Brain Research, 130 (1977) 229–238

ACTIVITY OF NEURONES IN THE INFEROTEMPORAL CORTEX OF THE ALERT MONKEY*

E. T. ROLLS, S. J. JUDGE** and MANJIT K. SANGHERA

University of Oxford, Department of Experimental Psychology, South Parks Road, Oxford OX1 3UD (Great Britain)

(Accepted November 18th, 1976)

SUMMARY

The activity of neurones in the inferotemporal cortex of the alert rhesus monkey was recorded while the monkey was shown visual stimuli, which included both food and non-food objects for comparison with the activity of neurones in the lateral hypothalamus and substantia innominata.

In the anteroventral part of the inferotemporal cortex, neurones were found with visual responses which were sustained while the animal looked at the appropriate visual stimuli. The latency of the responses was 100 msec or more. The majority (96/142 or 68%) of these neurones responded more strongly to some stimuli than to others. These units usually had different responses when objects were shown from different views, and physical factors such as shape, size, orientation, colour and texture appeared to account for the responses of some of these units.

Association of visual stimuli with a food reward (glucose solution) or an aversive taste (5% saline solution) did not affect the magnitude of the responses of the neurones to the stimuli either during the learning or after the period of learning. Nor did feeding the monkey to satiety affect the responses of the neurones to their effective stimuli.

INTRODUCTION

In a recent electrophysiological investigation of the monkey lateral hypothalamus and substantia innominata, neurones have been described which alter their activity before the monkey feeds[20]. This response occurs while the animal is looking

* This research was supported by the Medical Research Council.
** Present address: Laboratory of Neurobiology, National Institute of Mental Health, Bethesda, Md. 20014, U.S.A.

at the food, does not occur similarly to non-food objects[20], occurs only if the monkey is hungry[4], and becomes associated with the sight of food objects during learning[15]. Because of the nature of these responses, it is of interest to compare them with the responses of neurones in visual association cortex during the same behavioural tests. The part of visual association cortex chosen for analysis was the inferotemporal cortex, because it receives visual inputs after several earlier stages of visual cortical processing, and has connections to the lateral amygdala, through which visual information could influence the hypothalamus[9,11,16,22,23]. Further, in relation to feeding, it has been found that bilateral lesions of temporal cortex produce visual discrimination deficits and visual aspects of the Klüver–Bucy syndrome, which include a tendency to select non-food as well as food objects (ref. 1 and Weiskrantz, personal communication).

Recordings in anaesthetized monkeys have shown that neurones in the inferotemporal cortex have large visual receptive fields which include the fovea. Effective stimuli may be bars or edges, or sometimes much more complex stimuli seem to be necessary to produce a response[7,8]. So far there have been few reports on the activity of inferotemporal neurones in the unanaesthetized monkey, but in one study a small number of neurones in this area was found with responses which appeared to depend on whether the visual stimulus had been associated with reward in prior learning[17]. In the present experiments recordings were made from neurones in different parts of inferotemporal cortex to determine if there was an area in which the neurones showed responses during the same feeding and learning tests in which the units in the lateral hypothalamus and substantia innominata had been shown to be active. The responses of the inferotemporal neurones to different stimuli were measured and the effects of feeding the monkeys to satiety, and of learning and unlearning a food-related visual discrimination were determined. A preliminary report of this work has appeared[12].

METHODS

Recording method

Two juvenile male rhesus monkeys *(Macaca mulatta)*, weighing 2.5–3.5 kg, were implanted under Nembutal anaesthesia with stainless steel holders on which a Trent-Wells adaptor for chronic single unit recording could be placed during recording sessions. Stimulation electrodes (for another experiment) were implanted during the same operation. After a recovery period of two weeks or more, daily recording sessions started. Single unit activity was recorded using glass-coated tungsten microelectrodes (after Merrill and Ainsworth[14], but without platinum plating) while the monkey sat in a primate chair with head restraint to provide recording stability. The electrodes were lowered into the brain through a stainless steel guide tube whose tip was 3–7 mm below the dorsal surface of the dura. At the end of each track, X-rays were taken of the frontal and lateral aspects of the head to determine (to within $\pm$ 0.5 mm) the position of the tip of the recording electrode relative to the permanently implanted stimulating electrodes.

