

Figure 1 (Furtado). Schematic sequence of developmental events resulting in the specification of the main anterior telencephalic regions in reptiles and mammals, viewed in the coronal plane. Pax6 gene expression is shown in gray. Some gradients of inductors of pattern formation (segregation of isogenetic cell populations) are denoted by black arrows. The persistent expression of particular homeotic genes in dorsal areas of mammals could allow the specification of intermediate cell phenotypes within the dorsal cortex territory. BG, basal ganglia; DC, dorsal cortex; DP, dorsal pallium; DT, dorsal territory; DVR, dorsal ventricular ridge; IT, intermediate territory; LC, lateral cortex; MC, medial cortex; MP, medial pallium; S, septum; v, ventricle; VC, ventral cortex; VT, ventral territory.

connections in lateral, medial, and dorsal cortex. This suggests that the reptile/mammal common ancestral had a reptilian-like brain rather than an amphibian-like brain structure.

Brain changes in surface (area) and thickness (layers) that occurred in the synapsid lineage were not necessarily simultaneous. Fossil records suggest that the area enlargement did not occur until the Early Jurassic, exemplified by the brain of *Hadrocodium* (Luo et al. 2001). Nevertheless, the moment for the acquisition of new layers in the emerging isocortex is not very clear. The ecological scenario has to take into account the colonization of nocturnal ecological niches allowed by endothermy and the consequent exploratory behaviour driven by olfactory/auditory inputs. It is also necessary to include the nature of parental care, and maybe the coevolution of large-brained coelurosaurs.

Here we would like to suggest an alternative hypothesis that could conciliate the recapitulation hypothesis with the incompatibilities of the developmental criteria for homology, necessary to establish the origins of the isocortex. The hypothesis is based on the overlap (mixture) of two neurogenetic territories during the early stages of anterior telencephalon development. This overlap is possible if the border between the dorsal pallium territory and the intermediate territory (that will give rise to the lateral and ventral pallium) fails to be established (Fig. 1). The overlap led to the approximation of the audiovisual associative ADVR with the primary somatic-motor/visual/olfactory dorsal cortex, and allows the mixture and expansion of lemnthalamic/collothalamic systems within the dorsal pallium.

Pax-6 expression in pallial territory of avian embryo is interrupted early, but this does not occur in mammals (Puelles et al. 2000; Smith Fernandez et al. 1998; Stoykova 2000). Some mutation in the developmental genetic regulatory systems (Davidson

2001) could have led to a failure in the blockage of expression of Pax-6 (or another similar homeotic gene) within the pallial territory in the mammalian ancestral brain. This mutation could have gathered, in the same neurogenetic territory, cells that express pallial or intermediate territory-related homeotic genes. The maintained expression of Pax-6 in the mammalian dorsal pallium could have contributed to the specification of intermediate-like precursor cell, possibly radial glia (Götz et al. 1998; Malatesta et al. 2003), at the subventricular zone (Tarabykin et al. 2001) within dorsal pallium neurogenetic territory. These views suggest a homology between preplate/infragranular cells of mammalian isocortex with the dorsal cortex cells of reptiles and a homology between granular/supragranular cells with the ADVR cells. Inhibitory neurons came from subpallium in both taxa by tangential migration, following ancient and new routes to reach the isocortex (Anderson et al. 2001).

## Mesozoic mammals and early mammalian brain diversity

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**Abstract:** Fossil remains witness the relationship between the appearance of the middle ear and the expansion of the brain in early mammals. Nevertheless, the lack of detachment of ear ossicles in the mammaliaform *Morganucodon*, despite brain enlargement, points to other factors that triggered brain expansion in early mammals. Moreover, brain expansion in some early mammalian groups seems to have favored brain regions other than the cortex.

