Spread of current from monopolar stimulation of the lateral hypothalamus

ROY A. WISE
Department of Psychology, Sir George Williams University, Montreal, Canada

Wise, Roy A. Spread of current from monopolar stimulation of the lateral hypothalamus. Am. J. Physiol. 223(3): 545-548. 1972.—Electrically induced eating and drinking was studied in rats, using a movable electrode. Electrode movements of 1/8 mm produced minor fluctuations in the threshold when the electrodes were within the boundaries of the eating and drinking systems, but caused dramatic threshold changes when the electrode tip was near the boundary of a system. The characteristics of the thresholds suggest that, with intensities on the order of 25 μA, the effective spread of current from small monopolar electrodes may be as little as 1/8 mm. The changes in threshold with electrode movement also suggest that the lateral hypothalamic eating and drinking systems are homogeneous, have distinct boundaries, and are bordered on the ventral aspect by systems that do not mediate responses antagonistic to eating or drinking.

There has been considerable recent interest in the specificity of function within the lateral hypothalamic area (e.g., ref. 1). This interest has been generated partially by the findings that the same electrical stimulation in this area produces i) different responses in different animals, and ii) different responses in the same animal at different times. One of the problems of evaluating histological evidence from these studies in terms of localization of function is that it cannot be known exactly how far current effectively spreads from a stimulating electrode. Since tissue impedance and threshold for exciting neurons can vary in as yet undetermined ways, it is not yet possible to simply compute the boundaries of effective current spread from the laws of physics. Consequently, indirect evidence must be used to infer the extent of current spread. The method of approximation that has been used is to determine the threshold for a behavioral response when the stimulating electrode is set at varying distances from the target site. Using a variation of this approach, Olds (2) has suggested that hypothalamic stimulation at intensities on the order of 25 μA may spread effectively a full millimeter down from the tip of a bipolar electrode. Valenstein and Beer (7) have argued that monopolar stimulation should have even greater spread than bipolar stimulation.

More recent evidence suggests a much more restricted spread of current. The data on which the present discussion is based are from a study of electrically induced eating and drinking, in which a movable electrode1 was used to explore the vertical dimension of the lateral hypothalamus2 in awake, freely moving animals (8). The electrode was made of stainless steel wire of the same size (0.01 inch) as was used in the studies of Olds (2) and Valenstein and Beer (7); as in their studies, only the cross section of the wire was bared of insulation. The effects of stimulation were tested for 5 days with the electrode at each lateral hypothalamic site; each week the electrodes were moved approximately 1/8 mm further toward the base of the hypothalamus.

The details of the stimulation procedure are given elsewhere (8). The important data for the present discussion are those obtained during preliminary screening tests in which the animal was given daily threshold tests. Eating and drinking thresholds were taken for 5 days with the electrode at each lateral hypothalamic site, and it was lowered by 2 μA for the next train; conversely, if stimulation did not induce a response, stimulation intensity was raised by 2 μA. Thus the current intensity was varied between a

1 The movable electrode is described in detail elsewhere (8). Basically it was a piece of stainless steel wire soldered concentrically to a brass connector. The brass connector was externally threaded, and was mounted in a nylon receptacle that was internally threaded; the receptacle was mounted to the skull. The spacing of the threads (2-56) was such that the electrode could be lowered 1/8 mm by screwing the brass connector one-fourth of a turn deeper into the receptacle.

2 Histological reconstructions indicating the actual sites of stimulation are shown elsewhere (8). The general area explored was in the medial forebrain bundle-lateral hypothalamic area, just lateral to the fornix, at the level of the ventromedial nucleus. The boundaries of the effective area of stimulation do not correspond to the boundaries of any clearly defined anatomical structures defined by traditional histological techniques, however they do seem to correspond roughly to the boundaries of ascending noradrenergic and serotonergic fiber systems recently mapped by Ungerstedt and his associates (3) using histochemical fluorescence techniques. It is interesting to note that the effective area does not seem to correspond to the location of a nearby dopaminergic system that has been recently linked with normal food and water regulation (6).