The signal from the microelectrode was passed through a FET buffer amplifier mounted on the microdrive, amplified by conventional band-pass filtered amplifiers, and displayed on an oscilloscope. Data were analysed using an on-line PDP-11 computer, which was programmed to perform peristimulus time histograms, or to compute the mean firing rate (and its S.E.) of the neurones during stimulus presentations or control periods.

Presentation of stimuli

Stimuli were presented to the animal against a uniform background, in a circular aperture 15° in diameter (at a distance of 30 cm) in a screen which otherwise filled the animal's field of view. The stimuli used were real foods (such as peanuts and pieces of orange or banana), card or plexiglass cut into simple shapes such as bars, squares or triangles, or common laboratory objects, as these had been found useful in previous recordings in the inferotemporal cortex[7]. When a unit with a sustained visual response was found, different food and non-food stimuli were presented to determine whether physical factors such as the outline shape, size, orientation, colour or surface texture of the stimuli could account for the responses of the neurones. The animal's fixation was usually observed via a peephole, and the response to each stimulus was measured while the monkey looked at the stimulus. With some neurones, the latency of the visual response to an effective stimulus was measured by presenting the stimulus immediately behind a 6 cm diameter electromagnetically controlled shutter positioned in the circular aperture of the screen, and opened when the monkey was looking at the shutter.

Satiety and learning tests

The effect of satiety on the responses of a subset of the neurones was determined as follows. At the start of the experiment the animal was 12–14 h food-deprived. If the unit being tested responded to (amongst other things) a syringe of suitable size and orientation, the syringe was shown to the animal repeatedly, at intervals of about 90 sec, and at the end of each presentation the monkey was fed 5 ml of 25% glucose solution from the syringe. On each trial the syringe was shown to the animal either stationary, or for some neurones moving slowly towards the animal, over a period of 10 sec. The response of the neurone was measured during the first 5 sec or so of this presentation, while the animal was gazing at the syringe.

The activity of some neurones was measured while the monkey was learning an association between a visual stimulus and food. Two stimuli were selected, one of which was a highly effective stimulus for the neurone, and the other usually less effective. These stimuli were either in the form of plaques mounted on the syringes, or were themselves syringes of suitable size and colour. One syringe was filled with 25% glucose solution, and the other with 5% saline. Each syringe was presented to the monkey on alternate trials, and the neuronal response was measured as in the satiety experiments. The monkey was given 1 ml of the solution at the end of each trial. Trials were continued until the monkey consistently showed a positive response to the appearance of the glucose-filled syringe (reaching out and pulling the syringe

towards him, or opening his mouth as the syringe approached), and a negative response to the saline-filled syringe (shutting his mouth as the syringe approached or pushing the syringe away when it was advanced towards him). In some cases reversal training was performed by exchanging the solution in the syringe.

Localisation of recording sites

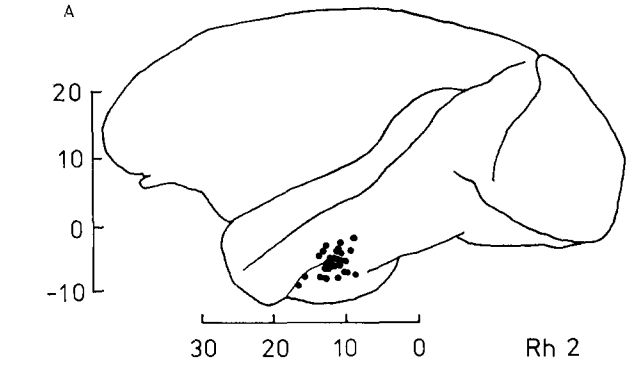
The recording sites of the neurones described in this paper were determined in two ways. Firstly, from the frontal and lateral X-ray photographs of the electrode at the end of its track, the position of each unit could be determined relative to the tips of the chronically implanted stimulation electrodes, the sites of which were histologically verified. Secondly, at the end of the recording period, lesions were made through the recording microelectrode to mark some typical units. This was done by passing either anodal or cathodal current of 60–100 μA for 60–100 sec. After a lethal i.p. dose of pentobarbitone sodium (Nembutal) the animal was perfused with 0.9% saline followed by formol–saline. After equilibration in sucrose–formalin, serial frozen 50 μm brain sections were cut and stained with thionin.

