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Neuropsychologia 44 (2006) 845–859

NEUROPSYCHOLOGIA

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Parieto-frontal interactions, personal space, and defensive behavior

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Received 4 April 2005; received in revised form 16 August 2005; accepted 17 September 2005

Abstract

In the monkey brain, two interconnected cortical areas have distinctive neuronal responses to visual, tactile, and auditory stimuli. These areas are the ventral intraparietal area (VIP) and a polysensory zone in the precentral gyrus (PZ). The multimodal neurons in these areas typically respond to objects touching, near, or looming toward the body surface. Electrical stimulation of these areas evokes defensive-like withdrawing or blocking movements. These areas have been suggested to participate in a range of functions including navigation by optic flow, attention to nearby space, and the processing of object location for the guidance of movement. We suggest that a major emphasis of these areas is the construction of a margin of safety around the body and the selection and coordination of defensive behavior. In this review, we summarize the physiological properties of these brain areas and discuss a range of behavioral phenomena that might be served by those neuronal properties, including the ducking and blocking reactions that follow startle, the flight zone of animals, the personal space of humans, the nearby, multimodal attentional space that has been studied in humans, the withdrawal reaction to looming visual stimuli, and the avoidance of obstacles during self-motion such as locomotion or reaching.

Keywords: Ventral intraparietal; Sensorimotor; Macaque; Avoidance; Motor cortex; Looming

> . . . "hunger and love" can take only second place. The satisfaction of hunger and sexual appetite can be postponed; not so escape from a dangerous enemy, and all animals, even the biggest and fiercest, have enemies. As far as higher animals are concerned, escape must thus at any rate be considered as the most important behavior biologically.
> Heini Hediger
>
> Constant vigilance!
> Alistar Moody

1. Introduction

A basic function of the motor system of all animals is to protect the body from attack or collision (e.g., King, Dykeman, Redgrave, & Dean, 1992; Landis & Hunt, 1939; Schiff, 1965; Yeomans, Scott, & Frankland, 2002). Protective mechanisms are essential in extreme, life-threatening situations; but they are also essential in every day life. They allow us to walk through a room without hitting the furniture, keep a healthy distance from a cliff edge, run through a twiggy forest without poking out an eye, brush away an insect, reach safely around a prickly object, or sit at a desk without bruising our elbows and arms as we work. Our lives would be impossible without these mechanisms in place and working in the background. In this description, defense of the body surface is not a single function, but rather a collection of processes all bound together by a similar goal and similar sensorimotor computations.

In mammals, protective mechanisms operate on both the cortical and subcortical level. On the subcortical level, for example, circuits in the brain stem mediate the startle reflex (Koch, 1999; Yeomans et al., 2002). Spinal mechanisms mediate the withdrawal reflex, an extremely sophisticated system that evokes a reaction dependant on the location of the noxious stimulus on the skin and the configuration of the limbs (Clarke & Harris, 2004; Schouenborg, Weng, Kalliomaki, & Holmberg, 1995; Sherrington, 1910). These reflexes apparently provide a rapid, first line of defense.

Cortical circuits may mediate a slower but more flexible reaction that can integrate information from many sensory modalities and allow the animal to avoid an impending impact. This spatially guided protection of the body surface is one of the most basic sensorimotor problems facing any animal. It requires

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0028-3932/$ – see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.neuropsychologia.2005.09.009

monitoring the location and trajectory of nearby objects, calculating the region on the body that is potentially threatened, and coordinating the appropriate defensive response. The responses can include squinting, ducking, withdrawing from the direction of the potential threat, navigational veering during locomotion to avoid obstacles, and blocking an impending object with one body part (e.g. the forelimb) to protect another body part (e.g. the face). Defense of the body surface does not need to involve an overt movement. It can be as subtle as biasing the animal's ongoing movements to avoid a dangerous object.

Recently, two interconnected cortical areas in the monkey brain have been implicated in the control of spatially guided defensive movements (Graziano, Taylor, Moore, & Cooke, 2002). These areas, shown in Fig. 1, are the ventral intraparietal area (VIP) and a polysensory zone in the precentral gyrus (PZ). Neurons in both areas are multimodal, responding to visual, tactile, and sometimes auditory stimuli (e.g. Colby, Duhamel, & Goldberg, 1993; Duhamel, Colby, & Goldberg, 1998; Graziano, Hu, & Gross, 1997a; Graziano, Reiss, & Gross, 1999; Rizzolatti, Scandolara, Matelli, & Gentilucci, 1981; Schlack, Sterbing, Hartung, Hoffmann, & Bremmer, 2002, in press). These sensory responses have a bias for objects that are near or approaching the body. Electrical stimulation of both areas leads to a characteristic set of defensive-like movements, including ducking, squinting, and blocking, as if the monkey were defending the part of the body where the sensory receptive fields of the neurons are located (Cooke & Graziano, 2004a; Cooke, Taylor, Moore, & Graziano, 2003; Graziano, Taylor, & Moore, 2002). These two cortical areas probably serve a range of functions, judging from their range of neuronal properties. These diverse neuronal properties, however, share a common theme of processing space and movement near the body. We propose that a major function of these cortical areas is to maintain a margin of safety around the body and to coordinate actions that defend the body surface.

One purpose of this review is to emphasize a more ethological approach to understanding the functions of the posterior parietal areas and their associated frontal areas. The physiological properties of a brain area may make most sense when placed in the context of the behavioral needs of the animal. For this reason, we begin by describing behavioral work on the defense of the body surface. We then describe the properties of parietal area VIP and frontal area PZ and discuss their possible role in defensive behavior.

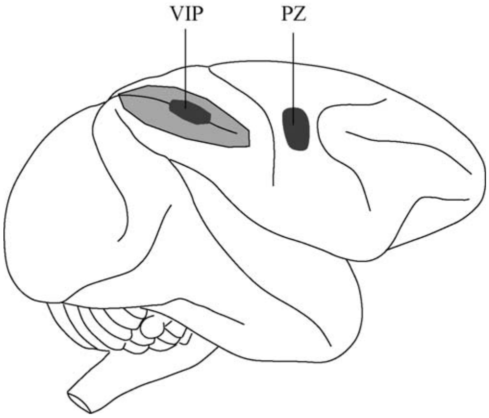

Fig. 1. Schematic side view of macaque monkey brain showing approximate location of the ventral intraparietal area (VIP) and the polysensory zone (PZ). Intraparioetal sulcus shown opened up, with light shaded area indicating buried cortex.

2. Defensive behavior

In this section, we review four ways in which the defense of the body surface has been studied: startle, personal space, looming, and obstacle avoidance during self-motion. These areas of research differ from each other, but all address the same underlying spatial and motor issues involved in protecting the body surface.

2.1. Startle and post-startle

In 1929, the German scientist Hans Strauss published the first systematic study of the startle reflex. He filmed psychiatric patients, war veterans, and infants while an assistant crept up and fired a pistol just behind the subject's head. Since then, the startle reaction has been studied extensively by many investigators in many species of animals (e.g., Davis, 1984; Koch, 1999; Landis & Hunt, 1939; Pfeiffer, 1962; Yeomans et al., 2002). The classic mammalian startle reflex, such as to a loud sound, involves a short latency and highly stereotyped set of movements. These movements appear to bring the body into a generalized defensive stance (Yeomans et al., 2002). The head draws down and the shoulders lift, as if to protect the parts of the neck that are vulnerable to predation. The eyes close, the facial muscles contract, lifting the upper lip in a characteristic sneer, the torso curves forward, the knees bend, and the arms pull in as if to protect the abdominal region. The magnitude of the startle reflex varies from subject to subject, and drops rapidly on repeated stimulus presentations in an apparent adaptation. In some cases, after adaptation or with a weak stimulus, only the blink remains of the reflex.

After the stereotyped startle reaction to an unexpected stimulus, the subject typically expresses a more flexible secondary reaction (e.g. King et al., 1992; Landis & Hunt, 1939; Schiff, Caviness, & Gibson, 1962; Strauss, 1929). These secondary movements are often spatially directed, involving orientation toward the stimulus, or ducking away from the stimulus, or squinting on the side of the face closest to the stimulus, or lifting the hands in a blocking gesture as if to ward off a threat. Thus, the initial startle reflex produces a generalized defensive stance, whereas the secondary reaction refines the defensive movement and tailors it to the specific location of the stimulus.

