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RESEARCH ARTICLE

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Face-selective and auditory neurons in the primate orbitofrontal cortex

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Abstract Neurons with responses selective for faces are described in the macaque orbitofrontal cortex. The neurons typically respond 2–13 times more to the best face than to the best non-face stimulus, and have response latencies which are typically in the range of 130–220 ms. Some of these face-selective neurons respond to identity, and others to facial expression. Some of the neurons do not have different responses to different views of a face, which is a useful property of neurons responding to face identity. Other neurons have view-dependent responses, and some respond to moving but not still heads. The neurons with face expression, face movement, or face view-dependent responses would all be useful as part of a system decoding and representing signals important in social interactions. The representation of face identity is also important in social interactions, for it provides some of the information needed in order to make different responses to different individuals. In addition, some orbitofrontal cortex neurons were shown to be tuned to auditory stimuli, including for some neurons, the sound of vocalizations. The findings are relevant to understanding the functions of the primate including human orbitofrontal cortex in normal behaviour, and to understanding the effects of damage to this region in humans.

Keywords Face identity · Face expression · Emotion · Orbitofrontal cortex · Vocalization

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Introduction

The primate orbitofrontal cortex is involved in emotion and motivation, and damage to it affects emotion and emotional behaviour (Rolls 1996, 1999a, b, 2000b, 2002, 2005; Baxter et al. 2000; Pears et al. 2003; Izquierdo et al. 2004). The orbitofrontal cortex receives taste and olfactory inputs from their primary cortical areas, and neurons in it respond to taste and olfactory stimuli (Rolls et al. 1990, 1996a, c; Baylis et al. 1994; Rolls and Baylis 1994; Critchley and Rolls 1996b, c). The orbitofrontal cortex also receives visual inputs from the inferior temporal cortex and cortex in the anterior part of the superior temporal sulcus (Pandya and Kuypers 1969; Barbas 1988, 1993, 1995; Webster et al. 1994), and auditory inputs from the superior temporal cortex auditory areas (Hackett et al. 1999). Neurons in the orbitofrontal cortex respond to visual stimuli, and learn and reverse in a very few trials the taste reward association of visual stimuli, thus implementing rapid stimulus-reinforcer association learning and reversal (Thorpe et al. 1983; Rolls et al. 1996b). Some neurons in the orbitofrontal cortex represent the reward value of visual, olfactory, and taste stimuli, as shown not only by their rapid stimulus-reinforcer association learning, but also by the fact that the responses of these neurons decrease to zero as the reward value of a food is devalued by feeding it to satiety, yet still respond to other foods which remain rewarding, thus implementing sensory-specific satiety (Rolls et al. 1989; Critchley and Rolls 1996a). Evidence consistent with these points is now accumulating from further studies in macaques (Schultz

et al. 2000; Tremblay and Schultz 2000) and rats (Lipton et al. 1999). Part of the importance of the primate orbitofrontal cortex in emotion may be that it learns the reward and punishment associations of visual stimuli (Rolls 1990, 1996, 1999a, 2005).

The temporal cortical visual areas that project into the orbitofrontal cortex contain neurons that respond to the sight of faces (Bruce et al. 1981; Perrett et al. 1982; Desimone et al. 1984; Baylis et al. 1987; Rolls 1992, 2000a; Tanaka 1996; Wallis and Rolls 1997; Rolls and Deco 2002). There are (at least) two populations of such neurons: one that by responding differently to different faces conveys information about face identity, and a second, found more commonly in the cortex in the depths of the anterior part of the superior temporal sulcus, that responds differently to different face expressions (Hasselmo et al. 1989a). The aim of the study described here is to investigate whether there are neurons with face-selective responses in the orbitofrontal cortex, and to investigate their response properties. The existence of such cells in the orbitofrontal cortex is suggested by an earlier recording study by Thorpe et al. (1983), who reported that among a population of 65 selective visual neurons, there were neurons that responded "selectively to particular classes of stimuli (e.g., *faces*, novel stimuli, etc.)".

There are also connections to the orbitofrontal cortex from auditory cortical areas in the superior temporal cortex (Romanski et al. 1999; Romanski and Goldman-Rakic 2001). It has been suggested that the more rostral auditory cortex in the temporal lobe, which projects to the orbitofrontal cortex, is primarily engaged in processing phonetic (vocal) information (Romanski et al. 1999; Cavada et al. 2000) and it has been reported in a 2-deoxyglucose study that the orbitofrontal cortex can be activated by auditory stimuli (Poremba et al. 2003), but we know very little from single neuron recording studies about possible orbitofrontal cortex neuronal responses and their tuning. Therefore in this study we included simple auditory stimuli, and some complex auditory stimuli such as vocalization, to investigate how such stimuli might activate individual neurons in the orbitofrontal cortex. A related region which has long been implicated in vocalisation is the anterior cingulate cortex (Jurgens 2002).

Part of the interest and importance of studying the properties of orbitofrontal cortex cells that respond to faces is that damage to them could contribute to the social and emotional changes found in patients with damage to the ventral parts of the frontal cortex (Rolls et al. 1994; Hornak et al. 1996, 2003). Indeed, in a recent study performed in patients with discrete surgical lesions of different parts of the orbitofrontal cortex, we (Hornak et al. 2003) found that small lesions restricted to the caudal orbitofrontal cortex can give rise to voice and/or face expression identification problems. We note that cells responding to faces have been found in some other parts of the prefrontal cortex than the orbitofrontal cortex. For example, face-responsive cells have been described in the periarcuate region and adjacent principal sulcal cortex of the dorsolateral aspect of the frontal lobe and the inferior convexity (Pigarev et al. 1979; O'Scalaidhe et al. 1997), but these areas are different to those with lesions in the patients of Hornak et al. (2003). The findings reported in this paper are therefore relevant to understanding the face and voice expression processing deficits in patients with small orbitofrontal cortex lesions (Hornak et al. 2003).

Methods

The responses of single neurons were recorded in the orbitofrontal cortex of three macaque monkeys (two rhesus and one cynomolgus) using methods described previously (Baylis et al. 1985; Hasselmo et al. 1989a). All procedures, including preparative and subsequent ones, were carried out in accordance with the "Guidelines for the use of animals in neuroscience research" of the Society for Neuroscience, the "Principles of laboratory animal care" (NIH publication No. 86-23, revised 1985), and were licensed under the U.K. Animals (Scientific Procedures) Act 1986. The monkeys performed a Go/NoGo visual discrimination task during much of the recording, in which a number of visual stimuli presented on a monitor were associated with reward (if the monkey licked a tube placed in front of his mouth, he could obtain a taste of fruit juice reward in what is termed a Go trial). If another stimulus appeared, the monkey was required to not lick, otherwise he obtained the taste of aversive saline from the lick tube in what is termed a NoGo trial. The video monitor was placed 1 m away from the monkey and subtended 12° at the retina. Images were presented in a pseudorandom order following a 0.5 s 500 Hz cue tone in the Go/NoGo visual discrimination task. Use of this Go/NoGo visual discrimination task ensured that the monkey looked at and processed the image shown on every trial, because if the monkey fixated the centre of the screen after the cue tone before a stimulus appeared, there was sufficient time for him to make three licks of the lick tube to obtain three rewards in the 1,000 ms visual stimulus presentation period. Most of the stimuli in the set (described below) were rewarded (these were Go trials) including a triangle, and one stimulus (a square of the same brightness and area as the triangle) was always punished if a lick was made on a NoGo trial. The neuronal responses were measured in a 500 ms epoch starting 100 ms after the visual stimulus was shown, ensuring that the neuronal responses on every trial reflected what the monkey had seen and indeed performed a visual discrimination on. Given the large receptive fields of inferior temporal cortex neurons, which send projections to the orbitofrontal cortex, measured with similar stimuli (Tovee et al. 1994; Rolls and Deco 2002), this is an appropriate way to measure the neuronal responses at this stage of processing.

