SEVERAL RECENT STUDIES have demonstrated that bilateral electrolytic lesions of the amygdala in female rats can result in marked hyperphagia and excessive weight gains. Daily food intake nearly doubles, and weight gains of 20–30 g during the first 3 days after lesions are not unusual (e.g., 45, 50–53, 84). Weight gains of ≥100 g in 20–25 days have been observed (50, 51). The lesions result in a marked preference for carbohydrates (53). Although food intake eventually returns to normal, the excessive weight gain is maintained indefinitely, with a marked increase in adipose tissue (50).

These results are similar to those reported many years ago for cats, dogs, and primates (including humans) given amygdaloid lesions or temporal lobectomies (e.g., 9, 32, 37, 70, 103). In the rat, the effective lesion site for hyperphagia and obesity has recently been identified as the posterodorsal part of the medial amygdaloid nucleus (MePD) and the intra-amygdaloid bed nucleus of the stria terminalis (BSTIA), together referred to as the posterodorsal amygdaloid area, or PDA (84). Lesions impinging on the basolateral, central, or corticomedial portions of the amygdala do not result in substantial overeating or obesity unless the lesions infringe on the posterodorsal region of the medial amygdala (84).

The medial nuclei of the amygdala have elaborate reciprocal connections with the medial hypothalamus (e.g., 10–12, 36, 74, 80) and thus are in a position to directly influence neuroendocrine status, as well as behavioral functions mediated by that area. Behavioral and endocrine changes suggest a close relationship between the phenomenon of amygdaloid obesity and obesity occurring after lesions of the ventromedial hypothalamic area. For example, after lesions in the PDA, hyperinsulinemia is observed during both restricted and ad libitum feeding regimens (46), as is also the case after lesions of the ventromedial hypothalamic area (for a review, see Ref. 48). This is in contrast to the overeating that occurs after lesions of the paraventricular hypothalamic nucleus, where hyperinsulinemia occurs only after ad libitum access to food (54). Lesions in the PDA also result in somewhat greater weight gains for females than for males (52), an effect also observed after lesions of the ventromedial hypothalamic area (e.g., 20, 49, 96).

Although it is well appreciated that the PDA is a complex area populated by a variety of distinct nuclei, it is also traversed by axons of passage interconnecting the amygdala with the basal forebrain and hypothalamus via the stria terminalis or ventral amygdalofugal pathway (1, 10, 12, 23, 24, 36, 80, 81). In the present study, the sensitive amino-cupric silver method (25) for impregnating degenerating axons and their terminals was applied to the brains of animals with obesity-inducing lesions. A dense pattern of degenerating terminals was found in the lateral septum, amygdala, ventral striatum, and ventromedial hypothalamus. Degeneration in the paraventricular nucleus of the hypothalamus was scarce or absent. Small retrograde tracer injections made in either the intra-amygdaloid bed nucleus of the stria terminalis or in the posterodorsal medial amygdaloid nucleus labeled cells in the amygdala, lateral septum, and hypothalamus, reciprocating the anterograde projections from the amygdala to these areas. The data suggest that subdivisions of the posterodorsal amygdala participate in the regulation of feeding in a manner that is similar to the better-known role of this part of the brain in mediating reproductive behavior. Although topographical differences may exist within the amygdaloid and hypothalamic subdivisions regulating these two sexually dimorphic behaviors, the relays engaged by feeding-related connections and those related to reproduction are remarkably parallel.
and bilateral lesions of the PDA. We additionally include here a description of retrograde labeling from tracer injections that were centered in the two most relevant subdivisions of this area as determined by the analysis of lesion damage, namely the MePD and the BSTIA. All together, a comprehensive picture of the afferents and efferents involved by obesity-inducing amygdala lesions is presented.

**METHODS**

**Animals and Surgery**

Nineteen adult female Long-Evans hooded rats were used (Harlan Sprague-Dawley, Indianapolis, IN). The animals weighed 275–335 g at the beginning of the study. Unilateral (n = 4) or bilateral (n = 10) electrolytic lesions were produced under pentobarbital sodium anesthesia (50 mg/kg) by passing a 1.5-mA anodal current for 20 s between the 0.25-mm uninsulated tip of an insulated stainless steel electrode (no. 0 insect pin) and a rectal cathode. Electrodes were positioned with a Kopf small animal stereotaxic instrument. With the upper incisor bar positioned horizontally at the level of the interaural line, the electrodes were positioned 2.1 mm posterior to bregma, 4.5 mm lateral to the mid sagittal suture, and 8.4 mm below the surface of the skull. In two of the unilateral cases the coordinates were deliberately varied; in one case (case 48), the lesion was aimed 0.5 mm more ventral, while in the second case (case 49), the lesion was targeted 0.5 mm more anterior. For sham operations (n = 2), the skull was drilled and the electrode was inserted, but no current was passed. Three additional animals were used for retrograde labeling (see below).

**Body Weight**

All animals were fed a standard lab chow ad libitum before and after surgery (laboratory rodent diet no. 5001, PMI Feeds, St. Louis, MO) and were weighed daily. Body weight was measured at the same time of the light cycle each day (2:00 PM), and postoperative body weight was compared with the body weight on the day of surgery. Because the purpose of the study was to trace anterograde degeneration in brains of rats with obesity-inducing lesions (and the animals had to be killed 1–3 days after surgery for optimal histological results; Ref. 111), a minimum criterion for weight gain of 10 g/day was used to select animals with bilateral lesions for inclusion in the group to be processed for silver staining. Ten grams per day at the high end of weight gain in the first few days after PDA lesions (50, 51). Animals with unilateral or control lesions were not screened according to this weight gain criterion.

**Cupric Silver Staining: Perfusion and Histology**

Ten animals with bilateral lesions underwent euthanasia 24, 48, or 72 h after surgery. Four animals with unilateral lesions and two with unilateral sham lesions underwent euthanasia 48 h after surgery. The animals were given transternal perfusion while under general pentobarbital sodium anesthesia. The rinse and fixation used were those recommended for the amino-cupric silver method (25). Briefly, the rats were rapidly perfused with 100 ml of a rinse consisting of 0.8% sucrose, 0.8% NaCl, and 0.4% glucose, followed by 300 ml of fixative consisting of 4% paraformaldehyde in 0.1 M cacodylate buffer (pH 7.2–7.4). After perfusion, the animals were decapitated, and the heads were immersed in the fixative at 4°C. Subsequently, the heads/brains were shipped to a commercial laboratory (Neuroscience Associates, Knoxville, TN) for histological processing. On receipt, the brains were removed from the calvaria, briefly rinsed, and then cryoprotected with a solution containing 10% glycerol, 10% sucrose, and 2% dimethyl sulfoxide. After 24–48 h of cryoprotection, multiple brains were subsequently embedded in single blocks of gelatin. After additional fixation and cryoprotection, the gelatin blocks were snap-frozen in isopentane cooled to −70°C and sectioned (40 μm) on a sliding microtome. Sections were collected in six series and stored in the same fixative used for perfusion. One series out of six was mounted on glass slides, dried, stained with thionin, cleared in Xylenes, and placed under coverslips with Permount. A second series was used to test the timing for the various silver impregnation steps, and a complete third series was then silver stained, mounted on glass slides, dried, cleared, and placed under coverslips.

