Anatomy. — *Introductory note on the phylogenetic and ontogenetic development of the Cortex cerebri.* By C. U. ARIËNS KAPPERS.

(Communicated at the meeting of April 26, 1941.)

To Dr. BRUMMELKAMP's paper in this issue of the Proceedings the following lines may serve as an introductory note.

Studying the development of the forebrain cortex of Amniotes we find that in the Amphibian pallium two different structural fields are found. In the lateral part of the pallium (fig. 1), which in its peripheral layer contains the unmyelinated fibres from the olfactory bulb, a very simple structure occurs, the cells being located in the ventricular matrix. Very few of these cells show a peripheral migration into the direction of the fibre zone or lamina zonalis. This is the most primitive form of the cortex (paleo-cortex). In the medial wall of the hemisphere, the archicortex or primordium hippocampi (prim. hipp. fig. 1), a more advanced arrangement is found.

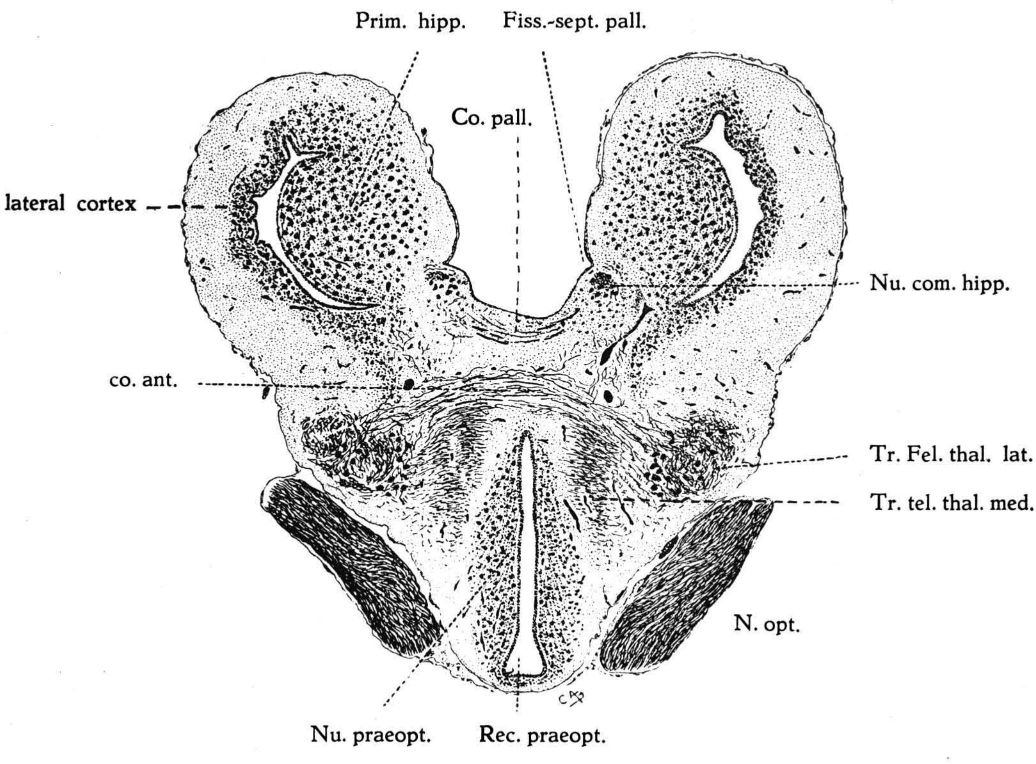

Fig. 1. Section of the posterior pole of the cerebral hemispheres of Rana catesbyana. Note the cell distribution in the primordium hippocampi.

In this field, which in its superficial zone contains myelinated — mostly tertiary olfactory fibres — the cortical cells are no more exclusively arranged in the ventricular matrix, but many of them have migrated in a peripheral direction approaching the lamina zonalis.

KUHLENBECK [1]) has called the attention to the fact that this migration is due to the neurobiotactic influence of the fibres in the lamina zonalis.

