and monkey 2 (*right*). Black dot at start of each trace indicates position of eye at start of air puff. Black oval indicates *x* and *y* SD of black dots (centered on mean position of black dots). Red dot at end of each trace indicates position of eye at time when eye position was most tightly clustered (166 ms after puff onset for monkey 1, 228 ms for monkey 2). Red oval indicates *x* and *y* SD of red dots. *B*: data from same trials shown in *A*. Here, *y*-axis shows mean distance to center, a measure of spatial dispersion of eye position (see text for explanation). Gray lines show SD. *x*-axis shows time during air puff trial. Horizontal line indicates time of air puff. *C*: same trials as in *A* but here *eye movement traces* show magnified view of beginning of eye movement, and *eye traces* are aligned on starting eye position. Each green line shows eye position on a single trial, starting at puff onset (plotted at center of graph) and ending at time that centering movement began (50 ms after puff onset for monkey 1, 68 ms for monkey 2, indicated by red dot). Black circles show average trajectory, moving in a downward and nasal direction. In each quadrant, N indicates number of trials for which eye moved into that quadrant.
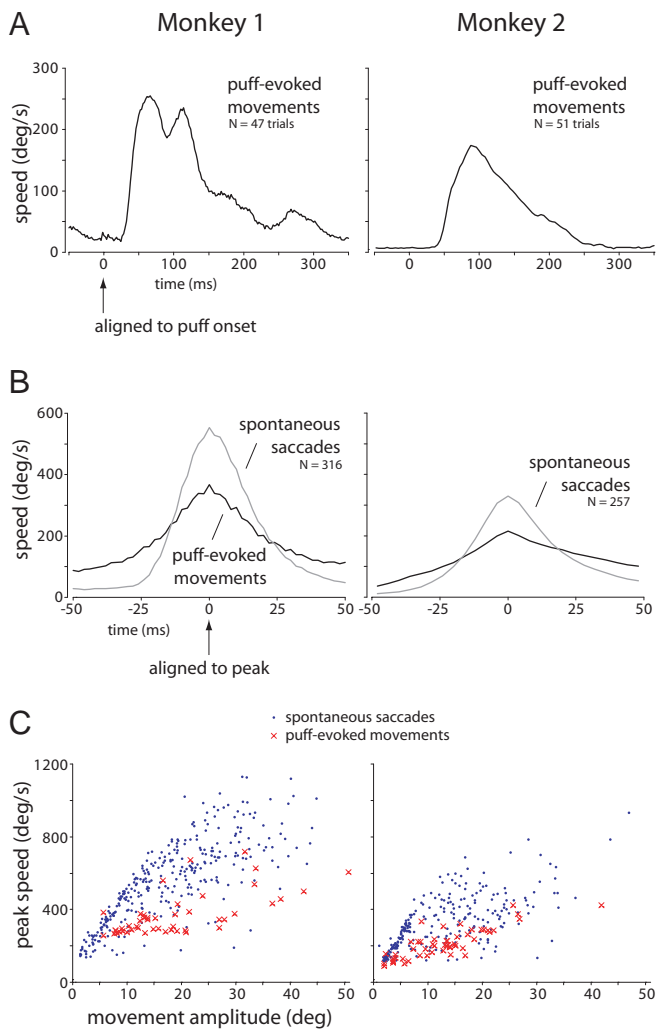
FIG. 4.   Comparison of puff-evoked eye movements and spontaneous saccades. *A*: average speed of eye before and during air puff. *B*: average speed of eye during air puff and during spontaneous saccades; each trial aligned on time of peak speed. *C*: main sequence (peak speed vs. amplitude of eye movement) for puff-evoked movements and spontaneous saccades.

differences, the overall pattern of results is the same for the 2 monkeys.