THERE HAS BEEN CONSIDERABLE RECENT INTEREST IN THE SPECIFICITY OF FUNCTION WITHIN THE LATERAL HYPOTHALAMIC AREA (E.G., REF. 1). THIS INTEREST HAS BEEN GENERATED PARTIALLY BY THE FINDINGS THAT THE SAME ELECTRICAL STIMULATION IN THIS AREA PRODUCES I) DIFFERENT RESPONSES IN DIFFERENT ANIMALS, AND II) DIFFERENT RESPONSES IN THE SAME ANIMAL AT DIFFERENT TIMES. ONE OF THE PROBLEMS OF EVALUATING HISTOLOGICAL EVIDENCE FROM THESE STUDIES IN TERMS OF LOCALIZATION OF FUNCTION IS THAT IT CANNOT BE KNOWN EXACTLY HOW FAR CURRENT EFFECTIVELY SPREADS FROM A STIMULATING ELECTRODE.
low level which never induced the response, and a higher level which always induced the response. The average of a series of such stimulations was taken as the threshold estimate. The criteria for stimulation-induced eating or drinking were three: i) that the animal actually appear to take food or water into the mouth and swallow it, ii) that the animal initiate this response during the stimulation period, and iii) that the animal terminate the response on termination of the stimulation train. The animals were sated during the tests; if an animal was observed to eat or drink during a period of no stimulation, it was returned for at least 30 min to a cage where it had free access to food and water. Animals rarely ate during the nonstimulation periods.

The mean eating and drinking thresholds at successive placements (0.113 mm apart) are shown in Fig. 1. These data indicate two important features of the systems mediating the eating and drinking which can be induced by lateral hypothalamic stimulation: i) the systems are large relative to the size of the field of stimulation, and ii) the systems are homogeneously sensitive to stimulation within their dorsal and ventral boundaries.

That the systems are large relative to the size of the effective field of stimulation is indicated by the fact that, while the threshold gradients change abruptly as the electrode is moved near the systems' boundaries, the gradients are quite stable when electrode movement is within the boundaries. If the stimulating field were large relative to the size of the target system, the thresholds would be constantly changing, since electrode movements would always be taking the electrode either closer to or farther from target. This is illustrated in cases I and II in Fig. 2. In case I, thresholds decline with electrode movement at the dorsal boundary of the system, since each electrode movement brings the electrode tip closer to the target system. As soon as the tip is within the target system, minimal stimulation is required to induce a response, and so long as the stimulating field remains entirely within the boundaries of the system there will be no further change in the current needed to produce a response. As the electrode tip approaches the ventral boundary of the system, a portion of the stimulating field will no longer be effective, since it will excite adjacent tissue, and higher stimulating intensities will be needed to reach the same number of elements in the target system. Thus again at the ventral boundary of the systems, threshold gradients will change dramatically.

Case II illustrates the condition where the stimulating field is large and the target system small. In this case the threshold gradients are always changing, since much of the stimulating current is spilling into adjacent systems. Any electrode movement that brings the electrode closer to the center of the target system will reduce the spillover, and thus reduce the amount of current needed for a response. That is, the less distant the system is from the electrode tip, the less spread of current will be necessary to activate a significant portion of the system. Thus the flat threshold gradients observed between the dorsal and ventral boundaries of the eating and drinking systems in the present study rule out the possibility that the spread of current might be large relative to the size of the systems stimulated.

In the present study the flat threshold gradients within the boundaries of the systems (especially animals 12 and 14) also indicate that the systems are homogeneous in sensitivity to stimulation. If they were not, electrode movements that brought the electrode to more sensitive areas could cause threshold reductions, even though the stimulating field might be completely contained within the system (see case III, Fig. 2).