Background artifactual staining in the amino-cupric silver method is generally well suppressed so that the best overview of the pattern of degeneration may be appreciated using low-magnification dark-field illumination. Despite this, it should be noted that some silver deposits found in normal tissue can be relatively intense; suppressed argyrophilia is usually recognizable and distinguished from actual degeneration on morphological grounds and, after unilateral lesions, by comparison with the structures on the unlesioned side of the brain.

**Lesion Assessment**

Estimates of the residual volumes of relevant amygdaloid and nearby nuclei on equally spaced Nissl sections were generated using the grid point counting method for the Cavalieri estimator (e.g., Ref. 38). The nuclear volumes of rats with sham lesions were also measured; because the electrode placement was also unilateral, this provided the means to estimate smaller, incidental damage owing to the passage of the electrode. Estimates of the normal volumes of the selected amygdaloid nuclei were based on measures made contralateral to the lesion.

Briefly, for volume measurement, the object to be measured was sampled by sections spaced at equal intervals throughout the entire axis perpendicular to the plane of the two-dimensional section. To estimate the volume, a two-dimensional grid of equally spaced points was superimposed on the area to be measured, and the number of points falling within the target area was counted. The spatial frequency of the dots was used to estimate the volume, once the intersection of the points with the entire sample of the two-dimensional sections had been tallied. For unbiased estimates, the first area measured was picked at random within the first sampling interval that included the area of interest. For measuring grid points that appeared to lie on a boundary line, the point was excluded if the north and east extension of perpendicular lines through the grid point lay outside the area measured. All measurements were made on the Nissl-stained series of sections produced for each of the experimental brains. Because for this material one in six sections was mounted and Nissl stained, this was chosen as the sampling interval for point counting.

For the control side of the brain, the nuclei of the amygdala were identified on Nissl-stained sections at low magnification using the divisions described by Alheid et al. (1). The boundaries of these nuclei were outlined with a personal computer-based drawing program (AutoCAD R13, Autodesk), coupled visually to the microscope via a digital color camera (Optronics) and a video frame grabber (Matrox, Marvel) using the overlay utility provided with the frame grabber. To facilitate
later measurements, the scale of the computer drawing was adjusted so that the units of the drawing coincided with the real dimensions of the sections being outlined.

Once the nuclei were outlined, a grid pattern of points was generated by the drawing program and superimposed on the outline. For each area being measured, the intersecting points were counted and entered into a computer spreadsheet for later analysis. A similar process was used for the measurement of the side of the brain with lesions. In this case, only the residual unlesioned tissue was included within the outline. Lesion size for individual nuclei was estimated by subtracting the residual area estimates for the lesioned nuclei from estimates for comparable intact nuclei on the contralateral side. Illustrations based on the computer-assisted drawings were directly produced from the program as encapsulated Postscript files.

Retrograde Tracing Experiments

Retrograde labeling was systematically examined in three adult female Long-Evans rats. One had a small injection of cholera toxin B subunit in the BSTIA and the other a FluoroGold deposit centered in the MePD. Together, the two injections accounted for the lesioned zones that best explained the observed weight gains. In the third animal the injection of FluoroGold involved the central amygdaloid nucleus and the BSTIA but completely avoided the MePD. The cholera toxin injection (low-salt cholera toxin B, List Biologicals) was made stereotaxically under general anesthesia through a glass pipette (internal tip diameter ~15 μm) filled with 1% cholera toxin B in 0.1 M sodium phosphate buffer, pH 6.0. The tracer was deposited in the brain by passing a positive (7 s on, 7 s off) current of 2 μA for 15 min. FluoroGold (Fluorochrome) was iontophoresed (1 μA for 5 min, 7 s on, 7 s off positive current) as a 1% solution in 0.15 M NaCl. The perfusion and staining techniques have previously been described in detail (93).

The retrograde-labeled cells were plotted using the same computer-aided method described earlier. A quantitative estimate of retrograde labeling was made. For each nucleus or area retrogradely labeled, a single unbiased counting frame (100 μm/side; see Ref. 98) was centered in the zone of maximal labeling, and the number of labeled cells was recorded and tabulated. The cytoarchitectonic parcellation and nomenclature, unless otherwise stated, were based on the rat brain atlas of Paxinos and Watson (79).

RESULTS

Body Weight

Weight gains are displayed in Table 1. Rats with bilateral lesions (prescreened for rapid weight gain) gained 11–16.2 g/day (see Table 1 for survival periods), whereas the weight gain of rats with unilateral lesions (not screened for minimal body weight gains) ranged from 2.5 to 12.8 g/day. Animals with sham lesions showed a slight loss in body weight during the short postoperative survival interval (~1.0 and ~3.5 g/day). The brains of five rats with bilateral lesions were excluded from analysis because the animals did not meet the minimal criterion for weight gain.

Lesion Damage

Areas sustaining direct damage in animals with bilateral lesions included the MePD, the BSTIA (a complex of cells intimately associated with the medial part of the vertical stria terminalis), the amygdalohippocampal transition area (called the posterior nucleus in some other schemes; Refs. 27, 80), and deep parts of the postero medial cortical amygdaloid nucleus. The lesion frequently involved caudal aspects of the posterior basomedial nucleus, and there was usually involvement of the caudal central amygdaloid nucleus and of the posterior basolateral nucleus, although the extent of damage varied. Destruction was also seen in the ventral subiculum and ventral hippocampus, but the extent of damage also varied considerably. The axons collecting to form the vertical limb of the stria terminalis were partially incorporated within the area of lesion. Other structures partially damaged in individual cases included the optic tract, the nucleus of the ansa lenticularis, ventral aspects of the caudal globus pallidus, the amygdalostratal transition area and adjacent portions of the ventral caudate putamen, and the ventromedial aspects of the lateral amygdaloid nucleus, as well as the large and paracapsular intercalated cell masses of the amygdala.