In one session we did not present air puffs and instead monitored spontaneous blinks and saccades. Figure 5*A* shows the pattern of eye movement during spontaneous blinks. Spontaneous blinks were often associated with long saccadic eye movements and sometimes associated with small deviations of gaze that began in a downward and nasal direction, in agreement with previous findings (e.g., Collewijn et al., 1985). However, there was no tendency toward centering. We calculated the mean distance to center at the start and 200 ms after blink onset (when most blinks had ended), and found no significant difference ($t = -0.53$, $P = 0.60$). Figure 5*B* shows the traces for spontaneous saccades that were not associated with blinks. Again, there was no tendency toward centering. We calculated the mean distance to center at the start and 100 ms after saccade onset (when all saccades had ended), and found no significant difference ($t = 0.09$, $P = 0.93$).

In summary, air puff to the face evoked an initial small, curved movement of the eyes in a downward and nasal direc-

tion. After 50–70 ms, the eyes then began to move toward a central position. This movement was on average slower than a normal saccade. In the case of spontaneous blinks and spontaneous saccades, no significant centering of the eye was observed.

Effect of magnitude of defensive movement on centering eye movements

As described above, the orbicularis muscle participates in blinking and squinting. In monkey 2, we measured EMG activity from the orbicularis muscle at the same time that we measured eye position. (In monkey 1, EMG and eye position were measured on separate trials.) For each trial we integrated the orbicularis EMG signal over the 500-ms air-puff period. Then we ranked the trials according to the amount of EMG signal. Two groups of air-puff trials were selected: the 33% of trials with the highest puff-evoked EMG activity and the 33% with the lowest EMG activity. Comparison with the video record confirmed that trials in the high EMG group corresponded to more pronounced facial flinches. Eye movements that occurred during these 2 trial types were then compared. Figure 6 shows the main sequence plot for air-puff trials with large EMG activity (red crosses), trials with small EMG activity (green triangles), and spontaneous saccades (blue dots). For a given amplitude of eye movement, the peak eye speed was faster for large EMG trials than for small EMG trials. These 2 distributions were significantly different (regression analysis, $F = 17.343$, $P < 0.001$). That is, larger facial flinches were associated with faster centering movements of the eye.

Effect of air-puff location

Are the centering movements of the eye reported above the result of the monkey saccading to the location of the air-puff stimulus? This explanation of the centering movements is unlikely because, as described above, their metrics are unlike those of normal saccades. To test the possibility explicitly, we placed 10 air nozzles around the monkey's head (see Fig. 2*A*) and presented air puffs at these different locations in a pseudorandom order. Figure 7 shows the mean eye position at the time of maximum centering during the air puff. The ovals in Fig. 7 show the *x* and *y* SD of eye position around the mean. There was no tendency for the final eye position to be aligned on the location of the air puff. Even a puff on the back of the head evoked a centering eye movement.

In both monkeys, however, the puff directed at the center of the nose (position 5) evoked an average final eye position that was elevated. The reason for this elevation is not clear. One possibility is that this particular air stream deflected from the top of the snout and hit the eyelid or ball. If so, then condition 5 was the only one in which air was puffed into the eye. This air in the eye might have resulted in a deviated final eye position, perhaps protecting the center of the cornea from the air stream.