The stimulus set used for screening of neuronal responses consisted of a range of complex and simple visual stimuli including human and monkey faces, gratings, boundaries and textures, as illustrated by Baylis et al. (1985). Some examples are included in Fig. 1. The Go/NoGo task required the monkey to attend on each trial. (There were seven face and five non-face stimuli in the standard set used to test for selectivity. If a response to any of these seven face stimuli was found, then the cell was tested with at least two other non-face stimuli. The mean brightness of all stimuli was 127 in the brightness range 0–255 used.) Typically the visual stimuli were presented for 1,000 ms with an intertrial interval of 4 s. Neurons responding preferentially to faces could thus be identified, as described below. Real visual stimuli could also be presented in the task (or independently of the task) by replacing the video monitor with a large aperture (6 cm) shutter (Compur 5FS), which opened after the tone to reveal the real object, and provided a viewing angle for the macaque of approximately 16°. The real objects included faces, a range of simple and complex objects of differing colours and shapes, and food stimuli. All of the face-selective neurons described here were tested with real objects, and almost none responded to these non-face objects or had much smaller responses than to the best face, as shown in Table 1. In addition, moving visual stimuli with precisely synchronized accompanying sounds could be presented by using an AVMaster card (FAST Gmbh) programmed using Video for Windows. This enabled short videoclips lasting 2 s to be presented with precise timing in the visual discrimination task, and for peristimulus time histograms to be time-locked to the movie clip. The stimulus material available included monkeys making prototypical face expressions and vocalizations, filmed both against a plain background, and in their natural habitat.

To test whether the neurons responded differently to different face expressions, the set of stimuli used and illustrated by Hasselmo et al. (1989a) was used. These stimuli included the faces of three different monkeys each making three different face expressions (threat, mild threat, and calm), providing a two factor design which allowed analyses of variance to be performed to investigate whether the neurons conveyed information about face expression, about face identity, or about both. In addition, in the shutter test situation, the effects of different face expressions on real faces were investigated.

For each cell, measures of responses were calculated from the total number of action potentials occurring on each trial in the period 100–600 ms following stimulus onset. The measure of the neuronal response to a stimulus used unless otherwise specified was the firing rate minus the mean spontaneous firing rate. Statistical analyses of the responses (one and two-way ANOVAs) were performed using the SPSS statistical package. The data are presented as mean evoked firing rates with error bars showing the standard errors of the mean, with typically data for six to eight presentations of each stimulus. To quantify how finely tuned the neurons were to the stimuli, the response sparseness of the tuning to a set of stimuli of a neuron was measured by

$$a_r = \frac{\left(\sum_{i=1,S} r_i/S\right)^2}{\sum_{i=1,S} \left(r_i^2/S\right)}$$

where r_i is the response (firing rate-spontaneous) to the ith stimulus in the set of S stimuli (see Rolls and Tovee 1995; Rolls and Treves 1998). This takes a maximal value of 1 if the neuron responds equally to all stimuli in the set, and a value of $1/S$ if the neuron responds to only one of the stimuli in the set. This measure of the fineness of tuning is used partly because it is a useful measure of how distributed the representation is which relates to the storage capacity of associative neural networks (see Rolls and Treves 1998; Rolls and Deco 2002).

The criteria for classification as a face-responsive neuron that were used previously for temporal cortex neurons (see e.g. Baylis et al. 1985) are as follows: first, the responses to the most effective face stimulus had to exceed twice that to the most effective non-face stimulus. Second, an analysis of variance performed over the set of face and non-face stimuli must show a significant effect for stimulus type and subsequent Newman–Keuls' analysis must show that the response to the optimal face stimulus was significantly greater ($P < 0.05$) than the response to the optimal non-face. In addition, we checked that the mean response to the face stimuli was different to the mean response to the non-face stimuli using t tests or ANOVAs with the results shown in Table 1 column 4. Also, Fisher exact probability tests as described in the Results section were performed to check that the number of significant neuronal responses found could not have arisen by chance. (The Fisher 1932 probability combination (or generalized significance or exact probability) test is well established and asymptotically Bahadur optimal; Littell and Folks 1971; Zaykin et al. 2002). When analysing orbitofrontal cortex face-selective neurons, we followed these criteria, which can be further clarified by knowledge of the firing rate distributions typical of face-selective neurons (e.g. Rolls and Tovee 1995; see Fig. 5.3 in Rolls and Deco 2002). The latency of neuronal responses was measured using the cusum (cumulative sum) statistic, which is sensitive to changes in the average frequency of occurrence of events (Woodward and Goldsmith 1964; Van Dobben De Bruyn 1968). (The statistic was calculated from the peristimulus time histogram array of the neuronal responses to 20 or more trials of effective stimuli, by cumulating across the bins of the array from time 0 onwards the number of spikes in each bin of the array with the mean spike count per bin subtracted first and estimated from 20 prestimulus bins).

