ACTA NEUROBIOL. EXP. 1973, 33: 623-648

THE AMYGDALA: HISTORICAL AND FUNCTIONAL ANALYSIS

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Abstract. The amygdala, part of the limbic system, is a small collection of neurons located in the ventral temporal lobe, and can be divided into two morphologically and functionally distinct nuclei — the corticomedial, a phylogenetically old group, and the basolateral, a phylogenetically more recent group. Both divisions of the amygdala have extensive interconnections with the hypothalamus, the corticomedial nucleus via the stria terminalis and the basolateral nucleus via the ventral amygdalohypothalamic pathway. The amygdala receives input from the orbital frontal cortex, the piriform cortex, the hypothalamus, the thalamus, and all sensory modalities as well as from the other structures of the limbic system. Early theories positing strictly emotional, olfactory, or visceral functions for the amygdala are at best incomplete. An intact amygdala seems to be essential for the successful performance of behavior patterns such as instinctive food getting and instinctive defensive reactions that are necessary for the survival of the individual organism and the species. Ablation of the amygdala produces many behavioral deficits that center around the inability to integrate changes in reinforcement contigencies into new behavior patterns.

ANATOMICAL DEFINITION OF THE AMYGDALA

The amygdala, located deep within the ventral temporal lobe of the brain in mammals, is a collection of nuclei that resembles — given the metaphoric imagination of the ancient anatomists — an almond (*amygdala,* Latin, an almond). In the lower phylogenetic orders, the amygdala is a small, undifferentiated cell mass in the telencephalon, merging with primordial piriform gray, while in tailed reptiles the amygdala becomes a more discrete gray mass related laterally to the piriform cortex (26). Although the amygdala of frogs, toads, and fishes can be divided into three nuclei, the mammalian amygdala has two main nuclear divisions;

a phylogenetically old group, comprised of the medial, central and cortical nuclei, and a phylogenetically newer group, the lateral and basal nuclei, that arose by migration of cells from the piriform cortex (68). The corticomedial amygdala is the larger in the lower animals while the basolateral group is the larger in the higher primates and reaches its highest morphological differentiation in man (17, 26). In an electron microscopic study comparing the medial and the lateral nuclei, Hall (58) observed much more glial cell contact in the medial nuclei while neurons in the lateral nuclei had many more dendritic spines. Using histological criteria, it is possible to subdivide these two amygdaloid areas further into numerous nuclei and subnuclei (86). From a functional standpoint, this appears unnecessary since current electrophysiological and behavioral analyses indicate that a division of the amygdala into the two areas suggested by Johnson (68) is quite adequate. However future research should be directed toward the understanding of the functional relationships and behavioral contributions of each of the various areas within the amygdala.

AFFERENT AND EFFERENT CONNECTIONS OF THE AMYGDALA

The amygdala is a part of the limbic system, a widespread organization of interconnected subcortical structures and associated fiber tracts that seem to exercise a regulatory influence over many central nervous system functions. The amygdala, as well as the rest of the limbic system, was long considered to be olfactory in function (129) — hence the term rhinencephalon (nose brain) to refer to the limbic system — due to the proximity of the nucleus of the lateral olfactory tract to the cortical amygdaloid area. However, Valverede (166) excluded the nucleus of the lateral olfactory tract from the amygdala on histological grounds and assigned the cortical amygdaloid area to the periamygdaloid and prepiriform cortices. Girgis (46) traced degenerating fibres from lesions in the olfactory bulbs and found scanty degeneration to the amygdala: only very little to the cortical amygdaloid nucleus and none at all to the basolateral amygdala. The olfactory bulbs project rather to the piriform cortex and gain access to the amygdala via the piriform-amygdala connections (131). In anosmatic mammals (e.g., the porpoise, 16) the entire amygdala, including the cortical amygdaloid area, is quite well developed. Furthermore, bilateral ablation of the amygdalae of dogs (3) and of monkeys (151) affects neither the retention nor the aquisition of olfactory discriminations. Thus the amygdala cannot be considered to have only specific olfactory functions.

The amygdala receives input from rather widespread and diverse central nervous system structures. Electrophysiological studies (114) in

which responses recorded in the amygdala could be evoked by stimulating anywhere in the entire baso-fronto-temporo-occipital cortical areas, and the histological tracing of direct fiber projections from the temporal cortex (166) and from the orbital and neighboring gyri (86, 166), reveal the extensive cortical influence on the amygdala.

The amygdala also has connections from various subcortical structures. The two amygdaloid areas, the corticomedial and the basolateral amygdaloid nuclei, are highly interconnected (57, 152, 166). The hypothalamus sends fiber to the amygdala via both the stria terminalis and the ventral amygdalofugal pathway (113). Electrical stimulation of the anterior hypothalamic area, the lateral hypothalamus, or the ventromedial hypothalamus leads to evoked responses that have different latencies and waveform characteristics depending on whether the recording site is in the corticomedial or in the basolateral amygdala (89). This supports not only the dual hypothalamo-amygdala projection systems suggested by Nauta and Haymaker (113), but also the adequancy of dividing the amygdaloid complex into only two functional nuclei.