DISCUSSION

Movement types

In this study we examined the movements evoked by a puff of air applied to the face and other body parts of monkeys. The
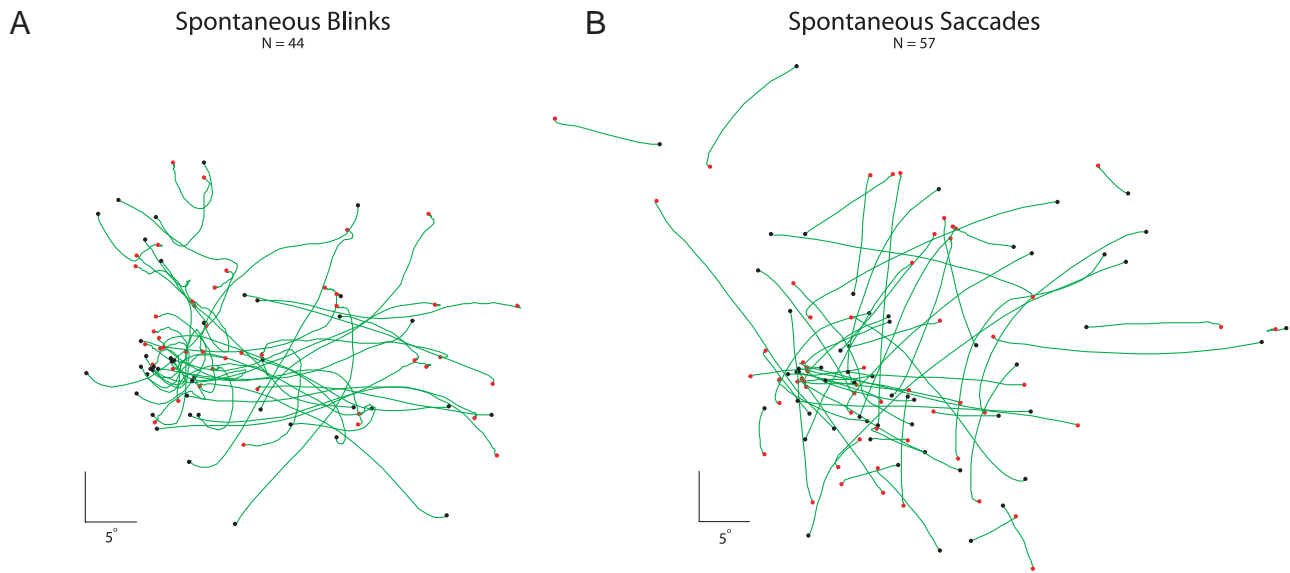
A
Spontaneous Blinks
N = 44

B
Spontaneous Saccades
N = 57

FIG. 5. Lack of centering of eyes during spontaneous blinks and spontaneous saccades. *A*: *eye traces* showing movement of eye in monkey 1 during spontaneous blinks. Spontaneous blinks were identified in video record and time of blink onset was then specified to nearest 10 ms by reference to orbicularis EMG record. Black dot shows position of eye at blink onset; red dot shows position of eye 200 ms later. For most cases blink had ended by this time. *B*: *eye traces* showing movement of eye in monkey 1 during spontaneous saccades not associated with blink. Black dot shows position of eye at saccade onset; red dot shows position of eye 100 ms later. For most cases this time was after saccade had ended and before next saccade had started.

purpose of the study was to compare these movements to those previously obtained by electrical stimulation of cortical areas VIP and PZ (Cooke et al. 2003; Dearworth and Gamlin 2002; Graziano et al. 2002a; Thier and Andersen 1998). As discussed in the following text, the movements were similar in a number of ways. Seven types of movement were observed in the present study. A similar 7 movements were evoked by electrical stimulation of sites in VIP and PZ. The movements included the following.

1) *Blink and squint*. This movement is one of the most reliable movements obtained in studies of startle and defense. Electrical stimulation of almost every site in VIP and PZ evokes a blink and squint (Cooke et al. 2003; Dearworth and
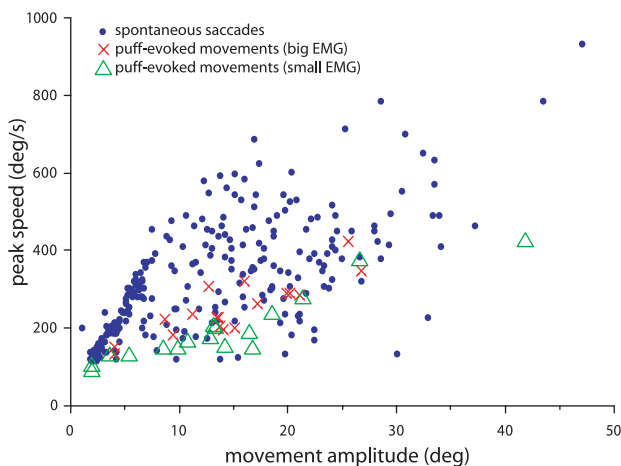

FIG. 6. Eye movements associated with large and small defensive reactions. Size of defensive reaction was measured by EMG in orbicularis muscle integrated over time period of air puff. Red crosses: eye movements on 33% of trials with greatest defensive reaction; green triangles: eye movements on 33% of trials with smallest defensive reaction; blue dots: spontaneous saccades. Data from monkey 2.