The issue of the origin of the mammalian isocortex raises the question of the various evolutionary factors that produced a uniquely mammalian structure. The suggestion of the authors is that the mammalian isocortex originated in large part as a consequence of a dorsalsizing influence in pallial development. The authors also assess how fossil evidence could shed light on isocortical origin. This is very welcome because, even in paleontological studies on early mammalian relationships, brain structure inferred from investigation of endocranial casts has been almost completely neglected (Kielan-Jaworowska 1997).

Besides functional demands involving the olfactory cortex, the dorsal cortex, and the hippocampus, an important functional correlate of the isocortical expansion is the detachment of the postdentary bones from the dentary, and the possible incorporation of these elements into the middle ear in early mammals (Luo et al. 2002; Rowe 1996b). The detachment of the auditory bones from the mandible and its coincidence with the enlargement of the brain is observed in several early mammalian fossil specimens.

There are some notable exceptions to this general pattern, such as the true mammalian form *Repenomamus* (Wang et al. 2001). As summarized by Luo et al. (2002), the brain vault is wider in the parietal region of *Hadrocodium*, and of the mammalian crown-group representative taxa, than in cynodonts and *Morganucodon*. *Hadrocodium* and the mammalian crown-group constitute a clade characterized by various diagnostic apomorphies. The mammalian crown-group is defined as the common ancestor of all living mammals and also includes the triconodonts (*Triconodon*, *Gobiconodon*, *Repenomamus*) and the multituberculates. The narrow braincase of some early true mammals such as *Repenomamus* and *Gobiconodon* is in concordance with the various evolutionary rates of the triconodont subgroups and with the paraphyletic nature of the triconodont group.

The consensus could be that mammals with enlarged isocortex have a fully evolved middle ear. The reverse is, however, not true.

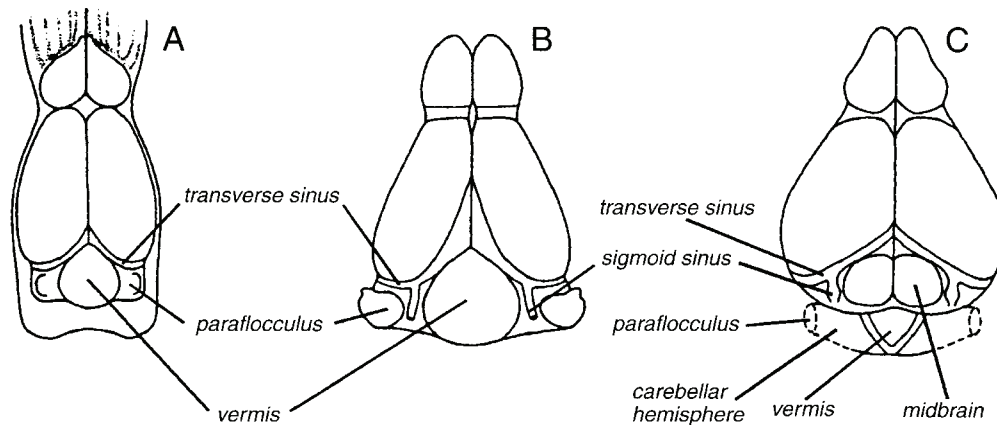


Figure 1 (Gilissen & Smith). Dorsal view of brain reconstructions in three Mesozoic mammals, based on endocranial casts. **A.** Triconodont *Triconodon*. **B.** Multituberculata *Chulsanbaatar*. **C.** Eutherian *Barunlestes*. A and B represent the cryptomesencephalic type, C represents the eumesencephalic type. Reprinted from Z. Kielan-Jaworowska, "Characters of multituberculates neglected in phylogenetic analyses of early mammals," *Lethaia*, 1997, vol. 29, pp. 249–66, by permission of Taylor and Francis AS.