The neural connections from the dorsal thalamus to the amygdala, first mentioned by Hilpert (61), were established histologically by Nauta (112) and confirmed electrophysiologically by Niemer, Goodfellow, Bertuccini and Schneider (115). About one half of the neural units in the amygdala tested by Sawa and Delgado (135) showed some changes either increased or decreased firing rates, to sensory stimulation. The input into the amygdala from all sensory modalities (49) probably arrives via these thalamic connections, but direct fibers from the various primary sensory cortices cannot be ruled out. Crosby et al. (26) state that the nucleus of the lateral olfactory tract projects directly to the basolateral amygdala. Such direct connections are also possible for other sense modalities (e. g. optical fibers, 61; sciatic nerve, 96).

The amygdala has two major efferent systems: the stria terminalis and the ventral amygdalofugal pathway. The former, a compact discrete bundle of nerve fibers, seems to be the dominate projection system in lower mammals, while the ventral amygdalofugal pathway reaches its greatest development in man with the stria terminalis becoming almost vestigial (166). Although the stria terminalis receives fibers from both the corticomedial and basolateral amygdaloid nuclei in the rat (25), the mouse (166) and the rabbit (9), only the corticomedial amygdala contributes fibers to the stria terminalis in the cat (47, 66, 166) with maybe a small contribution from the basal amygdaloid area (57). The ventral amygdalofugal pathway, a rather diffuse network of fibers that seem to arise in the basolateral amygdala in man (83), is very difficult to identify histologically in lower mammals but several electrophysiological studies

have demonstrated its existence in cats (50, 108). Short fibers interconnect the two amygdaloid nuclei and other short fibers project to various temporal cortex structures (166).

The target of most of the amygdaloid projections via either pathway is the various areas of the hypothalamus. Following lesions in the basolateral amygdala, degenerating fibers have been traced to the ventromedial hypothalamus (9, 25), the anterior, lateral, and ventromedial hypothalamic areas, and the medial forebrain bundle (9, 25, 57, 66). Lesions of only the stria terminalis place degenerating fibers in the anterior hypothalamus, in the medial forebrain bundle, and to the border of the ventromedial hypothalamic area where the fibers probably make axodendritic contacts with neurons from the ventromedial hypothalamus (60). Raisman (131) reported that the stria terminalis makes synaptic contact exclusively with the dendritic spines of neurons from the ventromedial hypothalamus and not the dendritic shafts. The functional significance of these connections has not been elucidated. Amygdalo-medial forebrain bundle connections were also described by Wright (174) and Klingler and Gloor (83). Thus the amygdala and the hypothalamus have very extensive interconnections with neural impulses passing both ways in the stria terminalis and the ventral amygdalofugal (sic) pathway (113). Based on evidence giving two way conduction to the latter pathway, the ventral amygdalofugal pathway might best be renamed the ventral amygdalo-hypothalamic pathway.

The amygdala also projects to the thalamus. Amygdaloid projections to the dorsomedial thalamic area were described by Klingler and Gloor (83) in man, by Nauta (112) in the monkey, and by Hall (57) and Ishikawa et al. (66) in the cat. Nauta (112) presents an amygdalo-thalamo-orbital frontal cortex system that gives the amygdala influence on the frontal association areas of the cortex. The amygdalo-thalamic connections are of importance in the propagation of epileptic seizures (166) and in the amygdaloid modulation of all sensory modalities.

Electrophysiological studies substantiate the monosynaptic connections of the amygdala revealed by histological and anatomical procedures as well as suggesting many new polysynaptic amygdaloid connections. Gloor (47, 48) recorded potentials evoked by amygdaloid stimulation from the septal area, anterior preoptic hypothalamic areas, and the cortex, and demonstrated potent multisynaptic amygdalo-hippocampal and amygdalo-piriform interconnections. Sutin (158) recorded responses evoked in the ventromedial hypothalamus by amygdaloid stimulation and Storozhuk, Vladimirova, Kozyreva and Nedel'kina (155) demonstrated a widespread amygdaloid influence on cortical activity. Amygdaloid stimulation typically alters the rate of spontaneous firing of neurons in the ventro-

medial hypothalamus (38, 50, 108). Although the direction of change in the firing rate does not seem to be precisely localized to a specific stimulation area in the amygdala, there does seem to be a specific response of ventromedial hypothalamic neurons to stimuli arriving over the stria terminalis as opposed to the ventral amygdalo-hypothalamic pathway. Amygdaloid stimulation: sometimes inhibits, sometimes excites, or maybe even both from the same electrode placement, or has no effect on neural units in the ventromedial hypothalamus (50, 108); usually depresses the EEG pattern recorded from the neocortex (35); but may either inhibit or excite neural units in the temporal cortex (177); but always inhibits auditory evoked potentials in the primary auditory cortical area (177). That the corticomedial and basolateral amygdaloid areas have different projection patterns was noted by Andy and Mukawa (8) who demonstrated that seizure discharges evoked in the corticomedial nucleus generally propagate to both the diencephalon and the mescencephalon, while basolateral evoked seizures propagate primarily to the diencephalon. Kreindler and Steriade (90) showed that the basolateral amygdala was more susceptible to seizures than was the corticomedial and that amygdaloid seizures readily propagate to the thalamo-hypothalamo-tegmental structures without involving the cortex. Thus the amygdala is comprised of two divisions, the corticomedial and the basolateral, that, while interconnected, seem to have different projection systems, different influences on neural activity, different thresholds of activation, and even different morphological ultrastructure (58).