In Reptiles (fig. 2) the cells of the lateral olfactory cortex have also

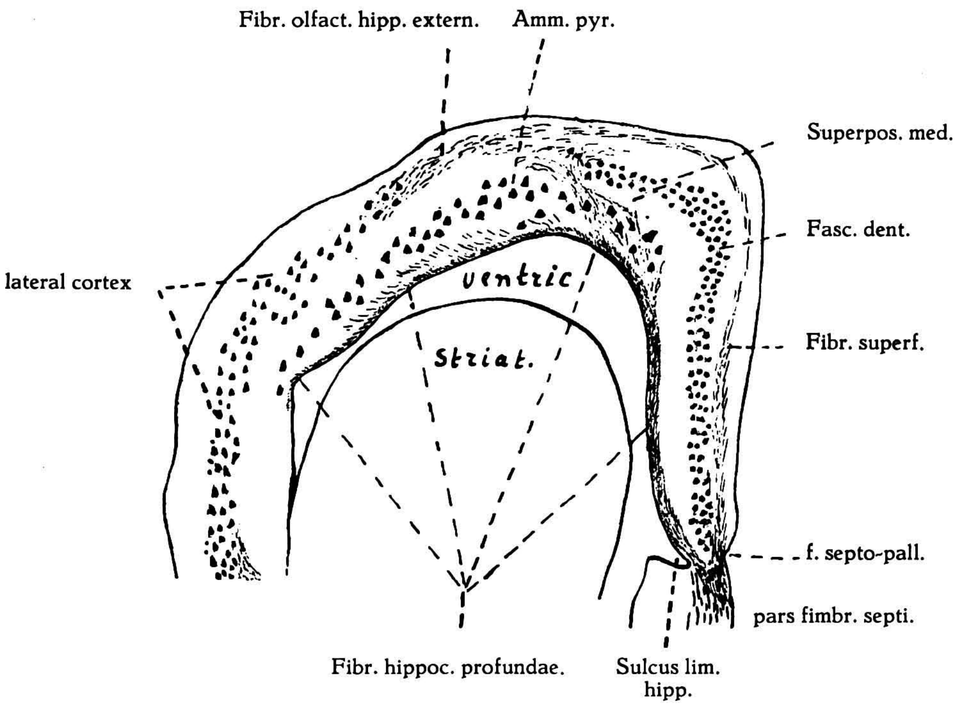

Fig. 2. Section of the left hemisphere of Boa constrictor showing the more superficial granular cells of the fascia dentata and the deeper partly subgranular position of the Ammon pyramids.

shifted peripherally forming an isolated layer underneath the fibre layer. Frontally in this cortex two layers are observed, a superficial granular receptive layer and a deeper pyramidal effectory layer. In the archicortex of these animals the differentiation is more distinct. Whereas the archicortex of Amphibia does not yet reveal a laminar differentiation of cells such a differentiation is obvious in Reptiles.

In the archicortex of these animals two layers are observed. The most medial one of these archicortical layers, which at the same time lies nearer to the periphery, is a layer of small granular cells (fasc. dent. fig. 2). It is a chiefly receptory layer i.e. it receives impulses from tertiary

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[1]) Ueber den Ursprung der Groszhirnrinde. Eine phylogenetische und neurobiotaktische Studie. Anat. Anz. **15** (1922).

olfactory fibres running in its lamina zonalis (fib. superf.). The second archicortical layer consists of large pyramidal cells, the Ammon pyramids (Amm. pyr. fig. 2) which partly extend underneath the granular layer (superpositio medialis).

From this deeper pyramidal layer descending and commissural fibres originate, the fibrae hippocampales profundae.

We thus find in Reptiles the first differentiation of the cortex in a receptory granular layer and an effectory (and commissural) pyramidal layer extending underneath the granular layer.

BRILL [1]) and ADOLF MEYER [2]) whose observations were confirmed by KAPPERS [3]) and CROSBY [4]), have been the first to realize that these two archicortical layers of Reptiles correspond with the two characteristic layers of the mammalian hippocampus: the granular layer being homologous to the fascia dentata, (see fig. 3), the pyramidal layer to the ammon pyramids of Mammals (Amm. pyr. fig. 3). A multilaminar neocortex chiefly related to non-olfactory functions does not yet occur in Reptiles.

