histone types can be closely correlated with the state of differentiation, and must produce major rearrangement of histone molecules within the chromosomes. In this instance, the changes in histones may be employed in a special differentiation process, perhaps taking place within the chromosomes to produce their condensed state in the mature sperm. Even so, the replacement of histones on this major scale probably lacks the genetic specificity which differentiation often displays. Such specificity may lie in mechanisms which precisely control the position of histones upon the chromosomes without regard to the relative amount of the histones (*5*, *6*).

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Interaction of Evoked Potentials of Neocortical and Hypothalamic Origin in the Amygdala

Abstract. *Evoked responses recorded from the amygdala of the cat after sequentially pairing neocortical and hypothalamic stimulation showed consistent suppression or depression of the response evoked by the test shocks, regardless of whether the cortical or subcortical site received the preceding conditioning shock. The possibility that functional interaction of neocortical and hypothalamic signals occurs in the amygdala is proved and an active inhibitory process is suggested.*

Much work on relationships between the brain and behavior in higher organisms has been focused on the interactions of the limbic system with other structures of the central nervous system. Anatomical and physiological evidence indicates close ties between the limbic system and the hypothalamus and, also, the neocortex. Hypothetically, limbic structures, such as the amygdala, can be viewed as correlating specific neocortical functions with motivational processes of hypothalamic origin (*1*). Neurophysiological details of such an interrelation at the neurophysiological level remain unspecified. The pilot experiments reported here were undertaken to define some of the neurophysiological variables involved in cortico-limbico-hypothalamic interactions.

In a series of 12 cats under chloralose anesthesia the cortex was stimulated through a pair of silver ball electrodes and concentric, stainless-steel electrodes were introduced stereotaxically to stimulate the hypothalamus and other sub-cortical structures. In the first experiments, stimulating electrodes were placed in the preoptic area and anterior hypothalamus and on the surface of the posterior ectosylvian gyrus, the homologue of the first temporal convolution of the primate brain (*2*). A bipolar recording electrode was placed in the lateral nucleus of the amygdala near its juncture with the corticomedial nuclei [F:12, L5, H-6 according to the atlas of Jasper and Ajmone-Marsan (*3*)]. A typical recording electrode site is shown in the photomicrograph of Fig. 1.

Monopolar and bipolar oscilloscopic recordings were made of responses in the amygdala to cortical and subcortical stimulation. Brief rectangular stimuli with a pulse duration of 1 msec were delivered at an intensity just sufficient to evoke reproducible waveforms at the recording electrode. Cortical stimulation elicited a complex triphasic response consisting of a high voltage (400 to 500 μv) 5- to 10-msec sharp potential with a latency of approximately 10 msec, followed by a slow wave of 40 to 70 msec duration appearing about 50 msec after stimulation; occasionally, tertiary waves were observed. Amygdaloid responses to preoptic and anterior hypothalamic stimulation consisted of a broad, 50 to 100 μv, slow wave commencing 20 to 25 msec after stimulation and, occasionally, included a high voltage short-duration component manifest at the crest of the slow wave. Representative traces are shown in Figs. 2 and 3.

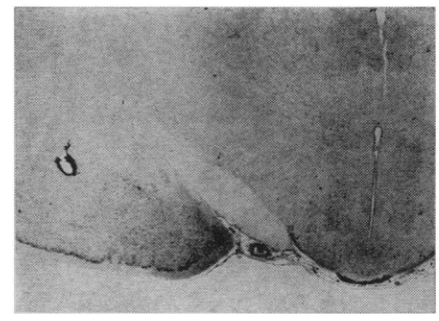

Fig. 1. Photomicrograph of a histological section through the amygdala showing a characteristic recording site represented by a small circular lesion within the substance of the amygdala (Nissl stain).

When sequential stimuli were delivered to both ectosylvian cortex and hypothalamus, the response to the second, or test stimulus, was regularly abolished or attentuated for periods up to 150 msec (Fig. 2). Abolition or attenuation of the response invariably resulted, whether the initial or conditioning stimulation was cortical or hypothalamic. The influence of the conditioning cortical stimulus was somewhat more profound and enduring than that of the test stimulus, but when complete blocking of the high-voltage response to cortical stimulation by prior hypothalamic stimulation occurred, it was no less dramatic.

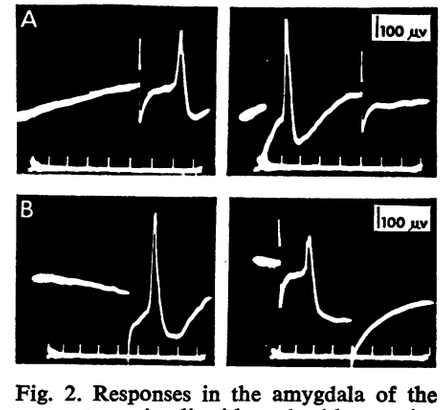

Fig. 2. Responses in the amygdala of the cat to test stimuli with and without prior conditioning stimulation. *A*, Stimulation of the anterior hypothalamus alone and preceded by stimulation of the posterior ectosylvian gyrus with an interval of 50 msec. *B*, Stimulation of the ectosylvian gyrus alone and preceded by stimulation of the anterior hypothalamus with an interval of 40 msec. Bipolar recordings, time scale, 10 msec; calibration, 100 μv.

