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FRONTOCLAUSTRAL INTERRELATIONS IN CATS AND DOGS

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Abstract. In 13 cats and 5 dogs various parts of the frontal lobe were removed. As a result terminal degenerations in the rostral quarter of the insular claustrum were found by Nauta and Fink-Heimer II methods. In cats with motor cortex lesions, the degenerations were localized more dorsally than in cats with removals of the frontoorbital cortex, but there is a large overlap between degenerating areas of the claustrum in both groups of animals. In the dog it even seems possible to differentiate claustral regions in which axons from various gyri of the frontal lobe mainly terminate. It was found under the electron microscope that degeneration affects asymmetrical axodendritic synapses which make contacts with small dendritic branches. Comparing these results with severe cellular degenerations found in the claustrum following large neocortical removals it seems that the rostral part of the claustrum is abundantly interconnected with the frontal cortex and interrelations between the frontal granular cortex and claustrum may be considered as close. There are two hypotheses concerning frontoclaustral relations: either the rostral pole of the claustrum belongs, like the dorsomedial nucleus of the thalamus mainly to the frontopetal ascending system which has frontoclaustral feedback connections or it is incorporated into a descending system through which the frontal cortex controls the functions of other subcortical structures.

Theories explaining the functions of the frontal granular cortex are supported by a vast experimental material of various cortical removals. But symptoms of the frontal cortex removal and their intensity depend not only on the localization and size of lesion but also on the integrity of other cortical and subcortical centers interconnected with the frontal lobe.

The role of these subcortical structures in the normal function of the frontal cortex had long been underestimated until stereotaxic lesions in the dorsomedial nucleus of the thalamus and in the head of the caudate nucleus as well as electrophysiological data stressed the importance of these structures for the activity of the frontal lobe neurons.

During the last few years we have paid special attention to connections of the claustrum with various neocortical regions (Narkiewicz 1964, 1966, Chadzypanagiotis and Narkiewicz 1971). It was found in agreement with some other authors (Mettler 1935, 1947, Nauta 1962, De Vito and Smith 1964, Druga 1966) that the claustrum is largely connected with the frontal cortex. We tried to explain characteristics of these connections as a basis for further research on the claustrum as a structure which may influence activity of the frontal lobe.

Our experimental material consisted of 13 cat's brains with various frontal cortex lesions. After perfusion with a 10% formalin mixture 10 brains were prepared by Nauta (1957) and Fink–Heimer II (1967) methods; survival time of animals 5–7 days after surgery. Three brains prepared for electron-microscopic examination were fixed with glutaraldehyde-osmium mixture and post-fixed in 2% osmium tetroxide. Ultrathin sections were stained with lead citrate and uranyl acetate.

Additionally brains of five dogs with frontal lobe lesions were used to study the more detailed topology of frontoclaustral connections. After 7 days of survival the brains were perfused with a 10% formalin solution and then treated by Nauta (1957) and Fink-Heimer II (1967) techniques.

The frontoorbital cortex of the cat which is probably a homologue of the primate frontal granular cortex occupies mainly the proreal gyrus. Its general structure is well known and will not be discussed here.

Certain general characteristicts of the cat's claustrum, however, require brief mention. The claustrum of the cat is a rather large structure

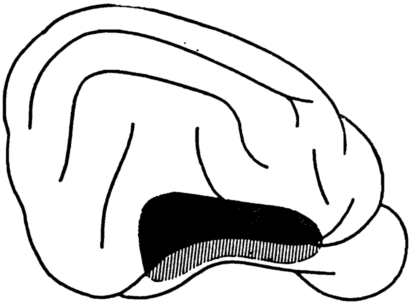

Fig. 1

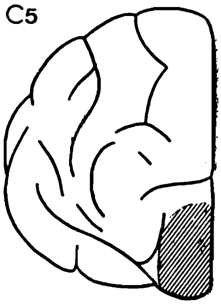

Fig. 2

Fig. 1. Outline of the claustrum projected on the lateral aspect of the brain of the cat. Crosshatches mark claustrum insulare; vertical lines, claustrum prepiriforme.

Fig. 2. Extent of cortical lesion confined mostly to the frontoorbital cortex.

the rostral pole of which lies in front of the presylvian sulcus (Fig. 1). The claustrum underlies the neocortex as well as paleocortex in the neighborhood of the rhinal sulcus. Its upper portion lying in close contact with the insular cortex is known as the insular claustrum. The lower part underlying the prepiriform cortex is designated the prepiriform claustrum.