Figure 1 is a dark-field photomontage of cupric silver-stained sections through the maximal extent of each of the unilateral lesion sites. The brightly stained areas in the vicinity of the lesions represent degeneration caused by the lesion, whereas the lesion itself is frequently free of silver deposits. The general arrangement of the nuclei measured by the point counting method is depicted in Fig. 2 for an intact brain. The quantitative estimates of the unilateral lesion damage for individual temporal lobe structures are presented in Table 2. Analysis of the unilateral and bilateral lesions revealed that three areas were extensively damaged in all animals: the BSTIA, the MePD, and the ventral hippocampal formation. A previous study from this lab found that lesions confined to this same area of the ventral hippocampal formation had no effect on food intake or body weight (45). As was found in another earlier study (84), incidental damage to the ventral globus pallidus attenuated the weight gain that followed damage to the BSTIA and MePD.

<table>
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<th>7</th>
<th>12</th>
<th>14</th>
<th>15</th>
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<td>48</td>
<td>24</td>
<td>72</td>
<td>48</td>
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<td>48</td>
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<td>12.3</td>
<td>12.0</td>
<td>12.4</td>
<td>16.2</td>
<td>12.8</td>
<td>2.5</td>
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In 2 cases, the electrode tip was deliberately placed 0.5 mm more ventral (case 48) or 0.5 mm more anterior (case 49) to the optimal target site for weight gain as determined by Rollins and King (84). C, operated controls; B, bilaterally lesioned rats; U, unilaterally lesioned rats.

Table 1. Body weight changes after amygdaloid lesions
Anterograde Degeneration AfterAmygdala Lesions That Result in Rapid Weight Gain

Although the variable lesion placements in the (un-screened) unilaterally lesioned animals led to a lower mean weight gain, the unilateral lesions that were best matched to the most effective bilateral lesions led to comparable weight gains in the first 48 h. We will focus our description of the degeneration of the unilateral lesioned animal with the greatest weight gain (case

Table 2. Estimated unilateral lesion size for individual nuclei

<table>
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<td>MePD</td>
<td>MePV</td>
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</table>

Values are lesion size in mm³. In 2 cases, the electrode tip was deliberately placed 0.5 mm more ventral (case 48) or 0.5 mm more anterior (case 49) to the optimal target site for weight gain as determined by Rollins and King (84). HPC, hippocampal formation; CeC, central amygdaloid nucleus, capsular part; CeL, central amygdaloid nucleus, lateral part; CeM, central amygdaloid nucleus, medial part; MePD, medial amygdaloid nucleus, posterodorsal part; MePV, medial amygdaloid nucleus, posteroverentral part; BSTIA, intra-amygdaloid bed nucleus of the stria terminalis; AHi, amygdalo-hippocampal transition area; PMCo, posteromedial cortical amygdalo- loid nucleus; BMP, basomedial amygdaloid nucleus, posterior part; BLA, basolateral amygdaloid nucleus, anterior part; BLP, basolateral amygdaloid nucleus, posterior part; La, lateral amygdaloid nucleus; GP, globus pallidus.

Fig. 1. Dark-field photomontage of cupric silver-stained sections through the maximal extent of damage in each of the unilateral lesion sites. The brightly stained areas in the vicinity of the lesions represent degeneration caused by the lesion. In 2 cases, the electrode tip was deliberately placed 0.5 mm more ventral (case 48) or 0.5 mm more anterior (case 49) to the optimal target site for weight gain.

Fig. 2. Sample of outlines from a control brain through the centromedial amygdala depicting the normal appearance of various subnuclei in this area. Superimposed on the outlines is a pattern of grid points similar to those used to estimate the area of the various nuclei. Adjacent to the outlines are the corresponding Nissl sections on which the drawings were based. ACo, anterior cortical amygdaloid nucleus; BLA, basolateral amygdaloid nucleus, anterior part; BLP, basolateral amygdaloid nucleus, posterior part; BLV, basolateral amygdaloid nucleus, ventral part; BMA, basomedial amygdaloid nucleus, anterior part; BMP, basomedial amygdaloid nucleus, posterior part; BSTIA, intra-amygdaloid bed nucleus of the stria terminalis; CeC, central amygdaloid nucleus, capsular part; CeM, central amygdaloid nucleus, medial part; cst, commissural component of the stria terminalis; ic, intercalated cell mass of the amygdala; La, lateral amygdaloid nucleus; MePD, medial amygdaloid nucleus, posterodorsal part; MePV, medial amygdaloid nucleus, posteroverentral part; opt, optic tract; PlCo, posterolateral cortical amygdaloid nucleus; PMCo, posteromedial cortical amygdaloid nucleus; st, stria terminalis.
43). Major areas of degeneration are described from rostral to caudal direction (see Fig. 3).

**Olfactory system.** Bilateral degeneration was seen in the glomeruli of the main and accessory olfactory bulbs, a replication of the well-documented normal cycle of degeneration and replacement of the olfactory nerve (e.g., Ref. 60). The ipsilateral accessory olfactory bulb contained terminal degeneration only in the granular layer, with little or no involvement of the mitral layer. Light degeneration also appeared in the lateral olfactory tract and in the dorsomedial portions of the anterior olfactory nucleus, especially caudally.

**Medial frontal cortex.** A pronounced band of degeneration was evident in prelimbic and infralimbic cortex with degenerating terminals in all layers, but with a particularly dense accumulation in layers 3–5.

**Ventral striatum.** Dense terminal degeneration was evident in the shell area of the nucleus accumbens and in the medial part of the olfactory tubercle (Fig. 3A).

**Septum.** Dense degeneration was also present in the ventrolateral septum (Fig. 3, B and C), in continuity with the degenerating terminals found in the dorsal part of the accumbens shell and in the medial bed nucleus of the stria terminalis.

**Extended amygdala.** This term designates the macrostructure extending from the centromedial amygdala to the bed nucleus of the stria terminalis and is divided into a medial corridor related to the medial amygdaloid nucleus and a central corridor related to the central amygdaloid nucleus (e.g., 1, 24). The lesion damaged portions of both the medial and central extended amygdala, as well as axons and cells of the cortical and basal amygdaloid nuclei that project to the extended amygdala.

Damage to the medial extended amygdala was reflected by dense degeneration in the unlesioned portions of the medial amygdaloid nucleus (Fig. 3, F and G) and in all the various subnuclei of the medial bed nucleus of the stria terminalis (Fig. 3, B–D), as well as among the medial supracapsular (Fig. 3, E and F) and posteroventral sublenticular neuronal columns (Fig. 3, D and E). In the central extended amygdala, degeneration was observed in the central nucleus of the amygdala (Fig. 3, F and G), as well as in the subnuclei of the lateral bed nucleus of the stria terminalis (Fig. 3, B–D), anterodorsal part of the sublenticular corridor (Fig. 3, D and E), interstitial nucleus of the posterior limb of the anterior commissure (3, B–E), and lateral part of the supracapsular bed nucleus of the stria terminalis (Fig. 3E).