RESULTS

One hundred and fifty-six neurones with visual responses were investigated. Of these the great majority (142) gave sustained, almost always excitatory, responses which lasted as long as but no longer than the animal looked at the stimuli. Thirty-two percent (46) of these neurones responded similarly to all stimuli, while the remaining 68% (96) responded more strongly to some stimuli than to others. The sites at which these units were recorded are indicated by dots in Fig. 1, and the results described below were obtained on units in this region of the inferotemporal cortex, in the anterior and ventrolateral part of area TE of von Bonin and Bailey[3]. Many additional neurones were noted which had no response, as judged by ear, to any visual stimulus presented.

Response characteristics

The responses of some of the differentially responding units appeared to be related to physical properties of the stimulus, such as its shape, size, orientation, colour, or surface texture. For example, the response of the unit illustrated in Fig. 2A occurred when elongated objects (whether food or non-food) were presented horizontally but not vertically, and did not respond when small non-elongated objects were presented. Another example of differential responsiveness was that some units responded strongly to large (10 ml) but not to small (1 ml) syringes. The responses of the units did not depend on whether the stimulus shown was a food or a non-food object, or had been previously associated with a food reward (glucose) or an aversive taste (saline or quinine). For example, the unit illustrated in Fig. 2A only responded to food objects such as the syringe and banana if these were presented in a particular orientation, responded to non-food objects if these were elongated and presented in the optimal orientation, and did not respond to food objects such as the peanut which