In a recent study, we examined the movements evoked by a puff of air directed at various points on the body surface of a monkey (Cooke & Graziano, 2003). Using recordings of muscle activity from a variety of muscles in the face and shoulder, we confirmed that the reaction began with a short latency, bilaterally symmetric startle. Within about 50 ms, the reaction evolved into a post-startle phase that was generally spatially directed toward the stimulus. Fig. 2A–E shows some typical components of the post-startle phase of the defensive movement. Many of these

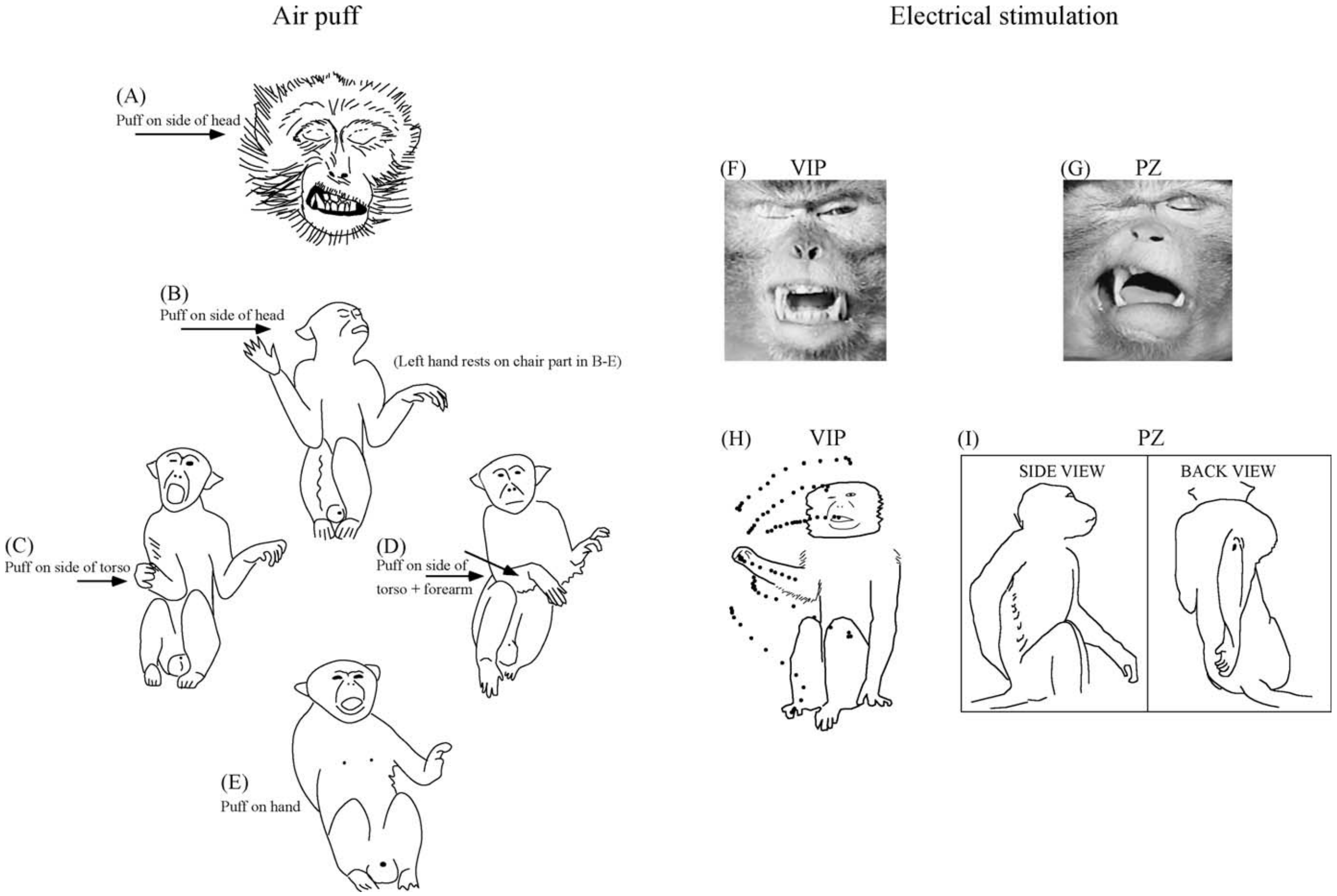

Fig. 2. Defensive behaviors evoked by air puff to the skin and by electrical stimulation of VIP and PZ. (A–E) Effects of 0.5 s air puff on different locations of a monkey's body. Tracings from video frames. The initial response to the air puff was a startle reaction that was not spatially directed. The spatially specific effects shown here occurred after the startle. (F–G) Effect of stimulating sites in VIP and PZ. Neurons at these sites had a tactile response on the side of the face and a visual response to objects near the side of the face. (H) Neurons at this site in VIP had a tactile response on the side of the face and a visual response to objects near the side of the face. Dots show the position of the hand in 33.3 ms increments. Each line of dots shows the path of the hand from a midline position to a lateral position during a 500 ms stimulation train. (I) Effect of stimulating a site in PZ. Neurons at this site had a tactile response on the arm and a visual response to objects near and approaching the arm. Stimulation evoked a rapid movement of the hand to a location behind the monkey's back.

components are familiar from everyday experience. We consistently observed seven components:

1. A blink and squint that was spatially specific, in the sense that it was more pronounced on the side of the air puff.
2. A lifting of the upper lip in a characteristic sneer, exposing the upper teeth, again more pronounced on the side of the air puff.
3. A retraction of the head away from the location of the air puff.
4. A folding of the ear against the head, more pronounced on the side of the air puff.
5. An elevation of the shoulders, more pronounced on the side of the air puff.
6. A variety of blocking or retracting arm movements. An air puff to the side of the face typically induced a lifting of the hand into the space near the side of the face, as if to block the stimulus. An air puff to the hand or forearm typically induced a fast withdrawal of the hand behind the back. An air puff to the side of the torso typically induced a retraction of the elbow to the side of the body as if to block the stimulus.
7. A distinctive, non-saccadic movement of the eyes. This defense-related eye movement is illustrated in Fig. 3A. The rotation of the eyes during a blink is thought to be a by-product of the protective retraction of the eyeballs into the head, caused by the co-contraction of the extra-ocular muscles (Bour, de Visser, Aramideh, & Speelman, 2002; Collewijn, van der Steen, & Steinman, 1985; Evinger, Shaw, Peck, Manning, & Baker, 1984). For example, in humans, the eyeball retracts 1–2 mm during a blink (Riggs, Kelly, Manning, & Moore, 1987). This co-contraction of muscles is thought to cause the distinctive, defense-related wobble in gaze direction. The eye first rotates several degrees in a downward and nasal direction, then rotates toward the center of gaze (Bergamin, Bizzarri, & Straumann, 2002; Bour, Aramideh, & de Visser, 2000; Collewijn et al., 1985; Evinger et al., 1984; Ginsborg & Maurice, 1959; Goossens & Opstal, 2000; Takagi, Abe, Hasegawa, & Usui, 1992). These convergent movements to the center of gaze do not have the same speed profiles as saccades or smooth pursuit eye movements (Cooke & Graziano, 2003, 2004a); they belong to a separate category of defense-related eye movement.