On transverse sections (Fig. 3, 5) through its central portion the insular claustrum is rather triangular in shape. Rostrally the insular claustrum becomes thinner and forms a strongly curved band which runs from the dorsolateral ventromedially.

The basic material prepared for the study of terminal degeneration in the claustrum was subdivided into three groups.

In the first group (five cats) lesions were confined strictly to the frontoorbital cortex of the proreal gyrus (Fig. 2). The removals affected the convexity of the hemisphere as well as its medial surface up to the rostral limit of the cingular cortex (according to Rose and Woolsey 1948). The animals were sacrificed 3–5 days after surgery.

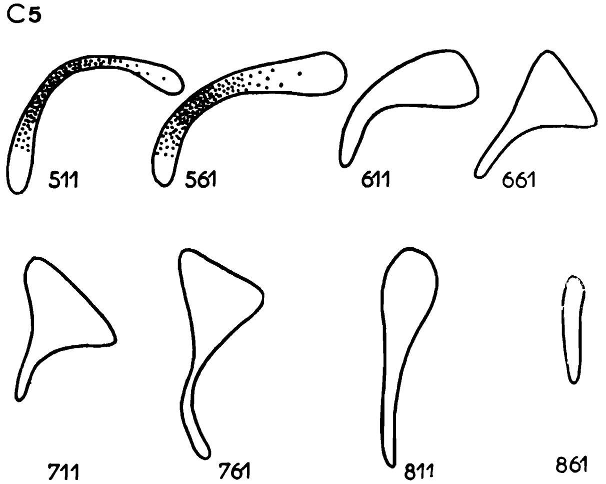

Fig. 3. Outline drawings of the insular claustrum in frontal sections showing location of terminal degenerations in cat 5. The drawing at upper left shows the most rostral section, the one at lower right — the most caudal one.

The degenerating corticofugal fibers enter the insular claustrum either sagittally from the white substance surrounding the rostral pole of the claustrum or from the external capsule. The rostrocaudal extent of the area in which the degenerated frontofugal fibers are present does not appear to extend over the rostral quarter of the claustrum[1] and is

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[1] For simplicity the term claustrum is used here instead of claustrum insulare as only this part is connected with the neocortex.

confined mainly to its rostral pole (Fig. 3). The degenerating structures are irregularly scattered in the clastrum suggesting that it is a true terminal degeneration (Fig. 7). Some more regular fibers are seen running through the medial zone of the claustrum on the border of the external capsule.

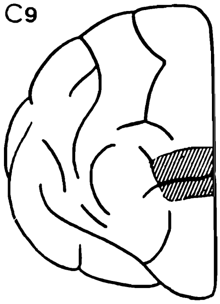

Fig. 4. Extent of cortical lesion confined mainly to motor and promotor cortex.

The second group of animals consisted of five cats with lesions the motor cortex (Fig. 4) encroaching in some cases on the frontoorbital and sensory areas.

As a result of these lesions terminal degenerations in the rostral quarter of the claustrum also appeared. But they were localized more dorsally then in those cats with removals of the frontoorbital cortex (Fig. 5). It must be stressed that there is quite a large overlap between degenerating areas of claustrum in both groups of animals.

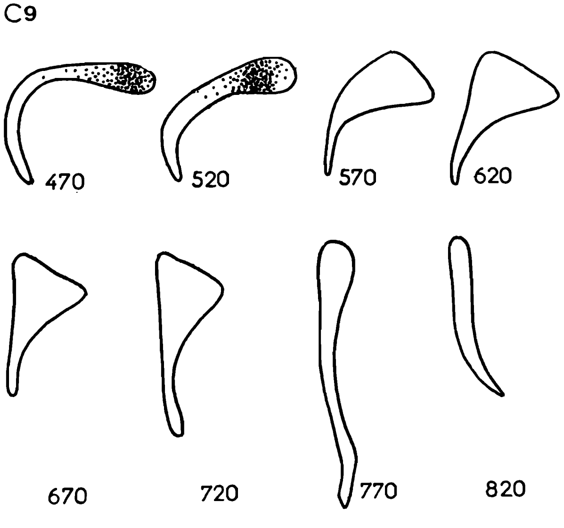

Fig. 5. Outline drawing of the insular claustrum in frontal sections showing extent and location of degenerative changes in cat 9. Legend as in Fig. 3.

