Brain Research, 164 (1979) 121–135

THE LATENCY OF ACTIVATION OF NEURONES IN THE LATERAL HYPOTHALAMUS AND SUBSTANTIA INNOMINATA DURING FEEDING IN THE MONKEY

E. T. ROLLS*, M. K. SANGHERA** and A. ROPER-HALL

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

(Accepted July 5th, 1978)

SUMMARY

To investigate whether the responses of neurones in the lateral hypothalamus and substantia innominata associated with the sight of food could control the responses of the hungry monkey to the food, the latency of activation of these neurones by food was measured. It was found that when an electromagnetically operated wide-aperture shutter opened to reveal food or non-food objects, these hypothalamic neurones responded with a latency of 150–200 msec to the food objects, and did not respond to the non-food objects. To measure the latency of the monkey's responses to the food, a visual discrimination task was set in which the monkey could lick a tube to obtain fruit juice if a food-related visual stimulus was shown, but obtained hypertonic saline, which was aversive, if a different visual stimulus was shown. In this situation the typical latencies of the neuronal responses to the food were 150–200 msec, of the lick responses 350–500 msec, and of the EMG activity associated with these lick responses 250–400 msec. Thus the responses of these hypothalamic neurones precede the monkey's responses to the food, and could mediate the feeding and other responses of the animal to the food.

It was also shown that a different population of hypothalamic neurones with responses associated with the sight of aversive visual stimuli had response latencies of 150–200 msec.

* To whom correspondence should be addressed.
** Present address: Department of Physiology, University of Texas Health Science Center, 5323 Harry Hines Boulevard, Dallas, Texas 73235, U.S.A.

INTRODUCTION

To investigate the neurology of feeding, the activity of neurones in different brain regions is being recorded in the monkey[11,12,16]. The activity of one population of neurones in the lateral hypothalamus and substantia innominata alters before eating starts, and is associated with the sight of food but not of non-food objects[14]. The responses of these neurones to food only occur if the monkey is hungry[1], and become associated with the sight of food during learning[8]. Further, the activity of these neurones is different to that of neurones in sensory and motor structures recorded in the same test situation. For example, the activity of neurones in the inferotemporal visual cortex occurs to visual stimuli independently of whether the stimuli are food-related, and is not modulated by hunger or by food-related learning[15], and the activity of neurones in the globus pallidus and region of the substantia nigra which occurs during feeding does not occur only during food-related movements, and is not modulated by hunger[7,16]. These findings are consistent with the possibility that the activity of neurones in the lateral hypothalamus and substantia innominata which is associated with the sight of food controls the responses which occur to the sight of food, such as feeding, and autonomic and endocrine responses. An alternative possibility is that the activity of these neurones occurs only as a result of feeding movements being made by the monkey. To investigate these possibilities, the latency of activation by the sight of food of these neurones was measured as described here, to determine whether these neurones fire before feeding movements are initiated, in which case these neurones could control the feeding or autonomic and endocrine responses to food, or after feeding movements are initiated in which case these neurones could not control feeding.

METHODS

Recording

Six juvenile rhesus monkeys (*Macaca mulatta*), weighing 2.5–3.5 kg, were implanted with thiopentone sodium 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[6], 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 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 analyzed using an on-line PDP-11 computer, which was programmed to perform peristimulus time histograms with the additional presentation of every trial individually as a dot display, or to compute the mean firing rate (and its S.E.) of the neurones during stimulus presentations or control periods.

The latency of the responses of hypothalamic neurones

The general test situation was similar to that used previously[14]. Food and non-food objects were introduced into the visual field at a distance of 1 m from the monkey and moved steadily over a 10 sec period towards the monkey before being placed in the monkey's mouth for consumption or rejection. The monkeys were fed daily after and during the test session, and were thus willing to accept and work for food in the test session. The neurones investigated were those classified previously as having responses associated with the sight of food, in that they responded in the 10 sec period with a sustained increase or decrease of firing rate when food but not non-food objects were shown, and did not have responses associated with arousal, movements made by the monkey, olfactory stimulation, etc.[12,14]. When the 'clinical' investigation of the responsiveness was completed, a screen was fitted to the monkey's chair to allow the visual stimulation to be more closely defined. Stimuli were presented to the animal against a uniform background, in a circular aperture 15° in diameter (at a distance of 30 cm) in the screen which otherwise filled the animal's field of view. The food and non-food stimuli could be presented through this aperture in the screen, and could also be moved to the monkey's mouth for feeding. The animal's fixation was observed via a peephole and the response to each stimulus was measured in the 10 sec period while the monkey looked at the stimulus. Then, to measure the latency of activation of the neurone, a 6 cm diameter electromagnetically controlled shutter (Compur 5FS) was positioned in the circular aperture of the screen and was opened to reveal the visual stimulus. Correct fixation of the shutter before it opened was usually obtained by providing a 0.5 sec signal tone immediately before the shutter was opened, and was monitored and noted through a peephole at one side of the screen. Fixation was usually good because the visual field apart from the shutter aperture was filled by the screen. Further, the shutter was timed to stay open for a relatively short period, 1.0 sec. The firing rate of the neurone was acquired on each trial by the on-line PDP-11, and presented as a peristimulus dot display and as a peristimulus histogram for the sum of the neuronal activity on 15 trials. Peristimulus time 0 was the time at which the shutter opened to reveal the visual stimulus. The latency of the neuronal responses to the visual stimuli could often be estimated from individual trials (see, for example, Figs. 1 and 2), but were measured from the sum buffer which contained the results of 15 trials. To assess the significance of the changes in firing rate found in the peristimulus time histograms, Mann–Whitney U-tests or tests appropriate to the Poisson distribution of the spikes in the bins of the sum buffer were used to compare the firing rate in 18 bins of 10 msec each in a 180 msec immediately prestimulus period with the firing rate in any set of poststimulus bins. These tests were used to find the shortest poststimulus time at which a significant change in the firing rate occurred from the prestimulus period.

