

## SOME CONNECTIONS OF THE ORBITO-FRONTO- TEMPORAL, LIMBIC AND HIPPOCAMPAL AREAS OF *MACACA MULATTA*\*

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THE PRIMARY olfactory pathways from the olfactory bulbs to the gray substance in the region of the olfactory trigone are well established (17). The studies of Broca, (5) Schwalbe (19), Zuckerkandl (24), Turner (20), His (11) and Minot (14) suggested secondary olfactory pathways through the adjacent trigonal area to the septal region, and also to medially located areas of the cerebral hemispheres which extend in an arch from in front of the rostrum of the corpus callosum around and above it to the splenium, then downwards and forwards to the medial part of the tip of the temporal lobe. This entire arch has been referred to as the limbic lobe, cingulate gyrus, or gyrus fornicatus. Others have restricted the terms cingulate or limbic gyrus to the dorsal half of the arch; the ventral half is known as the hippocampal gyrus. On the surface of the hippocampal gyrus, adjacent to the rest of the cortex of the temporal lobe, is the entorhinal region. Medially this region is continuous with an infolded strip of cortex—the presubiculum—which, in turn, adjoins the subiculum and the remainder of Ammon's formation, the hippocampus. Located at the rostral end of the hippocampal gyrus are the amygdaloid nuclei which are covered by the periamygdaloid cortex.

The interconnections and developmental history of these regions gave rise to the concept of an "olfactory brain" or rhinencephalon. More recently doubt has been expressed as to the olfactory function of many of these areas (1, 6, 13a, 15). Physiological studies (12) have implicated the cortex of the posterior orbital surface, anterior insula and temporal pole in any evaluation of the functions of this region. Since the method of physiological neuronography has proved so successful in elucidating the functional organization of the somatic sensorimotor cortex and the occipito-temporal cortex, it might prove equally helpful in clarifying the functional organization of the rhinencephalic and limbic cortex. Extensive neuronographic observations on the connections of the supracallosal cingulate areas (2, 8, 23) and the orbital and medial surfaces of the frontal and temporal lobes (3, 16) are available. The interrelations of the areas bordering the cingulate sulcus and of these areas with the lateral surface of the hemisphere are especially well worked out as are the connections of the entorhinal region with the lateral surface. However, little is known concerning the connections of the orbital and medial

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surfaces of the frontal and temporal lobes with the cingulate and hippocampal regions, or of these with each other. In an attempt to fill some of these gaps in our information, the present study was undertaken.

#### MATERIALS AND METHODS

Fourteen immature macaque monkeys were anesthetized with Dial (.4 cc./kg. body weight, half intramuscularly and half intraperitoneally). The orbital roof and contents, temporal muscle and zygoma were removed. The skull was removed well past the midline, exposing one entire hemisphere of the brain. The head was placed in whatever position gave maximum exposure of the areas studied: upright for the supracallosal regions, inverted for those ventromedially situated. In some experiments the parasagittal veins on the side opposite to that strychninized were coagulated and severed. In others the vein of Labbé had

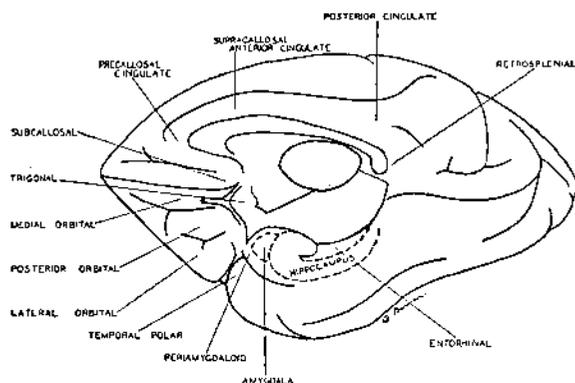


FIG. 1. Nomenclature used in subsequent legends.

to be sacrificed on the side studied. In a few experiments the contralateral frontal or occipital lobes were ablated. The amygdaloid nuclei and hippocampal formations were reached either with coated multilead electrodes (10) or by direct exposure through an incision in the inferior temporal gyrus. The brain was protected by a coating of mineral oil at all times. The animal was given subcutaneous infusions of isotonic solutions of saline and/or glucose as indicated. One-half to 1 cc. benzedrine subcutaneously was found to facilitate cortical activity toward the end of the experiments. Strychnine was applied over a 1×2 mm. surface by means of a piece of filter paper previously soaked in a saturated solution until spikes were recorded adjacent to the area strychninized, then removed.