**Other amygdaloid degeneration.** A dense field of degeneration filled the nucleus of the lateral olfactory tract (Fig. 3E). Terminal degeneration was also observed in the anterior and posterior basomedial nuclei, posterior basolateral nucleus, and posterior parts of the lateral nucleus (Fig. 3, F–H).

**Stria terminalis.** Dense degeneration was observed in the dorsal component and in the medial part of the ventral component of the stria terminalis (23, 93). Degeneration in the stria terminalis could have been due to the combined effect of damage to the medial amygdala and damage to the axons traversing the area of the lesion, as well as to more posterior amygdala zones included within the lesion, namely the amygdalohippocampal transition area and the posteromedial cortical amygdaloid nucleus (27). No degeneration was observed in the commissural component of the stria terminalis (Fig. 3, E and F), despite its proximity to the lesioned area.

**Hypothalamus.** Very heavy degeneration was seen in the medial preoptic (Fig. 3C) and anterior hypothalamic and the retrochiasmatic areas (Fig. 3E), as well as in the ventromedial hypothalamic nucleus (VMH). Labeling in the VMH was concentrated in its central and ventrolateral parts as well as in the shell area that surrounds the VMH (Fig. 3, F and G), whereas the dorsomedial part was only sparsely labeled. However, an effect on the dorsomedial part of the VMH cannot be excluded because the dendrites of neurons located in this region reach the dorsomedial part of the shell area, which was densely innervated by the PDA. Dense degeneration was also seen in the medial tuberal nucleus located ventrolaterally to the VMH (Fig. 3G). This latter degeneration was continuous caudally with terminal labeling in the tuberomammillary nucleus and in the dorsal and ventral premammillary nuclei. The argyrophilia seen in the arcuate nucleus (Fig. 3G) is also present in normal brains and represents a false-positive labeling.

In contrast to the heavy degeneration observed in the VMH, the paraventricular hypothalamic nucleus was relatively free of degeneration; only a few interrupted fibers were stained. Dense degeneration was seen, however, in the subparaventricular zone immediately ventral to the paraventricular nucleus (Fig. 3E).

Only diffuse, scattered silver deposits were observed in the lateral hypothalamus. Some of these appeared as broken strings of fibers and some as a diffuse, light field of terminal degeneration (Fig. 3, F and G). No degeneration in the fornix was seen past the level of the anterior hypothalamus/medial preoptic area, nor was degeneration evident in the nuclei of the mammillary body.

**Thalamus.** A small column of degenerating axons followed the course of the stria medullaris/inferior thalamic peduncle to the thalamic area, leading to a light terminal field in the vicinity of the nucleus reuniens and in the dorsal midline thalamic nuclei, including the paraventricular thalamic nucleus. A few degenerating axons continued in the stria medullaris reaching the level of the lateral habenula where a small terminal field was also apparent. At the caudal end of the thalamus a light field of degenerating axons or terminals was also seen ventral and medial to the medial geniculate nucleus, in the posterior intralaminar and peripeduncular nuclei. Because few, if any, thalamic projections appear to arise from the MePD (12, 36), the thalamic terminations presumably derived from direct or axonal damage to nearby structures. Some damage to the optic tract was observed, producing a modest
Fig. 3. Dark field of cupric silver-stained degeneration in the forebrain of a unilaterally lesioned rat (case 43). ac, anterior commissure; AcbSh, accumbens shell; acp, posterior limb of the anterior commissure; AH, anterior hypothalamic nucleus; AH1, amygdalohippocampal transition area; BM, basomedial amygdaloid nucleus; BST, bed nucleus of the stria terminalis; BSTM, bed nucleus of the stria terminalis, medial part; BSTL, bed nucleus of the stria terminalis, lateral part; CeA, central amygdaloid nucleus; CPu, caudate putamen; DLG, dorsolateral geniculate nucleus; GP, globus pallidus; HPC, hippocampal formation; IPAC, interstitial nucleus of the posterior limb of the anterior commissure; IPACm, interstitial nucleus of the posterior limb of the anterior commissure, medial part; LH, lateral hypothalamic area; lo, lateral olfactory tract; LOT, nucleus of the lateral olfactory tract; LSV, lateral septum, ventral part; MeAD, medial amygdaloid nucleus, anterodorsal part; MPA, medial preoptic area; MPO, medial preoptic nucleus; MTu, medial tuberal nucleus; ox, optic chiasm; Pa, paraventricular hypothalamic nucleus; SLEA, sublenticular extended amygdala; sm, stria medullaris; Tu, olfactory tubercle; VMH, ventromedial hypothalamic nucleus. See RESULTS for further description.
degeneration in the lateral geniculate nucleus (Fig. 3H) and superior colliculus.

Comparison with other cases. Generally speaking, among the brains with bilateral lesions, subcortical degeneration resembled that described for brains with unilateral lesions, except that bilateral degeneration was the rule and the terminal fields were more intensely labeled (e.g., Fig. 4, A and B). The survival period did not appear to be a factor. Degeneration in the nucleus of the lateral olfactory tract was a variable feature of the lesions but was absent in some cases that demonstrated excessive weight gain.

In case 2C, an operated control, degeneration resulted from the electrode passing through the fimbria of the fornix and into the ventral hippocampus. In the amygdala, degeneration was prominent in the amygdalohippocampal transition area and the posterodorsal, posteroverentral, and anterodorsal medial amygdaloid nuclei, as well as in the posteromedial cortical and posterior basomedial amygdaloid nuclei. Outside the
amygdala, the pattern of degeneration was similar in many respects to that described for the unilateral lesion resulting in weight gain, although the degeneration was much lighter.

**Retrograde Labeling from the BSTIA**

The injection site (Fig. 5A) was small (600- to 700-μm diameter) and centered in the zone between the medial border of the central amygdaloid nucleus and the lateral margin of the MePD. This area corresponds to the midrostral part of the BSTIA. The labeled halo surrounding the core of the injection potentially involved the lateral-most part of the MePD, dorsal part of the posteromedial cortical amygdaloid nucleus, and to some extent, anterior part of the amygdalohippocampal area. Although the halo of the injection site also appeared to overlap the caudomedial part of the central amygdaloid nucleus, very few labeled cells were observed in central extended amygdala components. The retrograde labeling from this case is diagrammed in Fig. 6 and summarized in Table 3.

**Cerebral cortex.** Retrogradely labeled cells were found in the medial face of the hemisphere rostral to the genu of the corpus callosum in the tenia tecta, dorsal peduncular, and infralimbic cortices (Fig. 6A), as well as in a region just anterodorsal to the rostral pole of the nucleus accumbens (VO in Fig. 6A), which is considered part of the ventral orbital cortex by Swanson (101). In addition, a dense retrograde labeling was noticed in the ventral subiculum (Fig. 6K), and a moderate one in the dorsal endopiriform nucleus and posterior part of the piriform cortex (Fig. 6, B–J).