Comparison of the latency of the neuronal and feeding responses to the sight of food

When it became clear that the latency of the responses of hypothalamic neurones to the sight of food could be measured with the shutter method described above, it became necessary to know whether this latency was less than the latency of the animal's responses to the food. A visual discrimination was therefore designed which would show whether the neuronal responses preceded and could therefore control the responses of the animal to the food. After a signal tone (usually set to 0.5 sec) the shutter opened to reveal a visual stimulus. If the reward-associated visual stimulus (S^D) was shown (usually a 2 ml syringe containing blackcurrant juice and mounted on a white plaque), then the monkey, who was food-deprived for 18 h during these experiments, could obtain fruit juice from a tube fixed in front of his mouth if he licked the tube during the shutter-open period of 1.0 sec. (The lick activated a pump which delivered 0.3 ml of fruit juice for the monkey to drink.) If the shutter opened to reveal the aversive visual stimulus (S^Δ) (usually a 1 ml translucent syringe containing 5% saline mounted on a black plaque), then the monkey obtained aversive hypertonic (5%) saline if he licked the tube. So that the animal could not predict the type of the next trial, trials were presented in a Gellerman series. Trial spacing was approximately 15 sec, and the usual level of performance was 80% correct. The animal's reaction time at this task was minimized by leaving the shutter open long enough (usually 1.0 sec) so that, if the monkey was fixating the shutter when it opened and if the reward-associated stimulus was shown, he could make a first lick quickly enough to be able to make a second or even third lick within the shutter-open period to obtain additional 0.3 ml amounts of fruit juice. The usual latencies from the shutter opening to a correct visually discriminated lick contact were approximately 400 msec for most of the monkeys, but individual monkeys could perform correct visually discriminated licks at 300 msec. One advantage to this test situation is that it enables neuronal responses to be measured in relation to the time at which a behavioural response is made, to determine whether the neuronal responses occur before and not as a result of motor responses. The motor response of a lick was chosen to be as simple as possible so that the only relevant muscles (given the head restraint) were those which open the mouth and protrude the tongue, so that the time of onset of the motor responses could be clearly defined by the EMG in these muscles. Regular unipolar EMG recordings from the region of the genioglossus muscle were made so that any EMG activity relevant to the task, including mouth opening and tongue protrusion, would be recorded. The latency to the onset of EMG from the time of opening of the shutter was measured on photographed traces of the EMG (see Fig. 5). A second advantage of this test is that it requires a visual discrimination between complex stimuli to be made, so that bypassing of the visual association cortex, and perhaps of the hypothalamus, which might occur with simple visual stimulation such as a flash of light, is unlikely to occur. The procedure was designed to utilize in the visual discrimination task the complex visual analysis implied by the response characteristics of hypothalamic food-related neurones, and to render it feasible to follow this processing through cortical to subcortical levels[11–13,16].

Other characteristics of these hypothalamic neurones

When it became clear that the responses of the hypothalamic neurones with activity associated with the sight of food preceded feeding, tests to further specify the function of these neurones were performed. First, with the monkeys both food (18 h) and water (18 h) deprived, the responses of these neurones were measured when food, or when water, was shown to the animal and then ingested. This test shows whether these neurones are part of a control system specific for hunger, or part of a control system which responds when the animal initiates behaviour to a variety of different rewards. Second, to obtain further evidence on whether the responses of these neurones were independent of actual movements made by the monkey, the responses of the neurones were measured while the monkey licked the tube used in the visual discrimination test, when every lick provided fruit juice (continuous reinforcement), and also while food was in the mouth. The activity of the hypothalamic neurones investigated here was found not to be related to movements made during these tests.

Characteristics of other hypothalamic neurones

The responses of some other groups of hypothalamic neurones which responded in the test situation were also investigated. First, some neurones responded primarily to aversive visual stimuli, for example to the 1 ml syringe which contained hypertonic saline, to the aversive visual stimulus in the visual discrimination, to a squeeze bulb used to puff air lightly onto the animal's face, and to a threat gesture from a human or monkey. The latency of the activation of these neurones by their effective visual stimuli was measured, to determine whether their function might be comparable to that of the hypothalamic neurones with food-related visual responses. Second, auditory and other responses noted in other hypothalamic neurones in the test situation were investigated.

Localization 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 the 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 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

Recordings were made in the lateral and anterior hypothalamus and substantia innominata of 6 rhesus monkeys (in which recordings were also made in some related brain areas[7,15,18]). Although, as in previous studies[1,8,14], neurones with food-related responses were not common, it was possible in the course of microelectrode tracks

made into the hypothalamus and substantia innominata to repeat the measurement of the latency of activation of the food-related neurones on 27 different neurones, as described below.