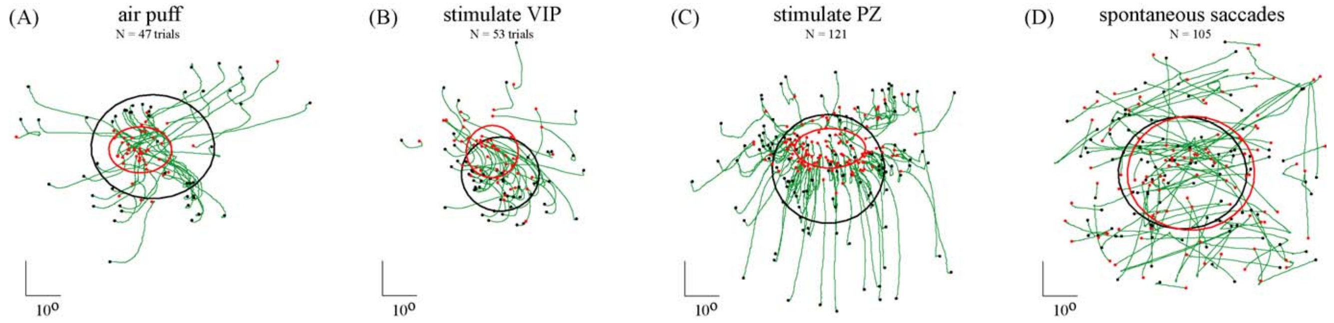

Fig. 3. Defense-related eye movements. (A) Air puff to the face evoked a distinctive eye movement including a brief down-and-nasal (in this plot, down-and-rightward) movement. This is followed by a movement that brings the eye to the center. These movements are believed to be caused by a protective retraction of the eyeball. Each green trace shows the movement of the eye during one air puff trial. The black dot shows the start position of the eye. The red dot shows the final position of the eye. The black oval shows the *x* and *y* standard deviation of eye position at start of air puff, and the red oval shows the *x* and *y* standard deviation of eye position at end of the sampled time. (B) Electrical stimulation of VIP evoked eye movements. These movements typically included a brief down-and-nasal movement followed by a movement toward a central location. The initial positions of the eye in this case were biased toward the lower right quadrant, but in general the eye moved from the starting position toward a central location. (C) Electrical stimulation of PZ evoked a down-and-nasal and centering movement. (D) Spontaneous saccades did not follow the same pattern as defense-related eye movements.

As described in a later section, a similar set of seven movement components are evoked by electrical stimulation of cortical areas VIP and PZ (Cooke & Graziano, 2004a; Cooke et al., 2003). Electrical stimulation of these areas does not appear to evoke a startle. The evoked reaction lacks the initial, bilaterally symmetric reaction. From the onset, the evoked movement appears to be spatially directed as if to protect the location of the receptive fields of the stimulated neurons. One possible interpretation is that there is a distinction between cortical and subcortical defensive mechanisms. In this hypothesis, the relatively simple startle reflex is mediated by fast, subcortical circuits that cannot distinguish the location or trajectory of the stimulus (Koch, 1999; Yeomans et al., 2002) and the post-startle reaction may be mediated by slower but more spatially sophisticated cortical mechanisms such as VIP and PZ.

2.2. *Flight zone, personal space, and peripersonal attention*

One of the first scientists to emphasize spatially directed defense was Hediger, director of the Zurich Zoo from 1954 to 1973. In his book on animal psychology (1955), Hediger argued that escape was the most urgent survival requirement of any animal, trumping the more postponable functions of sex and eating. Through his observations of wild and captive animals, Hediger formulated the concept of a flight distance, now often called a flight zone. In his formulation, escape is not a simple, stimulus-driven reflex. The sight of a predator is not enough to cause an animal to flee. Instead, the animal uses its active attention to its surroundings and its spatial cognition to construct a margin of safety around its body. When a threatening object enters this margin of safety or ‘flight zone’, the animal escapes. According to Hediger’s observations, grazing animals have an especially large flight zone of tens of meters that can expand or contract depending on circumstances. A domesticated animal will in general have a much smaller flight zone. The concept of a flight zone has even been applied explicitly to the practice of cow herding (Smith, 1998).

Hediger’s work on the flight zone led directly to the concept of personal space in humans. Many researchers noted that humans have an invisible bubble of protective space surrounding the body, generally larger around the head, extending farthest in the direction of sight (e.g. Dosey & Meisels, 1969; Hall, 1966; Horowitz, Duff, & Stratton, 1964; Sommer, 1959). When that personal space is violated, the person steps away to reinstate the margin of safety. Personal space, therefore, is the flight zone of a human with respect to other humans. The size of the personal space varies depending on context. A person who is placed in a potentially threatening context will have an expanded personal space; a person in friendly company will have a reduced personal space (Dosey & Meisels, 1969; Felipe & Sommer, 1966). In this view, personal space is fundamentally a protective space, a margin of safety.

The concept of a personal space surrounding the body has more recently been studied in the context of sensory attention. Psychophysical experiments on humans and experiments on the attentional deficits of brain-damaged humans have led to the hypothesis of a specialized attentional mechanism that is specific to the space near the body (di Pellegrino, Ladavas, & Farne, 1997; Halligan & Marshall, 1991; Ladavas, Pavani, & Farne, 2001; Ladavas, Zeloni, & Farne, 1998; Pavani & Castiello, 2004; Spence, Pavani, & Driver, 2000). This attention to space near the body is multimodal. For example, a touch on the hand will draw attention to the space near the hand, and speed the processing of a subsequent visual stimulus presented near the hand (Spence et al., 2000). A visual stimulus near the cheek will draw attention and enhance the processing of tactile stimuli on the cheek (Ladavas et al., 1998). These experiments on cross-modal attention have led to the concept of a shell of multimodal, attentional space that surrounds the body, conforming to the shape of the body and bending as the limbs bend.

One possibility is that this nearby attentional space is related to the protective personal space described by Hall and others and the defensive flight zone described by Hediger. In this view, the attention to objects near the body and the maintenance of a margin of safety around the body are linked functions. If purely subjective anecdote can be excused for a moment, there are some people whom everybody knows to be clumsy, who bruise themselves bumping into furniture, trip over obstacles, and knock over glassware without noticing. These people, at least superficially, give the impression of having deficient attention to the space near the body. They simply do not notice until it is too late. Perhaps the maintenance of a margin of safety around the body is an attentive process.

Neurons in cortical areas VIP and PZ are multimodal, responding to tactile, visual, and sometimes auditory stimuli (e.g. Colby et al., 1993; Duhamel et al., 1998; Graziano et al., 1997a, 1999; Rizzolatti et al., 1981; Schlack et al., 2002b, in press). The receptive fields are usually though not always confined to the space near the body. These receptive fields are like bubbles of space anchored to the body surface. The responses of these neurons can be altered by spatial attention (Cook & Mounsell, 2002; Graziano & Gross, 1998). Because of these properties, it has been hypothesized that the body-centered receptive fields in VIP and PZ form the neural basis for the peripersonal attentional effects described above (Ladavas et al., 2001; Spence et al., 2000). We speculate that these body-centered receptive fields in VIP and PZ could also form the neural basis for the psychological phenomenon of personal space and the ethological phenomenon of a flight zone (see Fig. 4). These possibilities, however, remain speculations. It will be useful to lesion the multimodal neurons in VIP and PZ and test for changes in peripersonal attention, personal space, and flight zone.

2.3. Looming

Gibson (1972) pointed out that visual looming is an essential component of threat. In Gibson's approximation, the animal can be considered a single point or eye. If an approaching object is expanding symmetrically, then it is on a direct collision course with the animal's eye. Asymmetrical expansion, in contrast, implies that the approaching object will not collide with the animal's eye. Thus, in Gibson's formulation, looming or symmetrical expansion is a sign of danger to trigger an evasive reaction.

Defensive reactions to looming have been found across a range of animals (Schiff, 1965; Schiff et al., 1962). Even human infants react defensively to looming stimuli, though there is still debate over whether the behavior is present from birth (Ball & Tronick, 1971; Nanez, 1988; Yonas, Pettersen, & Lockman, 1979). Neurons that respond selectively to looming have been identified in the fly brain, locust brain, and pigeon brain, and are hypothesized to play a role in obstacle avoidance during flight (Rind, 2002; Schuster, Strauss, & Gotz, 2002; Sun & Frost, 1998; Tammero & Dickinson, 2002). Looming, therefore, appears to be a fundamental signal for a threat to the body surface.

It is worth noting that visual looming in the Gibson sense of symmetrical expansion is only a limited class of stimulus. A stimulus that expands symmetrically is on a collision course with the eye, but a stimulus that expands asymmetrically may be on a collision course with another part of the body surface. It is obviously important to predict that point of impact on the body surface. If the threatening object is approaching your left cheek, you might squint your left eye and duck to the right. If the object is approaching your throat, you might tuck down your chin and lift your hands. Imagine that your hand is resting on a table and someone swings a hammer at it. This visual stimulus has no expansion component at all; instead it is entirely in the fronto-parallel plane. Yet it is still in a sense a "looming" stimulus, looming toward the hand.