Gamlin 2002; Graziano et al. 2002a; Thier and Andersen 1998).

2) *Lifting of the upper lip*. This movement was first described by Strauss (1929) and Landis et al. (1939) in humans during startle and defense. As those authors pointed out, sometimes the upper teeth are exposed in a "sneer." This movement is consistently evoked by stimulation of sites in VIP and PZ (Cooke et al. 2003; Graziano et al. 2002a; Thier and Andersen 1998).

3) *Folding of the pinna against the head*. This movement occurs consistently during startle and defense in animals with mobile ears and is the primary difference between the defensive pattern in humans and in nonhuman mammals (Koch 1999; Landis et al. 1939; Strauss 1929; Yeomans et al. 2002). This movement is also consistently evoked by electrical stimulation of VIP and PZ (Cooke et al. 2003; Graziano et al. 2002a; Thier and Andersen 1998).

4) *Shoulder shrug*. This movement occurs consistently during startle and defense (Koch 1999; Landis et al. 1939; Strauss 1929; Yeomans et al. 2002). One speculation is that it serves to protect the neck, the body location most vulnerable to predatory attack (Landis et al. 1939). Shoulder shrugs are consistently evoked by electrical stimulation in areas VIP and PZ (Cooke et al. 2003; Graziano et al. 2002a; Thier and Andersen 1998).

5) *Retraction of the head from the air puff*. Previous studies report that during startle, the head moves toward a central and downward position (Landis et al. 1939; Strauss 1929; Yeomans et al. 2002). After the initial startle, the head may withdraw from the direction of the stimulus (King and Cowey 1992; King et al. 1992; Landis et al. 1939; Schiff et al. 1962; Strauss 1929). In the present study, we observed mainly a retraction of the head from the direction of the air puff. In areas VIP and PZ, electrical stimulation evokes movements in which the head withdraws from the location of the sensory receptive fields of
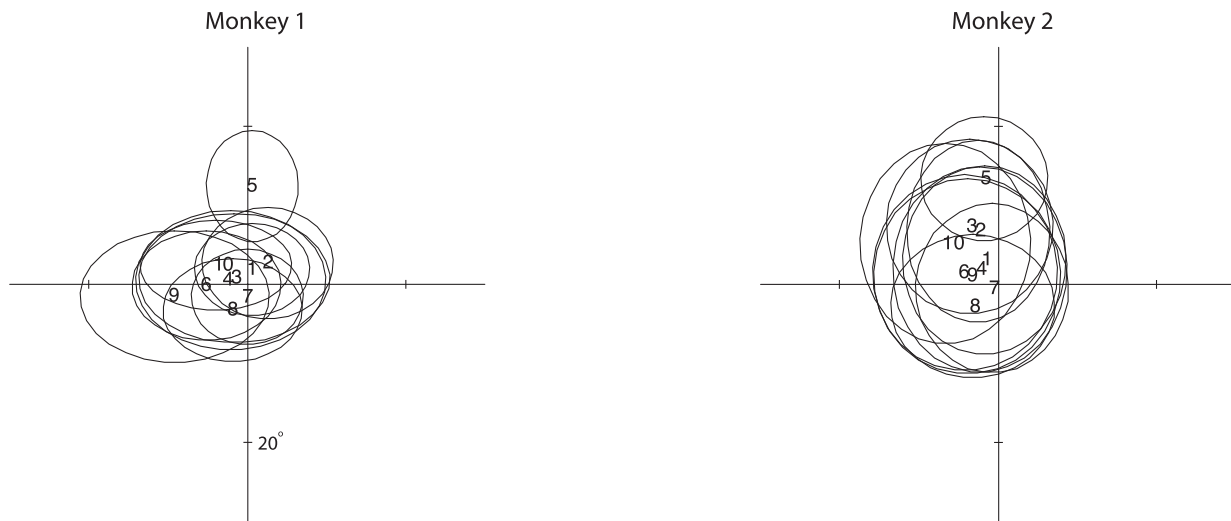
FIG. 7.   Effect of puff location on position to which eyes converge. Ten puff locations were tested, as illustrated in Fig. 2A. For each puff location, mean and the x and y SD of eye position were calculated 166 ms after puff onset for monkey 1 and 228 ms after puff onset for monkey 2. These times were selected because they represent time of maximum clustering of eye position (see Fig. 3). Numbers (1–10) show mean eye position for each puff location. Ovals show x and y SDs. Puff location had little effect on eye position: all 10 puff locations resulted in eyes centering on approximately same region.