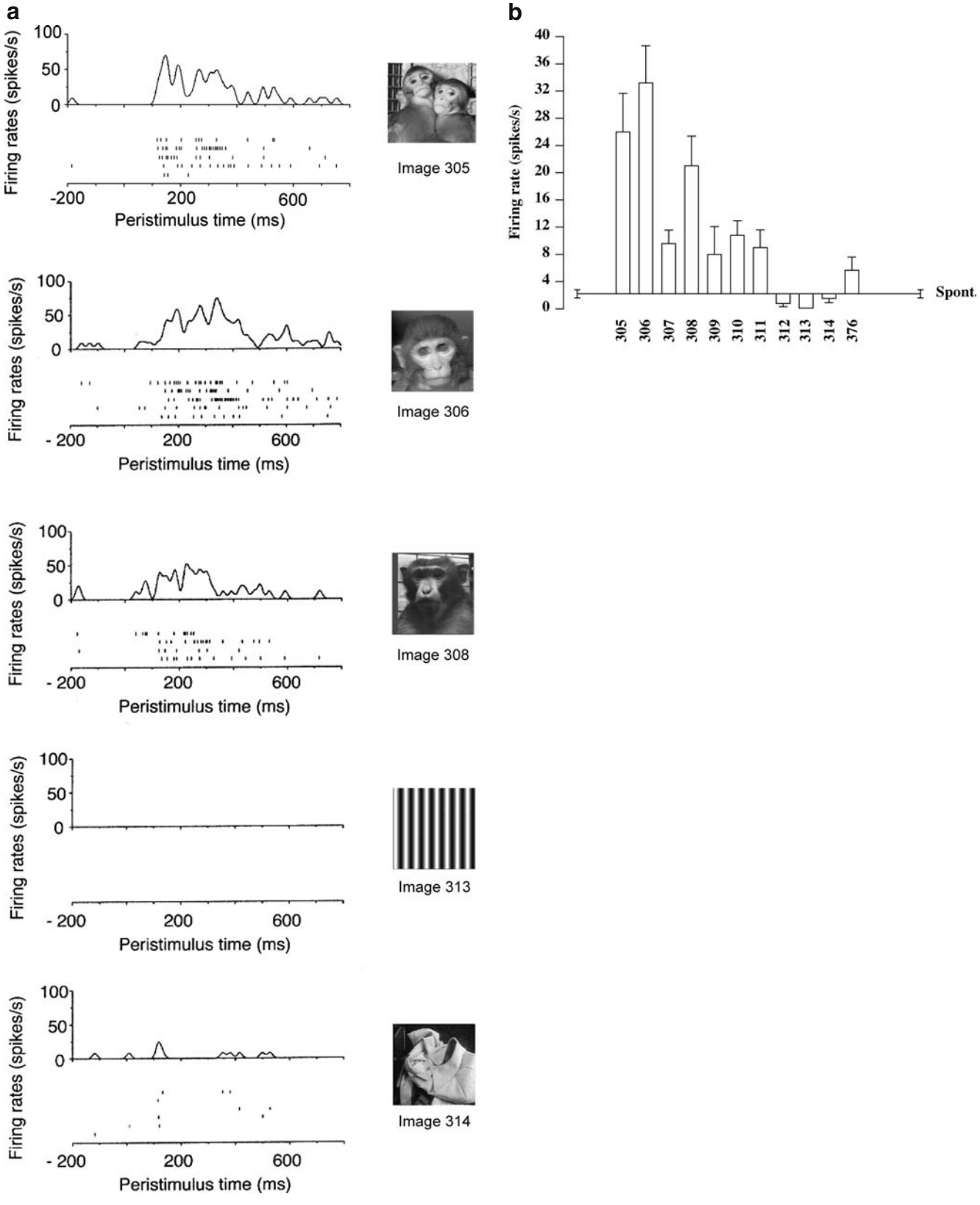

Fig. 1 **a** Raster and peristimulus time histogram of responses of cell au152 to examples of the test stimuli. **b** Firing rate histogram of cell au152 to different monkey face stimuli (305–308), human face stimuli (309–311) and different non-face stimuli (312 Fourier boundary curvature descriptor, 313 grating, 314 shirt, and 376 geometrical stimulus). The means and standard error of the mean (SEM) of the responses in spikes per second are shown as changes from the spontaneous rate (Spont) in this and subsequent figures

Table 1 Response properties of orbitofrontal cortex face-selective cells

Cell	Latency (ms)	Response ratio: best face/ best nonface	*P* (face vs. nonface)	View	Identity	Express-ion	Spon. (sp/s)	Mean face (sp/s)	Best face (sp/s)	Mean non-face (sp/s)	Best non-face (sp/s)	Sparseness within faces
Be003	280	2.7	2×10^{-4}	–	$P = 0.03$	–	1.5	8.1	11.4	2.4	4.3	0.94
Be0071	180	13.1	5×10^{-10}	NS	$P < 10^{-6}$	NS	1.1	5.0	15.8	1.0	1.2	0.37
Be0072	340	–	3×10^{-11}	–	–	–	1.4	–	–	–	–	–
Be009	160	8.0	1×10^{-4}	–	$P < 0.001$	–	0.7	4.1	7.9	0.9	1.4	0.62
Be011	260	3.8	7×10^{-8}	–	NS	–	1.8	5.8	8.7	1.4	2.3	0.82
Be118	280	8.3	7×10^{-16}	–	$P < 10^{-6}$	–	1.2	4.4	7.2	0.5	0.8	0.80
Aq093	100	2.4	3×10^{-16}	–	NS	NS	25.2	61.0	90.0	29.8	37.7	0.96
Au004	160	4.3	8×10^{-6}	–	$P < 0.001$	–	0.8	5.6	17.0	2.0	4.0	0.48
Au152	130	8.8	7×10^{-11}	–	$P < 0.001$	–	2.2	16.8	33.2	2.4	3.8	0.71
Au137	130	3.3	3×10^{-8}	–	NS	–	1.4	11.9	16.7	2.6	5.0	0.76
Au135	160	1.7	1×10^{-2}	–	NS	–	13.4	23.0	32.0	12.5	18.5	0.87
An088	320	6.0	5×10^{-6}	$P < 0.01$	–	$P < 0.05$	0.0	8.6	9.0	0.9	1.5	–
Aq045	280	4.7	2×10^{-11}	NS	–	$P < 0.05$	2.1	13.8	14.0	1.1	3.0	–
Aq0362	220	4.4	3×10^{-4}	$P < 0.05$	$P < 0.01$	NS	2.4	9.7	25.3	4.6	5.7	–

NS not significant

Results

Recordings were made from 3,168 single neurons in the region of the orbitofrontal cortex. 812 neurons (27%) were found to be visually responsive, as shown by statistically significant responses starting 100–200 ms after some visual stimuli were presented. Among these visually responsive neurons, some respond to visual stimuli if they are associated with primary reinforcers (Thorpe et al. 1983; Rolls and Baylis 1994; Rolls et al. 1996b; Deco and Rolls 2005) provided that they have not been devalued (Critchley and Rolls 1996a), and some respond to novel visual stimuli (Rolls et al. 2005). Thirty-two neurons from the orbitofrontal cortex had responses to faces which were significantly greater than those to non-faces, making up 3.9% of all the visual cells recorded in this area. From this set of 32 neurons, it was possible to perform further testing to investigate the face-selectivity further, using the tests described in Methods section, for 14 neurons with sufficient trials to allow statistical comparisons of the responses to the members of the stimulus sets. It is the response properties of these 14 neurons that are described here. All these neurons had statistically greater responses to the best face stimulus than to the best non-face stimulus. Further, as shown in Table 1 column 4, most neurons had very highly significant differences between the average response to faces and the average response to non-face stimuli, with 6 of the 14 neurons significant at $P < 10^{-9}$, and 10 significant at $P < 10^{-5}$. (For neuron be0072, the value shown is that for the ANOVA between the different types of head movement, as this neuron did not respond to still heads.) As a population the significant results in these 14 neurons could not have arisen by chance at $P < 2.6\times10^{-15}$ as shown by a Fisher generalized significance test ($z = 7.91$) (Kirk 1995), which assesses the likelihood that the probability values shown in Table 1 column 4 observed over the whole population of 3,168 neurons analyzed might have arisen by chance. The interpretation is thus that the responses observed in this population of orbitofrontal cortex face-selective neurons are very highly statistically significant.

Figure 1 illustrates the responses of a face-selective neuron (au152). The responses to some of the images in the visual discrimination task are shown in Fig. 1a as peristimulus time histograms plotted above rasters for individual trials. The response latency of the neuron was 130 ms. The responses of the neuron to a wide range of different face (images 305–311) and non-face stimuli are shown in Fig. 1b. The neuron was selective to monkey faces and was minimally responsive to human faces. The neuron discriminated very significantly between different faces (one-way ANOVA, $P < 0.001$). Non-face images elicited no significant responses, and the ratio of the response to the best face (33.2 spikes/s) to the best non-face (3.8 spikes/s) was 8.8.