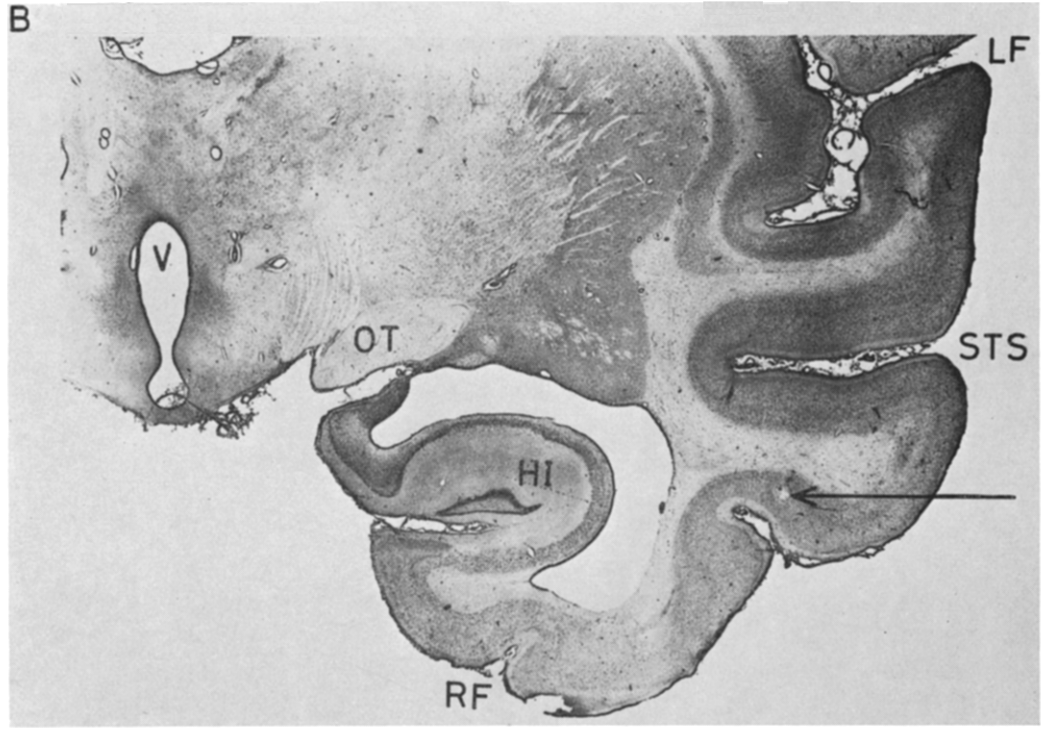


Fig. 1. A: the recording sites in the inferotemporal cortex of neurones which showed sustained responses to visual stimuli are indicated by filled circles (●) on these lateral views of one of the rhesus monkey brains (Rh2). The recording sites in all 3 monkeys were in the antero-ventro-lateral inferotemporal cortex (see B). The axes indicate mm on the stereotaxic planes[21]. B: vertical section of the rhesus monkey brain showing a lesion (arrow) to indicate a typical recording site in the inferotemporal cortex. HI, hippocampus; LF, lateral fissure; OT, optic tract; RF, rhinal fissure; STS, superior temporal sulcus; V, third ventricle.

were not elongated. In addition to the above-mentioned neurones, in agreement with Gross et al.[7,8], neurones were found which could apparently only be excited by more complicated visual stimuli.

The shortest average latencies of the responses of these neurones, measured

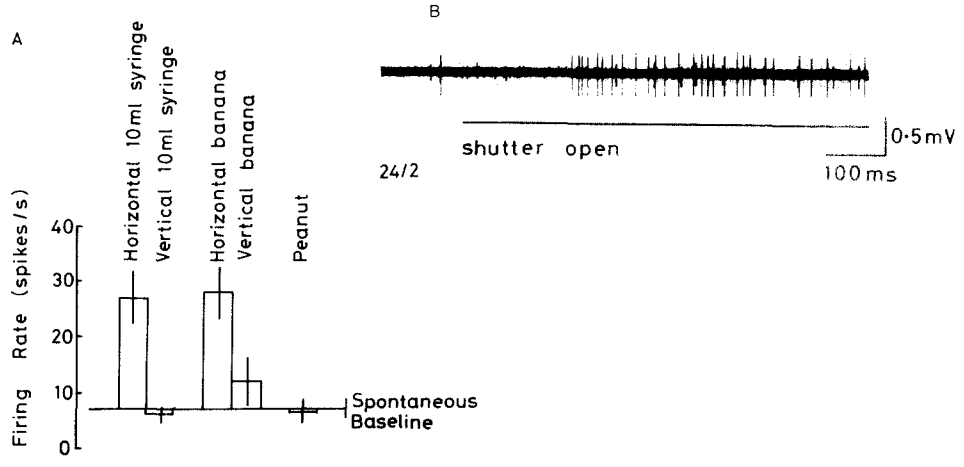


Fig. 2. A: an example of the responses (mean and S.E.M.) of inferotemporal neurones to different visual stimuli, measured over 5 sec periods in which the stimuli were presented. The neurone responded to elongated stimuli (whether or not these were food objects as illustrated), if they were shown horizontally but not if they were shown vertically. The unit did not respond to the sight of a peanut or to other small objects. B: latency determination using an electromagnetic shutter. A single trial is shown. Latency values ranged from 100 to 230 msec for different neurones in the inferotemporal cortex.

using the electromagnetic shutter, were 140–150 msec, and the range of latency values obtained was 100–230 msec for different trials. An example of a latency determination is shown in Fig. 2B. Care was taken to ensure that the monkey was already looking at the shutter before it opened to reveal the stimulus. If the monkey was looking away from the shutter before it opened, the response of the neurone was delayed by more than 100 msec, while the monkey made a saccade to fixate the stimulus.

Effects of satiety on the responses of the units

An example of an experiment in which the hungry monkey was fed to satiety is shown in Fig. 3. At the start of the experiment the unit fired at a high rate in the 5 sec period in which the monkey looked at the syringe before being offered 5 ml of the 25% glucose solution in the syringe, which monkey accepted. At about trial 18–19, the monkey started to reject the syringe, and after trial 20 the monkey was satiated as shown by consistent rejection of the syringe (by pushing away the syringe with the hand, and by keeping the mouth closed and not swallowing the solution), yet the response of the unit to the sight of the syringe continued unchanged. This type of result was found in all 7 of the units tested. Thus hunger and satiety did not affect the responses of these inferotemporal units.