The neurons in VIP and PZ could be described as looming detectors in this more complex or general sense (Colby et al., 1993; Rizzolatti et al., 1981; Graziano et al., 1997a). These neurons are typically bimodal or trimodal, with a tactile receptive field on some part of the body and a visual receptive field (and sometimes an auditory receptive field) extending into the adjacent space. An object touching, near, or approaching the tactile receptive field will usually drive the neuron. These neurons could

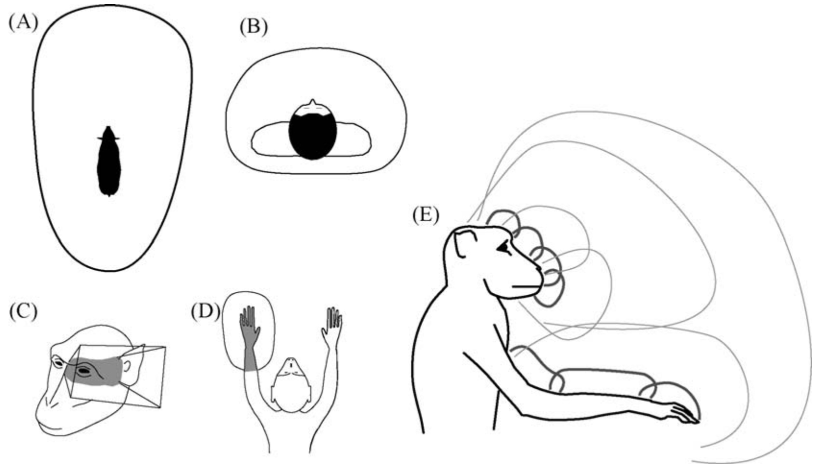

Fig. 4. Peripersonal space. (A) The flight zone of an animal. When a threat enters the flight zone, the animal moves away (based on Smith, 1998). (B) The personal space of a human. When another person enters the personal space, the subject moves away. (C and D) Some tactile receptive fields (shaded) and visual receptive fields (boxed) of neurons in monkey cortical area PZ. (E) Schematic diagram of visual receptive fields in PZ. Space near the body is represented by relatively more receptive fields, and space at increasing distances from the body is represented by fewer receptive fields.

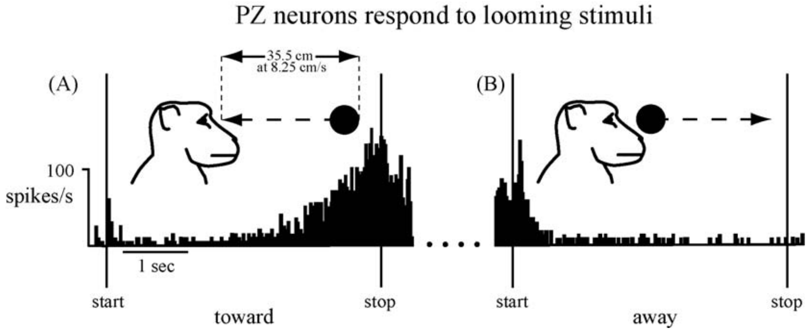

Fig. 5. Responses of a neuron in PZ to a 4 cm wide ball approaching and receding from the face. The neuron responded to tactile stimuli on the front of the face and to visual stimuli near the face. When the ball was stationary and distant from the monkey (37.5 cm away), the neuron's firing rate was low. As the ball approached, the firing rate increased. The increase was most pronounced at the end of the trajectory as the ball loomed toward the face. When the ball stopped moving (2 cm away), the firing rate dropped, but was still elevated above baseline. When the ball began to move away from the face, the neuron responded to the onset of movement with a transient burst of activity, then dropped to a low firing rate. Adapted from Graziano, Hu, and Gross (1997a,b) Fig. 4.

be said to encode looming toward a specific location on the body surface.

Fig. 5 shows the response of a typical bimodal, visual–tactile neuron in PZ to a visual stimulus that is looming directly toward the face (Graziano et al., 1997a). This neuron had a tactile receptive field on the face and a visual receptive field extending forward from the face. The neuron's activity rose as the stimulus loomed toward the face, remained high while the stimulus was stationary near the face, and dropped to a low level while the stimulus receded from the face.

2.4. *Obstacle avoidance during self-motion*

Navigation involves essentially two tasks: directing oneself toward a desired goal, and avoiding obstacles. Obstacle avoidance is usually thought of as a matter of adjusting one's direction of heading to avoid a collision (Gibson, 1972). In this model, the animal is essentially a point moving through the environment, swerving around obstacles. However, with a large, multi-jointed body, the problem is more complex and collision avoidance becomes more than adjusting the direction of heading. Imagine that you are walking through a doorway, and you adjust the angle of your shoulder to avoid hitting it on the door frame; or that you are walking through a cluttered room and lift your hand to avoid hitting it on a chair; or that you are walking through a twiggy forest, and shift your head slightly to one side while raising your hand to block a branch from hitting your face. These adjustments to your posture are all part of the collision avoidance response, but they protect specific subparts of the body rather than the body as a whole.

Reaching to a target with the hand also requires avoiding obstacles. Normally, the path of the hand is biased away from nearby objects even if they are not directly blocking the reach (Schindler et al., 2004; Tipper, Lortie, & Baylis, 1992; Tresilian, 1998; Vaughan, Rosenbaum, & Meulenbroek, 2001).

All of these tasks, including swerving around obstacles during locomotion, protecting specific parts of the body during locomotion, and reaching around obstacles, require similar sensorimotor computations. They all involve self-motion and all require monitoring the proximity and movement of objects relative to specific parts of the body. Visual receptive fields that are anchored to specific regions of the body surface and encode the location and movement of objects with respect to the body surface, such as visual receptive fields found in VIP and PZ, would be of use for this type of computation.

In the cortex of monkeys, two visual areas have been studied with respect to optic flow and navigation: MST and VIP. Neurons in both areas respond to optic flow, with a general preference for expanding flow fields (Bremmer, Duhamel, Ben Hamed, & Graf, 2002; Duffy & Wurtz, 1991; Froehler & Duffy, 2002; Graziano, Andersen, & Snowden, 1994; Saito et al., 1986; Schaafsma & Duysens, 1996; Tanaka & Saito, 1989; Zhang, Heuer, & Britten, 2004). Neurons in both areas also respond to vestibular signals that may participate in the encoding of self-motion (Bremmer, Klam, Duhamel, Ben Hamed, & Graf, 2002; Page & Duffy, 2003; Schlack, Hoffmann, & Bremmer, 2002). One distinction between the areas is that in VIP, the neurons appear to emphasize the space near the body, whereas in MST, no bias for nearby stimuli has been found. Some VIP neurons respond to expanding optic flow fields and also respond in a directional fashion to tactile stimuli that sweep over the face, as if the animals were running forward through leaves or grass (Bremmer, Duhamel, et al., 2002). On the basis of these properties, it has been suggested that VIP contributes to navigation with respect to nearby objects (Bremmer, Duhamel, et al., 2002). VIP, therefore, is a candidate for the task of obstacle avoidance during self-motion. Area PZ has not yet been tested with optic flow stimuli.

2.5. *Summary of defensive movements*

Defense of the body surface is a sensorimotor problem. It is partly served by reflexes such as the startle reflex, but much of defensive behavior is flexible and spatially guided. It involves an attentive encoding of the space near the body, such as the flight zone of grazing animals, the personal space of humans, or the multimodal attentional space that surrounds the skin. It involves visual processing to encode the trajectory of objects and especially the "looming" of objects toward the face or other body parts. Self-motion and obstacle avoidance are also essential components. Whether the object is moving to you, or you are moving toward it, a defensive mechanism must react to this relative motion. The motor output involves an elaborate set of components, including squinting, blinking, ducking, veering, shrugging, raising the arm to block a threat, withdrawing the arm or other body parts from a threat, and even a defense-related retraction of the eye into the orbit.

