The Lateral Hypothalamic Area

An Ultrastructural Analysis*

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Summary. An ultrastructural analysis of the rat lateral hypothalamic area (LHA) was undertaken in order to provide an initial step in the characterization of this complex area which appears to participate in a number of important neural functions. The organization of the normal tuberal LHA was compared to the area following acute and chronic denervating lesions. In the normal animal, the principal features of the LHA are the presence of lateral hypothalamic neurons, a major sagittal pathway (the medial forebrain bundle, MFB) and the interposed neuropil richly populated by a variety of synaptic terminal types. Alterations in the synaptic organization of the LHA following rostral and caudal MFB lesions were most pronounced in animals with acute and chronic caudal lesions. A 10% reduction of synaptic terminals containing 800–1000 Å diameter dense core vesicles and a 10% increase in terminals containing lucent core vesicles was observed in animals with caudal lesions while no significant redistribution of synaptic terminal types occurred with rostral lesions. The preliminary degeneration experiments indicate that identification of the numerous and diverse afferents to the LHA neuropil may be aided by this method but that a detailed and systematic ultrastructural analysis will be required to identify sources of input with certainty.

Key words: Lateral hypothalamic area — Synaptic organization — Rat — Ultrastructure.

Introduction

The lateral hypothalamic area (LHA) contains the axons of the medial forebrain bundle (MFB) and a prominent nucleus, the lateral hypothalamic nucleus (LHN).
(cf. Gurdjian, 1927; Bleier, 1963; Christ, 1969). The neurons of this nucleus give rise to ascending and descending projections into the adjacent medial hypothalamic zone (Guillery, 1957; Szentágothai et al., 1968; Millhouse, 1969; Raisman, 1971), and they receive input from the brainstem reticular formation, medial hypothalamus, other lateral hypothalamic neurons and basal forebrain (Guillery, 1957; Szentágothai et al., 1968; Millhouse, 1969; Nauta and Haymaker, 1969; Raisman, 1971). Since the medial hypothalamic nuclei receive relatively sparse projections from extra-hypothalamic sources (Nauta and Haymaker, 1969; Raisman, 1971), it is evident that the lateral hypothalamic nucleus is anatomically situated to represent a major integrating center between the brainstem reticular formation, basal forebrain and medial hypothalamus.

This is confirmed by a number of ablation and stimulation studies which have demonstrated that the LHA plays an important role in many functions (cf. Olds, 1962; Epstein, 1971; Rolls, 1975; Stricker and Zigmond, 1976 for reviews) but these have generally been attributed to the components of the medial forebrain bundle or related pathways traversing the LHA and adjacent areas. There has been little attention directed to the LHN even though its neurons appear to participate importantly in functions such as reward (Olds, 1973, 1974; Rolls, 1975). Because of its evident functional significance, the present ultrastructural study was undertaken in order to provide further information on the organization of the lateral hypothalamic area.

### Material and Methods

The animals used in this study were adult female albino rats of the Sprague-Dawley strain, 150–200 gm. They were anesthetized with pentobarbital (40 mg/kg) and perfused with glutaraldehyde-parafomaldehyde solutions described previously (Sipe et al., 1973). The LHA from the tuberal hypothalamus, between the optic chiasm and mamillary nuclei at approximately the level of the ventromedial nucleus, was dissected in a block approximately 1.5 × 1 mm, from 10 normal adult rats. The tissue blocks were post-fixed in cacodylate-buffered osmium tetroxide and aqueous uranyl acetate before dehydration and embedding in Epon. Thick sections were stained with methylene blue and used for further identification of areas to be examined by electron microscopy. Thin sections were mounted on uncoated grids, stained with both warm uranyl acetate in 50% methanol and lead citrate and examined in the coronal, sagittal and horizontal planes. A large number of photographs of randomly selected areas through the LHA was made at medium and high magnification for categorization and counting of synaptic terminal types and other structures. In addition, cresyl violet-stained celloidin sections in the coronal and horizontal planes were studied by light microscopy.

Two groups of animal were prepared with lesions. Each consisted of 6 animals with unilateral lesions either rostral to or caudal to the tuberal portion of the hypothalamus. The lesions were made as follows. With the animals under deep anesthesia, the head was placed in a small animal stereotaxic apparatus (Kopf Instruments, Tujunga, Ca) with the incisor bar 2 mm above the tooth bar. A burr hole was placed in the skull and a guillotine-type knife, 1.5 mm in diameter, was passed through the brain in the coronal plane until it reached the skull base. Both the rostral and caudal lesions were made with the center of the knife, 1.7 mm lateral to the midline. The rostral lesion was made at the level of the bregma and the caudal lesion 4.5 mm caudal to the bregma. Two animals at each time point from each group were sacrificed at 2 days, 4 days and at 4 and 8 months after the lesion was made. The method of sacrifice and preparation of tissue was as described above. The acute postoperative material, 2 and 4 day survival, was examined for evidence of axon terminal degeneration. The chronic brains were sectioned as described above and the terminals were categorized and counted from photographs of each lesion type.