Effects of learning on the responses of the units

The results of one learning experiment are shown in Fig. 4. The response of this neurone to the 2 ml syringe fitted with the square black plastic plaque (stimulus 'A') was greater than the response to the 2 ml syringe fitted with the wooden plaque of

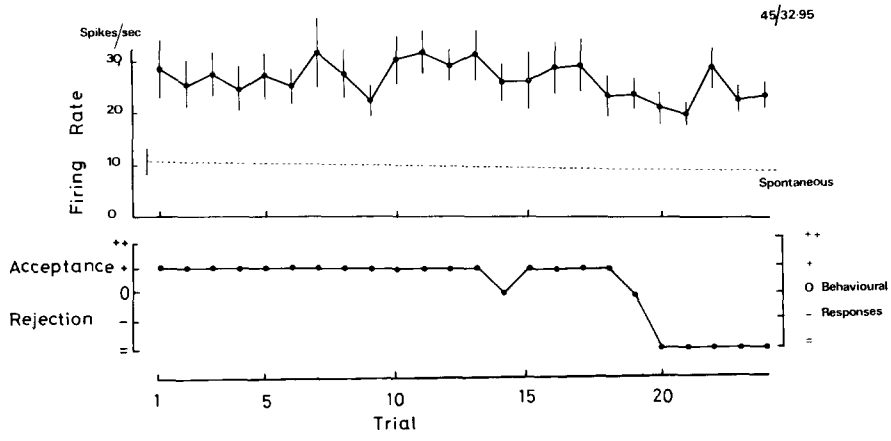


Fig. 3. Effects of satiety on the activity of an inferotemporal neurone. Upper trace: the mean firing rate (± S.E.) is indicated on successive trials when a 10 ml syringe containing a 25% solution of glucose was shown to the monkey for a 5 sec period immediately before the monkey was fed the glucose solution. Lower trace: the behavioural response of the animal on each trial is indicated in the following way: ++ = animal pulling syringe towards him; + = opening mouth in anticipation of syringe being placed in mouth; ○ = none of these actions; — = closing mouth firmly when syringe moved towards animal; = = pushing syringe away. On each trial the monkey was fed 5 ml of the 25% glucose solution, and by trial 20 he persistently rejected the glucose, but the neurone still responded above its baseline firing rate to the sight of the syringe.

the same size and shape (stimulus 'B'). On trials 1–5, the monkey learned that the stimulus 'A' syringe contained glucose solution, and the stimulus 'B' syringe saline. Learning was measured by whether the monkey accepted or rejected the syringe as it was moved towards him (see figure legend). On trial 22, reversal training was started, by exchanging the solutions in the two syringes. After a period of performance at chance, the monkey learned the reversed discrimination (by trial 34). The responses of the unit to the sight of each stimulus syringe remained constant throughout the learning experiment, and were not affected by whether the stimulus became associated during learning with a food reward or with an aversive taste. Similar results were obtained in 12 of the 13 neurones tested, and in one experiment the results were unclear.

DISCUSSION

We found that in an anterior part of the inferotemporal cortex of the alert monkey there were neurones whose responses to visual stimuli could be accounted for by simple physical aspects of the stimuli such as their outline shape, size, orientation, colour or surface texture. The responses of other neurones could not be accounted for in this way. The latencies of response of the inferotemporal neurones studied (100–230 msec) are similar to those reported by Gross et al.[8] for single units in the inferotemporal cortex of anaesthetized monkeys, and are comparable with the latencies of evoked potentials to patterned visual stimuli reported in this region[13].