The responses of another cell (be0071), with quite fine tuning within a set of faces, are illustrated in Fig. 2. The

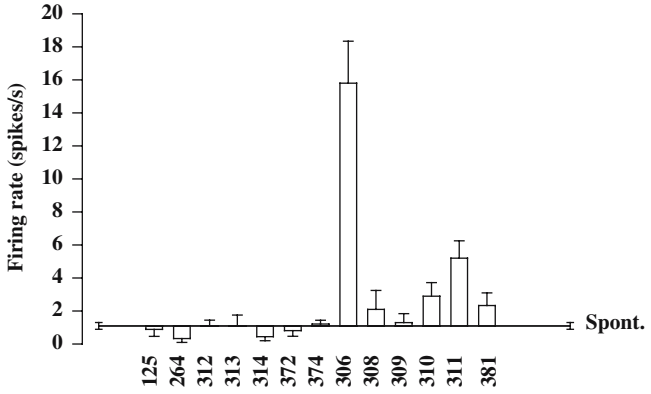

Fig. 2 Firing rate histogram of cell be009 to different face stimuli (306–311 and 381) and different non-face stimuli (125, 264, 312, 313, 314, 372 and 374) (Stimuli as in Fig. 1 except *381* monkey face, *125* hand, *372* triangle, *374* saline-associated square)

neuron increased its firing rate most to face 306 from a standard set of six faces (306, 308, 309, 310, 311 and 381), with quite small responses to the other face stimuli. The sparseness of its representation (firing rate distribution) across the six face stimuli was 0.37, and across the six face and seven non-face stimuli shown in Fig. 2 was 0.27. Non-face images (e.g., 125, 264, 312-314, 372 and 374) elicited no significant responses, and the ratio of the response to the best face to the best non-face was 13.

The responses of another cell (be009), with quite distributed tuning within a set of faces but no responses to non-faces, are illustrated in Fig. 3. The neuron increased its firing rate most to faces 306, 308 and 311 (with some response to 381) from the standard set of six faces, with no responses to the other two face stimuli or to non-face stimuli. The sparseness of its representation (firing rate distribution) across the six face stimuli was 0.62, and across the six face and seven non-face stimuli shown in Fig. 3 was 0.38. Non-face images elicited no significant responses, and the ratio of the response to the best face to the best non-face was 5.6.

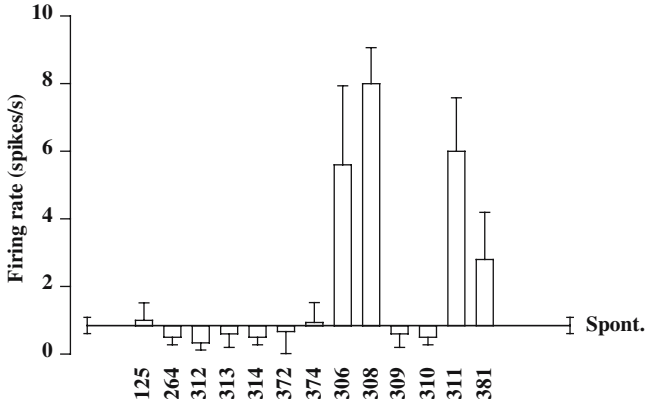

Fig. 3 Firing rate histogram of cell be0071 to different face stimuli (306–311 and 381) and different non-face stimuli (125, 264, 312, 313, 314, 372 and 374) (Stimuli as in earlier figures)

In that some of the cells respond differently to different faces, the neurons encode and make explicit information that would be useful in face identification. Of the 11 neurons tested for different responses to different faces, 7 had significantly different responses to the different faces, as shown by one-way ANOVAs performed on the firing rates to the set of faces (see Table 1). Whether the neurons encode information that could be useful in face identification independently of view is examined below.

The latencies of face responsive cells in the orbitofrontal cortex ranged from 100 to approximately 300 ms after presentation of the stimulus. The majority of responses occurred between 130 and 220 ms (see Table 1). Figure 4 is a histogram of the response latencies.

The most effective face stimuli for each cell elicited responses ranging from 7 to 90 spikes/s, as shown in Table 1. (The responses shown are the firing rate to a stimulus minus the spontaneous firing rate. The median response to the most effective face stimuli was 16 spikes/s and to the most effective non-face stimuli was 3.8 spikes/s.) The ratios of the response to the optimal face stimulus and the optimal non-face stimulus are shown in Table 1. It is clear that many of the cells in this population had a response to the best stimulus that was much more than twice that to the best non-face stimulus. The sparseness of the representation within the class faces provided by the different cells is shown in Table 1. For the neurons with significantly different responses to the different faces (as shown by the ANOVAs), the mean response sparseness was 0.65, which is typical of what can be described as sparse distributed representations for neurons with continuously distributed firing rates (Rolls and Tovee 1995; Rolls and Treves 1998; Treves et al. 1999).

Some of the cells responded better (or only) to moving heads or faces than to stationary faces. An example is shown in Fig. 5. The neuron did not respond

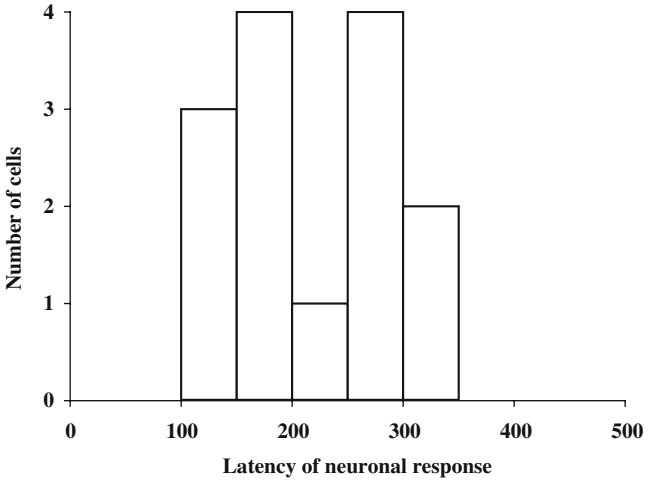

Fig. 4 Response latency histogram for the population of cells with responses to faces

