Central Trigeminal Structures and the Lateral Hypothalamic Syndrome in the Rat

Abstract. *Extrahypothalamic lesions of central trigeminal structures produce a syndrome of aphagia, adipsia, finickiness, and food spillage. The similarity of these effects to the lateral hypothalamic syndrome and the location of trigeminal structures within the diencephalon suggest that some components of the lateral hypothalamic syndrome are due to incidental damage to trigeminal fibers of passage.*

There is now considerable evidence that the deficits in eating and drinking seen after lesions in the "lateral hypothalamic area" are due in part to lesion effects upon fibers of passage rather than to the disruption of synaptic networks within the hypothalamus itself (*1*). Furthermore, although both earlier and more recent investigators have reported sensorimotor impairments after lateral hypothalamic damage in the rat (*2*), the lateral hypothalamic syndrome has been attributed to lesion effects upon motivational processes rather than to the disruption of sensory or motor mechanisms (*3*). The present report demonstrates the critical involvement of central trigeminal structures and pathways, adjacent to but outside the hypothalamus proper, in the neural control of eating and drinking. Our findings suggest that many of the deficits previously subsumed under the rubric of the "lateral hypothalamic" syndrome are actually the result of incidental damage to the trigeminal lemniscus.

Previous studies from our laboratories have shown that central trigeminal structures play a critical role in the neural control of hunger in the pigeon. Massive hypothalamic lesions had no effect on eating or drinking if central trigeminal structures were spared. However, lesions of central trigeminal structures abolished or dramatically reduced food intake in the pigeon without impairing drinking (*4*). Even after the resumption of feeding these birds failed to compensate in their intake for the body weight lost during the postoperative period of aphagia and anorexia. They showed a long-term reduction of body weight below preoperative free-feeding levels similar to that reported after lateral hypothalamic lesions in the rat (*5*).

The fact that such striking deficits in food intake and weight regulation are produced by damage to central sensory structures in the pigeon and can even be seen after peripheral deafferentation (*6*) led us to examine the role of central trigeminal structures in the neural control of feeding in the rat.

Figure 1A illustrates the longitudinal trajectory of the trigeminal lemniscus (LTr) at several levels of the rat brain (*7*). At the diencephalic level LTr lies lateral to the lateral hypothalamus proper, and all lesions were extrahypothalamic in order to avoid damage to the lateral hypothalamic region.

Preoperative data on intake, weight, and food spillage were obtained from 18 rats, both males and females (Holtzman strain, 300 to 600 g), divided into three equal groups: control, LTr, and VBm (see legend to Fig. 1). Food was removed 12 hours prior to surgery. Lesions were placed stereotaxically (*8*) with a d-c lesion-maker and were aimed at the loci indicated in levels 2, 3, and 4 of Fig. 1A. The location of the electrode tip in LTr was verified electrophysiologically by recording potentials evoked by stimulation of perioral regions. Appropriate surgical and lesion control cases were prepared. Animals who were aphagic or adipsic or both for four or more days were given access to a liquid diet (chocolate Nutrament) presented in both a dish and a drinking tube. Dry food (lab pellets) and water were continuously available. Histological analysis was carried out on sections cut at 25 μm and stained for both cells and fibers.

Lesions placed at levels 2, 3, or 4 had similar effects upon eating and drinking. However, lesions at level 3 inevitably impinged on substantia nigra and adjacent structures. Cases with lesions at levels 2 (LTr) and 4 (VBm) thus provide the most clear-cut data on the effects of central trigeminal lesions