**Amygdala.** The amygdalohippocampal transition area was, by far, the most densely retrogradely labeled structure (Fig. 6, I and J; Table 3). A less dense but still substantial cell labeling was observed in the anterior cortical, anterior basomedial bed nucleus of the accessory olfactory tract, large intercalated cell mass (Fig. 6F), lateral nucleus (in its dorsolateral and ventromedial divisions; Fig. 6, H–J), posterior basomedial (Fig. 6, H–J) and amygdalopiriform transition area (Fig. 6K). In addition, a few retrogradely labeled cells were detected in the molecular layer of the nucleus of the lateral olfactory tract, possibly representing interstitial neurons accompanying the accessory olfactory tract (Fig. 6E).

**Medial extended amygdala.** A robust retrograde labeling was observed in the various divisions of the medial nucleus, with slightly less dense cell labeling in the anterodorsal and anteroventral divisions (Fig. 6, F–H). Similar robust cell labeling was seen in the posterior part of the medial bed nucleus of the stria terminalis (chiefly in its lateral and intermediate columns and, to a lesser degree, in the medial, parvocellular column; Fig. 6D), as well as in the medial division...
Fig. 6. Line drawings depicting retrograde-labeled neurons resulting from the cholera toxin B injection site shown in Fig. 5. A11, A11 dopaminergic cell group; AAA, anterior amygdaloid area; Acb, nucleus accumbens; AcbC, nucleus accumbens, core; AOP, anterior olfactory nucleus, posterior part; APir, amygdalopiriform transition area; Arc, arcuate nucleus; BAOT, bed nucleus of the accessory olfactory tract; Cl, claustrum; DB, nucleus of the diagonal band; DEn, dorsal endopiriform nucleus; DP, dorsal peduncular cortex; DR, dorsal raphe nucleus; HDB, nucleus of the diagonal band, horizontal part; IL, infralimbic cortex; Ins, insular cortex; LPBS, superior lateral parabrachial nucleus; LS, lateral septum; PH, posterior hypothalamic nucleus; Pir, piriform cortex; PIR, posterior intralaminar thalamic nucleus; PMD, dorsal premammillary nucleus; PMV, ventral premammillary nucleus; PT, paratenial nucleus of the thalamus; SCP, superior cerebellar peduncle; SLEAm, sublenticular extended amygdala, medial part; SLEAc, sublenticular extended amygdala, central part; SLEAm, sublenticular extended amygdala, medial part; SPP, subparafascicular nucleus of the thalamus; SPF, subparafascicular nucleus of the thalamus, parvicellular part; TM, tuberomammillary nucleus; VO, ventral orbital cortex; VP, ventral pallidum; ZI, zona incerta. See RESULTS for further description.
<table>
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Continued
of the sublenticular extended amygdala (Fig. 6, D and E). Some retrogradely labeled cells were additionally observed in the anterior and ventral parts of the medial bed nucleus of the stria terminalis and, contralaterally, in the medial amygdaloid nucleus and BSTIA. Direct uptake of the tracer from dendrites near the injection site may have contributed to the large number of labeled cells found in the ipsilateral BSTIA. Remarkably, cell labeling was practically absent in the central extended amygdala (see Table 3). In good agreement with these cholera toxin observations, in the FluoroGold case that had an injection into the central amygdaloid nucleus and the BSTIA, cell labeling in the posterior part of the medial bed nucleus of the stria terminalis was found in its lateral and intermediate columns, sparing its medial, parvocellular column.

**Other telencephalic areas.** In the septodiagonal band complex, retrogradely labeled cells were observed mainly in the vertical and horizontal nuclei of the diagonal band and in the lateral septal area (Fig. 6, B and C). In addition, some scattered labeled cells were noticed in the dorsomedial part of the anterior olfactory nucleus and amygdalostriatal transition area.

**Hypothalamus.** Retrograde labeling in the hypothalamus was in general rather modest. Labeled cells were observed in the VMH (Fig. 6, G and H), arcuate nucleus (Fig. 6F), posterior hypothalamic nucleus (Fig. 6I), dorsal and ventral premammillary nuclei (Fig. 6, I and J), and tuberomammillary nucleus (Fig. 6J). Only a few labeled cells were found in the medial preoptic area, paraventricular nucleus, anterior hypothalamus, and retrochiasmatic area (Fig. 6, E and F).

**Thalamus.** Substantial retrograde labeling was observed in the paratenial (Fig. 6, D and E), paraventricular, and subparafascicular thalamic nuclei. In the paraventricular thalamic nucleus, labeling was largely concentrated in its posterior part (Fig. 6J), and in the
subparafascicular nucleus mainly in the caudolateral extent of its parvicellular part, i.e., as it reaches the vicinity of the medial geniculate nucleus (Fig. 6, J and K). In the posterior thalamus, some labeled cells were encountered in the posterior intralaminar (Fig. 6K) and peripeduncular nuclei. Additional labeling was seen just ventral to the boundary of the reuniens nucleus.

**Brain stem.** Retrogradely labeled cells were observed in the periventricular gray substance and in the linear and dorsal raphe nuclei (Fig. 6L). In the parabrachial complex, a cluster of labeled neurons was evident in the superior lateral subnucleus (Fig. 6L). Some labeled cells were also noted in the locus ceruleus, but no cell labeling was seen beyond that level.

With cholera toxin, anterograde labeling is also evident, although fiber labeling is often difficult to discriminate from terminal fields. Nonetheless, in the present case it is worth noting that a moderately dense terminal field was observed in the granular layer of the accessory olfactory bulb, possibly reflecting an involvement of the posteromedial cortical nucleus rather than the BSTIA (10, 26). Consistent with the terminal degeneration in lesioned animals, cholera toxin labeling was not observed in the mitral cell layer. No labeling was seen in the central division of the extended amygdala, whereas the components of the medial extended amygdala were well labeled. Finally, only light anterograde labeling was seen in the shell of the nucleus accumbens. In contrast to the cholera toxin case, a dense degeneration marked both the central extended amygdala and shell of the accumbens in all the cases with lesions in the PDA.

**Retrograde Labeling from the MePD**

The FluoroGold deposit was centered in the MePD and appeared to also include portions of the BSTIA (Fig. 5B). Although the halo of the 3,3′-diaminobenzidine tetrahydrochloride-stained injection site seemed to encroach on the central amygdaloid nucleus, structures that are known to project densely to it, such as the lateral bed nucleus of the stria terminalis, contained very few labeled cells (Table 3). This case was originally prepared for a report on the connections of the supracapsular bed nucleus of the stria terminalis, so that sections rostral to the level of the genu of the corpus callosum were not saved.