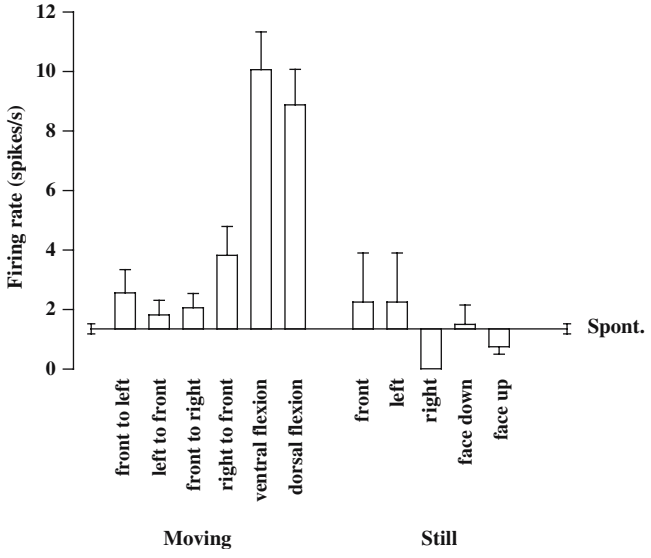

Fig. 5 Firing rate histogram of cell be0072 to moving face stimuli

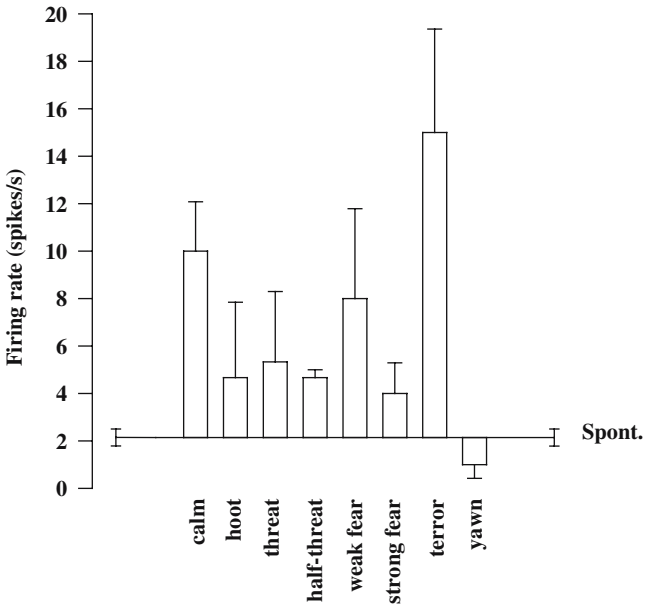

Fig. 7 Firing rate histogram of cell aq045 to different face expressions

to the still views of a face (shown on the right of Fig. 5), but did respond to ventral or dorsal flexion of the head at the neck (i.e., moving the head from lowered to look ahead at the subject and then up, or tilting forward the head from an upward looking position through looking straight ahead to looking down). Cells of this type are found in the cortex in the superior temporal sulcus (Hasselmo et al. 1989b). Of the 14 cells tested fully, 3 responded more to moving than to stationary faces (as shown by significantly greater responses in the post hoc test to the ANOVA for the most effective moving stimulus compared to the most effective stationary stimulus). The movements were head movements comparable to those illustrated in Fig. 5. These neurons did not respond to non-face objects moving in the visual field. We note that neurons of a similar type found in the cortex in the superior temporal sulcus do not respond to optic flow in visual field coordinates, in that those neurons respond to the same object-based motion, e.g. ventral flexion of the head at the neck, even when the head is inverted (Hasselmo et al. 1989b).

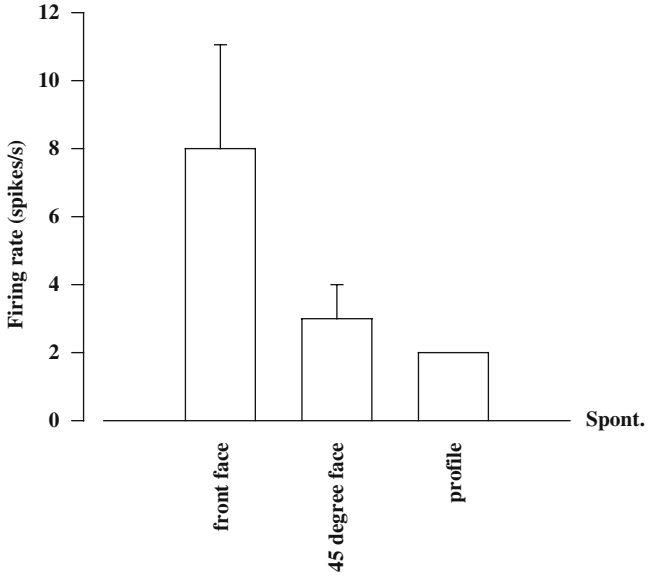

Fig. 6 Firing rate histogram of cell an088 to different views of a head

Some of the cells had view-dependent responses, and others had view invariant responses. An example of a view dependent cell is shown in Fig. 6. The cell had a greater response to the frontal view of a face than to a 45° view, or to the profile of a face. Of four cells tested in this way, two had responses which were different for different views of a face, and two had responses which were invariant across a set of views (see Table 1). The latter cells thus encode information about face identity that is invariant with respect to view.

Some of the cells had different responses to different face expressions, and others did not encode information about face expression. An example of a cell with different responses to different face expressions is shown in Fig. 7. The face expressions were classified according to Table 17 of Jolly (1972). Of five cells tested in this way, two had responses which were different for different face expressions (see Table 1).

Location of cells

The locations of the cells with selective responses to faces are shown in Fig. 8, which maps onto one hemisphere the sites of cells from histological reconstruction in three monkeys. The majority of these face-selective cells were located in both banks of the lateral orbital

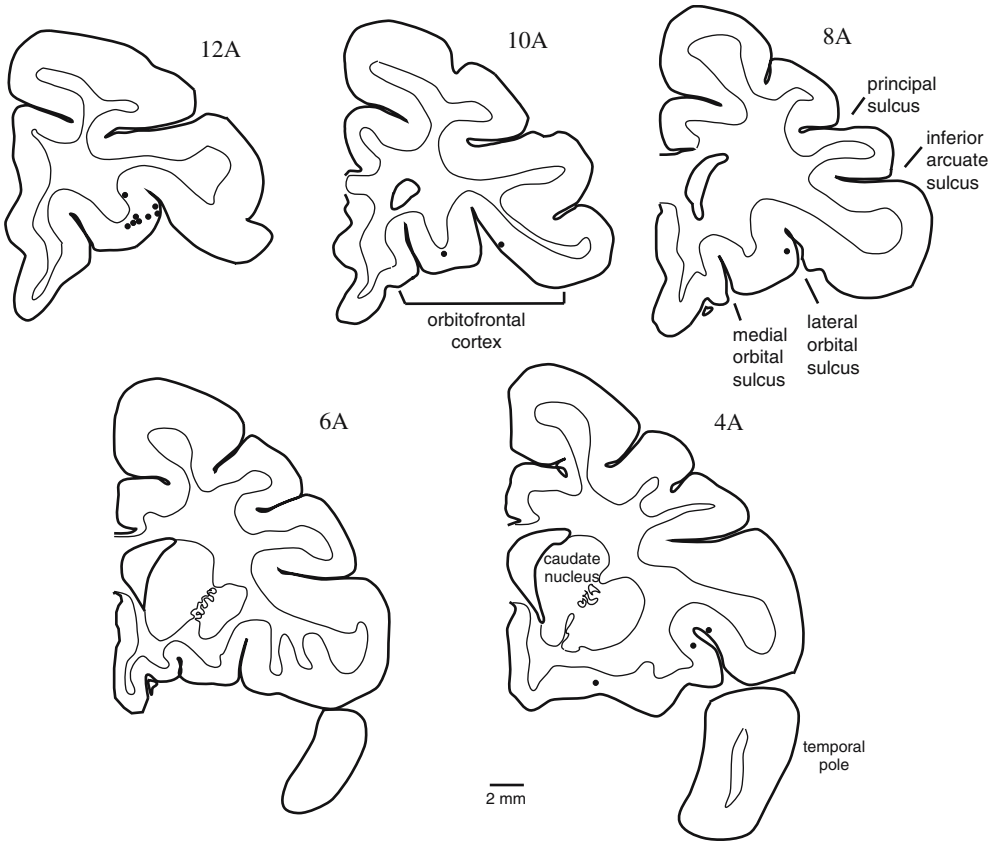

Fig. 8 The sites in the orbitofrontal cortex at which the different neurons with face-selective visual responses to faces were recorded. The coronal sections are at different numbers of millimetre anterior (A) to the sphenoid reference (see Aggleton and Passingham 1981)

sulcus of the orbitofrontal cortex, corresponding to the region described by Barbas (1988) as receiving predominantly from the anterior regions of inferior temporal visual cortex. This region largely corresponds (based on topological comparison) to the posterior part of area 11 l (in the Sect. 12A of Fig. 8) of Carmichael and Price (1994), with some neurons more posteriorly in area 13 and the transitional region to the agranular insula. This main cluster of neurons (at 12A) is slightly more anterior and medial to the areas in which neurons with visual responses to food-related stimuli have been found, in some cases in the same monkeys (Thorpe et al. 1983; Critchley and Rolls 1996a; Rolls et al. 1996b) and therefore may reflect a degree of anatomical specialization of the orbitofrontal cortex (see further Rolls and Baylis 1994; Kringelbach and Rolls 2004).