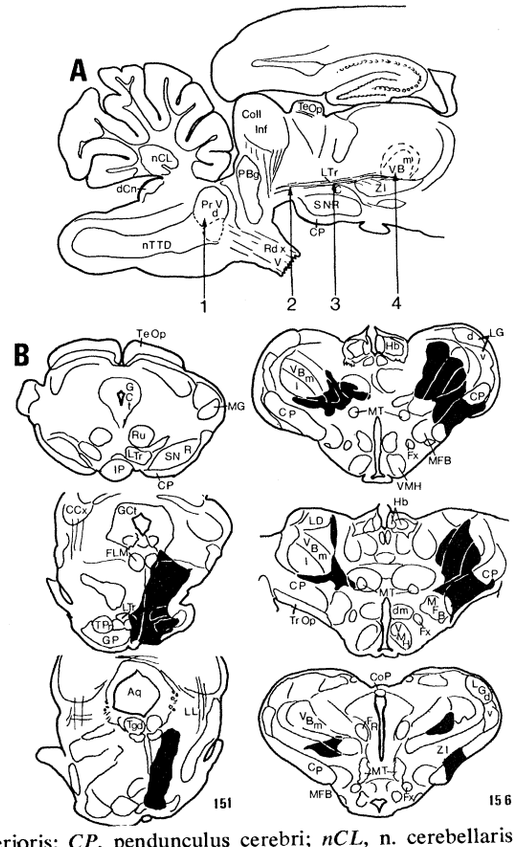

Fig. 1. (A) Sagittal section through the rat brain illustrating the trajectory of the trigeminal lemniscus at several levels, from its origin in PrV (level 1). After leaving PrV the lemniscus decussates at the level of the interpeduncular nucleus (level 2) and continues through the mesencephalon, lying immediately dorsal to the medial portion of the substantia nigra at the level of the ventral tegmentum (level 3). At the diencephalic level it gives off collaterals to the posterior thalamic region and to zona incerta before terminating in the medial portion of the ventrobasal complex of the thalamus (level 4). [Redrawn from Smith (*7*).] (B) Drawing of sections through the maximal extent of the lesions in cases 151 (LTr) and 156 (VBm). Because of its location at the level of the decussation of the trigeminal lemniscus, the lesion of case 151, although primarily unilateral, produced bilateral damage to LTr at this level. The lesion of case 156 produced bilateral damage to zona incerta and to the medial hilus of VBm, with complete sparing of the lateral hypothalamus, the mammillothalamic tract, the fornix, and the medial forebrain bundle. Abbreviations: *Aq*, aqueductus; *CCx*, n. centralis colliculus inferioris; *Coll. Inf.*, colliculus inferioris; *CP*, pendunculus cerebri; *nCL*, n. cerebellaris lateralis; *dCn*, n. cochlearis dorsalis; *FLM*, fasciculus medialis longitudinalis; *FX*, fornix; *GP*, peontine grey; *Hb*, habenula; *LG*, lateral geniculate nucleus; *LL*, lemniscus lateralis; *LTr*, lemniscus trigeminalis; *MFB*, medial forebrain bundle; *MT*, tractus mammillothalamicus; *PBg*, n. parabigeminalis; *PrVd*, n. sensibilis principalis trigemini, pars dorsalis; *RdxV*, radix nervi trigemini; *SN-R;C*, substantia nigra, pars reticulata; pars compacta; *TeOp*, tectum opticum; *Tgd*, n. tegmentalis Guddeni, pars dorsalis; *Tpr*, tractus pyramidalis; *nTTD*, nucleus et tractus trigeminalis descendens; *VBm*, n. ventrobasalis, pars medialis, thalami; *VMH*, n. ventromedialis hypothalami; *ZI*, zona incerta.

upon ingestive behavior. Figure 1B presents sections through the maximum extent of the lesions in two such cases. Effects upon ingestive behavior and body weight in these cases are illustrated in Fig. 2. With less extensive lesions the effects were more transient than those shown in Fig. 2, but in all cases lesions of LTr and VBm are followed by a disruption of food and water intake varying in severity with the bilateral extent of the lesion. Even after the resumption of eating and drinking, recovery to preoperative free-feeding body weight was retarded in the experimental groups. Median values and ranges for the three groups are as follows: control: 0 days of aphagia, 0 days of adipsia, 1.5 percent weight loss (range, 0 to 7 percent); LTr: 3 days of aphagia (2 to 14 days), 2 days of adipsia (2 to 9 days), 16.5 percent weight loss (5 to 26 percent); VBm: 2 days of aphagia (2 to 11 days), 2 days of adipsia (2 to 11 days), 13 percent weight loss (5 to 32 percent). For all measures, differences between control and experimental groups are significant beyond the 1 percent level (t-test).

Postoperatively, the prolonged periods of debilitation reported after large lateral hypothalamic lesions were not evident after LTr or VBm lesions. Animals were active within 24 hours and rarely showed impairments of posture or locomotion. Adipsic and aphagic rats showed no signs of aversion to food or water and would lick or swallow water or Nutrament applied to the mouth with a dropper. A significant effect upon food spillage ($P < .001$) was evident, with values increasing from a preoperative mean of 17.3 percent (standard deviation, 14.1 percentage points) to a postoperative mean of 51.3 percent (S.D., 23.2 percentage points) of the daily food ration.

We have shown that damage to central trigeminal structures disrupts eating and drinking in the rat. Although our lesions do not impinge either on the hypothalamus itself or on the so-called "lateral hypothalamic area," they produce deficits in food and water intake which are similar in many respects to those previously grouped under the rubric of the lateral hypothalamic syndrome (*9*).