As shown by CRAIGIE [5]) a typical multilaminar neocortex first occurs in birds, lateral to the archicortex, between this and the primary olfactory cortex. This multilaminar neocortex is especially evident in the Ratites. But even in these animals the larger part of this cortical field looses its characteristics cortical structure changing into a non laminated dense mass of cells which is continuous with the neostriatum (the hyperstriatum of EDINGER). In the Carinates the neocortex has lost its typical characters and gradually continues in striatal structures.

In Mammals the whole pallium located between the ventrolateral olfactory cortex and the medial archicortex or hippocampus shows a

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1) BRILL. The true homology of the mesial portion of the hemispheric vesicle in the Sauropsida. Medical Record, March 1890.

2) ADOLF MEYER. Ueber das Vorderhirn einiger Reptilien. Ztschr. f. Wiss. Zool., Bnd. **55** (1892). Id. Zur Homologie der Fornix commissur und des Septum lucidum bei Reptilien und Säugern. Anat. Anz. Bnd. **10** (1895).

3) ARIËNS KAPPERS. The phylogenesis of the palaeocortex and archicortex compared with the evolution of the visual neocortex. Arch. of Neur. and Psych. of the London Country Council, Vol. **4** (1909).

4) CROSBY. The forebrain of Alligator mississipiensis. Journ. Comp. Neur., Vol. **27** (1917).

5) CRAIGIE. The cerebral cortex of Apteryx. Anat. Anz., Bnd. **68** (1929); Id. Studies on the brain of the Kiwi (Apteryx australis). Journ. Comp. Neur., Vol. **49** (1930); Id. Multilaminar cortex in the dorsal pallium of the Emu, Dromiceius Novaehollandiae. Psych. en Neur. Bladen, Amsterdam (1934); Id. The hippocampal and parahippocampal cortex of the Emu (Dromiceius). Journ. Comp. Neur., Vol. **61** (1935); Id. The cerebral hemispheres of the Kiwi and the Emu (Apteryx and Dromiceius). Journ. of Anat., Vol. **69** (1935); Id. Some features of the pallium of the Cassowary, Anat. Anz., **81** (1935); Id. The cerebral cortex of the Ostrich (Struthio). Journ. of comp. Neur., Vol. **64** (1936); Id. Notes on the cytoarchitectoral features of the lateral cortex and related parts of the cerebral hemispheres in a series of Reptiles and Birds. Trans. Roy. Soc. of Canada, Vol. **30** (1936); Id. The cerebral cortex in Palaeognathine and Neognathine Birds. Journ. Comp. Neur., Vol. **73** (1940).

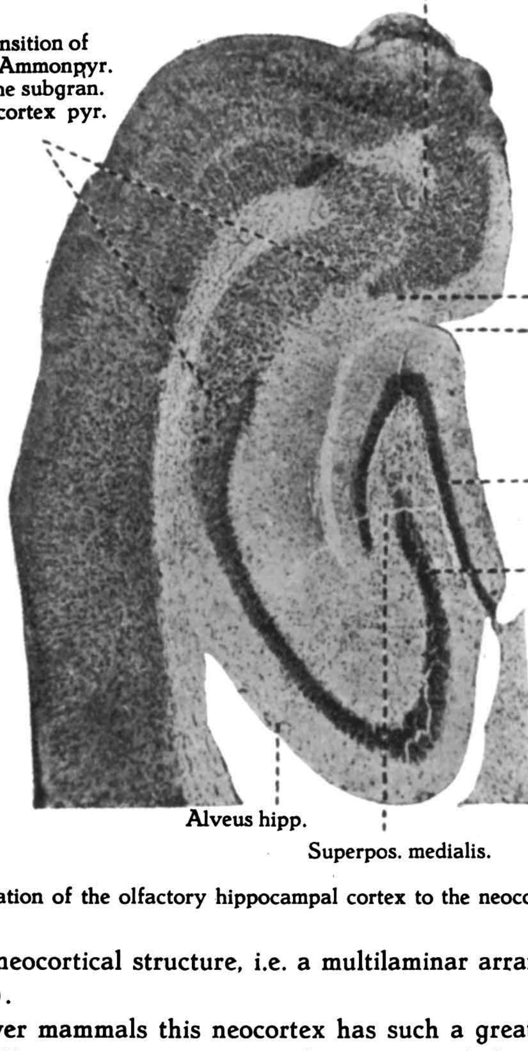


Fig. 3. Relation of the olfactory hippocampal cortex to the neocortex of the rat.

characteristic neocortical structure, i.e. a multilaminar arrangement of cells (fig. 3 and 4).