Orbitofrontal cortex cells with auditory responses

While making the recordings from face-selective cells in the orbitofrontal cortex, a population of cells was discovered with auditory responses. Some of these (8/16 analysed in monkey bk) responded to the 500 Hz 0.5 s tone cue used to signal the start of a trial in the task. Four of these cells responded also to visual stimuli used in the tasks, and typically the visual responses were not selective for only some images, though in one case the cell did respond more to novel than to familiar visual images.

Five auditory cells (of the 16 auditory cells analyzed, all in bk) had much more selective auditory responses. These cells did not respond to the tone cue, and to most sounds. Three of the cells responded with some selectivity to vocalization. An example is shown in Fig. 9. The cell had clear and very reproducible responses to 2 s video-with-sound clips of a monkey making a guttural defence call (Fig. 9a). The cell had no responses to the video alone (Fig. 9b), but had very clear and reliable responses to the sound alone (Fig. 9c). It is also shown in Fig. 9 that the cell had no responses to the 500 Hz 0.5 s tone cue that was presented from −500 to 0 ms. Because of the clear auditory responses of the cell, further investigation was performed. It is shown in Fig. 10 that the cell had no or small responses during percussive sounds, and talking. The neuron had some response to the sound of lip smacking and hoot imitations made by humans. The neuron had its maximal response to vocalization made deep in the throat by humans in an imitation of the guttural defence call made by monkeys (Fig. 10). The other two vocalization-related cells responded to monkey vocalizations made in the video-with-sound clips, but not to most other sounds, including the tone cue and talking. One further cell responded to a combination of vocalization and place, responding preferentially to a particular person's voice in a particular place (as shown by one-way ANOVA ($F(3,19) = 12.4$, $P \ll 0.001$) followed by post hoc analysis). The recording sites of the set of auditory

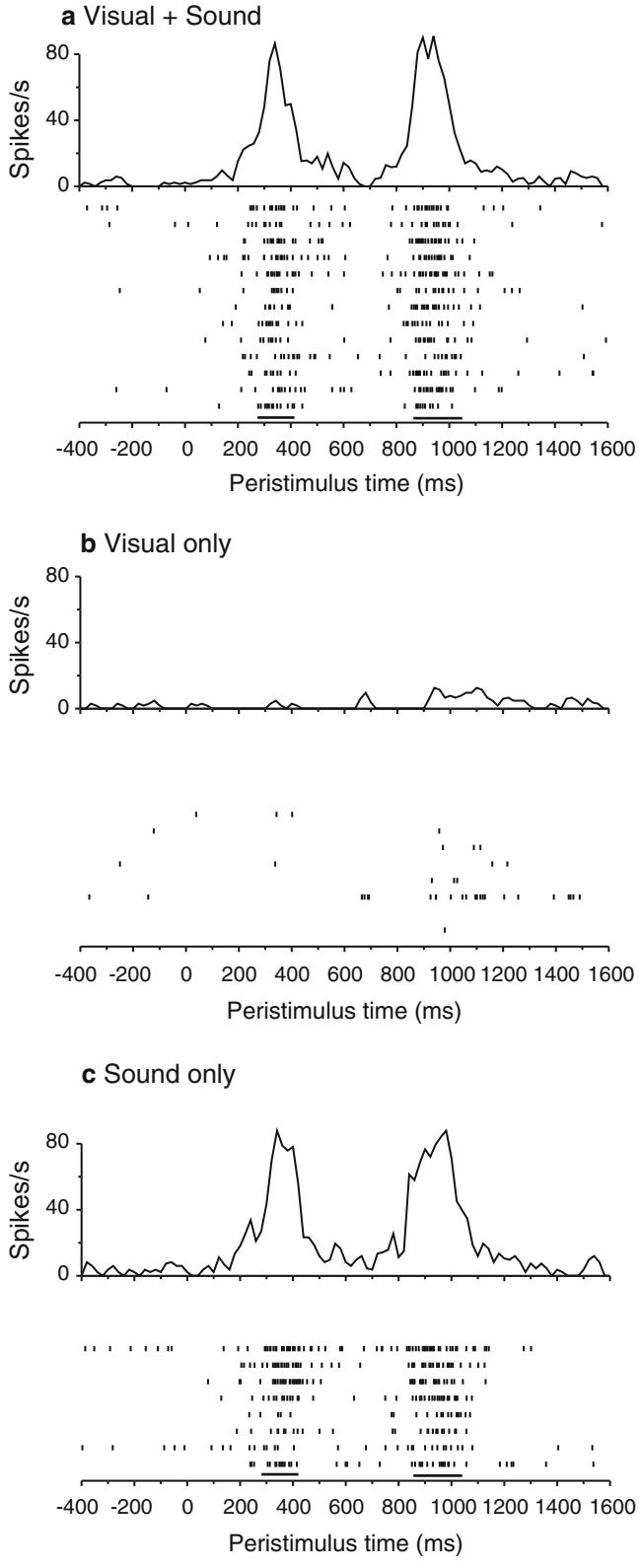

Fig. 9 Peristimulus histograms and rastergrams of an auditory cell tested with 2 s video-with-sound clips showing a monkey making a guttural defence call. The clip started at time 0, was preceded by a 500 ms 500 Hz cue tone. The vocalizations were made at the two times indicated by the *black bars*

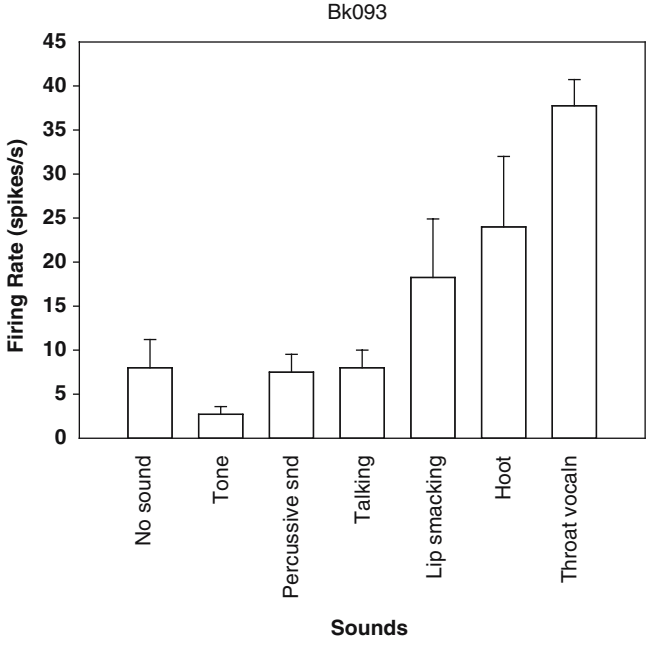

Fig. 10 The responses of neuron bk093 to a set of different auditory stimuli. The mean firing rate (±SEM) in a 1 s period in which the sounds were made are shown

neurons were mainly in the middle of the orbitofrontal cortex in the 12 m/13 l region (Carmichael and Price 1994) in the lateral orbital sulcus, and are shown in Fig. 11.