The latency of the responses of food-related neurones in the lateral hypothalamus and substantia innominata

An example of a latency determination is shown in Fig. 1. This neurone decreased its firing rate in the clinical test situation when the hungry monkey was shown food but not non-food objects. When the shutter opened (at peristimulus time 0) to reveal food, the unit decreased its firing rate, with a latency of approximately 200 msec from the time of the shutter opening (see top 4 dot displays of Fig. 1, and upper sum buffer containing the sum of the results of the 4 trials with food stimuli shown in this diagram). The response latencies of 27 neurones in the 6 monkeys in which the measurement was made were between 140 and 220 msec with most of the neurones having latencies between 150 and 200 msec. It can also be seen in Fig. 1 (and even more clearly in Figs. 2, 3 and 4) that comparable responses of these neurones to non-food stimuli, or to a blank control in which the shutter opens to reveal only the uniform white background field, are not obtained.

The latencies of the neuronal and feeding responses to food-related visual stimuli

An example of the measurement of the neuronal and feeding response latencies in the visual discrimination is shown in Fig. 2. This neurone increased its firing rate in the clinical test when the hungry monkey was shown food but not non-food related objects. In the discrimination task the neurone increased its firing rate approximately

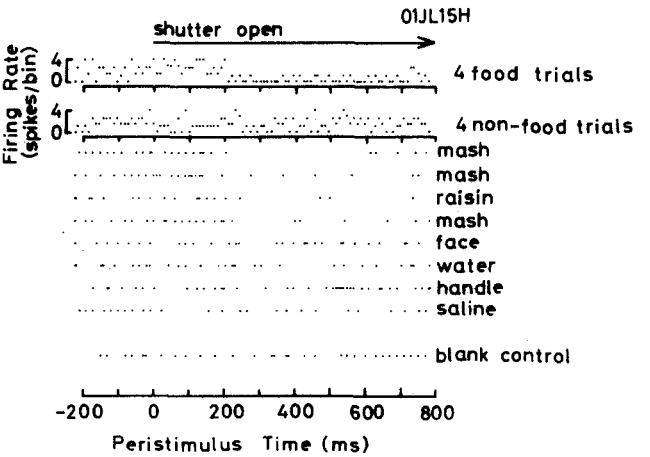

Fig. 1. Latency of responses of a hypothalamic neurone to the sight of food. At time 0 the shutter opened to reveal food (top 4 trials of the dot displays, grouped for clarity but originally presented in random order) or non-food objects (next 4 trials) or opened to reveal a blank screen (bottom trial). A decrease in firing rate occurred 150–200 msec after the shutter opened on food trials, and a similar response was not seen on non-food trials or on the control trial. The difference between food and non-food trials is also seen in the histograms showing the sum buffers for the 4 food and 4 non-food trials at the top of the diagram.

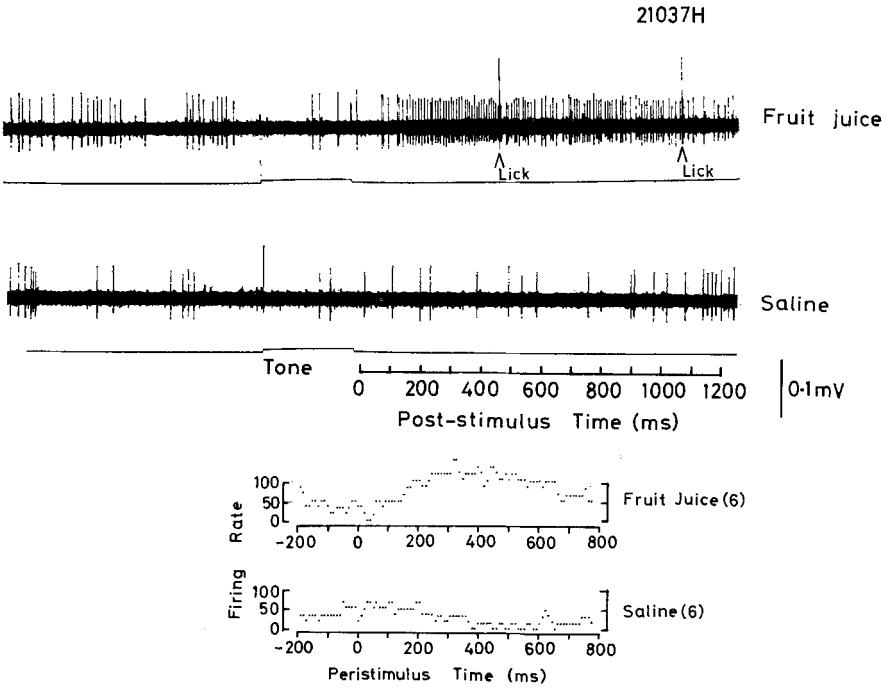

Fig. 2. Activity of a neurone in the substantia innominata during visual discrimination. Above, top trace, reward trial: at the end of the signal tone the shutter opened at time 0 to reveal a 2 ml syringe filled with red fruit juice and fitted with a white plate, the unit responded to the stimulus with a latency of 150 msec, and the monkey licked the tube in front of his mouth at approximately 470 msec to obtain fruit juice. Lower trace, saline trial: the shutter opened to reveal a 1 ml syringe containing clear saline and fitted with a black plate, the neurone did not respond to the stimulus, and correctly the monkey did not lick the tube, or he would have obtained hypertonic saline. Below: histograms, with 10 msec bins, of the average poststimulus activity for this neurone on 6 reward trials and 6 saline trials. The number of spikes/10 msec bin is expressed as the mean firing rate for a tiral.