To make sure that degenerations found in the claustrum by the Nauta method are terminal ones we used electron-microscopy. Our experimental material consisting of three cats with cortical lesions showed degeneration of the axon terminals in the appropriate portion of the claustrum. 3–5 days after the lesions many synaptic boutons had undergone changes. A marked increase in electron density of their axoplasm, loss of synaptic vesicles and swelling as well as fragmentation of mitochondria were found (Fig. 8*AB*). In the early stages of degeneration the synaptic vesicles of many boutons are still visible but their size usually varies. Later shrinkage and distortion of the synaptic boutons become pronounced and swollen processes of astroglial cytoplasm surround the degenerating terminals (Fig. 8*A*).

Degeneration affects the asymmetrical axodendritic synapses which make contacts with small dendritic branches and spines although sometimes also with the larger dendrites. These findings seem to prove that frontoclaustral connections do exist and that they are mostly if not exclusively axodendritic of an asymmetrical type which according to Gray's hypothesis may suggest that they are excitatory (Gray 1959).

These observations in the brains of cats imply that the frontoorbital and motor cortex have different although largely overlapping representation in the claustrum. Due to the comparatively small size of the proreal gyrus of the cat it is difficult on the basis of the above material to decide whether there is a topology of these connections inside the frontoorbital cortex. Therefore dogs — animals with a large frontal cortex subdivided into clearly demarcated gyri were used.

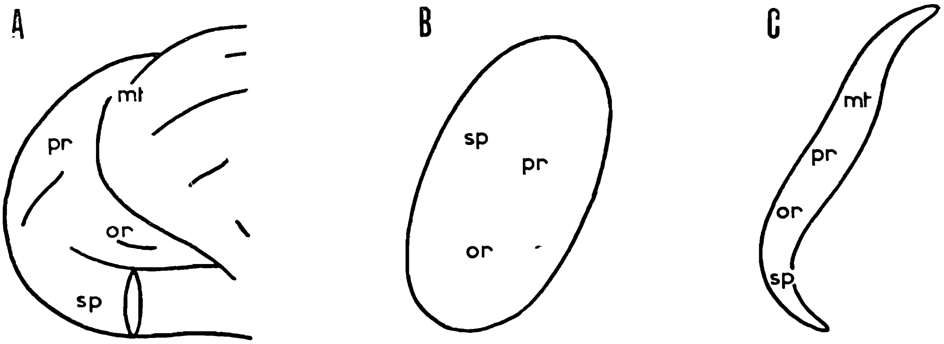

Fig. 6. Diagrams showing representation of various gyri of the dog's frontal lobe, in the dorsomedial thalamic nucleus and in the claustrum. *A*: *l*ateral aspect of the frontal lobe. mt, motor cortex; or, gyrus orbitalis; pr, gyrus proreus; sp. gyrus subproreus. *B*: transverse section through the central part of the dorsomedial thalamic nucleus with location of degenerations following removals of various frontal gyri. *C*: transverse section through the rostral part of the claustrum showing the areas of the heaviest terminal degenerations following removals of the various parts of the frontal lobe.

There are three main gyri in the frontal lobe of the dog: the proreal, orbital and subproreal (Fig. 6*A*) (Kreiner 1961). The proreal gyrus lies dorsally both on the lateral and medial aspects of the frontal lobe. The orbital gyrus forms the intermediate portion of the convexity. The subproreal gyrus, covered laterally by the olfactory bulb and olfactory peduncle — the ventral portion of the lobe.

All three gyri as well as the pregenual area situated on the medial surface of the hemisphere belong to the so-called frontoorbital, prefrontal, or from a comparative point of view to the frontal granular cortex. The posterolateral portion of the proreal gyrus is concealed within the depth of the presylvian sulcus which may be considered with some reservation as the posterior limit of the frontoorbital cortex. All these gyri receive projections from the dorsomedial thalamic nucleus (Narkiewicz and Brutkowski 1967). There are topographical relations between various portions of the dorsomedial nucleus and gyri of the frontoorbital cortex in the dog (Fig. 6*AB*).

The more medially situated parts of the dorsomedial thalamic nucleus project to the subproreal gyrus, the lateral — to the proreal and the ventral — to the orbital. Moreover, the more posterior to the rostral pole a given frontal area is located, the more peripherally it is represented in the dorsomedial nucleus of the thalamus.

From a comparative point of view it is important that the medial part of the dog's dorsomedial thalamic nucleus which in some respects is comparable to the magnocellular part of the dorsomedial nucleus of the macaca monkey, projects mainly to the subproreal gyrus and to the ventral part of the orbital gyrus. It suggests that in the dog the above mentioned portions of the frontal cortex are to some degree homologous to the orbital gyri of the frontal lobe of macaca (Narkiewicz et al. 1968).