NEURAL AND BEHAVIORAL EFFECTS OF ELECTRICAL STIMULATION OF THE AMYGDALA

Analysing the normal function of central nervous system structures generally poses many different problems at best. The conditions under which the analysis of the amygdala must be conducted are somewhat less that optimal. The amygdala is a rather small structure buried deep within the temporal lobe closely juxtaposed with several other small structures. This necessitates the destruction of the other areas in order to arrive at the amygdala and the inclusion of the other areas in any experimental manipulation of the amygdala. In addition, the amygdala is very prone to self-sustaining epileptiform seizure afterdischarges so any experimental stimulation of the amygdala must not initiate seizure afterdischarges for this would produce a functional (although temporary) lesion of the amygdala and would not reflect the normal neural influence of the amygdala at all. Many of the controversies concerning amygdaloid functioning disappear when the contributions to the dependent variable

from neural structures surrounding the amygdala or from amygdaloid seizure activity are removed.

Amygdaloid stimulation has a variety of effects on the spontaneous activity of neural tissue. Gloor (48) concluded that the amygdala exerts a flexible modulation on subcortical mechanisms but, because the effects of amygdaloid stimulation were so variable, that the normal action of the amygdala must be very subtle and discrete thus giving a high degree of flexibility to the activity of the central nervous system. The firing rates of neurons in all parts of the hypothalamus are driven, suppressed, increased, decreased, or unaffected by stimulation in the amygdala (32), while spontaneous electrical activity in the ventromedial (136) and lateral (120) hypothalamic areas is inhibited by long lasting inhibitory post-synaptic potentials exerted through the stria terminalis (121). Not only is spontaneous cortical electrical activity attenuated or depressed by amygdaloid stimulation but cortical evoked potentials (69) and olfactory bulb evoked potentials in the prepiriform cortex (21) are also inhibited. However only some of the electrode placements in the amygdala tested by Callens et al. (21) were effective. Amygdaloid stimulation also reduces the electrical activity of the hippocampus (161) and decreases the evoked responses of neural units in the globus pallidus to sciatic nerve stimulation (1, 2) while the spontaneous activity of units in the globus pallidus (116) are either facilitated or inhibited. Thus the variable effects of amygdaloid stimulation noted by Gloor (48) have been supported by many other investigators and attempts to localize the various amygdaloid influences have failed (38, 164) except that basolateral amygdaloid stimulation inhibits or decreases more often than it excites or increases (33, 108).

Electrical stimulation of the amygdala produces many alterations in the autonomic nervous system. The inhibition and facilitation of respiration following amygdaloid stimulation reported by Kaada (69) was supported by findings of MacLean and Delgado (98) and Kaada, Andersen and Jansen (70). Wood, Schottelius, Frost and Baldwin (173) found that the threshold for the respiratory influences of the amygdala was lower in the corticomedial than in the basolateral amygdala but that basolatal stimulation also inhibits respiration. Similary Ursin and Kaada (164) could not find a localized area of the amygdala that affected the respiratory or cardiac changes described for amygdaloid stimulation by MacLean and Delgado (98) and Koikegami (87). Amygdaloid stimulation increases heart rate and blood pressure (23), or decreases heart rate (132; R. B. Musty, personal communication) and blood pressure (171) via vagus nerve efferents (132, for bradycardia; 161, for blood pressure). Although these contradictory cardio-vascular effects of amygdaloid stimulation

have not been examined parametrically, the differences may be due to amygdala seizures produced by some stimulation parameters. Other reported autonomic effects of amygdaloid stimulation include pupil dilation, salivation, peristalsis, gastric secretion, defecation, ovulation, and initiation of labor (99, 148, 172, 173) thus demonstrating the widespread influences of the amygdala on innumerable autonomic nervous system activities.

The amygdala seems to be active in the processing of sensory information. Kaada (69), observing that electrical stimulation of the amygdala inhibited general motor activity, called this an orienting response (70), while others have termed it an arrest reaction (98), a state of alert attention (150), an attention response (165) and simply alerting (4). Lesse (92) demonstrated that the amygdaloid EEG became predominantly 40 to 45 Hz during attentive behavior and McLennan and Graystone (102) observed 40 Hz EEG burst activity in the amygdala during the attentive response to olfactory stimulation. Thus the amygdala seems to be involved in attentive behavior following sensory input.