Discussion

This investigation has shown that there are face cells in the primate (macaque) orbitofrontal cortex. They are found in for example areas 11 l of Carmichael and Price (1994), and are therefore in a different region from those found in either the dorsolateral prefrontal cortex of the inferior convexity or the prefrontal cortex in previous studies (Pigarev et al. 1979; O'Scalaidhe et al. 1997). Given that the regions in which face-selective neurons were recorded in the orbitofrontal cortex do have some projections to the dorsolateral prefrontal cortex (Carmichael and Price 1996), the orbitofrontal cortex could be a source of face-related information for the dorsolateral prefrontal cortex. The orbitofrontal cortex is the part of the prefrontal cortex involved in emotion and stimulus-reward or stimulus-punishment association learning and reversal. It receives its visual inputs from the anterior inferior temporal cortex (Pandya and Kuypers 1969; Barbas 1988, 1993, 1995; Webster et al. 1994), and therefore is expected to reflect information about what visual stimulus has been shown (Rolls 2000a; Rolls and Deco 2002). Consistent with this, the majority of the face-selective cells described here have differential responses

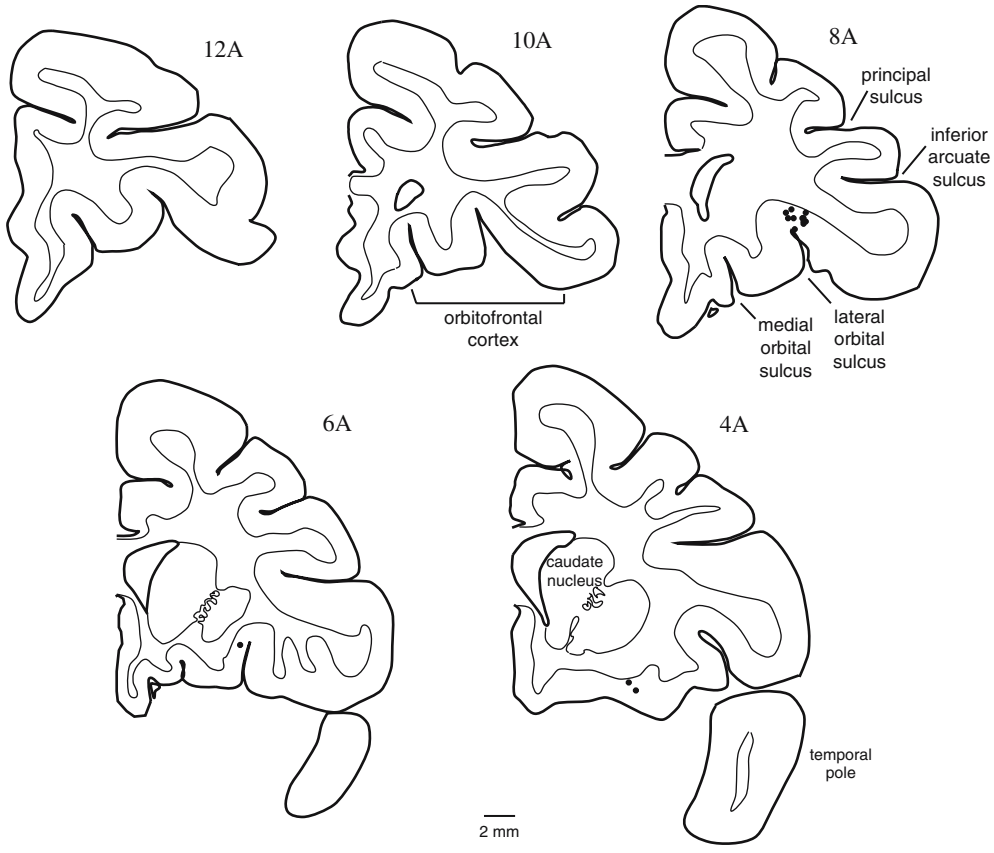

Fig. 11 The sites in the orbitofrontal cortex at which the different neurons with auditory responses were recorded. The coronal sections are at different numbers of mm anterior (A) to the sphenoid reference

depending on which face is being shown or on face expression. In contrast, the dorsolateral prefrontal cortex receives its visual inputs from parietal cortical visual areas and contains neurons that may be involved in spatial short term memory functions (see Fuster 1997; Rolls and Treves 1998), and the inferior convexity prefrontal cortex has neurons which may be involved in short term memory functions for objects and faces (Wilson et al. 1993).

The orbitofrontal cortex cells in this study responded to face stimuli with typical latencies of 130 to 220 ms. In contrast face-selective neurons in the cortex in the inferior temporal visual cortex and cortex in the superior temporal sulcus typically respond to face stimuli with a latency of between 80 and 160 ms (Baylis et al. 1985). The implication is that the majority of face-selective cells in this study are more than one synapse away from (i.e. may not receive direct projections from) the temporal cortical visual areas located in the middle (with respect to anterior–posterior location) of the temporal lobe (Baylis et al. 1987). The longer latency in the orbitofrontal cortex could be because the inputs come predominantly from rather anterior parts of the temporal cortical areas (Barbas 1993) in which the neuronal response latencies tend to be longer (Baylis et al. 1985, 1987); or because the orbitofrontal cells receive their face-related inputs from the amygdala, in which the latencies are longer than those in the inferior temporal cortex and similar to those in the orbitofrontal cortex (Leonard et al. 1985); or because of intrinsic connections within the orbitofrontal cortex. An additional factor is that the firing rates of face-selective neurons are lower in the orbitofrontal cortex than in the inferior temporal visual cortex, and this may reflect lower excitability, which may also result in more variation from trial to trial. However, the orbitofrontal cortex neurons do have highly significantly different responses to different faces and to non-face stimuli (see e.g. Fig. 1b), and across a population of such cells there would on any trial be considerable information about which stimulus was shown as the population firing rate vector is tolerant to individual neuron variability (Rolls et al. 1997, 2004; Rolls and Deco 2002; Franco et al. 2004).

The finding that some orbitofrontal cortex face-selective cells convey information about face expression is of considerable interest. Such cells could be part of a system that enables different emotional responses to arise when different face expressions are seen, and indeed, the finding that patients with ventral frontal lobe damage are sometimes impaired at even identifying face expression (Hornak et al. 1996, 2003; Rolls 1999b) is consistent with this. When producing emotional fresponses to a seen face, it may be important to take into account whose face it is, and this may be one function of the orbitofrontal cells that convey information about face identity (i.e., about which face has been

shown). Such cells probably receive their inputs from the neurons that respond to face identity in cortical areas in the gyral part of the inferior temporal cortex (area TE) (Hasselmo et al. 1989a). The cells that respond on the basis of expression probably receive inputs from the cells tuned to face expression in the cortex in the anterior part of the superior temporal sulcus (Hasselmo et al. 1989a). Similarly, the orbitofrontal cortex cells that respond to moving faces or heads probably receive their inputs from the cells in the cortex in the depths of the superior temporal sulcus, which are tuned to respond to moving faces or heads (Hasselmo et al. 1989b; Rolls 2000a). Such temporal cortex cells can for example respond when a head is turning from the view of either profile to the frontal view, and are responding to this type of object centred motion in that they do not respond to the frontal view when it is stationary (Hasselmo et al. 1989b). The significance of such neurons is that face gesture (including, e.g., moving the head) is significant in social situations, for it may mean breaking social contact (usually in macaques a sign of appeasement), or it may mean engaging in an agonistic social relationship by indicating a threat. Indeed, this interpretation is strengthened by the finding that some of the cells in the cortex in the superior temporal sulcus that respond to the head turning away (e.g., ventral flexion) may also respond to the eyes blinking closed with the head still, with both normally co-occurring when social contact is broken (Hasselmo et al. 1989b). Hebbian associativity at the neuronal level could account for these normally co-occurring stimuli activating the same set of neurons.