the stimulated neurons (Cooke et al. 2003; Graziano et al. 2002a). On stimulation of VIP, there is some evidence of the head moving initially to a central position (Thier and Andersen 1998).

6) Arm movements. Previous studies of startle report that the arms initially pull inward toward the abdomen (Koch 1999; Landis et al. 1939; Strauss 1929; Yeomans et al. 2002). After the initial startle, a more spatially specific reaction may occur in which the arms move rapidly to block a looming or threatening stimulus (Landis et al. 1939; Schiff et al. 1962; Strauss 1929). In the present study, in the video record we observed mainly a movement of the arm toward a guarding or blocking posture that depended on the location of the air puff. In areas VIP and PZ, electrical stimulation evokes postures of the arm similar to the postures obtained in the present study (Cooke et al. 2003; Graziano et al. 2002a). When cells at a cortical site have tactile and visual receptive fields related to the side of the head, stimulation evokes a movement of the arm that lifts the hand into the space near the side of the head (compare with Fig. 1B). When cells at a cortical site have sensory receptive fields related to the side of the torso, stimulation evokes a movement of the arm that brings the elbow tightly against the torso and the hand into lateral space (compare with Fig. 1C). When cells have sensory receptive fields related to both the side of the torso and the forearm, stimulation evokes a movement of the elbow against the torso and a movement of the forearm across the abdomen (compare with Fig. 1D). When cells have sensory receptive fields related to the hand and forearm, stimulation evokes a withdrawal of the hand behind the back (compare with Fig. 1E).

7) Movement of the eyes toward the center of gaze. This type of eye movement was similar but not identical to the goal-directed eye movements evoked by electrical stimulation of VIP and PZ (Fujii et al. 1998; Thier and Andersen 1998). This comparison is discussed in greater detail in a subsequent section.

The above list indicates that the movement components evoked by a puff of air resemble the movement components

evoked by electrical stimulation of brain areas VIP and PZ. There were, however, several apparent differences. One is that for both brain areas, stimulation evoked a movement that did not appear to adapt; it maintained a similar magnitude for hundreds of trials in a session, for many sessions over more than a year. In contrast, in the present study, air puff evoked a movement that had a reduced magnitude in later experimental sessions. Adaptation is common in defensive movements, even in reaction to extreme stimuli such as gunshots behind the head (Koch 1999; Landis et al. 1939; Yeomans et al. 2002). The apparent lack of adaptation in stimulation of VIP and PZ, even for low electrical currents and subtle movements, suggests that this brain stimulation does not simply mimic the effect of a startling sensory percept, but may activate a relatively direct motor pathway.

A second apparent difference between the effect of air puff and the effect of stimulation of VIP and PZ is that air puff evoked at least 2 phases of response, an initial startle followed by a more sustained, more spatially specific response; whereas for both brain areas, electrical stimulation evoked mainly a sustained, spatially specific response. This comparison is discussed in greater detail in the next section.

