Aboitiz, Morales, and Montiel (Aboitiz et al.) present an interesting review that attempts to integrate anatomical, developmental, and behavioral data to describe the evolution of the neocortex. Some data on the behavioral effects of lesions of the telencephalon in turtles may bear on the authors' hypotheses. These data suggest that the dorsal cortex of reptiles, rather than being an area that provides visual input to the medial cortex or hippocampus, actually functions more like the entorhinal/subicular cortex of mammals. Lesions of the dorsal cortex have no effect on visual processing but produce learning and memory deficits similar to those found after lesions of the hippocampal formation in mammals. Thus, the dorsal cortex may have been the progenitor of two parts of the cortex of mammals: the entorhinal and subicular cortices, on the one hand, and the primary sensory visual and somatosensory cortices, on the other (Butler 1994a; Day et al. 2001). The suggestion by Aboitiz et al. that dorsalization occurred in the evolution of the mammalian brain may be consistent with this idea. Perhaps the dorsal cortex of reptiles enlarged and subdivided to form both subicular/entorhinal and neocortical subdivisions in mammals. Evidence for this idea is reviewed below.

First, although it receives a projection from the dorsal part of the lateral geniculate nucleus in turtles (Hall & Ebner 1970; Hall et al. 1977; Ulinski 1988), the dorsal cortex does not function in vision. Dorsal cortex lesions do not produce deficits on retention of visual pattern or intensity discriminations (Reiner & Powers 1983, reviewed in Powers 1990). This finding, in comparison with the profound deficits seen after lesions of nucleus rotundus in the thalamus or the core nucleus of the dorsal ventricular ridge (Reiner & Powers 1978; 1983), suggests that the function of the dorsal cortex is not visual.

Rather, the dorsal cortex seems to be involved in learning and memory. Lesions of the dorsal cortex in reptiles produce deficits in acquisition and reversal of pattern discriminations (Blau & Powers 1989; Cranney & Powers 1983), acquisition and reversal of spatial discrimination in an operant chamber (Grisham & Powers 1990), acquisition and reversal of go/no go discriminations (Grisham & Powers 1989), acquisition of a simple operant (Grisham & Powers 1989), and acquisition and retention of maze learning (Avigan & Powers 1995; Day et al. 2001; Peterson 1980; Petrillo et al. 1994). Dorsal cortex lesions also disrupt long-term habituation of head withdrawal to a looming stimulus (Moran et al. 1998), a finding that is especially striking because no deficit was found on short-term (within-day) habituation. Thus, the deficit was not sensory but associative: Turtles with lesions of the dorsal cortex seemed not to remember the habituation from day to day.

The medial cortex of reptiles is involved in spatial learning. Lesions of the medial cortex of lizards disrupt the learning of a maze (Day et al. 2001), and lesions of the medial cortex of turtles disrupt the ability of the turtles to use cognitive mapping strategies to locate the goal (Rodriguez et al. 2002a; 2002b). In the case of lizards, it was not possible to determine the learning strategy that was disrupted (Day et al. 2001).

The medial cortex of reptiles does not appear to be involved in other tasks that are mediated by the hippocampus of mammals. In an operant chamber for turtles, no effects of lesions of the medial cortex were found. The tasks investigated were acquisition and reversal of spatial discriminations (Grisham & Powers 1990), acquisition and reversal of visual intensity discriminations (Grisham & Powers 1990), acquisition, retention, and reversal of go/no go discriminations (Grisham & Powers 1989), and acquisition, extinction, and reacquisition of a simple operant (Grisham & Powers 1989). Many of these tasks are impaired by lesions of the hippocampal complex in mammals (O'Keefe & Nadel 1978). In addition, turtles with lesions of the medial cortex are not impaired in a cued version of maze learning (Rodriguez et al. 2002a; 2002b).

In mammals, lesions of the hippocampus and of the subicular/entorhinal cortex may have different effects (e.g., Bannerman et al. 2001; Hunt et al. 1994). Although the findings in mammals do not seem to map directly on to the findings in reptiles, the fact that function differs is reminiscent of findings in reptiles, where lesions of the medial cortex, equivalent to the hippocampus (Butler & Hodos 1996), produce maze learning deficits (that can be shown to be spatial) but not cue learning deficits, and lesions of the dorsal cortex, similar to the entorhinal/subicular cortex (Butler & Hodos 1996), produce cue learning and reversal learning deficits in addition to deficits in maze learning.