In general, the retrograde labeling overlapped considerably with that seen after the cholera toxin injection in the BSTIA. Therefore, we have not diagrammed this case separately but instead have tabulated the resulting retrograde labeling (Table 3). Here, we will mainly describe those areas in which labeling differed from that seen after the cholera toxin injection in BSTIA.

**Cerebral cortex.** The most densely labeled “cortical” area was the ventral subiculum. Moderate labeling was seen in the entorhinal cortex and, to a lesser degree, in the agranular insular, caudal piriform, and perirhinal cortices.

**Amygdala.** The densest retrograde labeling was seen in the amygdalohippocampal transition area and in the posteromedial cortical nucleus (Table 3). The retrograde labeling in the posterior basolateral nucleus and amygdalopiriform transition area appeared to be more substantial in this case than after a cholera toxin injection into the BSTIA (Table 3).

**Extended amygdala.** There was a shift in the labeling of the posterior part of the medial bed nucleus of the stria terminalis, in that the most medial (small celled) column of this structure was more densely labeled after the FluoroGold injection. In contrast, after the BSTIA injection, the medial column was less densely labeled than the more lateral (medium celled) columns. The anterior part of the medial amygdaloid nucleus was more densely labeled than in the BSTIA case.

**Thalamus.** Retrograde labeling in the posterior thalamus, including the subparafascicular, posterior intralaminar and peripeduncular nuclei, appeared to be substantially greater compared with that observed in the BSTIA case. It is also interesting to note that the entire parvocellular part of the subparafascicular nucleus was robustly labeled in the MePD case, whereas in the BSTIA case only the lateral portion of this subdivision was substantially labeled (Table 3).

**Hypothalamus.** Generally, retrograde labeling of the hypothalamus from the injection in MePD was more widespread compared with the results of the cholera toxin injection in the BSTIA (Table 3). In particular, the MePD case labeled a proportionately higher number of neurons in the anterior hypothalamic area, VMH, dorsal and ventral premammillary nuclei, and in the posterior hypothalamic nucleus. Scattered neurons were observed in the lateral hypothalamus, including the perifornical and subperifornical areas as well as in the parasubthalamic nucleus. In contrast to the BSTIA case, no retrograde labeling was observed in the tuberomammillary nucleus.

**Brain stem.** A more extensive retrograde labeling was observed in the brain stem after the injection in MePD than after the injection in the BSTIA, especially in the parabrachial area (superior lateral, external lateral, medial, and waist subnuclei; see Table 3). Labeling in the superior lateral subnucleus was bilaterally distributed with an ipsilateral predominance. Dense cell labeling was also observed in the contralateral parabigeminal nucleus. This result probably should be ascribed to FluoroGold uptake by fibers running in the supraoptic decussation (106).

**DISCUSSION**

**Body Weight**

The results of the present study confirm our earlier reports of excessive weight gains after electrolytic lesions of the most posterodorsal aspects of the amygdala in rats (50, 51, 84). Mean daily weight gains ranged from 10.6 to 16.2 g in the first 2–3 days after lesions. Previous studies have shown that the excessive weight gains are preceded by marked hyperphagia (e.g., 45,
50, 52, 53, 84) and result in obesity, i.e., greatly elevated levels of adipose tissue (50). The weight gains are not due to changes in the estrous cycle or ovarian hormones (52). Although we cannot know what long-term weight gain would have been in the present study, the short intervals are optimal for quantification of the lesion because they minimize time-dependent changes in apparent lesion size (111). The results additionally show that rapid weight gains occur in the first 48 h after surgery even when such lesions are unilateral. Overeating has also been reported after unilateral lesions of the ventromedial hypothalamic area, although they were much less effective over an extended postoperative period than were bilateral lesions (62, 64).

Both the qualitative analysis of bilateral lesions and the numerical estimates of unilateral lesion size confirm and extend the recent finding of Rollins and King (84) that the critical nuclei are the BSTIA and the MePD. Incidental damage to the globus pallidus limited the excessive weight gain and contributed substantially to the variation in weight gain. It has been well established that aphagia and weight loss follow lesions directed at the globus pallidus (e.g., 22, 35, 59, 69) or after damage to its efferent pathways (2, 69). Because damage to the caudal pallidum is difficult to avoid when lesioning the ventrally adjacent PDA, it is possible that the effects caused by this procedure on ingestion have been consistently underestimated.

Finally, it is important to mention that in the scheme used for segmentation of the various amygdaloid nuclei, we have followed the plan outlined by de Olmos et al. (24), Krettek and Price (57), and Alheid et al. (1). In these schemes the BSTIA is found interposed between the dorsal parts of the medial and the central amygdaloid nuclei. The cells are immersed in a sheet of fibers that are condensing to form the compact columns of the stria terminalis. In another widely used scheme of amygdaloid organization the BSTIA is not depicted, and this area of the PDA is considered to be part of the (ventral) capsular portion of the central nucleus (27, 65, 80, 101).

Anterograde Degeneration and Retrograde Tracing Experiments

The anatomic results observed with the cupric silver stain and with the retrograde tracers, together with recently published Phaseolus vulgaris-leucaegglutinin (PHAL) studies of the posteromedial amygdala (10, 12, 27, 36, 80) and caudal globus pallidus (91), provide a comprehensive picture of the input-output relations of the lesioned areas. We must keep in mind that anterograde degeneration will result from damage to both the origin of a particular pathway and to axons of passage through the area of lesion. Behavioral changes, of course, could be attributed to either or both of these types of damage.

To our knowledge, the only other experiments to directly examine the afferents of the BSTIA were a single injection described over several papers by Ottersen (74–76) and Ottersen and Ben-Ari (77), whose results are indicated in our Table 3. Our results confirm the observations of Ottersen while identifying additional potential afferents. This is to be expected given the greater sensitivity of cholera toxin as a tracer compound compared with the horseradish peroxidase method used by Ottersen. In addition, our description is based on a more detailed cytoarchitectonic parcellation.

The silver degeneration method demonstrated the broad sweep of forebrain structures that are impacted by obesity-inducing amygdala lesions. Many of the areas suffering anterograde degeneration have previously been shown to be involved in various aspects of feeding and/or body weight regulation. These include the lateral septum (55, 108), shell area of the nucleus accumbens (61, 82, 99, 100), medial division of the extended amygdala (see below), medial preoptic nucleus (58, 63, 104), retrochiasmatic area (29), ventromedial hypothalamic area (e.g., 41, 48, 49), and ventral premammillary nucleus (30, 105).