The overt motor responses claimed to result from amygdaloid stimulation, primarily movements of the face and neck muscles such as sniffing, chewing, head turning (99, 150, 164, 173), biting (179) and turning to the side opposite the stimulation (70, 99), have a suspiciously high correlation with symptoms of seizure activity. All of the mentioned responses are identified by the respective authors as rhythmic and as lacking localization within the amygdala; the area with the lowest threshold for face and jaw movements, the basolateral (173), is also the area with the lowest seizure threshold (90); the larger motor acts such as head turning and turning to the side opposite the stimulation site are very stereotyped; these motor responses are accompanied by either clonic twitches (179) or outright seizures (4). The mechanisms whereby amygdala stimulation results in skeletal muscle activity require further elucidation.

Hilpert (61) suggested that the amygdala is involved with the excitation and mediation of defensive movements. This hypothesis has been supported by more recent investigators. Amygdaloid stimulation also produces a behavioral syndrome labeled defensive attack (98), fear, and anger (164, 172). Although both Zbrożyna (62, 178, 179) and Fernandez de Molina and Hunsperger (36, 37) agree that the amygdala elicited defense reaction is similar to the hypothalamic elicited defensive reaction, the former group describe it as a rage-fear-aggressive flight response that is conducted from the basal amygdaloid area to hypothalamic defensive centers via the ventral amygdalofugal pathway, while the latter group defines the defensive reaction as a hissing and growling response

that is conducted from the medial amygdaloid area to the hypothalamic defensive centers via the stria terminalis. Turner (162) implicates the stria terminalis in all rage reactions. This amygdala defensive reaction controversy is confounded further by the unseen and unreported possibility of seizure activity. Kaada et al. (70) turned an amygdala elicited orienting response into defensive rage by increasing the stimulating current. Alonso-de Florida and Delgado (6) noticed increased aggressive encounters in some cats receiving continuous amygdala stimulation, but these cats were also undergoing persistent amygdaloid seizures. Not only did Allikmets (4) find all amygdala elicited motor responses, including aggressive-defensive reactions, to be associated with seizure activity of the amygdala but also Zbrożyna (179) himself reported clonic twitches associated with the defensive responses. Perhaps the more violent definition given to Zbrożyna's defense reaction reflects abnormal seizure conduction while the more subdued hissing and growling of Ferandez de Molina's defensive reaction more closely approximates normal amygdalo-hypothalamic interactions. It is also possible that both types of elicited defensive reactions are seizure artifacts of amygdala stimulation.

Although the direct elicitation of motor activity by normal amygdaloid activation seems doubtful, it does appear that an amygdalo-motor activity interaction does exist in regard to amygdaloid modulation of behavior patterns elicited from the hypothalamus or the cortex. Stimulating different sites in the amygdala either inhibits or facilitates hypothalamically elicited attack behavior (33, 34), facilitates hypothalamically elicited flight (154), and inhibits motor activity produced by stimulation of the motor cortex (167). Thus it appears that the amygdala is involved in the modulation of behavior patterns organized at the hypothalamic or cortical level but that the exact nature of this modulation and its localization within the amygdala are following the hypothesis of amygdaloid function posited by Gloor (48), i.e., all parts of the amygdala either increase, decrease, or have no effect.

The data just presented suggesting an amygdaloid involvement in rage-type behavior might also suggest that amygdaloid stimulation would be aversive. It again appears that different parts of the amygdala produce different effects that cannot be localized to a particular site within the amygdala. Delgado, Rosvold and Looney (28) found that footshock and medial amygdaloid stimulation were equivalent aversive stimuli in an escape task and Wilkinson and Peele (169) reported that stimulation of the amygdala was negatively reinforcing. On the other hand, amygdaloid self-stimulation can produce both very high response rates with electrodes in the basolateral area (119) or low response rates (127). Wurtz and Olds (175, 176) demonstrated that corticomedial amygdaloid stimulation was

moderately positively reinforcing while basolateral stimulation was highly negatively reinforcing, i.e. produced high rates of escape. But here again, these effects were not localized within specific areas of the amygdala. Both escape and self-stimulation could be demonstrated everywhere in the amygdala, sometimes in the same electrode. Once again, Gloor's hypothesis is supported.

Amygdaloid stimulation experiments have also implicated the amygdala in the control of food consumption and instrumental behavior reinforced by food. Although Delgado and Anand (27) and Goddard (51) did not find that amygdaloid stimulation altered food intake, nor did Goddard (51) observe disruption of food reinforced hehavior during amygdaloid stimulation, several other authors have reported that stimulation of the basolateral (40, 41, 43, 44, 94, 104) or of the corticomedial (39, 134, 170), or of the anterior (56) amygdala produces an immediate and clear cut inhibition of ongoing food consumption and a partial inhibition of alimentary reactions (134). Conversely, stimulation of the dorsomedial amygdala increases food intake (41). Amygdaloid stimulation also disrupts learned, operant (43, 44) and instrumental (104) responses in both food reinforcement and medial forebrain bundle stimulation self-reinforcement situations (71) while leaving avoidance responses unaffected (40, 43, 44).