The abrupt changes in threshold as a function of electrode movements of ½ mm suggest that the spread of current is quite small. However, it is difficult to estimate the exact spread of current from these data because the slope of the threshold gradient is not only influenced by the nature of the current spread from points distant from the target system, but also by the nature of the influence of current on the adjacent systems. Cases IV and V (Fig. 2) illustrate that the slope of the threshold gradients can be greatly influenced by an antagonistic system bordering the target system and by the nature of the boundary between the target and antagonistic systems. When there is a bordering antagonistic system, thresholds are influenced by the fact that borderline stimulation activates not only the target system, but also activates tissue which antagonizes the response in question. If the excitation is not stronger than the inhibition, then an electrode placement will be ineffective even when it is still within the anatomical boundaries of the target system. In this case the electrode will appear to be out of range of the target system when it really is not.

Thus, before interpreting the rapid changes in eating and drinking thresholds which were found with electrode movement at the boundaries of the eating and drinking systems in the present study, it is necessary to determine
whether or not the systems are bounded by antagonistic circuitry. Responses such as crouching, escaping, and circling are frequently seen when stimulation is slightly off the lateral hypothalamic target, and these responses are clearly incompatible with eating and drinking. Current spread into the substrate of such responses would thus decrease the likelihood of eating. However, these responses seem to be obtained from placements medial and lateral to the target sites, and no such responses were observed at any of the sites immediately dorsal or ventral to positive sites for eating or drinking in the present study. Two further points suggest that the steep threshold gradients at the borders of the systems are not due to the existence of bordering antagonistic circuits. First, steep gradients were seen not only at the most ventral 1/2 mm of the lateral hypothalamus, but also in one case (animal 6) where the electrode path was medial, and the electrode penetrated the fornix. Thus if bordering antagonistic systems account for the steep threshold gradients, there must be remarkably similar antagonistic systems both in the ventral 1/2 mm of the lateral hypothalamus, and also in the fornix. Second, consider the data from animal 14. In this animal eating could not be induced from sites 8 and 9, while drinking was induced at low threshold from these sites. Thus, if the slope of the eating threshold gradient is sharp because of bordering antagonistic systems, then there must be additional antagonistic systems for drinking, and these must be located about 1/4 mm more ventral than the eating-antagonistic system. That is, at site 8 there would have to be the dorsal boundary of a system that is antagonistic to eating (but does not antagonize drinking), while at site 10 there would have to be yet another antagonistic system, this time one that antagonizes drinking. Thus if the slope of the threshold gradients is steep because of the interaction of borderline stimulation with antagonistic adjacent systems, there must be three such systems, one for eating but not drinking and a separate one for drinking in the ventral 1/2 mm of the lateral hypothalamus, and another that antagonizes both eating and drinking in the fornix. While this is possible, the possibility seems remote, and the assumption will be made that at least some of the ventral threshold gradients were simply due to movement of the electrode away from the target systems and into tissue that did not mediate responses that interacted with eating or drinking.

If the threshold changes can be assumed to be simply due to movement of the electrode out of range of the eating and drinking systems without complication from antagonistic systems, then the present data suggest a much smaller spread of current than has been previously suspected. The data from animals 6 and 14 would suggest that electrode placements medial and lateral to the target, which were 20- or 30-μA field was completely contained within the boundaries of the system, to a site where a 100-μA current was not sufficient to significantly activate the target system. The data from animals 6 and 14 suggest a more modest but still limited spread of current; here the spread of current at 100-μA intensities would appear to be on the order of 1/4-1/2 mm. Thus, the present study suggests that the spread of current in hypothalamic stimulation studies, where a small monopolar electrode tip is left uninsulated, can be as small as 1/8 mm or less for
stimulation intensities around 25 μA, and on the order of \( \frac{1}{4} \) or \( \frac{1}{2} \) mm or less for intensities as high as 100 μA. These estimates seem surprisingly low in terms of the estimate by Olds (2) of spread from a bipolar electrode; however, it is not the case that monopolar electrodes necessarily activate more tissue than bipolar electrodes (3, 4). At the threshold intensities used in the present experiment, it is likely that the current spread from monopolar electrodes is less than would be obtained from bipolar electrodes of the same wire diameter.

This study was supported by the National Research Council of Canada (APA 0362).

Received for publication 16 November 1971.

REFERENCES