Both monopolar and bipolar recordings were made with silver-silver chloride electrodes and a Grass ink-writing six-channel amplifier. Eight to ten fixed electrodes (22), one at the site of strychninization, and a roving bipolar electrode were used. The results were charted in a manner similar to that used in previous studies (16).

#### RESULTS

*Trigonal area* (Fig. 2). Strychnine placed on the cortex of the olfactory tubercle resulted in two separate firing patterns which could alternate during the same strychninization. The first firing pattern (Fig. 2A) extended through the medial orbital area and the subcallosal area to the precallosal cingulate area. The second firing pattern (Fig. 2B) involved the posterior orbital area, the anterior insula, the temporal polar area and the periamygdaloid area. Spikes were recorded from the region of the amygdaloid nuclei and the region of the hippocampus whenever this second firing pattern obtained. See page

of the strychnine to the adjacent posterior part of the anterior perforate area could not be ruled out.

*Medial orbital area.* (Fig. 3A). Strychnine applied to the cortex medial to the posterior part of the olfactory tract fires the subcallosal area maximally. It also results in less pronounced spiking of the precallosal cingulate area, the trigonal area and the posterior orbital area. No firing was obtained of the supracallosal cingulate, temporal polar or periamygdaloid areas.

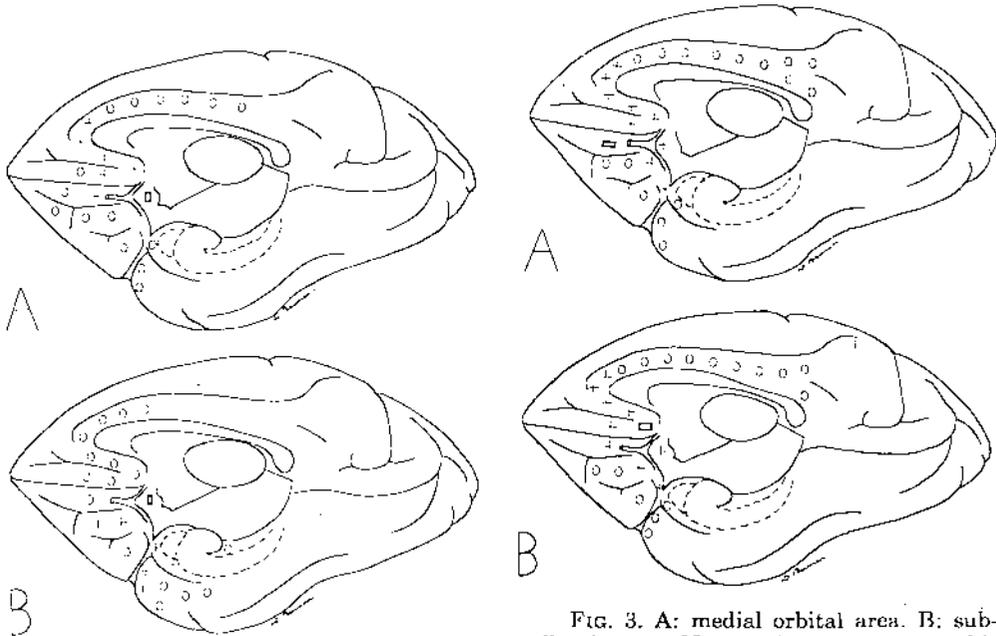


FIG. 3. A: medial orbital area. B: subcallosal area. No previous neuronographic data. These two areas have been identified as FL cytoarchitecturally by von Bonin and Bailey (4).

FIG. 2. Trigonal area. A: firing pattern 1. B: firing pattern 2. No previous neuronographic data.

*Subcallosal area* (Fig. 3B). Strychnine applied to the cortex situated under the genu of the corpus callosum fired the precallosal cingulate area, the medial orbital area, from which the largest spikes were recorded, the trigonal area and the posterior orbital area. No firing was recorded from the supracallosal cingulate areas, the temporal polar area or the periamygdaloid area.

*Precallosal area* (Fig. 4A). Strychnine applied to the precallosal part of the cingulate gyrus was followed by feeble firing of the subcallosal area only.

*Anterior supracallosal cingulate area* (Fig. 4B). Strychnine applied to the rostral cingulate gyrus gave rise only to restricted firing at all times.

*Posterior supracallosal cingulate area* (Fig. 5A). Strychnine applied to the cortex of the posterior part of the supracallosal cingulate gyrus resulted in local firing only. (No attempt was made to map the dorsal or lateral extent of the firing pattern.)