The similarity of the two syndromes and the location of the LTr within the diencephalon of the rat (*7*) suggest that many of the deficits formerly attributed to lateral hypothalamic lesions are not due to hypothalamic damage

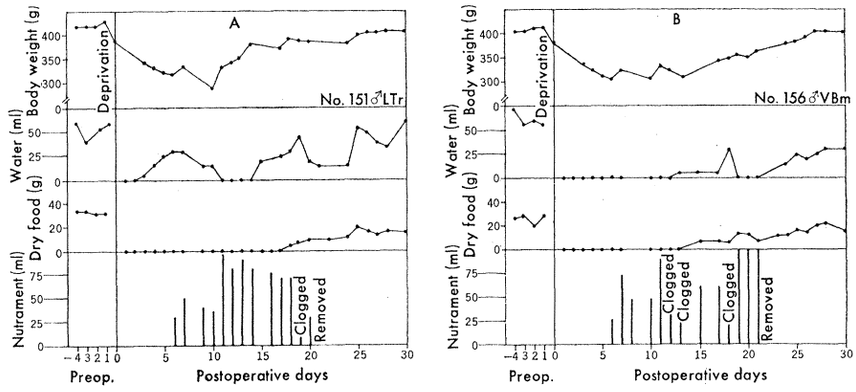

Fig. 2. Effects of lesions of central trigeminal structures upon food and water intake and body weight in the rat. (A) Lesion of LTr at level 2. Case 151 did not respond to the food pellets until the fourth day postoperatively. From day 5 to day 14 there was considerable gnawing at the food but no measurable food intake until day 18. For days 18 through 30 daily spillage ranged from 55 to 65 percent of the ration given. (B) Lesion of VBm at level 4. Case 156 made no responses to either food or water until the 13th postoperative day. Spillage over the next 2 weeks ranged between 55 and 75 percent of the food ration given. In both cases the rats were "finicky" in the sense that they ingested large quantities of chocolate Nutrament during periods when intake of dry food or water was absent or reduced below preoperative levels.

but—as in the pigeon—are the result of incidental damage to trigeminal fibers of passage coursing through adjacent portions of the diencephalon. A review of the histological material accompanying published studies of the lateral hypothalamic syndrome suggests that the "characteristic" lateral hypothalamic lesion always impinges upon LTr fibers or on their areas of termination within the diencephalon.

A review of studies which have implicated extrahypothalamic mechanisms in the neural control of eating and drinking also suggests the critical involvement of central trigeminal structures. Aphagia and adipsia have been reported after lesions of VBm (*10*) and after electrolytic or chemical lesions of ventral mesencephalic regions (*11*). The reconstructions accompanying the latter reports indicate that the effective lesions impinge on LTr at the level of the red nucleus, the substantia nigra, and the area ventralis of Tsai (*12*). Electrical stimulation of a variety of sites in or near the trajectory of LTr at the level of the diencephalon and mesencephalon have been reported to elicit eating and drinking and to support self-stimulation (*13*).

Further studies will be required to specify more precisely the differences between the trigeminal and the lateral hypothalamic syndromes and to identify the anatomical substrates related to these differences. However, to the extent that the deficits seen after lateral hypothalamic lesions are indeed related to trigeminal damage, several hitherto puzzling aspects of the lateral hypothalamic syndrome (spillage, somatosensory "neglect," and, perhaps, finickiness) would become more readily explicable. The trigeminal system is highly developed in the rat (*14*) and the pigeon (*4*) and may be expected to play a major role in the oral monitoring of intake and in the neurosensory control of eating and drinking. Moreover, in both species inputs from the oral region appear to have motivational as well as sensory properties (*15*).

The analysis of ingestive behavior in vertebrates has focused largely upon one species, the rat, and, with some exceptions, upon one brain structure—the hypothalamus. Moreover, while the contribution of peripheral sensory factors is well documented in the rat (*16*), there is relatively little direct evidence on the relation between central sensory systems and ingestive behavior in any vertebrate. Our findings on the pigeon and the rat suggest that a comparative analysis of such relationships across a broader spectrum of vertebrate classes would yield significant dividends for the study of neurobehavioral mechanisms underlying hunger and thirst.