Startle versus spatially directed defensive movements

A sudden or intense stimulus can evoke a short latency startle response. This response is similar in most mammals. It is stereotyped, bilaterally symmetric, and relatively insensitive to the type of stimulus (Koch 1999; Landis et al. 1939; Strauss 1929; Yeomans et al. 2002). It is thought to be an important adaptation for putting the body into an initial protective posture. After the initial startle response, a variety of more complex secondary responses can occur (e.g., King and Cowey 1992; King et al. 1992; Landis et al. 1939; Schiff et al. 1962; Strauss 1929). These responses, such as ducking and veering, depend on a more complex analysis of stimulus properties such as location and trajectory. In the present study, we found evidence of both an initial startle response and a more sus-

tained, spatially specific response. The 2 phases of response were most clearly seen in the EMG recordings from facial and shoulder muscles (Fig. 2). The air puff evoked an initial, transient spike in muscle activity. This spike was relatively bilaterally symmetric, and thus resembled the previously described startle response. After the initial spike, a more sustained muscle activity was observed. This more sustained activity was largest in the muscles on the same side of the face as the air puff.

Electrical stimulation of cortical areas VIP and PZ evokes activity in the same facial and shoulder muscles that were studied in the present experiment. For both brain areas, stimulation evokes activity that is sustained throughout the stimulation train and that is more pronounced on the same side of the body as the sensory receptive fields of the stimulated neurons (Cooke et al. 2003; Graziano et al. 2002a). The evoked activity lacks an initial, bilaterally symmetric spike. In these respects, stimulation of VIP and PZ does not evoke a startle response, but instead evokes a response that resembles the more sustained, spatially specific component of a defensive reaction.

One interpretation of these results is that the simple, bilaterally symmetric startle reflex and the more complex, spatially specific defensive movements may be mediated by separate mechanisms. The startle reflex is thought to be mediated by a set of subcortical structures (Koch 1999; Yeomans et al. 2002). Its latency (e.g., 18 to 34 ms in the present study) is thought to be too brief to depend on cortical circuits. We suggest that cortical areas VIP and PZ could contribute mainly to the secondary phase of defensive movement that requires processing of stimulus location and movement. Such a role is consistent with the properties of neurons in VIP and PZ. In both areas, the neurons are sensitive to spatial location, speed, and direction of movement of tactile, visual, and auditory stimuli (Bremmer et al. 2002; Colby et al. 1993; Duhamel et al. 1998; Fogassi et al. 1996; Graziano and Gandhi 2000; Graziano et al. 1997, 1999; Rizzolatti et al. 1991; Schaafsma and Duysens 1996; Schlack et al. 2000). It will be important to lesion or reversibly deactivate areas VIP and PZ to determine whether this spatially specific component of the defensive reaction is attenuated.

Eye movements

In this section, we suggest that the centering of the eye in the orbit during defensive movements may be secondary to a previously described protective retraction of the eyeball into the orbit.

The movement of the eye during blink has been studied in many animals including humans, monkeys, rabbits, cats, and guinea pigs (e.g., Collewijn et al. 1985; Evinger et al. 1984; Schlag et al. 1983). It was once thought that the eye consistently rotates upward during a blink (Bell 1823), but modern methods of tracking eye position have not confirmed "Bell's reflex" (Collewijn et al. 1985; Evinger et al. 1984; Takagi et al. 1992). A variety of blinking-related eye movements have been described, including a torsional movement; a slight, curved deviation of gaze in a downward and nasal direction; and a retraction of the eyeball into the orbit (Bergamin et al. 2002; Bour et al. 2000, 2002; Collewijn et al. 1985; Evinger et al. 1984; Takagi et al. 1992). This

retraction of the eyeball is caused by the cocontraction of the extraocular muscles that normally rotate the eye (Evinger and Manning 1993). In most animals (but not primates), a specialized muscle, the retractor bulbi, also participates in the retraction of the eyeball. It is now generally thought that rotational movements of the eye during blink, such as torsional movements and small deviations of gaze, are a secondary effect of the cocontraction of muscles, and that the primary movement is the protective retraction of the eye into the orbit (Bour et al. 2000; Evinger and Manning 1993). In humans, this retraction is about 1–2 mm (Evinger et al. 1984). It is also generally thought that the movements of the eye during blink are not caused by mechanical interactions between the eyelid and the ball (Bour et al. 2000; Collewijn et al. 1985; Evinger and Manning 1993; Evinger et al. 1984).