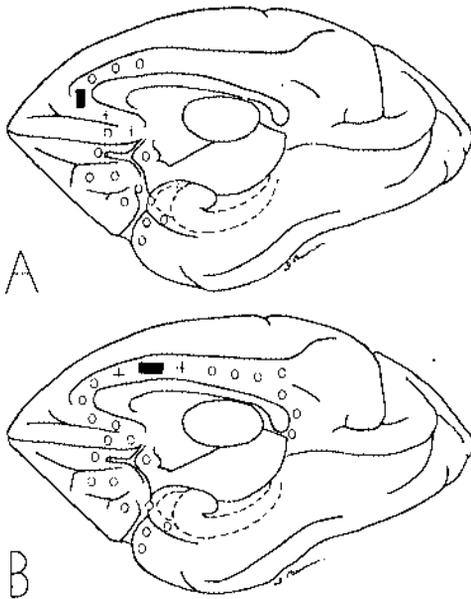


FIG. 4. A: precallosoal area. Homologies of the area are uncertain—probably LA<sub>2</sub> of von Economo (9). B: anterior supracallosoal cingulate area. Consistent with previously reported data by Bailey *et al.* (2) corresponds to area LA of von Bonin and Bailey (4). Projection area of anteromedial thalamic nucleus in subprimate mammals (18).

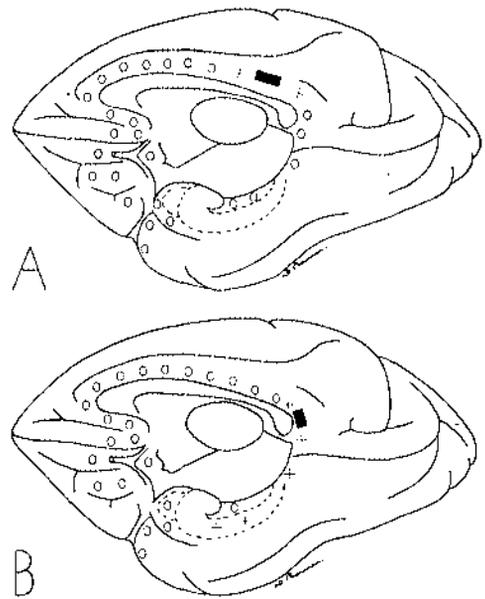


FIG. 5. A: posterior cingulate area. Consistent with previously reported data by Bailey *et al.* (2). Corresponds to area LC of von Bonin and Bailey (4) or 23 of Brodmann (7). Projection area of anteroventral thalamic nucleus in subprimate mammals (18). B: retrosplenial area. Consistent with previously reported data by Bailey *et al.* (2) who also reported firing to anterior thalamic tubercle. Projection area of anterodorsal thalamic nucleus in subprimate mammals (18). Corresponds to area LC<sub>1</sub>, LD, etc., of von Economo (9) or 29 of Brodmann (7).

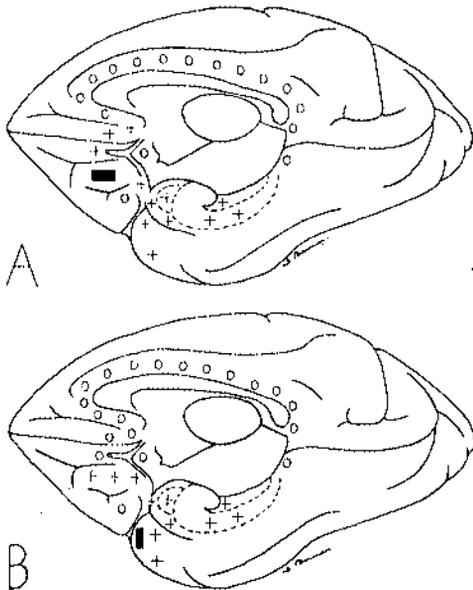
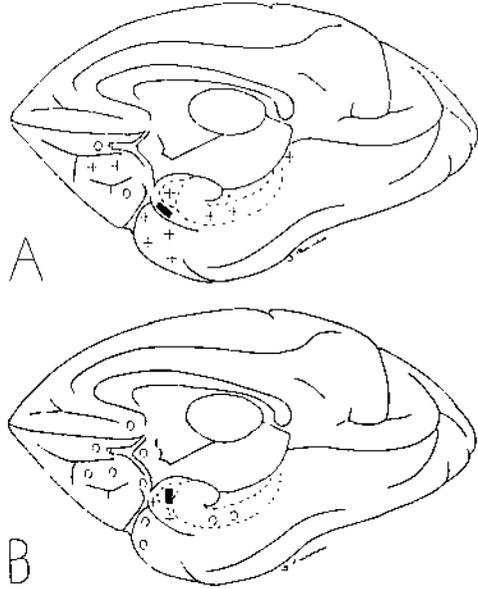


FIG. 6. A: posterior orbital area. As previously reported by Bailey *et al.* (3) except that firing of medial orbital and subcallosal areas had not been investigated. Relations to amygdala and hippocampus also new. Corresponds to area FF of von Bonin and Bailey (4) and 13 of Walker (21). B: temporal polar area. Consistent with previous reports by Bailey *et al.* (3) and Petr *et al.* (16). Corresponds to area TG of von Bonin and Bailey (4).