These effects on operant and avoidance conditioning are in direct opposition to data presented by Ikeda (65) and Goddard (51) which showed that amygdaloid stimulation disrupted fear and avoidance conditioning while leaving food reinforced operant responding intact. Goddard (51, 52) concluded that stimulation of the amygdala prevented the consolidation of fear and of aversive stimuli by demonstrating a retrograde disruption of conditioned emotional response acquisition. But the data presented by others does not support this suggestion. Fonberg (40) noted that amygdaloid stimulation inhibited the fearful emotional behaviors associated with shock avoidance but had no effect on the avoidance response itself. Similarly Lidsky, Levine, Kreinick and Schwartzbaum (95) reported that amygdaloid stimulation did not produce retrograde disruption of conditioned emotional reponse acquisition. In fact, Fonberg and Delgado (43, 44) established a conditioned emotional response to a cue stimulus that preceeded amygdala stimulation, thus demonstrating a lack of retrograde disruption of behavior. Perhaps, as before, the insidious seizure phenomenon and the resulting production of a functional lesion in the amygdala is responsible for the discrepancies in these data. Ikeda (65), who, like Goddard (51), reported avoidance behavior to be disrupted by the amygdaloid stimulation, also reported amygdaloid seizure afterdischarges in his subjects. Pellegrino (125) who found that amygdaloid

stimulation by high frequency low amperage current impaired passive avoidance acquisition, also found the identical behavioral effect produced by ablation of the basolateral amygdala (126). Karli, Vergnes and Didier-georges (72) summarized data that indicate that amygdaloid lesions abolish mouse killing in rats. Vergnes and Karli (168) demonstrated an identical effect on mouse killing by stimulation of the amygdala, but only when the stimulation also caused seizures; subseizure stimulation of the amygdala had no effect. Thus any experiment investigating the effects of amygdaloid stimulation must prevent the confounding effect of seizure afterdischarges. The opposing data presented by Goddard (51) versus Fonberg (40) and Lidsky et al. (95), and the paradoxical data presented by Pellegrino (125, 126) can be reconciled by a parametric analysis of the manner in which the stimulation current affects the individual neurons, whether by constant hyperpolarization (109) or by seizure activity, both of which would inactivate the amygdala by producing a functional lesion. Many investigations have examined amygdaloid contributions to behavior by directly destroying amygdaloid neural tissue, observing various behavioral patterns following these intentional lesions of the amygdala, and then inferring the normal functions of the amygdala from the lesion-produced behavioral abnormalities.

THE BEHAVIORAL EFFECTS OF AMYGDALOID ABLATION

One of the most intriguing behavioral consequences of destruction of neural tissue is the syndrome produced by ablation of the infero-temporal lobes. Brown and Schaeffer (18) characterized a monkey with infero-temporal lobe ablation as having lost, in great measure intelligence and memory. This monkey repeatedly investigated the same objects over and over again and became very tame, hypoactive, and hyperphagic. These abnormal behaviors, described as psychic blindness, hyperorality, and hypersexuality by Klüver and Bucy (84, 85), became known as the Klüver–Bucy syndrome. Although psychic blindness, an emotional flattening, a loss of fear or a taming effect, and reduction in agressiveness are common results of temporal lobe and/or amygdaloid ablation (7, 45, 59, 101, 107, 110, 111, 128, 137, 139, 157, 167), Bard and his coworkers reported that temporal lobectomies or amygdala ablation increased agressiveness and rage (10–12). Green, Clemente and de Groot (55) also found increased aggressiveness after amygdaloid lesions but only if the lesion also produced seizure activity. Thus the insidious seizure phenomenon confounds research involving ablation of amygdaloid structures as well as research involving stimulation of the amygdala.

The hypersexuality following amygdaloid lesions is marked by a wide

increase in the range of sexual behavior–copulation is attempted with whatever is at hand. Hypersexuality has been produced in male and female cats (137–139), in male and female monkeys (79, 101), and in humans (159). Hypersexuality might have been present in the monkey described by Brown and Schaeffer (18) but the vernancular of Victorian England could give "uncontrollable passion on the approach of other monkeys" (p. 318) an interpretation other than hypersexuality. Schreiner and Kling (137, 138) demonstrated that the hypersexuality in cats could be abolished along with other Klüver–Bucy behaviors by lesions of the ventromedial hypothalamus. Hypersexuality could also be abolished in male cats and monkeys (80) by castration and could then be reinstanted by hormone replacements. On the other hand, hypersexuality was not found in rats (140, 160), in cats (157), in dogs (45) nor in man (59, 111). In fact, a number of reports could not demonstrate Klüver–Bucy behaviors of any kind following amygdala lesion (20, 59, 111, 157). A possible solution to the controversy concerning amygdaloid involvement in hypersexuality and other Klüver–Bucy behaviors was suggested by Green et al. (55) who produced hypersexuality by ablation of the piriform cortex, sparing the amygdala proper. This piriform hypersexuality was abolished by castration just as Klüver–Bucy hypersexuality was (138). The earlier experiments on the Klüver-Bucy syndrome typically ablated the entire infero-temporal lobe, removing the piriform and entorhinal cortices and the hippocampus as well as the amygdala. However the more recent experiments typically use an electrolytically produced lesion that can result in a very small, very precise area of destruction that can leave sizeable portions of a target as large as the amygdala intact and not disrupt normal functioning. Thus the lack of agreement on amygdaloid function is probably due as much to differing methodologies as to the ablation of several temporal lobe structures and the labelling of the resultant effects as reflecting amygdaloid functions.