The cocontraction of the extraocular muscles during a blink might be expected to cause the eye to rotate from any initial position toward a central position. However, such centering movements of the eye have not been consistently reported. Where they have been reported, they are generally small movements that bring the eye only a few degrees closer to the center (Bour et al. 2000; Evinger et al. 1984; Ginsborg and Maurice 1959; Goossens and Opstal 2000; Riggs et al. 1987). One possible reason for the differences between studies is that some examine spontaneous blinks, some examine blinks performed on verbal command, some examine blinks evoked by a mild stimulus to the eye, and some examine blinks evoked by a strong stimulus such as a 12 psi puff of air to the face. Centering movements of the eye, caused by the cocontraction of the extraocular muscles, might occur more reliably during a strong or sustained defensive reaction than during a brief spontaneous blink.

In the present study we found that a puff of air directed at the face for 500 ms evoked a consistent pattern of eye movement. This pattern included an initial movement that was in a downward and nasal direction, matching previous reports of eye movements during blinks (Bergamin et al. 2002; Bour et al. 2000, 2002; Collewijn et al. 1985; Evinger et al. 1984; Takagi et al. 1992). We also found that during air puff, after the initial downward and nasal movement, the eye made an apparent goal-directed movement, toward and sometimes reaching a location that was near the center of gaze. On trials when the air-puff–evoked squint was greater, as measured by the muscle activity in the orbicularis muscle, the speed of the centering eye movement was significantly faster; on trials when the air-puff–evoked squint was smaller, the speed of the eye movement was slower. These centering eye movements do not appear to be saccades but rather represent a type of movement specific to the defensive reaction.

In both VIP and PZ, electrical stimulation has been reported to evoke goal-directed movements of the eyes (Fujii et al. 1998; Thier and Andersen 1998). For both brain areas, the movements are slower than spontaneous saccades; in area VIP the movements were described as being in the range for memory-guided saccades. Because these movements converge on a location and are hypometric, they resemble the air-puff–evoked centering of the eyes observed in the present study. It is important to note, however, that these stimulation-evoked eye movements do not necessarily converge on the center of gaze; other goal positions can also be obtained. In the present

study, puff-evoked eye movements were usually (although not always) directed to a region within about 15° of the center of gaze.

We hypothesize that the goal-directed eye movements evoked by stimulation of VIP and PZ may be partly a defense-related centering of the eyes. One possibility is that the brain stimulation sometimes evoked a combination of normal, vector saccades and defense-related centering of the eyes, resulting in off-center convergence evoked from some stimulation sites. Kurylo and Skavenski (1991) stimulated sites across the posterior parietal lobe; when stimulation of a site caused a squint, it typically also caused a goal-directed eye movement. They concluded that the "goal-directed" component was a side effect of the squint.

Goal-directed saccades almost certainly have a variety of functions including those unrelated to defense. For example, they may be related to fixation of a target in head-centered spatial coordinates (Thier and Andersen 1998). Saccades that converge toward a final position, and that are thought to be involved in acquiring a fixation target, have been evoked by stimulation of other brain areas such as the dorsomedial frontal cortex (Tehovnik and Lee 1993). Whether the goal-directed saccades in VIP and PZ are related to defense or to fixation of targets is now open to debate. As found in the present study, many of the components of defensive movements are the same as those found on stimulation of VIP and PZ, including specific movements of the face, ear, head, shoulder, and arm. We therefore suggest that the "goal-directed" eye movements evoked from these two particular areas might be part of the constellation of defensive movements.

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