150 msec after the reward-associated visual stimulus was shown (top trace), and the monkey licked the tube to obtain fruit juice 470 msec after the visual stimulus was shown. On trials when the visual stimulus associated with hypertonic saline was shown, there was no neuronal response and, correctly, no lick was made (see, for example, bottom trace).

The responses of another hypothalamic neurone, which increased its firing rate when the monkey looked at food but not at non-food related objects in the clinical tests, are illustrated in a different form in Fig. 3. On the reward (r) trials (grouped together here as rows 1–8 for clarity as the original trials were run in a Gellerman series), the neurone increased its firing rate approximately 150 msec after the shutter opened to reveal the reward-associated visual stimulus, and the licks (indicated by double dots in the dot display) were made at latencies of 370–480 msec after the shutter opened. (The 3 vertical columns of dots near time 0 represent the shutter opening pulses.) On trial 2 the animal was not fixating the shutter when it opened, and the neuronal and lick responses were delayed by the time for fixation. On the trials on which the shutter opened to reveal the saline-associated visual stimulus (s), no

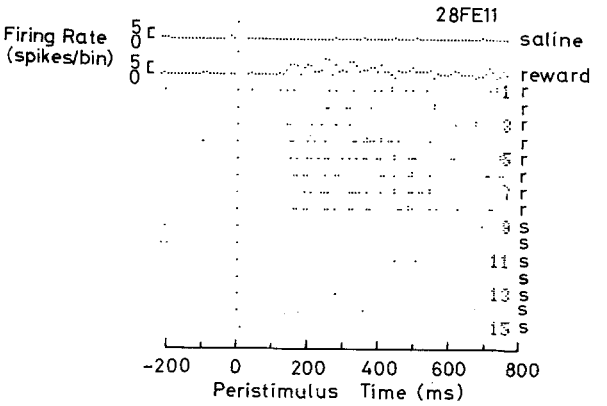

Fig. 3. Dot displays of a different neurone showing activity on a number of reward (r) and saline (s) trials, which were presented in random order but are grouped together for convenience in this diagram. The shutter opened at time 0 (the column of dots near time zero was due to a shutter control pulse), and on reward trials the neurone responded at approximately 150 msec, and the animal contacted the tube to obtain fruit juice at 380–500 msec (double dot). (On the second reward trial shown, the animal had to fixate the visual stimulus after the shutter opened, and the neuronal and lick responses were delayed by the fixation time.) The histograms above show the sum of the neuronal activity on the 8 reward and 7 saline trials illustrated, with a bin width of 10 msec.

neuronal responses and, correctly, no licks appear in the dot displays. The neuronal responses on the 8 reward and 7 saline trials are summed in the peristimulus histogram shown at the top of Fig. 3.

The responses of 27 neurones with activity related to the sight of food were measured in this visual discrimination. The shortest neuronal responses were between 140 and 200 msec for the different neurones in the different animals. The shortest correctly visually discriminated licks in most of the animals occurred with latencies of 300–400 msec. Thus on fast correctly discriminated trials the neuronal responses preceded the lick responses by approximately 170 msec (e.g. 150 msec for neuronal vs. 320 msec for lick responses). Typical values for most trials ranged from 150 to 200 msec for neuronal responses and 330–600 msec for lick responses.

In 3 monkeys the relation between the time of initiation of EMG responses in the genioglossus muscle and the time of the lick contact with the tube containing fruit juice was measured. For each monkey it was found that even on fast visually discriminated trials, the hypothalamic neuronal responses always preceded the EMG responses (for almost all neurones by 50 msec or more), and that the EMG responses preceded the lick contact by 50–100 msec (see Fig. 4). On slower trials, this sequence was more spaced, with the EMG responses often following the hypothalamic neuronal responses by several hundred msec. Although it was not often possible to measure the neuronal and EMG responses simultaneously, it was possible to repeat the simultaneous measurement on different neurones in 3 different monkeys. An example of the recording of the EMG is shown with a dot display of a neuronal response in Fig. 5. It is clear that the neuronal responses which occurred when the food-associated stimulus was shown preceded the EMG response from the region of the genioglossus muscle by