*Retrosplenial area* (Fig. 5B). Strychnine applied to the cortex just above or behind the splenium of the corpus callosum fired locally only. On one occasion small and irregular spikes were recorded from the region of the hippocampus.

*Posterior orbital area* (Fig. 6A). Strychninization of the posterior orbital gyrus fired the adjacent cortex of the anterior insula and the temporal polar area maximally. Minimal spiking was recorded from the medial orbital area

FIG. 7. A: periamygdaloid area. Consistent with previous report by Petr *et al.* (16) except for firing of posterior orbital area. Corresponds to allocortical area H of von Bonin and Bailey (4). B: amygdaloid nuclei. No previous neuronographic data.



and the subcallosal area. No firing was recorded from the pre- or supracallosal cingulate areas or from the trigonal area, periamygdaloid cortex or the entorhinal areas. Spikes were recorded from the region of the hippocampus on two occasions but never from the region of the amygdaloid nuclei.

*Temporal polar area* (Fig. 6B). Strychnine applied to the temporal pole fired the cortex of the anterior insula and the posterior orbital area. Firing was also recorded from the periamygdaloid cortex, the anterior part of the fusiform gyrus, and from the region of the amygdaloid nuclei and the region of the hippocampus. No spikes were obtained from the trigonal area, medial orbital or subcallosal area, the pre- or supracallosal cingulate areas, the retrosplenial or posterior entorhinal areas.

*Periamygdaloid area* (Fig. 7A). Strychninization of the periamygdaloid cortex resulted in extensive firing of the entorhinal areas, the temporal pole, anterior insula, posterior orbital and trigonal areas. No firing was recorded from the medial orbital or subcallosal areas nor from the pre- or supracallosal cingulate or retrosplenial areas. Both the regions of the amygdaloid

nuclei and the hippocampus fired synchronously with the periamygdaloid cortex.

*Amygdala* (Fig. 7B). Strychnine applied to the amygdaloid nuclei fired the periamygdaloid cortex only. No spikes were obtained from the exposed hippocampal formation, the temporal polar, posterior or medial orbital areas or the trigonal area.

*Entorhinal area* (Fig. 8A). Strychnine applied to the most medial portions of the ventrally accessible temporal cortex usually resulted in local

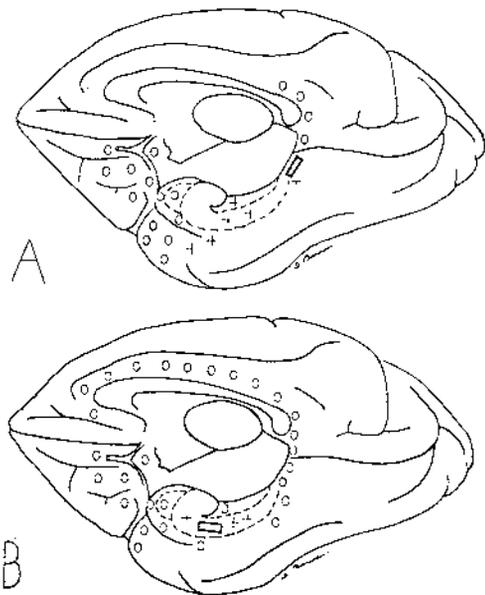


FIG. 8. A: entorhinal area. Previous report by Petr *et al.* describes neuronographic connections with lateral surface (16). May correspond to medial part of area TF of von Bonin and Bailey (4), 28 of Brodmann. B: hippocampus. No previous neuronographic data.

firing only. (No attempts were made to map the lateral extent of the firing pattern.) On several occasions spikes were obtained from the region of the hippocampus but none from the region of the amygdaloid nuclei.

*Hippocampus* (Fig. 8B). Strychninization of the exposed hippocampal formation resulted in local firing only. (This exposure entailed cutting a window in the inferior temporal gyrus which may have affected the results.)

