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EFFECTS OF SATIETY ON SELF-STIMULATION OF THE ORBITOFRONTAL CORTEX IN THE RHESUS MONKEY

F. MORA*, D.B. AVRITH**, A.G. PHILLIPS† and E.T. ROLLS††

Department of Experimental Psychology, University of Oxford, South Parks Road, Oxford (United Kingdom)

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SUMMARY

Self-stimulation of the orbitofrontal cortex of the rhesus monkey was found to be attenuated after the monkeys were fed to satiety. Self-stimulation at some other sites (e.g. the nucleus accumbens septi, the region of the substantia nigra, and the caudate nucleus) was relatively unaffected in the same test sessions by the satiety. In recordings from single neurons in the monkey orbitofrontal cortex, neurons of the type found in the lateral hypothalamus with sustained responses associated with the sight of preferred foods were not found. However, some orbitofrontal neurons did respond to the removal of food or other desired objects. These experiments show that self-stimulation of the monkey orbitofrontal cortex in modulated by hunger, and show that some orbitofrontal neurons have complex responses which could be related to the control of feeding.

There are neurons in the lateral hypothalamus and substantia innominata of the monkey with activity which is related to the presentation and consumption of food [7,11,14]. These neurons only respond to food if the monkey is hungry [3]. These finding-related neurons are also activated during self-stimulation of a number of brain sites, which frequently include a self-stimulation site in the orbitofrontal cortex [9,10; E.T. Rolls et al., unpublished]. These findings suggest a close relationship between the

* Departmento de Fisiologia, Facultad de Medecina, Universidad de Granada, Granada, Spain.
** University of Cambridge, Physiological Laboratory, Downing Street, Cambridge, United Kindgom.
† Department of Psychology, University of British Columbia, Vancouver V6T 1W5, Canada.
†† To whom correspondence should be sent.

orbitofrontal cortex and lateral hypothalamus, and self-stimulation and feeding behaviour. It was therefore of interest when it was found in the squirrel monkey that satiating the animal not only suppressed self-stimulation of the lateral hypothalamus (E.T. Rolls et al., unpublished), but also of the orbitofrontal cortex (E.T. Rolls and M.J. Burton, unpublished, 1975). (Self-stimulation of some other brain sites was not attenuated by satiety.) This work led to the demonstration that in the rat sulcal prefrontal cortex, which may correspond with the monkey orbitofrontal cortex [6], self-stimulation is facilitated by hunger [5]. Because of these findings and because lesions of this region produce a transient aphagia and adipsia in rhesus monkeys [1] and in rats [4] and affect food preferences in rhesus monkeys [2], the following investigations were performed. First, the effects of hunger and satiety on self-stimulation of the orbitofrontal cortex (and other brain regions for comparison) of the rhesus monkey were measured. Second, the responses of a number of single neurons in the orbitofrontal cortex were recorded during feeding to determine whether their activity was related to feeding, as had been shown for neurons in the lateral hypothalamus and substantia innominata (see refs. above).

Five rhesus monkeys weighing 2.5—3.5 kg were implanted with monopolar stimulation electrodes (00 gauge stainless-steel pins) in the caudal orbitofrontal cortex (area 13) and other brain areas (F. Mora et al., unpublished. The single unit recordings and the electrical brain stimulation were made using the parameters and general procedures described elsewhere [8,11; F. Mora et al., unpublished].

The effects of satiety on self-stimulation were investigated both with the chronically implanted stimulation electrodes and with microelectrodes used for self-stimulation at the end of a recording session. Monophasic, 0.5 msec, negative, rectangular, capacitatively coupled pulses at a frequency of 100 Hz in trains lasting 0.3 sec were applied to the electrode under test when the monkey contacted a bar in front of him. (Pulse trains were generated with a Grass S8 stimulator followed by a Grass S1U5 stimulus isolation unit.) Current return was via the screws permanently implanted in the skull. The current of the constant current stimulation pulses was monitored continuously with a Tektronix 502A oscilloscope. After self-stimulation was found at a particular site, the threshold was determined by increasing the current, starting from a subthreshold intensity. The curve relating self-stimulation rate to current intensity was repeated then by decreasing the current from a suprathreshold intensity. Two or three further points in the rate-intensity curve were then determined in random order. After that, the animals were fed to satiety with blackcurrant juice (Ribena brand diluted to 20%) with glucose added to saturation. Satiety was measured by the refusal of the animal to drink more blackcurrant juice. The juice was very acceptable at the start of the experiment as the animals were deprived of food for 4—6 h. After active rejection of the blackcurrant juice, the animals were offered water to drink and then