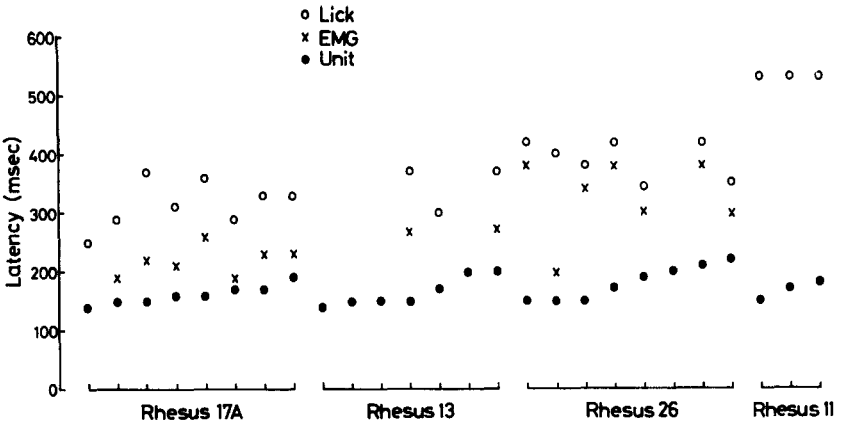

Fig. 4. The relation between the response latencies of hypothalamic neurones (●) to the food reward-related visual stimulus and the latency of the licks (○) made to obtain fruit juice, and where possible, the EMG (×) associated with the lick movement. Results for 26 neurones in 4 monkeys are shown in this diagram. The latencies shown are the shortest neuronal and associated lick response latencies obtained for each neurone on correct visually discriminated trials, measured relative to the time of shutter opening. On more typical trials, the neuronal response was similar to that shown, but the lick and EMG responses were less fast, so that they were further separated from the neuronal responses. These neurones did not respond on trials in which the saline-associated visual stimulus was shown.

several hundred msec. Thus the neuronal responses could not have been produced by the lick movement.

These experiments show that the responses of neurones in the lateral hypothalamus to the sight of food occur with a latency of 150–200 msec, and precede the lick responses and the associated EMGs when feeding is initiated to the sight of food.

The activity of these hypothalamic neurones during the initiation of drinking

To determine whether the activity of these neurones was associated with the

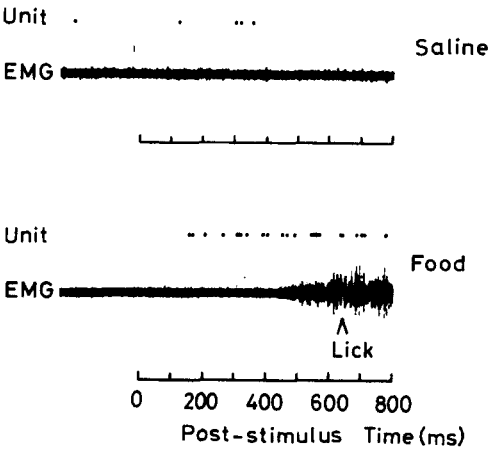

Fig. 5. Neuronal (dot displays) and EMG activity in the region of the genioglossus muscle recorded simultaneously during the visual discrimination. The response of the unit on the reward trial preceded the onset of the EMG associated with the lick made to obtain fruit juice. The shutter opened at time 0,

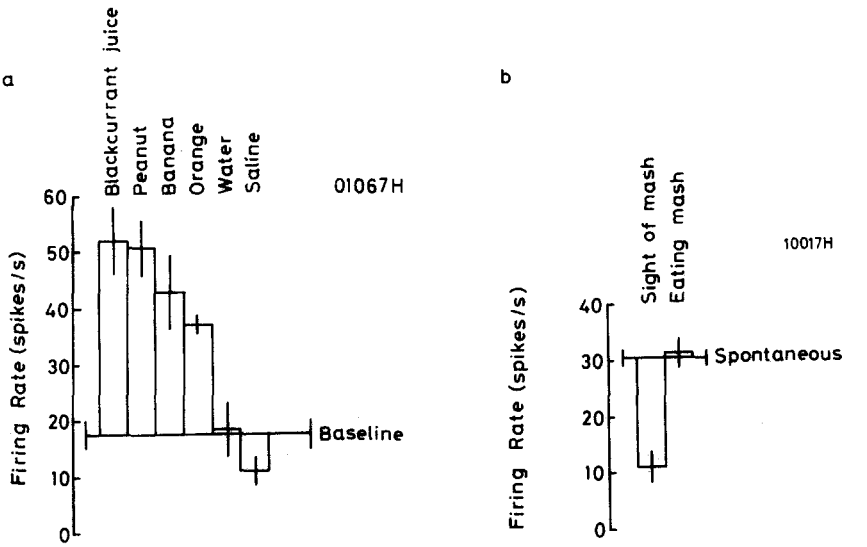

Fig. 6. a: responses of a hypothalamic neurone to the sight of food stimuli, and to non-food stimuli including water. The mean and S.E.M. of the firing rate were measured in a 5 sec period in which the monkey looked at each object as it was brought steadily towards the monkey's mouth, for ingestion of the substance shown. In the hungry and thirsty monkey, this neurone responded to the sight of the food-related stimuli (including a 2 ml syringe from which the monkey was fed blackcurrant juice), but not of the water-related stimulus (a 10 ml syringe from which the monkey was given water), or the saline-related stimulus (a 10 ml syringe from which the monkey was given 2% saline). b: the firing rate (mean ± S.E.M.) of this neurone in the lateral hypothalamus decreased when the monkey looked at food but not while he ate the food.

sight of water in addition to the sight of food in the thirsty and hungry monkey, the firing rate of these neurones was measured during a 5–10 sec period in which either a 10 ml syringe containing water, or different food objects including a 2 ml syringe containing 5% glucose, were shown to the monkey and gradually approached the monkey's mouth before ingestion. An example of the response of a unit which responded to food-related visual stimuli but not to the sight of a syringe from which the hungry and thirsty monkey was given water is shown in Fig. 6a. Of 10 units tested under these conditions, 4 responded to the sight of food but not of water, 4 responded to both food and water, and 2 responded primarily to food but had weak responses to water.