In the following sections, we describe the properties of cortical areas VIP and PZ in the monkey brain. Neurons in these areas respond selectively to the stimuli described above that pose a potential threat to the body, and electrical stimulation of these cortical areas evokes the movement components that are typical of a defensive reaction. Whether these cortical areas are specialized for defense of the body surface or serve a range of other functions is briefly discussed in the final section.

3. Physiology of VIP and PZ

3.1. Parieto-frontal interactions

The relationship between the primate posterior parietal lobe and the frontal lobe follows a distinctive pattern. Specific regions in the parietal lobe connect to corresponding regions in the frontal lobe with similar properties (Burnod et al., 1999; Matelli & Luppino, 2001). The parietal and frontal regions are subtly different, a parietal area generally emphasizing sensory or representational processing, attention, and planning, and the corresponding frontal area generally emphasizing motor output. However, the functions overlap extensively and no clear distinction can be made between a purely sensory area and a purely motor area. Indeed, the differences between a parietal area and its corresponding frontal area often seem to be more in the interpretation than in the actual data.

Examples of this interaction between the parietal and frontal lobe include the control of eye movements by the lateral intraparietal area (LIP) and the frontal eye fields (FEF) (e.g. Andersen, Brotchie, & Mazzoni, 1992; Bruce, Goldberg, Bushnell, & Stanton, 1985); the visual guidance of grasping by the anterior intraparietal area (AIP) and frontal area F5 (e.g. Fogassi et al., 2001; Rizzolatti et al., 1988; Sakata, Taira, Murata, & Mine, 1995); and the spatial guidance of reaching by the parietal reach region (PRR) and the dorsal premotor cortex (e.g. Batista, Buneo, Snyder, & Andersen, 1999; Hocherman & Wise, 1991; Johnson, Ferraina, Bianchi, & Caminiti, 1996; Messier & Kalaska, 2000; Snyder, Batista, & Andersen, 1997). Arguably, another example is the processing of language in Wernicke's area on the parieto-temporal junction and Broca's area in the frontal lobe (Damasio & Geschwind, 1984). It was originally thought that Wernicke's area subserves language perception and that Broca's area subserves language production, but it is now known that both areas contribute to some extent to both functions. In each of these cases, a specific class of behavior is emphasized by a specific posterior–frontal circuit. These behaviors – saccadic eye movements, grasping, reaching, speaking – represent sensorimotor tasks of ethological importance to the animal. We propose that parietal area VIP and frontal area PZ provide another example of this pattern, and that a sensorimotor task that is at least emphasized by these areas is the defense of the body surface.

It should be pointed out, however, that although the parietal subdivisions may emphasize different types of processing and thus different behavioral tasks, they are unlikely to function as independent modules, since they are densely interconnected. Perhaps these specialized parietal areas could be thought of as players on a team, interacting, sharing information, depending on each other, and yet also each one specializing to some degree in a particular type of task. In particular, though we suggest that defense of the body and maintenance of a margin of safety may be emphasized by VIP, that is unlikely to be its only function, and VIP is likely to participate in a range of other functions. The degree of specialization and independence of function may be greater in the frontal areas to which the parietal areas project.

3.2. The ventral intraparietal area

The ventral intraparietal area was first defined as the projection zone of visual area MT into the intraparietal sulcus (Maunsell & Van Essen, 1983). VIP also receives projections from other cortical visual areas including area MST, and from somatosensory, auditory, and vestibular regions of cortex (Boussaoud, Ungerleider, & Desimone, 1990; Cavada & Goldman-Rakic, 1989; Lewis & Van Essen, 2000; Seltzer & Pandya, 1986). VIP is therefore a region of convergence of multimodal sensory input. It can be identified by its distinctive multimodal neurons that have corresponding tactile and visual receptive fields and a high degree of direction selectivity (Colby et al., 1993; Duhamel et al., 1998).

One caution is worth keeping in mind: the floor of the intraparietal sulcus is a large cortical region that might contain many subregions with different properties. It is sometimes difficult to tell if the VIP studied in one experiment is the same as the VIP studied in another experiment. Our attempt to draw together the different properties of VIP into a coherent defensive function should therefore be taken with some caution, since we might be incorrectly gluing together different properties from different areas.

3.3. Sensory properties of VIP

In this section, we summarize the sensory properties of neurons in VIP, including the encoding of the location and trajectory of objects near the body, and the encoding of self-motion with respect to nearby objects. In the next section, we summarize the effect of electrical stimulation of these neurons, including the production of defensive-like movements.

Most neurons in VIP are multimodal, responding to visual and tactile stimuli (Colby et al., 1993; Duhamel et al., 1998). The tactile receptive fields are usually on the head but can sometimes be on the chest, shoulder, or arm. The visual receptive field usually matches the location of the tactile receptive field. For example, a neuron with a tactile receptive field on the right shoulder will typically have a visual receptive field in lower right space. A neuron with a tactile receptive field on the left eyebrow will typically have a visual receptive field in upper left space.

For at least some neurons, the visual and tactile receptive fields appear to remain in register even when the monkey moves its eyes (Duhamel, Bremmer, Ben Hamed, & Graf, 1997). For these neurons, when the monkey fixates different locations on a screen, the visual receptive field remains fixed at one screen location. It has been suggested that these receptive fields are anchored in head-centered coordinates, fixed to the tactile receptive field on the face. This head-centered coding of visual space is not complete in VIP. About half the neurons have this spatial property; others have visual receptive fields that are anchored to the retina, moving as the eyes move; and others have intermediate properties. One interpretation of this mix of properties is that VIP serves as an intermediate station in spatial processing (Avillac, Deneve, Olivier, Pouget, & Duhamel, in press; Pouget, Fisher, & Sejnowski, 1993; Salinas & Abbott, 1995). In this view, different sensory and motor areas represent space in different coordinate systems, and VIP might act as an intermediary that participates in the transformation or cross-communication from one type of coordinate system to another.

The visual receptive fields in VIP emphasize the space near the body. About half of VIP cells respond best to visual stimuli within 30 cm of the body, and many respond only within a few centimeters (Colby et al., 1993). This preference for nearby stimuli is independent of the size of the stimulus. The depth cues that are used by VIP neurons are not yet known but probably include binocular disparity (Bremmer et al., 2001). Although VIP neurons seem to greatly emphasize the space near the body, more distant space is also represented, since at least some neurons have visual receptive fields that are not confined in depth.

In addition to the visual and tactile responses, auditory responses have also recently been reported in a high percentage of neurons in VIP (Schlack et al., 2002b, in press). The location of a neuron's auditory receptive field generally matches the location of its tactile and visual receptive fields. It is not known whether the auditory receptive fields are confined to the space near the body. The auditory responses have not yet been studied in as much detail as the tactile or visual responses. It is clear, however, that VIP neurons encode the locations of objects in a supramodal fashion; the neurons respond whether the object is felt, seen, or heard.

A high proportion of neurons in VIP are directionally selective (Colby et al., 1993; Duhamel et al., 1998). VIP neurons are typically directionally tuned in a matching fashion in both the tactile and visual domain. (The auditory domain has not been studied in this respect.) For example, a neuron may have a directionally tuned tactile receptive field on the cheek, responding preferentially to tactile movement from the left to the right; the same neuron will respond to visual stimuli near the cheek, and will prefer visual motion from left to right. Some VIP neurons are sensitive to the three-dimensional trajectory of objects, and many neurons respond best to a visual stimulus on a collision course with the tactile receptive field. About half of VIP neurons respond during smooth pursuit eye movement in a directionally selective fashion, with an emphasis on fast pursuit such as is typically employed for tracking objects near the body (Schlack, Hoffmann, & Bremmer, 2003).