Even when occasionally the amygdaloid responses to hypothalamic stimulation were not obvious in the record, responses to test stimulation of the ectosylvian cortex were still markedly reduced. On the other hand, when high voltage components were present in the response to hypothalamic stimulation, the period of test response attenuation was extended, in one instance for as long as 500 msec.

Two questions arose immediately: What physiological mechanism is involved? Is the observed attenuation specific for the areas tested? When the cortex or hypothalamus was stimulated at intervals of less than 20 msec, attenuation of test responses did not occur, nor was there any evidence of response facilitation; stimuli spaced further apart still attenuated the test responses in the same preparation (Fig. 3). This was taken as evidence that the recording substrate was not rendered refractory by the conditioning stimulus, and that the mechanism of response blocking was not passive occlusion. Active inhibition is probably involved.

Similar phenomena could be elicited from a wide variety of stimulated cortical and subcortical sites. Stimulation of the posterior hypothalamus, dorsal hippocampus, and caudate nucleus attenuated amygdaloid responses to ectosylvian cortex stimulation; the same effect was obtained when two different cortical sites were employed for conditioning and test stimulation. Whenever the amygdaloid-evoked response appeared, it interacted reciprocally with the response from another cortical source and the interaction resulted in attenuation of the test response.

When a specific cortical placement was stimulated repeatedly, it was observed that the early responses of short duration could not be sustained at rates greater than 4 to 5 per second. Coincident with this failure of the early high-voltage component, the secondary slow wave of the response became more prominent and seemed to have an earlier onset. Whether the short-duration component prevented the early appearance of the slow wave or whether the true waveform of the slow component was unmasked by the elimination of the high voltage potential, remains uncertain. Upon occasion, unpaired cortical stimulation also failed to produce a high voltage potential, and similar displacement of the slow waves was observed.

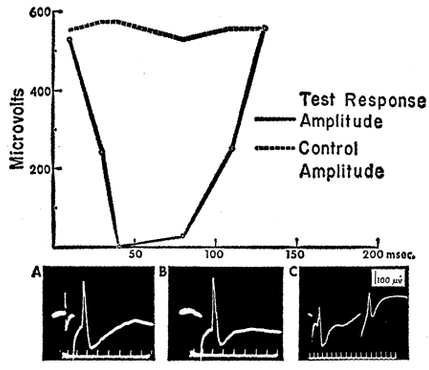

Fig. 3. Excitability cycle in amygdala following anterior hypothalamic stimulation, when tested with responses elicited by stimulations to the posterior ectosylvian cortex (graph). *A*, *B*, and *C* records taken from same animal. *A*, Stimulation of anterior hypothalamus followed after 10 msec by stimulation of posterior ectosylvian cortex: no inhibition of test response. *B*, Stimulation of the same cortical site alone: control response. *C*, Stimulation of the anterior hypothalamus followed after 110 msec by stimulation of posterior ectosylvian cortex: partial recovery of test response. Time scale, 10 msec; calibration, 100 μv. (Note the sweep speed reduced in *C*).

The placement of the recording electrode is apparently of some significance. While investigations of this parameter have not been completed, it was apparent that slight changes in the position of the recording electrode in the amygdala definitely altered the evoked response.

These observations confirm first, that impulses generated at neocortical and hypothalamic sites converge in the amygdala and, second, that the evoked responses elicited in this structure mutually interact. In our experiments, this interaction exclusively resulted in attenuation of the test response, suggesting that cortical and hypothalamic impulses are mutually linked to cause inhibition in the amygdala.

The technique of paired stimulation at diverse locations has been used before, with the reticular formation (*4*), for example, to study interactions of diverse sensory inputs. More recently, Albe-Fessard and Gillet (*5*) have investigated interactions in the thalamic center median nucleus of responses to paired peripheral and cortical stimuli. Their experimental design was similar to ours, and they also reported that ubiquitous attenuation occurred even when the conditioning stimuli produced no observable responses in macroelectrode recordings. These workers also suggested that active inhibition is responsible for the attenuation rather than passive occlusion or refractoriness. However, refractoriness of possible intervening structures or long pathways may be concerned in this effect.

The question may be raised as to whether the use of chloralose as an anesthetic may be an important factor in explaining the long-lasting mutual inhibition. Recent evidence cited by Albe-Fessard (*6*) however, makes it highly unlikely that chloralose anesthesia is a significant factor in this effect. The similarity of our results to those of Albe-Fessard and Gillet (*5*), raises the question of whether we are dealing here with two instances of a more general neurophysiological mechanism. Whether or not this is so, our observations demonstrate that at least one limbic structure, the amygdala, provides for the mutual interaction of neocortical and hypothalamic activity. An extension of investigations to other limbic areas should permit a more precise interpretation of our findings.

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