Recording sites

The sites of the units with food-related activity in which latency determinations were performed are shown in Fig. 7. The units were found in a ventral forebrain region which included the lateral hypothalamus and substantia innominata, and continued in an anterior direction beyond the anterior commissure as shown. In this general region, of many hundreds of neurones recorded, the activity of 83 units with activity which was related to feeding was observed. Of these 83, 67 had responses which were classified as visual, with 35 showing food-related responses (the latency determinations were performed on 27 of these), 4 showing responses to aversive visual stimuli

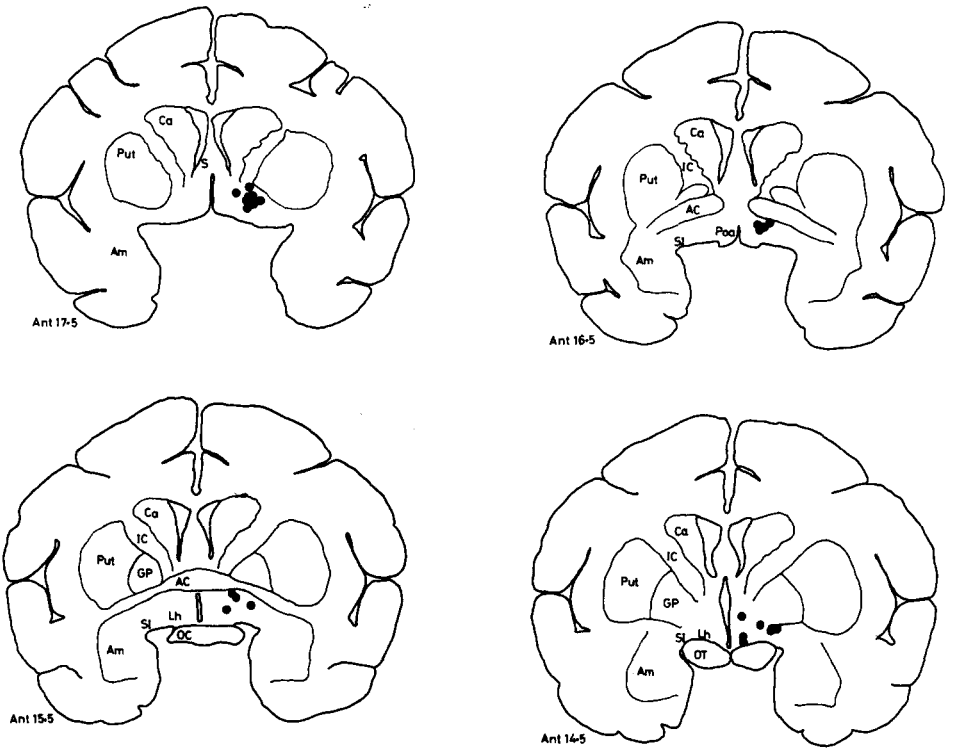

Fig. 7. The recording sites of the neurones which responded to the sight of food-related visual stimuli and were investigated in this study are shown by filled circles. Abbreviations: AC, anterior commissure; Am, amygdala; Ca, caudate nucleus; GP, globus pallidus; IC, internal capsule; Lh, lateral hypothalamus; OC, optic chiasm; OT, optic tract; Poa, preoptic area; Put, putamen; S, septal region; SI, substantia innominata. The plane of each section anterior to ear bar zero is shown in mm.

(see below), and 28 showing unselective visual responses. Of the remaining 16 units, 9 showed auditory responses, 1 showed multi-modal responses, while 2 units had activity associated with taste and 4 with movements made by the monkey.

Activity of other hypothalamic neurones related to aversive visual stimuli

During the course of these experiments it was noted that some hypothalamic neurones responded primarily to the sight of aversive visual stimuli, such as the sight of a syringe from which the monkey was fed hypertonic saline, or the sight of a squeeze bulb from which air was puffed onto the face. To obtain evidence on whether these were visual responses, and on whether the activity of these neurones preceded the responses of the monkeys to the aversive visual stimuli, the latency of the activation of these neurones was measured when the shutter opened to reveal aversive and non-aversive visual stimuli (see, for example, Fig. 8), and in the food vs. saline visual discrimination. These tests were repeated on 4 different neurones, and the latencies of the responses were all in the range of 150–200 msec after the aversive visual stimuli were shown. One of these units was excited and 3 were inhibited by the aversive visual stimuli.