The sensitivity of VIP neurons to motion has been studied in greater detail in relation to optic flow stimuli such as might occur during self-motion. The majority of neurons in VIP prefer an expanding visual flow field; some neurons prefer a contracting visual flow field; and some prefer rotating flow fields (Bremmer, Duhamel, et al., 2002; Gabel, Misslisch, Gielen, & Duysens, 2002; Gabel, Misslisch, Schaafsma, & Duysens, 2002; Schaafsma & Duysens, 1996). On the basis of this sensitivity to flow fields, it was suggested that VIP may play a role in visual navigation. During locomotion, the flow field on the retina will in general depend on both the direction that the animal is moving through space and on the movement of the animal's eye, but some neurons in VIP can apparently subtract the effect of an eye movement. These neurons respond in relation to the direction of the animal's heading that is implied by the visual flow field, even during a smooth pursuit eye movement (Zhang, Heuer, & Britten, 2004). Some neurons that are sensitive to visual flow fields are also apparently sensitive to matching tactile flow fields. For example, a neuron that prefers an expanding visual pattern may also respond to tactile stimuli that move across the skin in a divergent fashion from the tip of the snout toward the back of the head (Bremmer, Duhamel, et al., 2002). Because of this matching sensitivity to visual and tactile flow fields, and because of the typical preference for visual stimuli near the body, it has been suggested that VIP contributes to navigation with respect to nearby objects, such as branches or leaves that the animal may be moving through (Bremmer, Duhamel, et al., 2002).

Recently, vestibular signals have been reported in VIP (Bremmer, Klam, et al., 2002; Klam & Graf, 2003; Schlack, Hoffmann, & Bremmer, 2002). In a system designed to detect the direction of self-motion, vestibular signals and visual signals might be expected to be paired in a specific fashion. For example, a neuron that encodes forward motion might respond both to the vestibular signals indicating a forward movement of the head and also to an expanding visual flow field. A neuron that encodes backward motion might respond to vestibular signals indicating a backward movement of the head and also to a contracting visual flow field. These pairings, however, are not consistently found in VIP. In one study of forward and backward motion (Schlack, Hoffmann, & Bremmer, 2002), neurons were equally likely to prefer mis-matching vestibular and visual signals as matching signals. The function of this range of properties, including both matches and mismatches, is not known. A similar mixture of matching and mismatching of the vestibular and visual properties has been reported in cortical area MST (Page & Duffy, 2003), an area in the monkey extrastriate cortex that is also hypothesized to play a role in optic flow analysis.

In another experiment, side-to-side rotations of the head were tested and a consistent pairing between vestibular and visual signals was obtained (Bremmer, Klam, et al., 2002). For example, a VIP neuron that responded best to the vestibular signal of leftward rotation of the head would almost always respond best to a leftward moving visual stimulus, instead of the expected rightward moving stimulus. That is, the vestibular and visual signals matched in their direction, but mismatched in terms of their expected pairing for the encoding of self-motion. One interpretation of this mismatch is that, when the head turns to the left, under some specialized conditions objects that are near the body will move in a leftward direction across the retina (Bremmer, Klam, et al., 2002). In this view, the neurons in VIP encode the motion of the head and also the motion of objects that are especially near the body.

It is worth considering a second possible function of the vestibular signals in VIP. A sudden movement of the head that is not self-generated is a sign of collision or attack. It is believed that when an animal is attacked, the vestibular signal of the sudden head movement, along with the tactile signal, contributes to the rapid defensive reaction (Yeomans et al., 2002). Consider a neuron whose purpose is to encode the direction of threat, such that the output of the neuron can be used to trigger a spatially guided defensive movement, such as a withdrawal or a blocking movement. Suppose this neuron has a tactile receptive field on the front of the face, encoding a threat from that direction. Such a neuron should therefore also respond to visual stimuli approaching the front of the face, or visual stimuli that expand. The neuron should also respond to an unexpected or externally generated head movement in a backward direction, indicating that the head has been hit on the front. Each of these signals indicates a threat to the front of the face. If the stimulus is a visual one, the threat is impending. If the stimulus is a tactile or vestibular one, then the threatening object has already come in contact with the head. In all of these cases, the motor output should be of the same type: blink, squint, retract the head, and lift the arms to push away the object. This pairing of the vestibular signal (head moves back) and visual signal (expanding flow) is an appropriate pairing for detecting the direction of a collision, but is the opposite of that expected for detecting the direction of self-motion.

We speculate that neurons in VIP might use vestibular input for a range of related functions. Some neurons may be related more to detecting the direction of self-generated motion; other neurons may be related more to detecting the direction of non-self-generated motion such as might be produced by an impact to the head. We speculate that this range of functions results in a range of pairings between vestibular and visual signals in VIP.

3.4. Electrical stimulation of VIP

Early studies of electrical stimulation in the monkey posterior parietal lobe reported, among other movements, a blink and facial squint evoked by stimulation of some cortical sites (Kurylo & Skavenski, 1991; Shibutani, Sakata, & Hyvarinen, 1984). These sites typically had neuronal responses to visual stimuli near the face. It was therefore suggested that these sites participate in the detection of visual looming and the generation of defensive reactions. At some of these sites, the stimulation also evoked a movement of the eyes toward the center of gaze (Kurylo & Skavenski, 1991). These convergent eye movements were interpreted to be a side effect of the defensive blink. As described in a previous section (startle and post-startle), a defensive blink can include a distinctive centering of the gaze, believed to be caused by a retraction of the eye into the orbit.

The exact location of the blink-related sites in these earlier studies is not clear, since these studies were conducted mainly before the recognition of distinct functional zones in the intraparietal sulcus. The blink-related sites were found in a scattered fashion across the posterior parietal lobe. No cluster of blink-related sites was reported, perhaps because the studies explored mainly the gyral surface and not the floor of the intraparietal sulcus.

In a more recent study (Thier & Andersen, 1998), electrical stimulation was tested systematically in both banks and the floor of the intraparietal sulcus. On the floor of the sulcus, in a relatively restricted region, a distinctive set of movements was evoked. The monkey blinked and squinted, the ear folded back against the head, the shoulder shrugged, and the eyes moved from any initial position toward a final goal position. The authors suggested that the evoked movement of the eyes represented a saccade to a goal position. Goal-directed saccades have been evoked from other cortical areas (e.g. Tehovnik & Lee, 1993). Other regions within the intraparietal sulcus, especially the lateral bank, are believed to be involved in the control of saccadic eye movements (e.g. Andersen et al., 1992). Therefore, it is plausible to hypothesize that the convergent eye movements evoked from the floor of the intraparietal sulcus represent saccades. However, it is also possible that some of the convergence of the eyes to a goal position obtained by Thier and Andersen (1998) may have been the result of a defense-related centering of the eyes.

Recently, we found that electrical stimulation in area VIP evoked defensive-like movements whereas stimulation of surrounding sites did not (Cooke et al., 2003). The movements evoked by stimulation were almost always strongest on the contralateral side of the body and included a squint and blink, a lifting of the upper lip in a grimace, a backward folding of the ear against the head, a shrugging of the shoulder, a retraction of the head from the contralateral side of space, and a lifting of the contralateral arm and movement of the hand into lateral or upper lateral space (see Fig. 2F and H). We also observed a movement of the eyes that followed a distinctive pattern (Fig. 3B). The eye first moved in a downward and nasal direction, and then moved toward a central location. These movements, including the facial, arm, and eye movements, resemble the movements evoked by an air puff to the side of the head. Stimulation with low currents tended to produce weaker defensive movements, sometimes only a blink; stimulation with higher currents, up to 150 μA, tended to produce stronger defensive movements in which all the components were present.

In a more recent study, Stepniewska, Fang, and Kaas (2005) systematically mapped the parietal lobe of prosimians using electrical stimulation and found distinct functional zones in which different types of movement were evoked. These movements included eye movements, reaching, bringing the hand to the mouth, aggressive displays, and defensive movements. The defensive movements were obtained on stimulation of the floor of the intraparietal sulcus, in a location similar to that of VIP in macaque monkeys.

In summary, activation of specific sites in the posterior parietal cortex results in defensive-like movements. These defense-related sites are clustered in the floor of the intraparietal sulcus, in area VIP. Neurons in VIP encode the location and trajectory of objects, with an emphasis on objects that are near or approaching the body and objects that may be streaming past the face during self-motion. We therefore hypothesize that VIP may be part of a cortical system that contributes to the sensorimotor task of defense of the body surface, including withdrawing, blocking, and veering during self-motion.

In the following sections, we describe the properties of cortical area PZ, which receives input from VIP and is more closely linked to the motor system.