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9. Similar deficits have been produced by peripheral trigeminal deafferentation in the rat. Lesions of the Gasserian ganglion and the Vth nerve, not involving the trigeminal motor system, were produced under electrophysiological control by using an intracranial approach to the nerve (H. P. Zeigler, A. Marwine, H. J. Karten, paper presented at Eastern Psychological Association, Philadelphia, 18 April 1974).
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12. The deficits seen after injections of 6-hydroxydopamine were originally attributed to a selective destruction of neurons in medial substantia nigra. However, more recent studies suggest that such injections produce severe, nonspecific neurotoxic effects distributed over a considerable area. It thus seems likely that the effects upon ingestive behaviors seen after chemical lesions of these regions are due to the almost inevitable damage to the overlying LTr [C. Sotelo *et al.*, *Brain Res.* **58**, 269 (1973); L. L. Butcher and C. K. Hodge, paper presented at Society for Neuroscience, San Diego, 1973].
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Death of American Ground Sloths

Abstract. *Organic remains, especially dung, of extinct ground sloths provide ideal material for radiocarbon dating. Rampart Cave, Arizona, revealed periodic occupation at intervals by the Shasta ground sloth from before 40,000 years ago until 11,000 years ago. Dates from other caves in the arid Southwest indicate that the Shasta ground sloth disappeared at or very soon after the time of Clovis big game hunters. Ground sloth remains in South America are slightly younger. The timing of ground sloth extinction is in accord with the model of explosive overkill.*

Among the most remarkable of the organic deposits known to survive, rivaling the frozen carcasses of mammoths and woolly rhinoceroses in the Arctic, are the dung balls, hair, and even hide of extinct ground sloths. Under conditions of low humidity and uniform temperature in certain caves the dung escapes fungal, bacterial, or insect attack and endures for at least 10,000 years. The deposits look and smell fresh, leading paleontologists of the last century into the belief that the ground sloths were not extinct. Radiocarbon dating has supported more conservative views and made possible a more critical assessment of ground sloth chronology.

In the Northern Hemisphere, ground sloth dung of *Nothrotheriops* (formerly *Nothrotherium*) *shastense* Sinclair is known from half a dozen caves in the arid Southwest. The least disturbed stratified deposit is found within the Grand Canyon at Rampart Cave (elevation, 525 m; 36°06′N, 113°56′W) (*1*). In the Southern Hemisphere the best known sloth dung deposit is Gruta del Milodon or Eberhardt Cave, 30 km north-northwest of Puerto Natales, Chile. More recently ground sloth dung has been found in Cuevo del Indio near San Rafael, Argentina (*2*). These are the only two South American deposits of ground sloth dung known to us.

Our purpose was to determine the time of ground sloth extinction, refine the provisional radiocarbon chronology of organic deposits in Rampart and other caves established a decade ago (*3*), and compare the results in the Northern Hemisphere with those from the Southern Hemisphere. Thirteen new radiocarbon dates are now available from Rampart Cave alone, with a total of 30 on organic remains from various ground sloth cave deposits.

We sought samples younger than the 10,000-year age reported by Martin *et al.* (*3*). In Rampart Cave, Long and Martin collected four apparently undisturbed dung balls from the surface of the deposit. Three of the softball-sized (7 to 10 cm in diameter) specimens were found about 3 m east of a trampled dung surface dated on both humic and nonhumic fractions at about 10,000 years in age (L-473A).

Rather than being younger, the new dates (A-1041, 1066, 1067, and 1068) are significantly older. Close examination of the profile point where Shutler collected L-473A (*3*) revealed that postglacial or modern wood rat (*Neotoma*) feces and food material was mixed into trampled and disaggregated dung fragments of *Nothrotheriops*. The possibility of wood rat contamination at this point is greater than in the case of the unaltered dung balls that are the source of our new dates.

In addition, we attempted to replicate I-442, 10,400 ± 275 (unpublished date by Teledyne Isotopes) by dating the remaining half of a dung ball so labeled in Remington Kellogg's (Smithsonian Institution) Rampart collection. Our result was significantly older, suggesting that the two dates were not from the same specimen.

We recollected samples from a profile in Kellogg's trench originally collected by Shutler. Except for the surface dates, our samples replicate or extend the original Lamont dates (Table 1). At the position of the profile, a buried wood rat (*Neotoma*) midden between 63 and 98 cm divides the sloth dung deposit. It is formed of stocks, seeds, and fecal pellets of rodents and artiodactyls with occasional animal bones (*Marmota, Oreamnos*). Sloth dung above 61 cm was deposited from about 12,500 to 11,000 years ago. We estimate that the main part of the deposit covers 180 m^2 with the upper sloth dung unit averaging no more than 0.5 m in thickness. The entire late-glacial dung layer represents an average annual rate of deposition of 0.1 m^{-3}, perhaps less than a week's elimination of one adult sloth (*4*). There is no suggestion of a decline in deposition rate toward the top of the deposit as might be expected if the population were coming under stress gradually.

These three units, the upper sloth (A), the pack rat (B), and the lower