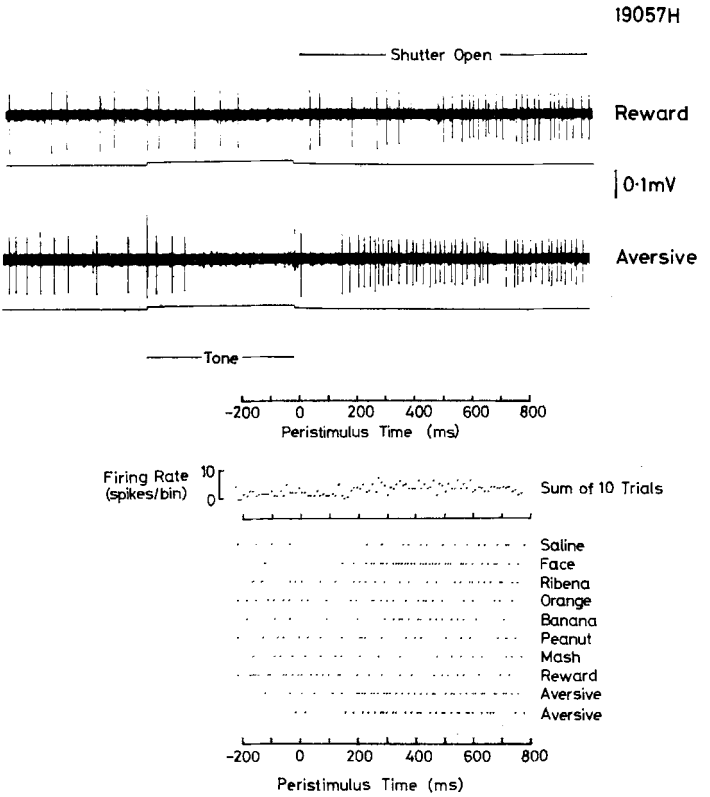

Fig. 8. The latency of activation of a hypothalamic unit responding primarily to aversive stimuli. The top trace shows unit activity when the reward-related visual stimulus was shown (see also trial 8 in dot display below). The lower trace shows the unit responding to the aversive-related visual stimulus with a latency of approximately 150 msec (see also trials 9 and 10 in dot display). The dot display below shows that the unit also responded well to a face which the monkey found aversive and to a syringe which the monkey knew contained hypertonic saline. There were no clear responses to any of the other stimuli.

DISCUSSION

These experiments show that neurones in the lateral hypothalamus and substantia innominata with activity associated with the sight of food respond with a latency of 140–200 msec to the food. Comparable responses to non-food objects are not seen in these neurones, and usually not even minor short-latency responses (e.g., 1 or 2 action potentials at 140–200 msec) are found. This differentiation between food and non-food stimuli was clearly shown in the visual discrimination situation, in which the neurones responded only to the food-related visual stimuli, and in which the neuronal responses preceded the fastest visually discriminated lick movements and their associated EMG activity which each monkey could make to the visual stimuli. Typical values for fast responses were 150–200 msec for the hypothalamic neurones, 250–300 msec for the EMG activity, and 350–400 msec for the lick contact. (For comparison, in the same test situation, a human subject's shortest latency licks were 390–400 msec.) These findings show that the activity of hypothalamic neurones with responses

associated with the sight of food cannot be caused by movements made by the monkey to obtain the food. The sequence of responses is consistent with an alternative possibility, that the hypothalamic neuronal responses mediate the feeding responses of the animal to the sight of the food, and this possibility is discussed below.

This evidence on the latency of activation of these hypothalamic neurones may be considered with other evidence on their function. First, these neurones do not appear to be motor in that their responses precede the initiation of movements made to the sight of food (see above), and in that their activity is not associated with mouth or arm movements[10,11]. Further, in the course of the experiments described here the observation[14] that some of these neurones respond to the sight of food but not while food is in the animal's mouth was confirmed (see Fig. 6b). This observation also shows that the activity of these neurones can not simply reflect salivation, although it could mediate autonomic responses to the sight of food. Some of these neurones responded both to the sight of food and of water in the hungry and thirsty monkey, and some responded only to the sight of food. Thus some of these neurones could be involved in responses to a range of rewarding stimuli, and others in responses specific to food. It was found, as previously[14], that some neurones responded to the sight of food with an increase of firing rate (17/27), and others with a decrease (10/27). Five of the 17 units which increased their firing rate to the sight of food showed some decrease of firing rate when aversive stimuli such as a syringe which contained saline or a squeeze bulb from which air was puffed onto the monkey's face was shown. This evidence is consistent with the possibility that these neurones mediate at least some of the responses of the hungry monkey to the sight of food. These responses include autonomic and endocrine responses, and the initiation of feeding. These neurones do not respond when non-food related visual stimuli are shown.

The function in feeding of the neurones in the lateral hypothalamus and substantia innominata with activity related to the sight of food can be discussed in terms of what is known about pathways related to feeding[11–13,16]. Neurones in the inferotemporal visual cortex fire 100–140 msec or more after visual stimuli are shown to the monkey[15]. The inferotemporal cortex is a region of visual association cortex which receives a visual input after processing through several different cortical visual areas[4], and which has connections to the lateral amygdala[3,4] which in turn has connections to the hypothalamus[9]. Neurones in the inferotemporal cortex fire independently of whether the visual stimulus is food-related (the responses of a number of inferotemporal neurones can be accounted for by simple physical dimensions of stimuli), are not affected by food-related learning, and are not affected by hunger[15]. Thus the food-related significance and the motivational state of the animal do not affect neuronal responses at this stage. If recordings are made in the dorsolateral part of the amygdala, which anatomically has been shown to receive an input from the inferotemporal cortex[3,4], then neurones which respond to visual stimuli with latencies of 100–140 msec and up to 180 msec are found[18]. None of these neurones recorded responded only to food-related visual stimuli, and the responsiveness of most of the neurones tested was not influenced by food-related learning. Thus, the responses of these amygdaloid neurones did not appear to be due to the