The responses of these inferotemporal neurones to visual stimuli did not

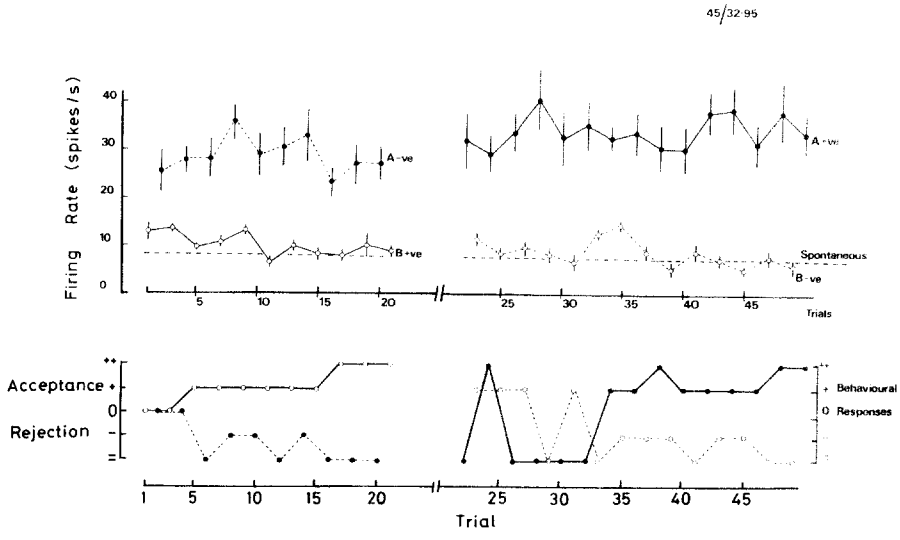


Fig. 4. An example of the responses of an inferotemporal neurone during visual discrimination learning and reversal. The discriminanda were a 2 ml syringe fitted with a square shiny black plastic plaque (filled circles, A), and a 2 ml syringe fitted with a natural wooden plaque of the same size and shape (open circles, B). Initially syringe B contained 25% glucose solution, and syringe A, 5% saline. The lower trace (using the conventions of Fig. 3) shows that the monkey learned in a few trials to accept the glucose-containing syringe (B) and to reject the saline-containing syringe (A). As shown in the upper trace, during this learning the neurone consistently responded more to the A stimulus (the mean and S.E.M. firing rate were measured in the 5 sec period immediately before the monkey was fed the solution). At trial 22 the contents of the syringes were exchanged. The monkey learnt over several trials to accept the A stimulus and reject the B stimulus, yet the neurone continued to respond consistently more to the A stimulus than to the B stimulus.

depend on whether the stimulus had been associated in previous learning with a food reward or an aversive taste. Although Ridley and Ettlinger[17] reported on a very small number of inferotemporal neurones whose responses appeared to depend on a previously learnt association of the stimuli with food reward, more neurones of this type have not been described subsequently, and it is a possibility that this type of association between visual stimuli and rewards is manifest at a stage of processing after the inferotemporal cortex.

It is of interest to compare the activity of the inferotemporal neurones with that of neurones in the lateral hypothalamus and substantia innominata of squirrel monkeys and rhesus monkeys recorded in the same test situation[4,15,20]. The hypothalamic neurones respond when the monkey looks at food but not at non-food objects, whereas the inferotemporal neurones responded independently of food reward and often on the basis of physical characteristics such as orientation or shape of the stimuli. The hypothalamic neurones alter their responses as the monkey learns or unlearns associations between visual stimuli and food reward, whereas the inferotemporal neurones continue to respond to a particular physical stimulus independently of its changing association with food reward. Further, the hypothalamic neurones only respond in association with the sight of their effective stimuli when the monkey is hungry. Thus

the significance in terms of food reward of the objects shown to the monkey can be used to predict the responses of the hypothalamic neurones, whereas in contrast physical aspects of the objects can be used to predict the responses of the inferotemporal neurones described. The similarity between the responses of the inferotemporal and hypothalamic neurones is that both showed responses which were sustained while the monkey looked at appropriate visual stimuli. These comparisons are consistent with the view[10,18,19] that the inferotemporal cortex is at a relatively early stage in the processes which mediate the feeding, autonomic and endocrine reactions to the sight of food, and that the effects of learning and satiety take place at a later stage of processing. It is possible that the association of visual stimuli with food rewards, which we have shown is not likely to be subserved by inferotemporal neurones, may take place in the amygdala (see refs. 2, 6 and 10) for recent evidence on this hypothesis). Further recordings in the amygdala may be able to resolve whether or not this is the case, and whether the amygdala could provide a link between visual association cortex and the hypothalamus.