The hyperorality aspect of the Klüver–Bucy syndrome suggests that the amygdala is normally involved with food consumatory behaviors. Much conflicting data indicate that amygdaloid lesions either reduce, augment, or have no effect on food intake. Anand and Brobeck (7) and Kemble and Beckman (74) found no change in food intake after amygdala lesions. Kling and Schwartz (82) and Kling (79) demonstrated that amygdaloid lesions in infant rats or cats have no effect on food intake, while similar lesions in post-weanling rats and adult cats produce severe anorexia. The anorexia, hypophagia or aphagia reported to follow amygdaloid ablation (19, 24, 55, 81, 82, 130, 140) occurs when the lesion includes or is restricted to the dorsomedial (41, 42) or corticomedial (149) amygdala. However, Morgane and Jacobs (105) conclude that amygdaloid

(sic) aphagia is really due to lesions in the globus pallidus, a structure lying just dorsal to the amygdala, while the amygdala itself normally inhibits food intake. If this is so, then ablation of the amygdala should remove this inhibitory influence producing hyperphagia. And it does (5, 18, 45, 88, 105, 106, 159, 171), but only when the ablation includes the basolateral nucleus (41, 55). Thus there is a functional division in the amygdala with respect to food consumption. As discussed earlier, stimulation of the basolateral amygdala inhibits and of the dorsomedial amygdala increases, food intake. Similarly, lesions of the basolateral amygdala increases and of the dorsomedial inhibits, food intake. Fonberg (41) noted that the reciprocal effects on food consumption of these two amygdaloid areas parallel the reciprocal effects on food consumption of the lateral and ventromedial hypothalamic areas. The role of the amygdala in food intake mechanisms have been reviewed by Morgane and Jacobs (105) and by Stevenson (153).

Another of the original Klüver–Bucy symptoms that can be considered as the prototype for subsequent investigations, is the taming, or emotional flattening, or fear reduction noted by Brown and Schaffer (18) and demonstrated in monkeys, cats, the Canadian lynx (139), dogs (45) and in man (59, 111). The taming or emotional flattening produced by amygdaloid lesions seems to reflect a decrease in the reaction to aversive stimuli. Not only do animals with amygdaloid lesions fail to react normally toward humans (and are therefore described as tamer) and other noxious stimuli (e.g., fire, 128) but the autonomic nervous system arousal (as measured by the galvanic skin response) is also decreased (63). Allikmets and Ditrikh (5) found that amygdaloid lesions decreased general emotionality in addition to increasing the level of electric shock necessary to elicit shock induced fighting in rats. A decrease in reactivity to painful stimuli following lesions of the amygdala was also noted by Goldstein (54) for electric shock in rats and Jelasic (67) for trigeminal neuralgia in man. But these experiments need not be interpreted only as demonstrating a reduction in pain thresholds after amygdaloid lesions. Other data (22, 133) suggest that rats with amygdaloid lesions have a tendency to crouch in response to electric footshock, thus making shock induced fighting unlikely and spuriously suggesting a lack of pain. In fact, Nakao (110) reported no change in reactivity to painful stimuli or in shock escape performance following amygdaloid lesions. Nor did Ursin (163) observe disruption of escape behavior even though lesions of the amygdala did impair avoidance responding, suggesting that amygdaloid lesions disrupt the behavioral response to fear and not just to pain.

Many experiments have investigated the effects of amygdaloid lesions on fear motivated (i.e., avoidance) behaviors with little agreement in

the resulting data. Allen (3) reported no effects of amygdaloid lesions on olfactory discriminated avoidance conditioning while an internally cued go–no go avoidance task was disrupted. Although Brady, Schreiner, Geller and Kling (15) and Weiskrantz (167) found that amygdaloid lesions disrupt the acquisition, but not the retention, of two-way shuttle box avoidance, Kling (77) and Allikmets and Ditrikh (5) could not find amygdaloid lesion impairment of a two-way avoidance task. In fact, Kemble and Beckman (73) reported that amygdaloid lesions facilitate the acquisition of two-way avoidance by reducing the reluctance of the subjects to reenter the compartment in which they had just been shocked (i.e., a passive avoidance deficit). Impairment of passive avoidance behavior following amygdaloid lesions also has been demonstrated by Ursin (163) and Suboski, Marquis, Black and Platenius (156). Pellegrino (126) found passive avoidance deficits in rats to follow lesions of the basolateral amygdala while Horvath (64) showed that basolateral amygdaloid lesions in cats had no effect on passive avoidance. The conflicting data presented by Horvath (64) and Pellegrino (126) probably represent a species difference in neuroanatomical structures. When the passive avoidance component is removed from two-way avoidance making the task one-way avoidance, then amygdaloid lesions do seem to disrupt the avoidance behavior (53, 64, 103, 163). Thus amygdaloid lesions may produce the taming effect by impairing the behavioral responses to fear.