#### DISCUSSION

An attempt has been made in the legends of the figures to homologize the areas strychninized with the most commonly used cytoarchitectural nomenclature. Admittedly this is less satisfactory than defining areas in terms of their thalamocortical or other subcortico-cortical projection systems. However, except in the case of the supracallosal cingulate and retrosplenial areas (18), such relationships are as yet largely undetermined.

One factor complicating the neuronographic analysis is the fact that areal differentiation in the allocortical regions is primarily along narrow

strips running perpendicular and adjacent to the callosal fibers or buried in the invagination of the hippocampal gyrus. This arrangement limits the mass of cortex of one subdivision strychninized at one time and frequently means that parts of several such subdivisions have been strychninized simultaneously. In spite of this limitation, the present experiments suggest that the cortex of the orbito-fronto-temporal and limbic areas is functionally interconnected by relatively short fibers with none of the long anteroposterior association tracts so prominent on the lateral surface. On the other hand, previous experiments (2, 3, 8, 16, 23) have demonstrated long and heavy connections of several of these areas with various aspects of the lateral surface.

The facility of the trigonal area to fire at different times either the areas extending medially or those laterally suggests that two independent systems are involved. This is consistent with the fact that both the medial and lateral olfactory striae originate in this area. A close functional relation between the precallosal and subcallosal areas seems definite. The latter forms a unit with the medial orbital gyrus as indicated by von Bonin and Bailey (4).

The functional unity of the cortex of the posterior orbital surface, anterior insula and temporal pole is again confirmed. Its relation to the trigonal area and periamygdaloid cortex on the one hand and the hippocampal formation on the other is made evident. Excitation of the trigonal and pyriform areas (allocortical) is elaborated in the adjacent isocortex. It appears that the hippocampal formation may receive this excitation from either the allocortical or the isocortical areas. The occasional firing of the hippocampus on strychninization of the posterior orbital surface was one of the few really long connections demonstrated in these experiments and reemphasizes the importance and close relationship of the orbital portions of the frontal lobes with the medial and polar temporal regions, presumably through the uncinate fasciculus. The importance of the periamygdaloid area to this region is demonstrated not only by the extent of its connections but by the facility with which it responded to strychninization. The almost invariably present spontaneous spiking recorded from this area throughout these experiments has been reported elsewhere (13).

The connections suggested for the amygdaloid complex and hippocampal formations are tentative as the techniques employed were extremely crude. No accurate determination could be made, whether recording was from nuclear structures or from adjacent fibers. However, often—at the onset of strychninization—the area strychninized would fire restrictedly and only later would synchronous spikes appear from the depth electrodes. Direct exposure of these structures served as another check. Nevertheless, a more accurate and more extensive investigation of the connections of these structures with more refined techniques is planned.

As Bailey has pointed out repeatedly, in order to understand the functional organization of the cortex it is imperative to examine the sulci. Stud-

ies on the connections of the borders of the cingulate sulcus exist (areas LC [23] and 31 and 32 and the band of cortex connecting them). The present experiments did not attempt to extend this information so this and the other major sulci on the medial and orbital surfaces await exploration.

#### SUMMARY AND CONCLUSIONS

1. By means of the technique of physiological neuronography some of the connections of the rhinencephalic and limbic areas of *Macaca mulatta* have been investigated in an attempt to extend reports of previous studies.

2. The following areas can be recognized by differences in their firing patterns: trigonal, subcallosal and medial orbital, precallosal cingulate, supracallosal anterior cingulate, supracallosal posterior cingulate, retrosplinal, posterior orbital and anterior insular, temporal polar, periamygdaloid, and entorhinal. An attempt has been made to correlate these with cytoarchitectural differences and with subcortico-cortical connections whenever possible. Some of the connections of the hippocampus and amygdala were also investigated.

3. The cortico-cortical interconnections of these areas suggest that they fall into three groupings. (i) The trigonal, subcallosal and medial orbital, precallosal cingulate, posterior orbital and anterior insular, temporal polar, periamygdaloid and entorhinal areas are heavily interconnected. This group may be referred to as the orbito-fronto-temporal region. (ii) The second group includes the projection areas of the three divisions of the anterior thalamic nucleus. There are three of these areas: supracallosal anterior cingulate, posterior cingulate, and retrosplinal. According to previous studies, these areas are closely related to the cortex surrounding the cingulate sulcus and to certain aspects of the lateral surface of the hemispheres. They are functionally interconnected by extremely short fiber systems. This group may be referred to as the limbic region. (iii) Finally, the consideration of the hippocampal formation as a separate region is tentative until its relation to the orbito-fronto-temporal and the limbic areas is further clarified and any possible connections with the lateral neocortex investigated.

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