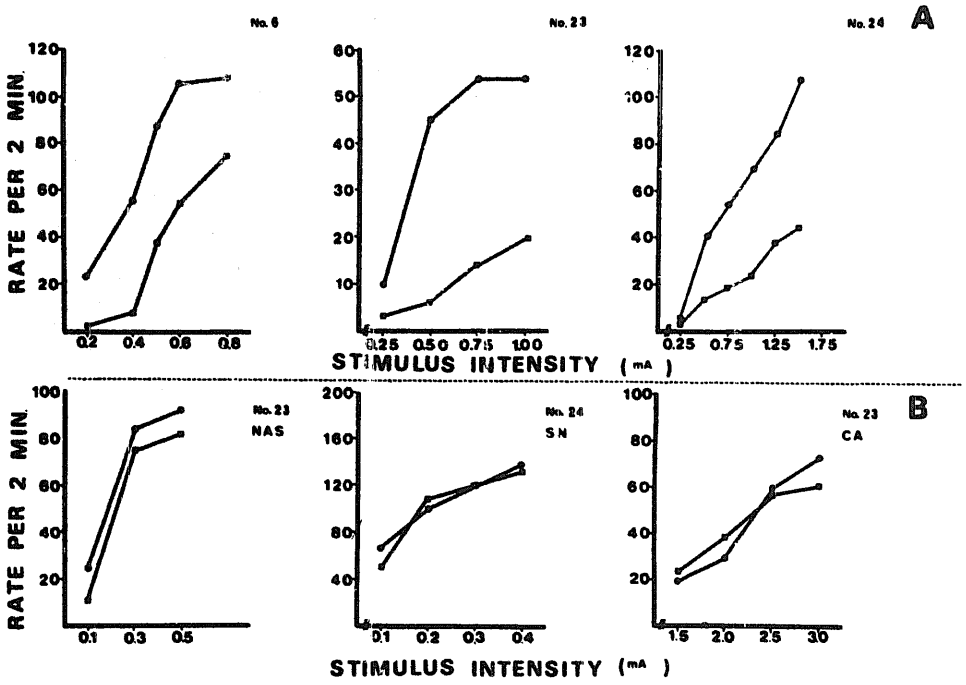

Fig. 1. A: effects of satiety on self-stimulation of the orbitofrontal cortex in the rhesus monkey. B: effects measured in the same test session of satiety on self-stimulation of the nucleus accumbens septi (NAS), region of the substantia nigra (SN) and caudate nucleus (CA). ●——●, hungry; ■——■, satieted.

the rate-intensity curves for all the available self-stimulation sites were determined again in the same way as before.

Fig. 1 shows the effects of satiety on self-stimulation of the orbitofrontal cortex in rhesus monkeys 6, 23 and 24. In these three animals, satiety caused a significant decrease of self-stimulation in the orbitofrontal cortex ($P < 0.005$, Wilcoxon matched-pairs signed ranks test), while self-stimulation measured in the same test session of the caudate nucleus, region of the substantia nigra and nucleus accumbens septi, was unaffected. In two other monkeys tested, feeding the animal to satiety after this relatively mild food deprivation did not attenuate orbitofrontal self-stimulation. The effect on self-stimulation of food deprivation was also tested in all of these animals but periods of up to 12 h of deprivation did not produce a significant facilitation of self-stimulation.

In the second investigation, the activity of single neurons was recorded in the orbitofrontal cortex of 2 monkeys during feeding. No neurons recorded had activity like that of hypothalamic food-related neurons, that is sustained activity associated with the sight of preferred foods in the hungry monkey (see refs. above). Although the sample of neurons in the rhesus monkey was small (35 neurons), to this can be added a further sample of 61 orbitofrontal neurons in the squirrel monkey, which similarly

did not have responses associated with the sight of food (E.T. Rolls and M.J. Burton, unpublished, 1975). However, in the rhesus monkey, it was observed that some of the neurons showed a transient increase in firing rate immediately after some foods or preferred objects were taken away from the monkey. These responses were not consistent, often diminishing if this procedure was repeated. However, if after a delay of 1—2 min the preferred object or food was presented to the monkey, there was again a neuronal response when the object was removed. In this situation some of the responses were associaed both with the removal of food and of preferred non-food objects.

Thus, in the experiments described here it has been shown that self-stimulation of at least some sites in the caudal orbitofrontal cortex, area 13, of the rhesus monkey is attenuated by satiety. The effect appeared to be related directly to the satiety, and not to, for example, drowsiness produced by the satiety, in that self-stimulation of some other brain sites (e.g. the caudate nucleus, region of the substantia nigra and nucleus accumbens) was not attenuated. The results are consistent with those found in the orbitofrontal cortex of the squirrel monkey (E.T. Rolls and M.J. Burton, unpublished, 1975) and suggest that function of the caudal orbitofrontal cortex is related in some way to self-stimulation and feeding. The failure to observe a facilitation following food deprivation of self-stimulation in the orbitofrontal cortex, similar to that observed in the sulcal prefrontal cortex of the rat [5], may be due to the mild levels of food deprivation (i.e. 12 h) employed in the present study. The recordings made from single neurons in the caudal orbitofrontal cortex suggest that its role in feeding and self-stimulation is different to that of the lateral hypothalamus and substantia innominata (see refs. above and refs. 12 and 13), but the findings described here suggest that further investigation of a relation between the function of the orbitofrontal cortex and self-stimulation and feeding is deserved. The observation that some neurons in the orbitofrontal cortex respond to the removal of food has led to an investigation in the rat sulcal prefrontal cortex, in which neurons with similar responses have now been recorded (E.T. Rolls and J.M. Koolhaas, unpublished, 1976). The activity of these neurons may be related to the resulting inhibition of feeding behavior.

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