Even in lower mammals this neocortex has such a great extension, that the primary olfactory cortex is pushed in a ventral direction, while the archicortex, especially its pyramidal layer adjacent to the neocortex, is lifted up in a dorsal direction (fig. 3), thus giving rise to the peculiar folded form of the archicortex from which its names cornu Ammonis and Hippocampus are derived.

A comparison of the neocortex with the older forms of cortex, the lateral olfactory and medial archicortex shows that, notwithstanding considerable differences, the same principles obtain in it.

This principle is that the upper layer(s) has (have) a receptory function, the deeper layer(s) an effectory and commissural function.

Whereas each of these functions in the primary olfactory and archicortex, however, is represented by one cell layer only, the receptory function in the neocortex is divided over three layers, all of which may be considered as derivatives of the originally single granular layer. This also appears from VAN 'T HOOG's [1]) comparisons of the same neocortical field in small and large representatives of the same order of mammals, which

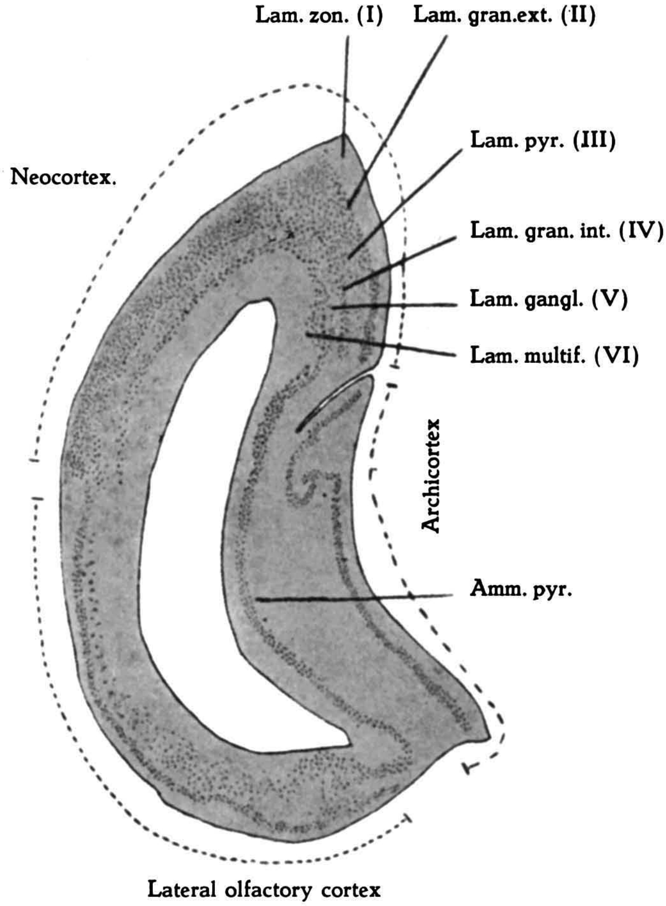


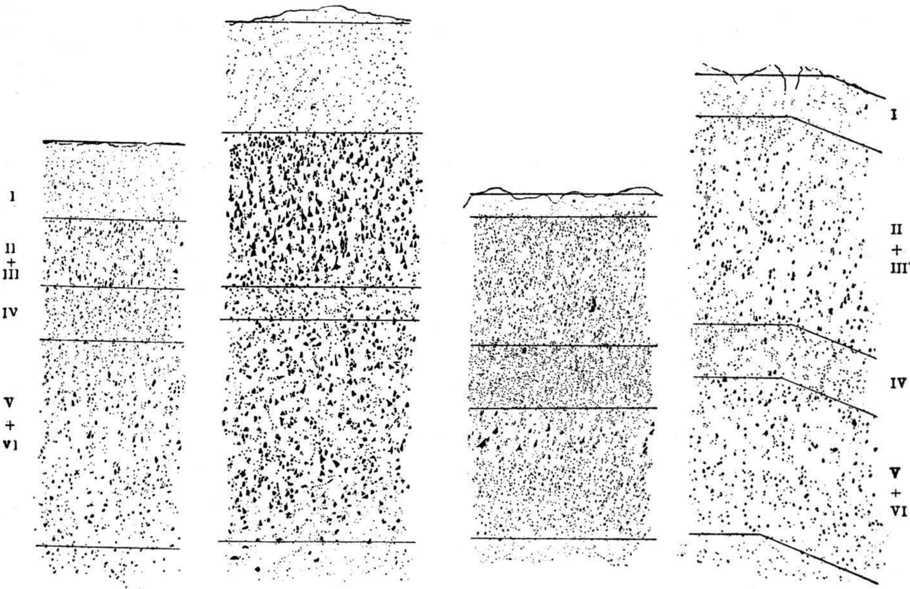
Fig. 4. Cerebrum of an embryo of Dasypus novemcinctus showing the six layered neocortex between the two-layered lateral olfactory and archicortex.

shows that the supragranular layers (II + III) in the large animals increase at the expense of the (internal) granular layer (IV, fig. 5). The effectory function being divided over two subgranular layers, the lam. ganglionaris (V) and multiformis (VI) this makes five cell layers together. Adding the lamina zonalis the neocortex thus consists of six layers.

That the neocortex has a six-layered character is proved for various mammalian orders and for man by BRODMANN [2]) who also showed that in the prenatal stage this six-layered structure is very much the same

[1]) VAN 'T HOOG. Ueber Tiefenlokalisation in der Grosshirnrinde. Psych. en Neur. Bladen, Amsterdam (1918).

[2]) BRODMANN. Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellbaues, Leipzig (1909).