In this investigation auditory neurons were also described in the orbitofrontal cortex. The auditory information probably reaches the orbitofrontal cortex through auditory association cortical areas, which have direct connections to the orbitofrontal cortex (Barbas 1988, 1993; Hackett et al. 1999; Romanski et al. 1999). Some of the neurons responded to simple auditory stimuli such as the 500 Hz pure tone used to signal the start of a trial. Other neurons had rather interesting auditory responses, responding for example to vocalization better than to most other auditory stimuli tested. These observations are the first we know of the types of auditory stimuli to which orbitofrontal cortex neurons are tuned, and indicate that further much more detailed exploration of the nature of the auditory stimuli to which orbitofrontal cortex neurons are tuned is in order. The neurons could provide information useful in social and emotional behaviour, by responding to signals that have emotional meaning. Although the prevalence of neurons with auditory responses cannot be determined from this study because not all cells encountered could be tested with auditory stimuli, the 16 cells do appear to be a sample of what does appear to be a significant population functionally, in that, we have shown that lesions of the human orbitofrontal cortex can impair the ability to identify the emotional expression in a voice (while leaving identification of the nature of the sound unimpaired) (Hornak et al. 1996). Indeed, partly on the basis of the types of auditory response described in this paper, we have now studied a group of patients with surgical lesions circumscribed to small parts of the orbitofrontal cortex, and have shown that patients with even unilateral lesions, if they are in the caudolateral orbitofrontal cortex, have problems in identifying the emotional expression conveyed by vocalization (Hornak et al. 2003). This paper is the first we know to describe some of the properties of the neurons that may when damaged contribute to this deficit. Although the proportions of face-selective and auditory neurons found in this investigation were low, these neurons do appear to be functionally important, as shown by the deficits in face and voice expression identification of patients with damage to this region (Hornak et al. 1996, 2003). Indeed, part of the interest of the study is that the proportion of face-selective neurons was quite low, and yet lesions of the orbitofrontal cortex can influence face processing. Further evidence that quite low proportions of neurons may be functionally relevant is that only approximately 3.5% of macaque orbitofrontal cortex neurons respond when reward-related errors are made (Thorpe et al. 1983), for example in the reversal of a visual discrimination task, yet lesions of the orbitofrontal cortex do impair visual discrimination reversal in macaques (Butter 1969) and humans (Hornak et al. 2004), and, further, activation of the human orbitofrontal cortex can be shown with functional magnetic resonance imaging (fMRI) to occur specifically at the time of visual discrimination reversal (Kringelbach et al. 2003). It is also perhaps not generally known that even in the brain areas with the highest proportion of face-selective cells known in the brain, areas TEa and TEm, the proportion of face-selective neurons is only 20% of the visual neurons (Baylis et al. 1987). Thus, small proportions of neurons in a given brain area with a particular type of response do not mean that these neurons are unimportant. The only way that evidence can be obtained about the proportions of neurons with a particular type of responsiveness, and indeed, about the details of the types of response they have, is with studies of the type described here. These studies are quite demanding when the proportions are low.

When making different emotional responses to a visual stimulus, including the sight of a particular individual, the emotional, or reward/punishment, association of the visual stimulus with a primary (unlearned) reinforcer must normally be learned. The orbitofrontal cortex is involved in this learning, as shown by single neuron recording evidence that some orbitofrontal cortex neurons learn and rapidly reverse associations between visual stimuli and primary reinforcers such as taste (Thorpe et al. 1983; Rolls 1996, 1999a, b, 2000b, 2002, 2005, Rolls et al. 1996b). The effects of lesions of the orbitofrontal cortex are consistent with this (Butter 1969; Baxter et al. 2000; Pears et al. 2003; Izquierdo et al. 2004; Rolls 2005), although in most lesion studies direct associations to primary reinforcers

such as taste are not strictly tested, as the food reinforcer is typically seen and possibly heard, and these are secondary reinforcing stimuli. For example, 71% of a sample of orbitofrontal cortex cells responded in relation to the learned reinforcement association of visual stimuli, which were simple shapes or objects (Rolls et al. 1996b). For the face-selective cells described here in the orbitofrontal cortex, there is incomplete evidence so far on the extent to which they reverse the face to which they respond when the taste reward association of the face is reversed (glucose vs. salt). When considering face association learning, however, the nature of relevant primary reinforcers should be considered, and for faces this might include touch, and perhaps vocalisation (e.g., a threat call vs. the sound of appeasing lip-smacking). For neurons that respond in relation to face expression, it could be that they provide a primary reinforcing signal (e.g., the sight of a threat face expression vs. one of lip-smacking), or alternatively the reinforcement value of the face expression could be learned by association with another primary reinforcer. In either case, one might expect that face expression neurons should not alter their responsiveness rapidly during a reversal learning situation, because the reinforcement value of face expression is normally rather stable, and is reliable as an indicator of reinforcement in primate social situations. This raises the interesting possibility that during the learning of stimulus-reinforcement associations by neurons responding on the basis of face identity, the (primary) reinforcer might be conveyed by a different population of neurons responding to face expression. There is evidence consistent with this in humans, in that activation of the human medial orbitofrontal cortex is related to facial attractiveness and to the face expression of smiling (O'Doherty et al. 2003). In any case, the face-selective neurons described here are among the population of orbitofrontal cortex visual neurons that do not reflect associations with taste reward, in that in the Go/NoGo visual discrimination task they did not respond differentially to the rewarded stimuli (most of those in the set) vs. the saline associated (NoGo) stimulus, the square.

In conclusion, face-selective neurons are present in the orbitofrontal cortex. Some of these face cells respond to identity, others to facial expression. Some of the neurons do not have different responses to different views of a face, which is a useful property of neurons responding to face identity. Other neurons have view-dependent responses, and some respond to moving, not still heads. The neurons with face expression, face movement, or face view-dependent responses would all be useful as part of a system decoding and representing signals important in social interactions. The representation of face identity is also important in social interactions, for it provides some of the information needed in order to make different responses to different individuals. The findings are relevant to understanding the normal functions of the orbitofrontal cortex, and the effects that are produced by damage to it. In particular, disordered social and emotional behaviour is seen in human and non-human primates following lesions affecting this brain area (see Rolls 1999a). Patients with such lesions are impaired in identifying facial expressions (Hornak et al. 1996, 2003), and in addition are impaired at reversal of learned reward/punishment associations to visual stimuli (Rolls et al. 1994; Fellows and Farah 2003; Berlin et al. 2004; Hornak et al. 2004). Together these data suggest that the human orbitofrontal cortex may have an important role in the use of facial information in social and emotional behaviour. The social sequelae of frontal lobe damage, particularly involving the orbitofrontal region, in humans and non-human primates are likely to result from disruption of mechanisms that integrate representations of socially relevant stimuli such as face expression and identity with the reinforcement associations of these stimuli (Rolls 1999a, b; Rolls 2000b; Kringelbach et al. 2003).

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