Before we proceed, mention must be made of the damage incurred in the ventral hippocampal formation of one of the control animals. This resulted in a pattern of degeneration (albeit lighter) involving many of the same areas as the experimental animals, but with no weight gain. A previous study found that even large lesions of the ventral hippocampal formation have no effect on food intake or body weight (45). The targets of the medial amygdala and the ventral hippocampus are generally similar (80). It may be that the topography of the projections differs sufficiently so that one could postulate that subcompartments within a given target may serve different aspects of goal-directed behaviors. Another alternative may be that common areas innervated by the ventral hippocampal formation and the posterior amygdala target circuits that influence feeding but that the transmitter(s) used by the two areas differ. Thus denervation of the same target could have unique or even opposite effects. For example, glutamate is the likely transmitter in the projection emanating from the ventral subiculum, whereas GABAergic cells are likely to provide a substantial contribution to the afferents derived from the PDA. With this caution in mind, the areas impacted by the PDA lesions will now be examined.

Nucleus accumbens. Degeneration was observed in the nucleus accumbens, and Kelley (see Ref. 44 for a review) has shown that food intake may be specifically elicited from the caudal shell of the nucleus accumbens by locally blocking glutamate receptors (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionate but not N-methyl-D-aspartate) or by injection of GABA_A or GABA_B agonists. Interestingly, degeneration of uncertain origin is also observed in the nucleus accumbens after knife cuts in the medial hypothalamus that also produce hyperphagia (71). The shell of the accumbens sends a GABAergic projection to the medial part of the ventral pallidum and beyond this terminates along a broad rostrocaudal extent of the lateral hypothalamus (40).
It is noteworthy that the meager projection to accum-
bens emanating from the MePD (8, 10) and the limited
evidence for input from the BSTIA (8, present results)
suggest that the dense degeneration seen in the shell
was not primarily the result of damage to these two
structures. Other potential sources of these terminals
include the amygdalopiriform transition area (8, 94),
the ventral subiculum (13), the posterior basolateral
amygdaloid nucleus (8, 56, 66), and the basomedial
nucleus, which also projects densely to the VMH (81).
The anterodorsal medial amygdala is another possible
source of afferents to the shell of the accumbens (12,
36), but the virtual lack of degeneration in the mitral
layer of the accessory olfactory bulb and lateral hypo-
thalamus indicates that our lesions largely spared
the anterior part of the medial amygdaloid nucleus. For
the ventral subiculum, our incidental control lesion did
not result in overeating, nor was this behavior induced
after deliberate lesion of this structure in our earlier
experiments (45). Lesions of the basolateral amygdala
have been reported to result in obesity in the rat (34),
but Rollins and King (84) found that excessive weight
 gain does not occur after basolateral amygdaloid le-
sions unless damage impinges on the PDA. Finally, the
direct involvement of the basomedial amygdaloid nu-
cleus by our lesions did not seem to contribute to
prediction of the increase in body weight.

Medial extended amygdala. Anatomically, and to
some degree functionally, the various subdivisions in
the area of the PDA appear to be interconnected and
paired with similar subdivisions in the medial bed
nucleus of the stria terminalis (1, 19, 24, 110). The
MePD appears to be homologous with the small-celled
medial part of the posteromedial bed nucleus of the
striatal terminalis, whereas the homologous subdivision
for the BSTIA is less clear. This may include portions
of the anterior medial bed nucleus of the stria termi-
nalis (see Ref. 1) or an intermediate zone wedged
between the lateral and medial subdivisions of the bed
nucleus of the stria terminalis (i.e., the intermediate
bed nucleus of the stria terminalis described by Ref.
24). The role of the analogous subdivisions in the me-
dial bed nucleus of the stria terminalis in ingestion is,
however, less clear. To ascertain this, it may be impor-
tant to confine lesions to the medial sector of the bed
nucleus of the stria terminalis, minimizing involve-
ment of adjacent structures such as the lateral septum,
lateral bed nucleus, or globus pallidus. Lesions in the
lateral septum do result in weight gain for female but
not male rats (108). The gender-specific effect is remi-
niscent of the earlier observation that after lesions of
the ventromedial hypothalamic area females gain pro-
portionately more weight than males (e.g., 20, 49, 96),
as well as the recent observations of preferential
weight gain by female rats after posterodorsal amygd-
aloid lesions (52).

The obesity-inducing lesions in the present study do
not seem to depend on damage to the central amygd-
aloid nucleus as judged by the lack of terminal degen-
eration in several of its major targets, e.g., the postero-
lateral hypothalamus or brain stem autonomic centers.
Although the central extended amygdala does not seem
to be innervated by the MePD (12, 36) or by the BSTIA
(present results), all its components (including the cen-
tral amygdaloid nucleus, its sublenticular and supra-
capsular extension, the interstitial nucleus of the pos-
terior limb of the anterior commissure, and the lateral
bed nucleus of the stria terminalis) showed moderate
to dense degeneration after our lesions. As with the
degeneration in the shell of the accumbens (discussed
previously), this degeneration is likely to arise from
extrinsic sources such as the basomedial nucleus (81),
the posterior basolateral amygdaloid nucleus (56, 67,
88, 92, 93), or the amygdalopiriform transition area
(67, 94), whose axons might have been inadvertently
damaged by our lesions.

Thalamo-amygdaloid-hypothalamic circuits in moti-
vated behaviors. The parvocellular subparafascicular
nucleus relays visceral information from the parabrachial
to the amygdala and cortex (5, 115). Midline
thalamic nuclei also appear to be crucially involved in
visceroceptive processing (e.g., 5, 86; for additional
references see Ref. 83). More recently, the peripedun-
cular area also was reported to receive strong projec-
tions from the caudal interoceptive part of the nucleus
of the solitary tract (86). Winans Newman (110) has
suggested that the posterior amygdala, medial bed
nucleus of the stria terminalis, lateral septum, medial
preoptic area, anterior hypothalamic nucleus, VMH, and
central gray/central tegmentum form a circuit of broadly
interconnected structures involved in social behaviors.
This includes activities such as sex and parental be-
havior, as well as aggression. For example, in male
hamsters or rats that are allowed to ejaculate or cop-
ulate to satiety, c-fos is upregulated in cell columns of
the MePD and posterior bed nucleus of the stria termi-
nalis (17, 18, 78) that appear to be paired structures
to the extent that they are neurochemically similar,
have similar afferents and efferents, and are densely
interconnected with one another (1, 19). Cells in the
lateral, parvocellular part of the subparafascicular nu-
cleus, MePD, posterior division of the medial bed
nucleus of the stria terminalis, and medial preoptic
nucleus represent a network with reciprocal intercon-
nections with the medial preoptic nucleus that is acti-
vated by ejaculation in the male rat (18). The argument
by Winans Newman (110) suggests that the balance of
activity within different portions of this network and
its extension in the VMH and central tegmentum may
serve to direct the output to impact on distinct behav-
oriority within different compartments of these struc-
tures. The BSTIA lies just lateral to the MePD and to
the columns within the MePD that are activated by sexual
activity. Similarly, retrograde labeling in the posterior
part of the medial bed nucleus of the stria terminalis
from the BSTIA is centered somewhat lateral to the
neuronal labeling from the MePD. These results sug-
that a circuit mediating feeding satiety could be
described that would parallel that observed for copula-
with the relevant cell columns in the amygdala
and bed nucleus of the stria terminalis occurring lat-
eral to the corridors responding to sexual satiety within each of these structures. At least within the thalamus, some resemblance of this topography may remain, since in the parvocellular division of the subparafascicular nucleus projections to the BSTIA are essentially derived from its caudolateral part, and, to a much lesser degree, from its rostromedial part. The parvocellular part of the subparafascicular nucleus is a potential target for nociceptive, visceral, and gustatory stimuli, presumably relayed via the external medial portions of the parabrachial nucleus (5, 14, 115). Finally, the subparafascicular nucleus, including its caudolateral part, is the recipient of a relatively dense projection from the VMH (11). The latter therefore projects directly to the BSTIA and MePD as well as via a synaptic relay in the posterior thalamus (Ref. 11; present study). It is noteworthy that the densest VMH projections to the caudal part of the subparafascicular nucleus derive from its ventrolateral part, which is more closely associated with reproductive behaviors.