Tragulus meminna. Small ungulate. Rusa hippelaphus. Large ungulate. Hapale jacchus. Small monkey. Ateles paniscus. Large monkey.

Fig. 5. (After VAN 'T HOOG) Increase of the supragranular cell layers (II + III) at the expense of the internal granular layer (IV) in larger animals of the same orders.

over the whole neocortex. Personally we had an opportunity to confirm this for Dasypus novemcinctus as shown by our figure 4. Of these six layers the upper one contains fibres only. In the other five nerve cells are predominant. Comparing the five cell layers of the mammalian neocortex with the original two layers of the olfactory cortex, it appears that the granular receptive layer of the latter is represented in the neocortex by the lam. granularis interna, the supragranular pyramid and stellate cells, the effectory pyramidal layer of the olfactory cortex is represented by the subgranular pyramids, the so called laminae ganglionaris and multiformis.

The receptive and associative function of the three upper cell layers of the neocortex clearly appears from the researches of MOTT, BROUWER, LORENTZ DE NO, the effectory motor and commissaral function of the two deep layers from the work of NISSL, VAN VALKENBURG, BIELSCHOWSKY, DUSSER DE BARENNE.

The regional differentiations occurring in the further development of the pallium, which is the cause that so many regions may be distinguished in the adult, may be explained by the fact that in some of these regions the effectory or commissural, in others the receptive and associative-receptive functions prevail [1]).

[1]) ARIËNS KAPPERS. Vergleichende Anatomie des Nervensystems der Wirbeltiere und des Menschen. Bnd. II (1921), Bonn, Haarlem. Id., HUBER and CROSBY. The comparative anatomy of the nervous system of vertebrates including Man, Vol. II (1936), Macmillan, New York and London (1936).

So in the motor or prerolandic area the deeper effectory layers of large pyramidal cells prevail. In the sensory, visual and acoustic area the granular layers are very obvious and in the associative-receptory regions, as the frontal and parietal cortex, the supragranular pyramids.