In this context, the reference to *Morganucodon* is particularly interesting because it is the most completely known Late Triassic–Early Jurassic mammaliaform. *Morganucodon* and living mammals represent a clade characterized by a large suite of derived dental characters and basicranial features, but the ear ossicles are still attached to the lower jaw in *Morganucodon*, despite a clear brain enlargement when compared to mammal-like reptiles (Luo et al. 2002). This could be explained by contributions of hippocampal and multimodal association circuits to the enlargement of the isocortex more than to enhanced hearing, as suggested elsewhere by the authors. In any case, the importance of the transcallosal interhemispheric connections of the binaural cells makes the telencephalic auditory spatial processing a largely isocortical and, therefore, mammalian feature.

We acknowledge that mesozoic mammals are characterized by cerebral hemispheres diverging posteriorly. Nevertheless, according to Kielan-Jaworowska (1986), two distinct types of brain morphology can be defined within this pattern (Fig. 1). In some primitive mammals such as triconodonts, and especially multituberculates, the vermis and the paraflocculi are very large with no apparent cerebellar hemispheres and no dorsal midbrain exposure. In this type, the so-called "cryptomesencephalic type," the large vermis seems to push the cerebral hemispheres laterally, and the breadth of the posterior part of the brain is increased by the presence of the large paraflocculi. Therefore, the cerebral hemispheres appear to be larger posteriorly but this does not reflect expansion of the posterior part of the isocortex.

In the other type of brain morphology, the so-called "eumesencephalic type," the cerebral hemispheres are actually well developed, the presence of cerebellar hemispheres is apparent, and there is a large dorsal midbrain exposure. All extant mammals are derived from this second type. It must be emphasized that variability in dorsal midbrain exposure shows a huge variability even within orders of extant mammals (Kaas & Collins 2001). The eumesencephalic type is represented by the Cretaceous theria *Barunlestes* (Kielan-Jaworowska 1986) and possibly by the primitive mammaliaform *Morganucodon* (Kielan-Jaworowska 1986; 1997). It is not clear, however, if the partial expansion of the posterior part of the brain in *Morganucodon* is due to an enlargement of the posterior part of the cerebral hemispheres, because the posterior part of the endocranial cast is not well identified at the anatomic level in *Morganucodon*. Interestingly, the posterior part of the brain of cynodonts such as *Therioherpeton* also appears to be enlarged when compared to other cynodonts (cf. target article, Fig. 7; Kielan-Jaworowska 1986).

In view of the studies of Kielan-Jaworowska (1986; 1997), it is well possible that the posterior enlargement of the endocranial cast can in some cases be due to enlargement of the vermis and paraflocculi rather than to enlargement of the posterior part of the isocortex. This could be the case for the Mesozoic true mammalian group multituberculates. Such differences in mesozoic mammalian brain patterns obscure the scenario of a single trend leading to enlarged posterior parts of the isocortex from mammal-like reptiles to more advanced mammalian taxa.

The authors mention the observation that gross morphology of Mesozoic mammals resembles that of some present-day insectivores. It would be of high interest to better understand what kind of ecological micro-niches Mesozoic mammals occupied and, hence, if early mammalian brain evolution was already characterized by various trends comparable to or exceeding the situation that can be observed in extant Insectivora (Catania 2000).

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The dorsal thalamic connection in the origin of the isocortex

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**Abstract:** The origin of the isocortex may be seen as a series of gradual changes (each one with an adaptive value) from a reptilian-like cerebral cortex, as proposed by Aboitiz et al., or as a new dorsal pallium derivative in mammals which undergoes a surface expansion concomitant with the expansion of the dorsal tier of the dorsal thalamus.

The vision of the evolutionary origin of the isocortex offered by Aboitiz et al. must be applauded as an effort directed to integrate diverse connective, developmental, and functional data, as well as to reconcile two completely different scenarios of the evolution of the isocortex. Overall, I agree with the main point of the target article – that the isocortex and the dorsal cortex of reptiles are field homologous because both are derivatives of the dorsal pallium. Aboitiz et al. present a very interesting review of the literature and analyze just up to the molecular levels, the events they consider