Another explanation for the taming effect of amygdaloid lesions is a reduction in reactivity to all types of stimulus change, and not just to aversive stimuli, perhaps by interfering with the integration of the internal representation of stimulus changes into new behavior patterns. Although the amygdala receives input from all sensory modalities, an intact amygdala is not necessary for the adequate processing of simple external sensory information. Amygdaloid lesions do not alter the acquisition or the retention of simple discrimination tasks in olfactory, visual, auditory, or tactile modalities (3, 78, 101, 128, 144, 151, 163). Nor does amygdaloid ablation interfere with rather complex spacial alterations, go–no go discriminations, and reversals (126) or sequential discrimination (14) as long as the correct response is cued or indicated by an external environmental stimulus. However these same tasks without the external cue, and other tasks depending on internally produced cues to guide behavior such as discrimination reversals, (146), timing behavior, (126, 130) and learning set problems, (14) are disrupted by amygdaloid lesions. Pellegrino (126) demonstrated that lesions of the basolateral but not corticomedial amygdala were responsible for the disruption of the internally cued inhibition of behavior required on a timing task (DRL-20).

That this disruption is due to more than simple memory deficits is demonstrated by the lack of effect of amygdaloid lesions on delayed response tasks (100, 122, 128). But when the delayed response is made slightly more complex by requiring the animal to respond differentially relative to his previous behavior, then amygdaloid lesion deficits are observed. Fuller et al. (45) added a discrimination requirement to the delayed response and observed amygdaloid lesion deficits both in retention and in relearning. Although Orbach et al. (122) and Mahut and Cordeau (100) did not find disruption of delayed response, they did find amygdaloid lesion disruption of delayed alternation responding. Pellegrino (126) reported deficits in non-signalled bar press alternation following basolateral amygdaloid lesions. Even the acquisition of simple position discrimination in a T-maze (e.g., left turn) and the reversal of this discrimination are disrupted by lesions of the amygdala (74). Thus, when the correct behavior depends upon altering an old response based on the reinforcement contingencies associated with that response, animals with amygdaloid lesions have difficulty acquiring the new behavior. But the correct behavior pattern for all of these tasks involve the elimination of non-rewarded responses.

Amygdaloid ablation also reduces the response supression effects of nonreward. Animals with amygdaloid lesions make more bar presses during the nonreward discriminative stimulus in a two tone auditory discrimination operant conditioning task (147), make more nonrewarded presses on timing tasks (FI-30, Pubols (130); DRL-20, Pellegrino (126)), and keep responding longer in extinction (75). Since nonreward and electric shock are both aversive events (91), the reduction by amygdaloid lesions in the response suppression effects of nonreward may be considered a passive avoidance deficit as was discussed above for electric shock. If the amygdala is involved in reactivity to aversive nonreward, then amygdaloid lesions should disrupt the behavioral reaction to reduction in the magnitude of reward. Amygdaloid lesions do attenuate the response rate decrement following quantitative (144) or qualitative (76) reduction in reward, or habituation (143, 148). However amygdaloid lesions also attenuate the response rate increase following quantitative (141), or qualitative (130, 142) or deprivation induced (145) increases in the magnitude of reward. While the former effect of amygdaloid lesions might be considered as an extention of the passive avoidance deficit for aversive stimuli, the latter cannot. Nor can the demonstration by Kemble and Beckman (73) that amygdaloid lesions disrupt the behavioral response to changes in the magnitude of negative reinforcement. The attenuating effect of ablations of the amygdala on the behavioral reaction to making a positive reinforcement more positive or a negative rein-

forcement more negative, require a hypothesis concerning reactivity to stimulus change. However, the amygdaloid lesion deficit is not just a disruption of attention processes as suggested by Klüver and Bucy (85), but rather a disruption of the incorporation of internal representations of cue stimuli into new behavior patterns.