Yet, in all these regional differentiations the pre-adult five layer structure may be observed also in the adult neocortex notwithstanding the differences in density and size of cells and the variations in the depth of the neocortical columns in the adult. It is here that the researches of BOK and BRUMMELKAMP give us more light. BOK [1]) and his pupils gave us valuable informations concerning the influence of the folding of the cortex on the height of its various layers, the relations existing between the volume of the cell bodies and dendrites on one hand and their distance to the zonal layer on the other, and concerning the width of the interfibrillar spaces (RENES [2])). BRUMMELKAMP [3]) showed the striking fact that notwithstanding the changes in the adult the nuclear mass in neocortical columns of equal diameter is the same at every spot of the neocortex. Together with VAN VEEN [4]) he could confirm this for the human cerebrum, counting and measuring more than 20.000 nuclei in various neocortical columns of equal diameter. In his paper in this issue BRUMMELKAMP shows that the equality of nuclear volume holds good already for the neocortical matrix and persists in the adult. Since in each single row of cells the nuclear volume remains the same whatever the change in the size of the cells and nuclei may be, the number of single cell rows in each cortical region is the same notwithstanding the great differences in the depth of these regions. He furthermore shows that the surface extension of a functionally homogeneous region originates from juxtapositional

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1) BOK. Der Einflusz der in den Furchen und Windungen auftretenden Krümmungen der Groszhirnrinde auf die Rindenarchitektur. Zeitschr. f. d. ges. Neur. u. Psych., Bnd. **121** (1929). Id. A quadratic relation between the volumes of the nucleus and body of ganglion cells of different sizes. Psych. en Neur. Bladen, Amsterdam (1934). Id. Messungen an den Ganglienzellen der Groszhirnrinde. I. Die Einheitlichkeit der einzelnen Hauptzonen. Zeitschr. f. mikrosk.-anat. Forschung. Bnd. **36** (1934). Id. A quantitative analysis of the structure of the cerebral cortex. Verh. d. Kon. Akad. v. Wetensch., Amsterdam, (2e sectie), **35**, No. 2 (1936). Id. The branching of the dendrites in the cerebral cortex. Kon. Akad. v. Wetensch., Amsterdam, Vol. XXXIX (1936).

BOK and VAN ERP TAALMAN KIP. The size of the body and the size of the cerebral cortex. Acta Neerl. Morph., II (1939). Id. The size of the body and the size and the number of the nerve cells in the cerebral cortex. Acta Neerl. Morph., III (1939).

BOK. Cephalization and the boundary values of the brain- and body sizes in mammals. Kon. Ned. Akad. v. Wetensch., Amsterdam, Vol. XLII (1939). Id. The different structures of the cyto-architectonic fields of the cerebral cortex as different manifestations of a general scheme, each being mainly indicated by the value of one varying proporty, called the field exponent. Kon. Ned. Akad. v. Wetensch., Amsterdam, Vol. XLII (1939).

2) RENES. Over de vezelrijkdom van de hersenschors. Diss. Leiden (1940).

3) BRUMMELKAMP. Normale en abnormale hersengroei in verband met de cephalisatieleer. Dissertatie, Amsterdam (1937).

4) BRUMMELKAMP and VAN VEEN. The distribution of the nervous nucleus volume in the Neocortex. Verh. Ned. Akad. v. Wetensch., Amsterdam, Sectie 2. Vol. **39** (1941).

growth of this area in which the equi-nuclear volume agains persists. This he explains by the fact that for juxtapositional growth no extra energy in the lines of the neurobiotactic field of power is required.

This juxtapositional growth apparently acts an important part also in the development of other surface extensions, such as the cerebellar cortex and tectum opticum which also increase by surface extension in a principally homogeneous field.

And the same holds good for what we have called "internal cortical" structures [1]), which do not increase in thickness but by lamellation i.e. by surface extension, such as the inferior and superior olives, the nucleus dentatus, and — in some animals — the nuclei of the posterior columns and substantia gelatinosa Rolandi, all of which are structures intercalated in an equi-energetic ascending system.

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[1]) ARIËNS KAPPERS. Ueber das Rindenproblem und die Tendenz innerer Hirnteile durch Oberflächenvermehrung statt Volumzunahme zu vergrösseren. Fol. Neurobiologica, Bnd. 8 (1914).