3.5. The polysensory zone

The precentral gyrus of monkeys contains a restricted zone in which the neurons have polysensory properties, responding with short latency to tactile, visual, and sometimes auditory stimuli (Fogassi et al., 1996; Gentilucci et al., 1988; Graziano & Gandhi, 2000; Graziano et al., 1997a, 1999; Rizzolatti et al., 1981). These polysensory neurons were first reported in ventral area 6, or the ventral premotor cortex (PMv) (Graziano et al., 1997a; Rizzolatti et al., 1981). Their location was specified further to a posterior part of PMv termed F4 (Matelli, Luppino, & Rizzolatti, 1985). In a mapping study in anesthetized monkeys, the polysensory neurons were found to be clustered in a more restricted region that may roughly match the dorsal half of F4 (Graziano & Gandhi, 2000). We refer to this region of polymodal sensory properties as the polysensory zone (PZ). The size and exact location of PZ varies somewhat among monkeys, and polysensory neurons can sometimes be found scattered in the precentral gyrus outside of this zone of greatest concentration (Graziano & Gandhi, 2000).

The specific anatomical connections of PZ are not yet clear. Luppino, Murata, Govoni, and Matelli (1999) report that area F4 receives a dense projection from VIP. Lewis and Van Essen (2000) also report a dense projection from VIP to the precentral gyrus, to a region that we believe to be consistent with PZ. Given the striking similarity between the neuron properties of VIP and of PZ, it seems likely that this dense connection from the intraparietal sulcus to the precentral gyrus does indeed interconnect VIP with PZ. However, the connections of PZ have yet to be confirmed by locating the area through its polysensory properties and then injecting tracers into it.

Much of the precentral gyrus, presumably including PZ, projects to primary motor cortex, to subcortical motor structures, and directly to the spinal cord (e.g. Dum & Strick, 1991; Kunzle, 1978; Wu, Bichot, & Kaas, 2000). Thus, it appears that PZ receives its sensory input mainly from VIP, and influences movement via its projections to a variety of motor structures.

3.6. Sensory properties of PZ

The sensory properties of PZ closely resemble those of VIP. Most neurons in PZ respond to tactile and visual stimuli (Fogassi et al., 1996; Graziano et al., 1997a; Graziano, Yap, & Gross, 1994; Rizzolatti et al., 1981). For these bimodal cells, the tactile receptive field is located on the face, shoulder, arm, or upper torso, and the visual receptive field extends from the approximate region of the tactile receptive field into the immediately adjacent space. For almost all cells the visual receptive field is confined in depth (Graziano et al., 1997a). About 46% of the neurons give a strong, sustained response only when the visual stimulus is within 5 cm of the body surface; about 40% give a response when the visual stimulus is within 20 cm of the body surface; about 7% give a response within a meter of the body; and about 5% respond robustly to visual stimuli at all distances tested. These neurons therefore strongly over-represent the space near the body, but to some extent also represent distant space.

Neurons with a tactile response on the side and back of the head are often trimodal, responding to auditory stimuli in addition to tactile and visual stimuli. These neurons respond to sound sources near the head, within about 30 cm (Graziano et al., 1999). They respond weakly or not at all to more distant sound sources, regardless of the intensity of the sound. The auditory parameter that is used by these neurons to encode the distance to the stimulus is not known, but it is thought that primates use the reverberation of the sound to estimate the distance to the source (Blauert, 1997).

Most neurons in PZ are directionally selective in the visual modality and have a matching directional preference in the tactile modality (Graziano et al., 1997a). Auditory directional selectivity has not yet been tested in PZ.

For most neurons, the spatial match between the visual and tactile receptive field is preserved even when the monkey moves its eyes, limbs, or head. For example, for almost all bimodal cells with a tactile receptive field on the arm, when the arm is placed in different positions, the visual receptive field moves in the same direction as the arm (Graziano, 1999; Graziano et al., 1997a; Graziano, Yap, et al., 1994). When the eyes move, the visual receptive field does not move, but remains anchored to the arm (Gentilucci, Scandolara, Pigarev, & Rizzolatti, 1983; Graziano & Gross, 1998; Graziano et al., 1997a; Graziano, Yap, et al., 1994). Similarly, for most bimodal cells with a tactile receptive field on the face, when the head is rotated, the visual receptive field moves with the head (Graziano, Hu, & Gross, 1997a,b). When the eyes move, the visual receptive field does not move, but remains anchored to the head (Fogassi et al., 1992, 1996; Gentilucci et al., 1983; Graziano & Gross, 1998; Graziano et al., 1997a; Graziano, Yap, et al., 1994). Such visual receptive fields can encode the locations of nearby stimuli relative to the body surface.

The multisensory neurons in PZ therefore represent the space surrounding the body through touch, audition, and vision. These neurons monitor the location and movement of objects with an emphasis on items that are near and approaching the body surface. Some neurons even appear to monitor the remembered locations of nearby stimuli in the dark, if the monkey is given a brief glimpse of the stimulus before the lights are turned out (Graziano, Hu, & Gross, 1997b).

We hypothesized that if PZ neurons contribute to defensive movements, then they should respond in a manner that is correlated with defensive output. We tested neurons in PZ by presenting an air puff to the monkey's cheek (Cooke & Graziano, 2004a). We monitored both neuronal activity and the monkey's defensive reaction. To measure defensive reaction, we recorded EMG activity from the orbicularis muscle, which surrounds the eye and participates in blinking and squinting. Although the air puff stimulus was the same on each trial, the neuronal response and the monkey's defensive reaction varied from trial to trial. The trials on which the PZ neurons gave a larger response corresponded to the trials on which the monkey gave a larger defensive reaction to the air puff. The neuronal activity in PZ, therefore, was correlated with the magnitude of the defensive output. This result suggests that there is indeed some relation between PZ neuronal activity and defensive behavior. However, to test this relationship more directly requires causal experiments such as activation or inactivation of neuronal tissue. The following sections present evidence from both approaches.

3.7. Electrical stimulation of PZ

We electrically stimulated sites within PZ and studied the evoked movements (Cooke & Graziano, 2004a; Graziano, Taylor, & Moore, 2002). The movements were consistent with avoiding, withdrawing, or protecting the part of the body on which the tactile receptive field was located (Fig. 2G and I). For some cortical sites in PZ, the neurons responded to tactile stimuli on the side of the head and to visual stimuli near and approaching the tactile receptive field. Stimulation of these sites evoked a constellation of movements including blinking, squinting, flattening the ear against the side of the head, elevating the upper lip, 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. For other cortical sites, the neurons responded to tactile stimuli on the hand and forearm and to visual stimuli near and approaching the hand. Stimulation of these sites evoked a fast withdrawal of the hand to a guarding-like posture behind the back. Stimulation of non-polysensory sites surrounding area PZ did not result in defensive-like movements.

Other studies have reported blinking, squinting, and other defense-related movements on stimulation of a similar region of cortex just posterior to the bend in the arcuate sulcus (Dearworth & Gamlin, 2002; Smith, 1936). In one of the first systematic studies of the precentral gyrus, Ferrier (1873) described an area posterior to the bend in the arcuate sulcus that, when stimulated, evoked a set of facial grimaces. Recently, a region of motor cortex in the rat has been described for which stimulation evokes a withdrawal of the whiskers, a facial grimace, a retraction of the ear, and possibly movements of the forelimb into the space beside the head (Haiss & Schwarz, 2005). One interpretation of these evoked movements is that the rat motor cortex also includes a subregion that emphasizes defensive reactions.

One of the most distinctive components of a normal defensive reaction is a movement of the eyes from any initial position toward the center of gaze. These centering eye movements are slower than normal saccades and begin with a characteristic downward and nasal curve. Fujii, Mushiake, and Tanji (1998) obtained centering eye movements on stimulation of the ventral precentral gyrus. However, whether these centering movements were true saccades or defense-related eye movements, and whether they were obtained from polysensory cortex or surrounding, non-polysensory cortex, was not directly examined in that experiment. To address this issue, we stimulated sites within and outside of PZ and measured eye movement. We found that for most sites in PZ, stimulation evoked a characteristic, defensive-like centering of the eyes, illustrated in Fig. 3C. An analysis of speed and trajectory showed that these evoked movements closely resembled defense-related movements and not saccades (Cooke & Graziano, 2004a). Stimulation of cortical sites just outside of PZ did not evoke eye movements.

In summary, electrical stimulation of sites in PZ evokes a set of arm, head, facial, and eye movements resembling the defensive movements that occur during air puff.