**Superior lateral parabrachial subnucleus.** Besides receiving parabrachial inputs relayed by the thalamus, the MePD and BSTIA are the targets of direct afferents from the superior lateral subnucleus of the parabrachial complex. Within the context of feeding behavior, this subnucleus is particularly relevant because it is the main source of cholecystokinin afferents to the dorsomedial part of the VMH (4, 33, 116). Cholecystokinin has been implicated as a satiety-producing hormone with both central (e.g., 89, 95, 109) and peripheral receptors (e.g., 97). In at least one instance, the central inhibition of food intake has been linked to the cholecystokinin neurons in the superior lateral parabrachial nucleus and their projection to the dorsomedial subdivision of the VMH (102). The involvement of the superior lateral parabrachial nucleus in the inhibition of food intake is reinforced by the report that administration of leptin in doses that reduce food intake also increases c-fos expression in the superior lateral parabrachial nucleus (30, 31).

**Medial hypothalamus.** In parallel with the circuit proposed to mediate social behaviors, a feeding-related circuit could include the medial preoptic nucleus, the subparaventricular zone (31, 109), retrochiasmatic area (29), and periventricular hypothalamus. Somatostatin neurons in the periventricular hypothalamus presumably serve directly or indirectly as a relay for hypothalamic and amygdaloid influences on the release of growth hormone (43, 72). The periventricular hypothalamus is additionally targeted by afferents from the superior lateral subnucleus of the parabrachial complex (4). The subparaventricular area, a site of dense degeneration after our obesity-inducing amygdala lesions, provides an important relay for afferents from the suprachiasmatic nucleus to many of the same areas targeted directly by the suprachiasmatic nucleus (107). The projections of the subparaventricular nucleus include the dorsomedial hypothalamic nucleus, which has been implicated in ingestive behavior (e.g., Ref. 3), and the dorsal part of the VMH shell. The latter also displays degenerating terminals after amygdaloid lesions resulting in obesity; these terminals may represent synaptic contacts on distal dendrites of neurons located within the dorsal part of the VMH (68). The dorsomedial portion of the VMH is the sector more closely associated with food intake and energy balance, in view of its numerous leptin receptors (e.g., 31, 39, 90) and its activation by leptin administration (30). Although the ventrolateral VMH has also been implicated in obesity (41), this portion of the VMH has been more closely associated with the expression of sexual behavior (see Ref. 11 for references).

It should be noted that in a recent comprehensive PHAL study of efferent projections from the rat amygdala, Petrovich et al. (80) caution against the idea that the amygdala participates in reproductive and ingestive behaviors via parallel, segregated pathways to the hypothalamus. Their work showed that the amygdala may influence the medial hypothalamus via multiple pathways, including direct inputs via the stria terminalis, via ventral hippocampal-hypothalamic or ventral hippocampal-lateral septal circuits, via relays through the bed nucleus of the stria terminals (27), or via prefonto-hypothalamic projections. In their theoretical scheme, function is organized in a network of diverging and converging amygdaloid projections. These differences in theory about amygdaloid functional organization do not diminish the present results. In fact, identification of the specific nuclei affected by obesity-inducing lesions may help to resolve the issue.

It must also be noted that the present study used electrolytic lesions. Because all previous studies that reported weight gain after amygdaloid lesions in female rats had employed electrolytic lesions, the present study also used electrolytic lesions to elucidate the anatomic substrate involved in this model of obesity. In addition to destroying local populations of neurons, electrolytic lesions also sever fibers coursing through the lesioned area. Future research should explore the effects of knife cuts and excitotoxic lesions (e.g., ibotenic acid) to determine the contribution of each. However, several cautions must be mentioned. Three studies have reported that severing the stria terminalis did not result in excessive weight gain in rats, but this may have been due to the use of males (6, 7, 73). Although electrolytic lesions have obvious shortcomings, excitotoxic lesions also have limitations: 1) damage to axons occurs at some sites, 2) lesions sometimes occur at distant sites (presumably by transynaptic activation), and 3) incomplete cell loss sometimes occurs (15, 16, 28, 42, 85, 87, 113). There is also the problem of widespread diffusion when ibotenic acid is injected into the amygdala (114), often necessitating high dosages to get effects. Despite these limitations, a combination of techniques should help to ascertain the etiology of this model of obesity.

**Perspectives**

Lesions in the MePD and BSTIA resulted in dramatic weight gain. The results of our analysis suggest...
that the degeneration produced by our lesions may be divided into two classes. The first one originates in the posterodorsal region of the medial amygdala and is concordant with the projections of this amygdaloid region to different structures that are likely to take part in a network controlling food intake. These structures include the lateral septum, medial bed nucleus of the stria terminalis, medial preoptic area, subparaventricular area, VMH, and ventral premammillary nuclei. The second class consists of anterograde degeneration that is unlikely to emanate from the posteromedial amygdala but that nonetheless is likely to have an impact on feeding behavior. Among the latter class are projections to the accumbens shell and central extended amygdala. Interestingly, many of the areas of the first group are also included within the circuits implicated in the organization of reproductive behaviors as discussed by Winans Newman (110). The present results extend this into the realm of food intake. Overall, a greater appreciation of the importance of active inhibition as a rate-limiting factor in food intake has evolved over recent years (e.g., 112). The areas of the posterodorsal medial amygdala are likely to play a pivotal role in negotiating this inhibition based not only on metabolic and visceral signals, but also from other competing demands such as sodium balance, thermoregulation, and reproductive behaviors such as copulation, parenting, and aggression.

REFERENCES


OBESITY-INDUCING AMYGDALA LESIONS