A RESTRICTED THEORETICAL VIEW OF THE AMYGDALA

Hilpert (61) suggested that the amygdala, as part of the visceral brain system, was involved with the excitation and mediation of general reactivity and defensive movements. Papez (123, 124) and MacLean (97) posited a visceral brain function for the limbic system in which the amygdala had a parasympathetic modulating effect on feeding, digestion, elimination, and sleep. In addition to connections with the sciatic and vagus nerves, the amygdala also receives input from all sense modalities (96). Therefore the amygdala has the neural connections to play a role in the modulation of visceral activities by acting as a nonspecific gating system for autonomic nervous system functioning as suggested by Barratt (13) as well as in the modulation of all sensory data. Domino and Ueki (30) and McLennan and Graystone (102) recorded strong 20 to 40 Hz electrical activity bursts from the amygdala. Although Domino and Ueki (30) concluded that the 40 Hz burst was due entirely to respiration, McLennan and Graystone (102), recording from the olfactory bulbs as well as from the amygdala, noticed that the 40 Hz burst started in the amygdala and spread to the olfactory bulbs. McLennan and Graystone concluded that this electrical activity represented an amygdaloid gating mechanism scanning the olfactory bulbs for relevant sensory data. However there is no reason to doubt that the amygdala scans the other sensory modalities too.

Weiskrantz (169) observed that animals with amygdaloid lesions have difficulty in identifying reinforcing stimuli, thus suggesting that the normal function of the amygdala is involved in the interpretation and integration of reinforcing stimuli. Douglas (31) created a functional model of the limbic system in which the amygdala acted as a reinforcement register, guiding behavior based on the occurrence of positive reinforcement. The involvement of the amygdala in the processing of information associated with reward was demonstrated electrophysiologically by Norton (117) who reported an increase in the amplitude of the electrical activity of the amygdala following rewarded bar presses by rats but not following nonrewarded responses. Lesse (92, 93) found that the electrical activity of the amygdala of cats assumed a high amplitude 40 to 45 Hz waveform following any attentive response to excitant stimuli, either

positive (food, a mouse) or negative (a dog, electric shock). In fact the shift to 40 to 45 Hz can be classically conditioned to a buzzer by pairing the buzzer with electric shock. After many trials of presenting the buzzer alone, the ability of the buzzer to elicit 40 to 45 Hz extinguishes. Goddard (52) considered the amygdala to be of importance in the association of fear and avoidance behavior with previously neutral stimuli. O'Keefe and Bouma (118) demonstrated that certain neural units in the amygdala of cats respond only to a specific complex sensory pattern, such as hearing the song of a bird or seeing a black mouse, and that there was no change in this response with changes in alertness of the cat nor during habituation trials. This specificity of amygdaloid action was also suggested by Summers and Kaelber (157) who found none of the usual effects of amygdaloid lesions, except that their cats became indifferent to a mouse. Some of the amygdaloid units monitored by O'Keefe and Bouma (118) remained active for a while after the stimulus object (the black mouse) had been removed thus suggesting that the amygdala maintains the neural response to a complex stimulus pattern in the absence of the stimulus. Not only do these findings support the involvement of the amygdala in the internal representation and manipulation of stimuli as suggested by the lesion experiments discussed above, but these findings also suggest an amygdaloid involvement in instinctive food getting (118) and defensive (92, 93) behaviors.

The effects of amygdaloid stimulation or ablation on food intake and avoidance conditioning also support the hypothesized involvement of the amygdala in instinctive survival behaviors. Karli et al. (72) reported that amygdaloid lesions abolish mouse killing in rats and Cherkes (24) demonstrated that cats with amygdaloid lesions no longer attack a mouse or a bird. Cherkes suggested that the amygdala is involved in the emotional aspect, the urgent mobilization, necessary for instinctual survival and prey-killing behaviors. Amygdaloid lesions completely abolish the prey killing behaviors by eliminating the mechanism for urgent mobilization while the same lesions in the same cat only slightly disrupt instrumental food getting behaviors because the emotional urgent mobilization is not a necessary component of eating laboratory chow from a dish. The disruption of instinctive defensive behaviors by amygdaloid lesions is manifested in deficits in the avoidance of aversive stimuli, either electric shock or nonreward as was discussed earlier. In the laboratory experiment, it is perhaps difficult to envision the threat to survival posed by an avoidance deficit, but this is vividly demonstrated in a natural environment. Dicks, Myers and Kling (29) trapped five monkeys from bands of free-ranging monkeys maintained on an island colony, gave four monkeys amygdaloid lesions and one a sham operation, and

released them again after a postoperative recovery period. The major behavioral effect of the amygdaloid lesions was reported as a social indifference and a lack of foresight. Inasmuch as a lack of foresight may be considered to be an avoidance deficit, then the major effect of the amygdaloid lesions was an avoidance deficit. The four monkeys with amygdaloid lesions were found dead shortly after release while the sham operated monkey continued as before. Thus it appears that the amygdala is involved with the successful behavioral adaptation to the positive and negative emotional aspects of various reinforcement contingencies, and exerts this influence via the extensive connections that the amygdala has with hypothalamic centers for emotional and homeostatic mechanisms.

Much appreciation is extended to Dr. Richard E. Musty for continuing intellectual stimulation and the critical evaluation of early drafts of this manuscript. The stenographic contributions of Miss Joann Golden and Miss Margret McGrenna are gratefully acknowledged.

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Received 15 November 1972

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