food-related significance of the effective visual stimuli. Nevertheless a number of neurones (22/133 with visual responses) in this part of the amygdala responded mainly but not uniquely to food-related visual stimuli, so that there is a possibility that this is a stage of processing at which food-related significance is starting to operate, although its operation is still incomplete[18]. In the lateral hypothalamus and substantia innominata, as shown here, neurones respond in the same test situation with latencies of 150–200 msec. As the responses of these neurones precede feeding movements made to the visual stimuli, as described here, and because they are associated with the food-related significance of the visual stimuli[8] and only occur in the hungry animal[1], they predict the responses of the animal to food and non-food related visual stimuli, and could control whether or not feeding is initiated when the animal sees food. In this context, it is of interest that neurones with cell bodies scattered in the region of the lateral hypothalamus and substantia innominata, the basal forebrain nuclei of Meyenert, send axons directly to a wide range of cortical areas[2,5]. Although this provides a possible output from this region which could be related to the initiation of feeding, the sequence of processes which initiates feeding movements is largely uninvestigated. It has been found that pallidal neurones with activity related to mouth movements fire approximately 300 msec after the visual stimuli are shown in the visual discrimination described above. According to these findings the hypothalamic neurones described could play an important role in feeding, by responding when visual stimuli are food-related and when the monkey is hungry, so that feeding, autonomic, and/or endocrine responses can be initiated on the basis of these signals (see also refs. 11–13, 16). In concluding, it may be mentioned that although the activity of these neurones could lead to autonomic responses such as salivation when food is seen, it is unlikely that the activity of these neurones reflects autonomic responses, in that in most cases these neurones do not respond when food is in the mouth (see above). Also the findings described here are consistent with the evidence that the activity of these hypothalamic neurones is related to food reward[10].

ACKNOWLEDGEMENTS

This work was supported by the Medical Research Council.

REFERENCES

1 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.
2 Divac, I., Magnocellular nuclei of the basal forebrain project to the neocortex, brain stem, and olfactory bulb. Review of some functional correlates, *Brain Research*, 93 (1975) 385–388.
3 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.
4 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.
5 Kievit, J. and Kuypers, H. G. J. M., Subcortical afferents to the frontal lobe in the rhesus monkey studied by means of retrograde horseradish peroxidase transport, *Brain Research*, 85 (1975) 261–266.
6 Merrill, E. G. and Ainsworth, A., Glass-coated platinum-plated tungsten microelectrodes, *Med. Biol. Engng.*, 10 (1972) 662–672.

7 Mora, F., Mogenson, G. J. and Rolls, E. T., Activity of neurons in the region of the substantia nigra during feeding in the monkey, *Brain Research*, 133 (1977) 267–276.
8 Mora, F., Rolls, E. T. and Burton, M. J., Modulation during learning of the responses of neurones in the lateral hypothalamus to the sight of food, *Exp. Neurol.*, 53 (1976) 508–519.
9 Nauta, W. J. H., Fibre degeneration following lesions of the amygdaloid complex in the monkey, *J. Anat. (Lond.)*, 95 (1961) 515–531.
10 Rolls, E. T., The neurophysiological basis of brain-stimulation reward. In A. Wauquier and E. T. Rolls (Eds.), *Brain-Stimulation Reward*, North-Holland Publ., Amsterdam, 1976, pp. 65–87.
11 Rolls, E. T., Neurophysiology of feeding, *Life Sci.*, 2 (1976) 21–42.
12 Rolls, E. T., Activity of hypothalamic and related neurons in the alert animal. In P. J. Morgane and J. Panksepp (Eds.), *Handbook of the Hypothalamus*, Dekker, New York, 1978.
13 Rolls, E. T., Neurophysiology of feeding, *Trends Neurosci.*, 1 (1978) 1–3.
14 Rolls, E. T., Burton, M. J. and Mora, F., Hypothalamic neuronal responses associated with the sight of food, *Brain Research*, 111 (1976) 53–66.
15 Rolls, E. T., Judge, S. J. and Sanghera, M. K., Activity of neurones in the inferotemporal cortex of the alert monkey, *Brain Research*, 130 (1977) 229–238.
16 Rolls, E. T. and Rolls, B. J., Activity of neurones in sensory, hypothalamic and motor areas during feeding in the monkey. In Y. Katsuki, M. Sato, S. Takagi and Y. Oomura (Eds.), *Food Intake and Chemical Senses*, University of Tokyo Press, Tokyo, 1977.
17 Rolls, E. T., Roper-Hall, A. and Sanghera, M. K., Activity of neurones in the substantia innominata and lateral hypothalamus during the initiation of feeding in the monkey, *J. Physiol. (Lond.)*, 272 (1977) 24P.
18 Sanghera, M. K., Rolls, E. T. and Roper-Hall, A., Visual responses of neurones in the dorsolateral amygdala of the alert monkey, *Exp. Neurol.*, submitted.