3.8. Reversible activation and inactivation of PZ

In order to further test the role of area PZ in the coordination of defensive movements, we disinhibited neuronal activity in PZ by injecting the chemical bicuculline and inhibited neuronal activity by injecting the chemical muscimol (Cooke & Graziano, 2004b).

When bicuculine was injected into PZ, not only did the local neuronal activity increase, but the neurons also began to fire in intense spontaneous bursts of activity with approximately 5–30 s between bursts. Each spontaneous burst of neuronal activity was followed at short latency by the standard set of defensive-like movements, including blinking, squinting, flattening the ear against the side of the head, elevating the upper lip, 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. That is, chemical stimulation of neurons within PZ produced the same effect as electrical stimulation.

In addition to evoking defensive-like movements by inducing bursts of neuronal activity, bicuculline also altered the monkey's actual defensive reaction to an air puff directed at the face. After the injection of bicuculline into PZ, the monkey gave an exaggerated defensive reaction to the air puff. The magnitude of the defensive reaction, as measured by orbicularis EMG, was approximately 45% larger after bicuculline injection than before injection. The orbicularis muscle participates in blinking and squinting and is active to some degree during a range of behaviors including chewing, eyebrow movements during gaze shifts, and making threat faces. We found, however, that the injection of bicuculline into PZ did not alter the muscle activity measured during these other behaviors. Instead the effect was limited to the defensive reaction.

When muscimol was injected into PZ, thereby inhibiting neuronal activity, the monkey's defensive reaction to the air puff was reduced. The magnitude of the defensive reaction, as measured by orbicularis EMG, was approximately 30% smaller after muscimol injection than before injection.

These results demonstrate that disinhibing PZ can result in enhanced defensive reactions, and inhibiting PZ can result in reduced defensive reactions, indicating that PZ may indeed play a role in defensive behavior.

4. Relationship between PZ and VIP

Neurons in VIP and PZ respond to similar types of sensory stimuli, and electrical stimulation in both areas leads to similar defensive-like output. Their properties, however, are not identical. The differences are most apparent in the stimulation-evoked movements, since these were tested using similar procedures in both areas (Cooke & Graziano, 2004a; Cooke et al., 2003; Graziano, Taylor, & Gross, 2002). As expected, the differences tend to suggest that VIP is relatively more involved in sensory processing for nearby space and PZ is relatively more involved in defensive motor output.

The current threshold for evoking a movement is much lower in PZ than in VIP. A current of 20 μA is usually sufficient to evoke a visible movement in PZ, whereas a current as high as 100 μA is often required to obtain a movement in VIP. This difference in threshold is consistent with the known connections of PZ to cortical and subcortical motor structures (e.g. Dum & Strick, 1991; Kunzle, 1978; Wu et al., 2000).

The movements evoked from PZ remain even when the monkey is anesthetized. In VIP, in contrast, anesthesia eliminates or greatly reduces the electrically evoked movement. This result again suggests that the pathways from PZ to the motor output are more robust.

In PZ, the defensive-like movements are evoked on every stimulation trial with a mechanical reliability. The magnitude of the evoked movement does not change even over hundreds of trials. In VIP, in contrast, we found that for about 20% of the stimulation sites, the evoked movement diminishes over repeated trials in an adaptation-like fashion. After adapting a site in VIP in this fashion using a sequence of stimulation trials, if a long inter-trial interval is then introduced such as a 10 or 15 min rest, then the stimulation effect recovers and stimulation once again evokes a large reaction.

In PZ, after each stimulation train ends, the evoked movement ends. Even when the movement resembles a violent flinch, the reaction stops abruptly on stimulation offset. The monkey returns within about 100 ms to its previous behavior, such as feeding or grooming itself, with no sign of distress or of having experienced any noxious percept associated with the stimulation. In contrast, for about 20% of the sites in VIP, we observed after-reactions of the monkey that suggested a possible sensory percept. In these cases, after the stimulation-evoked movement, the monkey continued to palpate the side of its head with its hand as if trying to find an object that it had sensed in that location. Thus, our purely subjective impression was that stimulation of PZ never evoked a sensory percept associated with the receptive fields of the neurons, whereas stimulation of VIP sometimes did.

It is tempting to construct a simple model of a cortical loop in which visual, tactile, and auditory information converges in VIP to represent nearby space, VIP communicates to PZ, and PZ sends motor commands to subcortical structures, resulting in an appropriate defensive reaction. In this view, VIP and PZ are connected in series and lie along a specific sensorimotor pathway. This view might be partially correct. However, it is not complete and cannot explain at least one curious aspect of the data. Stimulation of VIP evokes a blink with a latency as short as 10 ms, whereas stimulation of PZ evokes a blink with an average latency of about 30 ms, and a minimum latency of about 20 ms. Somehow, VIP has a privileged, fast route to the motor output that PZ does not have. One possibility is that VIP connects directly to subcortical structures involved in blink.

Clearly, VIP and PZ are not connected in a simple sequence, but rather are embedded in a network of cortical and subcortical areas. It is not yet clear what these other areas may be. There is evidence to suggest at least some defensive, obstacle-avoidance, or looming detection functions of the putamen (Graziano & Gross, 1993), parietal area 7b (Graziano & Gross, 1995), and the superior colliculus (Dean, Redgrave, & Westby, 1989). The spinal cord also contains machinery for the spatially directed withdrawal of body parts from noxious somatosensory stimuli (Clarke & Harris, 2004; Hagbarth, 1960; Schouenborg et al., 1995; Sherrington, 1910). Subregions of the amygdala, the hypothalamus, and the periaqueductal gray contribute to the emotional reaction to noxious stimuli (Brandao, Troncoso, de Souza Silva, & Huston, 2003), perhaps helping to enhance or suppress defensive reactions under different circumstances. All of these brain areas presumably work together to produce a normal defensive reaction.

5. Assigning a function to a brain area

Is it helpful to assign the function of defense of the body surface to areas VIP and PZ? Consider one cortical area that has been particularly thoroughly studied: the frontal eye fields (FEF). Electrical stimulation of this area evokes saccadic eye movements in a systematic map, and neurons in this area fire bursts of activity just before and during saccades (Bruce et al., 1985; Robinson & Fuchs, 1969). Recent results show that the FEF is more than a saccade generating area. It has been implicated in decision making, particularly in selecting which target to saccade to next (Murthy, Thompson, & Schall, 2001; Schall, Hanes, Thompson, & King, 1995; Thompson, Hanes, Bichot, & Schall, 1996). It has also been implicated in the shifting and focusing of spatial attention (Moore & Armstrong, 2003; Moore & Fallah, 2004). One possible lesson to be learned from the FEF is that a brain area may participate in a bundle of related functions, ranging from simple sensory or motor functions to more subtle cognitive functions.

In a similar spirit, we propose that areas VIP and PZ probably contribute to a bundle of related functions. At the most concrete level, neurons in these areas respond to stimuli that are near, approaching, or impacting the body surface, and electrical stimulation of these areas results in overt defensive behavior. On a more complex level, these areas may participate in spatial processing, navigation, and in the general allocation of attention to objects near the body.

These cortical areas could even play a role in social behavior, in the following fashion. Defensive mechanisms place special emphasis on protecting certain parts of the body, such as the face, neck, and abdomen. Dogs expose their abdomens in a submissive social gesture. During pair bonding, humans touch their mouths to each other's bodies with an emphasis on vulnerable portions such as the face and throat. We speculate that these social interactions take advantage of the body's natural defensive mechanisms. Trust and submission can be achieved, and also communicated to others, by actively suppressing the normal defensive reactions and allowing conspecifics into the most heavily defended parts of personal space.

Our point here is that brain areas that participate in the defense of the body surface need not be restricted to simple reflex-like functions, but can participate in highly complex and subtle behavior. In this view, it is not correct to assign a single or rigid function to areas VIP and PZ. We suggest that whereas one basic function of these areas may be to protect the body surface, they may have a wide variety of other, closely or distantly related functions.

Acknowledgements

We thank Ann P. Fox for her many insights into animal behavior and helpful knowledge of the literature on defense, and Frank Bremmer for helpful comments on the manuscript.

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