REFERENCES

1 Akert, K., Gruesen, R. A., Woolsey, C. N. and Meyer, D. R., Klüver–Bucy syndrome in monkeys with neocortical ablations of temporal lobe, *Brain*, 84 (1961) 480–498.
2 Ben Ari, Y. and Le Gal la Salle, G., Plasticity at unitary level. II. Modifications during sensory association procedures, *Electroenceph. clin. Neurophysiol.*, 32 (1972) 667–679.
3 Bonin, G. von and Bailey, P., *The Neocortex of Macaca mulatta*, University of Illinois Press, Urbana, Ill., 1947, pp. 1–136.
4 Burton, M. J., Rolls, E. T. and Mora, F., Effects of hunger on the responses of neurones in the lateral hypothalamus to the sight and taste of food, *Exp. Neurol.*, 51 (1976) 668–677.
5 Dean, P., Effects of inferotemporal lesions on the behaviour of monkeys, *Psychol. Bull.*, 83 (1976) 41–71.
6 Fuster, J. M. and Uyeda, A. A., Reactivity of limbic neurones of the monkey to appetitive and aversive signals, *Electroenceph. clin. Neurophysiol.*, 30 (1971) 281–293.
7 Gross, C. G., Inferotemporal cortex and vision, *Progr. in Physiol. Psychol.*, 5 (1973) 77–123.
8 Gross, C. G., Rocha-Miranda, C. E. and Bender, D. B., Visual properties of neurons in inferotemporal cortex of the macaque, *J. Neurophysiol.*, 35 (1972) 96–111.
9 Herzog, A. G. and Van Hoesen, G. W., Temporal neocortical afferent connections to the amygdala in the rhesus monkey, *Brain Research*, 115 (1976) 57–69.
10 Jones, B. and Mishkin, M., Limbic lesions and the problem of stimulus-reinforcement associations, *Exp. Neurol.*, 36 (1972) 362–377.
11 Jones, E. G. and Powell, T. P. S., An anatomical study of converging sensory pathways within the cerebral cortex of the monkey, *Brain*, 93 (1970) 793–820.
12 Judge, S. J., Rolls, E. T. and Sanghera, M. K., Responses of neurones in the inferotemporal cortex of the monkey, *J. Physiol. (Lond.)*, 260 (1976) 50–51P.
13 Lieb, J. P. and Karmel, B. Z., The processing of edge information in visual areas of the cortex as evidenced by evoked potentials, *Brain Research*, 76 (1974) 503–519.
14 Merrill, E. G. and Ainsworth, A., Glass-coated platinum-plated tungsten microelectrodes, *Med. Biol. Eng.*, 10 (1972) 662–672.
15 Mora, F., Rolls, E. T. and Burton, M. J., Modulation during learning of the responses of neurons in the lateral hypothalamus to the sight of food, *Exp. Neurol.*, 53 (1976) 508–519.
16 Nauta, W. J. H., Fibre degeneration following lesions of the amygdaloid complex in the monkey, *J. Anat. (Lond.)*, 95 (1961) 515–531.
17 Ridley, R. M. and Ettlinger, G., Visual discrimination performance in the monkey: the activity of single cells in infero-temporal cortex, *Brain Research*, 55 (1973) 179–182.
18 Rolls, E. T., *The Brain and Reward*, Pergamon Press, Oxford, 1975.

19 Rolls, E. T., Neurophysiology of feeding. In T. Silverstone (Ed.), *Appetite and Food Intake*, Dahlem Konferenzen, Berlin, 1976, pp. 21–42.
20 Rolls, E. T., Burton, M. J. and Mora, F., Hypothalamic neuronal responses associated with the sight of food, *Brain Research*, 111 (1976) 53–66.
21 Snider, R. S. and Lee, J. C., *A Stereotaxic Atlas of the Monkey Brain*, Univ. of Chicago Press, Chicago, Ill., 1961.
22 Whitlock, D. G. and Nauta, W. J. H., Subcortical projections from the temporal neocortex in Macaca mulatta, *J. comp. Neurol.*, 106 (1956) 183–212.