The structure of the dog's claustrum is similar to that of the cat with perhaps one important difference, namely, that its rostral portion which is connected with the frontal lobe seems to be larger in the dog. We tried to ascertain whether in this rostral portion there is a topographical organization of the frontoclaustral connections similar to that found in the dorsomedial thalamic nucleus.

Our experimental material consisting of five dogs' brains with various frontal lesions is not sufficient to permit making a decisive statement in this respect. But it would seem that in spite of the overlap which in the claustrum is much clearer than in the thalamus, it is possible to differentiate claustral regions in which axons from various gyri of the frontal lobe mainly terminate (Fig. 6*C*). It seems that the subproreal gyrus is represented ventrally, close to the prepirifirm claustrum while areas receiving fibers from the orbital and proreal gyrus are situated

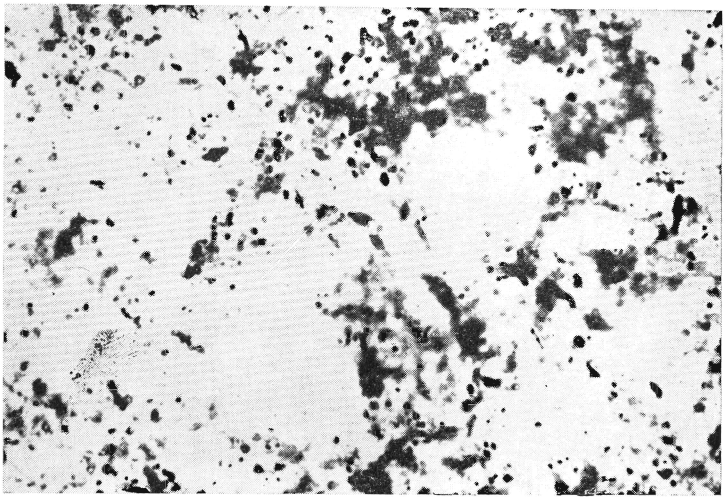

Fig. 7. Terminal degenerations in the rostral pole of the claustrum following frontoorbital cortex removal. Fink–Heimer II. × 780.

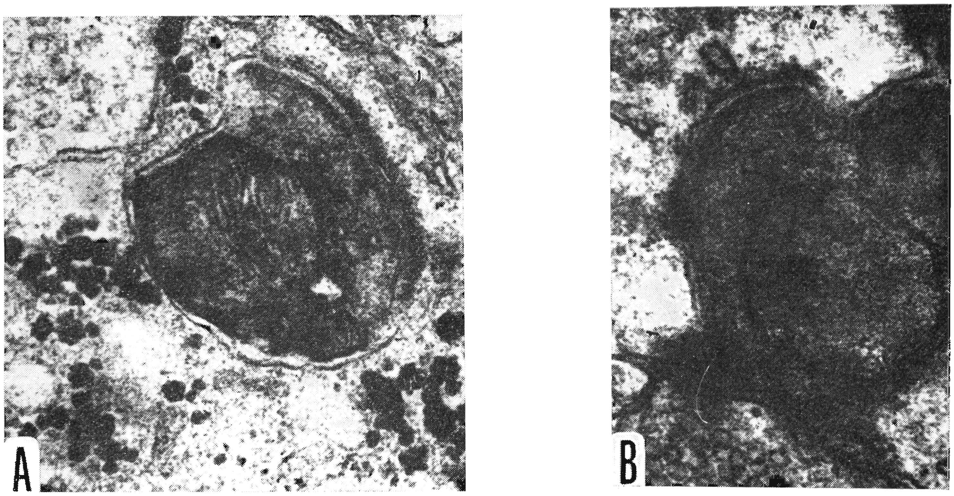

Fig. 8. Electron-micrographs of degenerating axon terminals ending by means of asymmetrical synaptic contacts on dendrites of claustral neurons. *A*: a dark degenerating terminal which appears to be surrounded by the astrocyte; a mitochondrium inside the terminal and some synaptic vesicles are still preserved. *B:* a dark degenerating terminal with complete loss of synaptic vesicles; inside the terminal a distorted mitochondrium is still visible. 6 days survival. × 57,000.

more dorsally. The motor cortex projects to the dorsolateral margin of the claustrum.

It must be stressed that these results are not conclusive owing to the small number of experimental animals. But it is highly probable that there is quite a definite topology inside the frontoclaustral connections.

The topology of the frontoclaustral connections agrees in general with our previous results. As found by Carman et al. (1964) and by us (Narkiewicz 1964) the claustrum, like the striatum and thalamus, is connected with the whole or almost the whole neocortex. The arrangement of these connections may be described as follows: the anterior cortical areas are connected with the anterior parts of the claustrum and the posterior areas of the cortex with the posterior claustral regions.

Taking into account only those results obtained by both the silver impregnation and electron-microscopy methods it may be supposed that the frontal cortex is connected with the claustrum exclusively by corticofugal axons. But other data suggest that there are also claustrocortical, ascending axons which are perhaps no less important than the descending ones.

As shown by our experimental material with a longer survival time the removal of large neocortical regions causes severe degeneration of corresponding claustral cells. The localization of these cellular degenerations is similar to those found by silver impregnation methods.

The question arises as to whether degenerations of the claustral neurons are transsynaptic or retrograde. They can conceivably be the result of anterograde transsynaptic changes if the input to the degenerating sector of the claustrum is supplied almost exclusively by the corticofugal fibers. This hypothesis cannot be excluded. But degeneration of claustral neurons after neocortical removal is very severe. There are extensive changes with loss of neurons and marked gliosis. With a longer survival time removal leads to severe devastation of the claustrum (Chadzypanagiotis and Narkiewicz 1971). Such changes in adult animals are typical not for transsynaptic but rather for retrograde degenerations.

In this respect the rostral pole of the claustrum is similar to the dorsomedial thalamic nucleus. After removals of the neocortex, including the frontal lobe, both structures show severe cellular degenerations. In both degenerations have been found in silver impregnated specimens and under electron microscope, and the two structures probably have descending as well as ascending connections with the frontal lobe.

Another similarity between the claustrum and thalamic nuclei is that cortical connections of both structures are more or less topically organized — more precisely in the thalamus, less so within the claustrum.

These similarities suggest that the rostral pole of the claustrum like the dorsomedial thalamic nucleus may be a structure incorporated into afferent systems of the frontal lobe whereas descending frontoclaustral connections may form a feedback mechanism which controls functions of both subcortical nuclei. In this respect it is interesting to compare cortical connections of the claustrum and thalamus with those of the striatum.

A very accurate correspondence between cortical areas and parts of the striatum was described for the rat (Webster 1961), rabbit (Carman et al. 1964) and cat (Webster 1965). Nauta (1964) found that in the monkey the laterodorsal frontal cortex projects to the anterodorsal part of the caudate nucleus and the frontoorbital cortex to the ventrolateral part.

These results suggest that in spite of an absence of cytoarchitectonic difference the striatum is topically organized and that each cortical region including the frontal granular cortex has a corresponding area in the striatum. In this respect the localization in the striatum seems to be defined by its cortical input (Divac 1968).

Though the striatum receives a large input from the cortex and especially from the frontal lobe its cells contrary to neurons of the claustrum and specific thalamic nuclei show a great independence of the neocortex. Even very extensive cortical removals do not cause any visible changes in structure and size of striatal cells (Burandt et al. 1961).

The independence of the striatal cells is probably due to the lack or lesser importance of striatocortical connections. Most authors studying this problem (Voneida 1960, Szabo 1962) tend to deny their existence. Some, especially those who use the thiocholine histochemical method for AChE (Krnjević and Silver 1965) suppose that there are specific cholinergic systems ascending from the striatum to the neocortex. However, if such connections exist they seem to be rather collaterals of the striatofugal axons, the removal of which does not lead to retrograde degeneration of neurons in the putamen and caudate nucleus.

Dissimilar reactions of the claustral and striatal neurons to the removal of the neocortex imply different functions of the two structures. The rostral portion of the striatum which receives afferents from the frontal cortex may perform some integrative functions even after complete removal of the frontal lobe and from a theoretical point of view the striatum may be considered as a vicarious cortex.

The claustrum as a corticodependent relay nucleus probably has a different role to play. We consider that it may form a link between neocortex and some limbic structures as for instance the amygdaloid complex (our unpublished data).

Taking this hypothesis into account it would be interesting to study the influence of lesions in the rostral portion of the claustrum on the frontal cortex functions as well as on the limbic system.

Additional anatomical research and new experimental data are needed to solve the problem to which morphological and physiological system the claustrum belongs. But our findings seem to prove that the claustrum is abundantly connected with most of the neocortical areas and that the functional interrelation between the frontal granular cortex and the claustrum must be considered as close.

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