The dorsal cortex of some reptiles (e.g., turtles) is also the recipient of both visual and somatosensory projections from the thalamus. In lizards, the visual projection from the thalamus terminates in a lateral region termed the "pallial thickening" (Bruce & Butler 1984a). It is noteworthy that, in spite of this difference, the function of the dorsal cortex in lizards appears to be similar to that in turtles, in that lesions in both orders disrupt learning and memory (Day et al. 2001; Peterson 1980; Petrillo et al. 1994). Our data on the behavioral effects of lesions in the dorsal and medial cortex suggest that the dorsal cortex is not, as postulated by Aboitiz et al., a sensory area that provides sensory input to the medial cortex/hippocampus. Rather, these effects are consistent with the dorsal cortex being similar to entorhinal/subicular cortex.

Nonetheless, the dorsalization hypothesis proposed by Aboitiz et al. suggests a solution to the dilemma posed by the clear demonstration that the dorsal cortex is involved in learning and memory like the hippocampus of mammals but also contains sensory areas that seem to be the forerunners of primary sensory neocortex in mammals. The dorsalization hypothesis is consistent with the idea that, in the transition to mammals, the dorsal cortex may have expanded medially to become the entorhinal/subicular cortex and laterally to become the primary sensory cortices for vision and touch. The function of the dorsal cortex seems to correspond more to that of the entorhinal/subicular cortex, but the structural increase in area implied by the dorsalization hypothesis may have allowed an increased functional role for visual information in the thalamofugal system.

The data do not support the hypothesis

Anton Reiner

Department of Anatomy and Neurobiology, University of Tennessee Health Science Center, Memphis, TN 38163. **areiner@utmem.edu**

Abstract: The position that Aboitiz et al. have taken on the regions of the stem amniote brain from which neocortex arose, and on homologies among telencephalic pallial regions in mammals and sauropsids, is premature. Nonetheless, if their intent is to promote thought, discussion, and experimentation on this important topic, then their paper is valuable.

Aboitiz et al. conclude that (1) stem amniotes possessed a dorsal cortex that was the antecedent of mammalian cerebral cortex medial to temporal sulcus (i.e., superior neocortex); (2) temporal neocortex (lateral to temporal sulcus) arose as an expansion of superior neocortex; and (3) the DVR of birds and living reptiles, which has many of the connections and functions of temporal neocortex, evolved from the same antecedent structures as parts of mammalian amygdala and claustrum, and any similarities between DVR and temporal neocortex are coincidental. I believe a major premise by which Aboitiz et al. reach their conclusions is flawed, and that recent findings render the latter two of the above conclusions problematic.

First, Aboitiz et al. use as their point of departure the Northcutt and Kaas (1995) dichotomy of opinions on evolution of cerebral cortex and DVR into an "outgroup" camp and a "recapitulation" camp. The former proposes that temporal neocortex has no homologue in living sauropsids, and the latter posits that stem amniotes possessed a DVR that was transformed into temporal neocortex in the mammalian lineage, and that this process is recapitulated during mammalian development. Aboitiz et al. reject the recapitulationist view for the valid reason that there is no evidence from brain endocasts of stem amniotes or from the brains

of living amphibians that stem amniotes possessed a DVR, or that the evolution of DVR into temporal neocortex is recapitulated during development. They thus embrace the seemingly default "outgroup" position. These two positions, however, do not exhaust all possible evolutionary scenarios for the relationship of DVR and cerebral cortex (Reiner 1996). Both Butler and I have suggested that the dorsal pallial sector of stem amniotes may have possessed a more lateral zone that was the forerunner of both DVR in sauropsids and temporal neocortex in mammals (Butler 1994a; Reiner 1993). Thus, a rejection of the recapitulationist view does not exclude the possibility that DVR and temporal neocortex both arose from a structure in stem amniotes that was not yet either a DVR or neocortex (Reiner 2000).

The evidence typically offered for homology of temporal neocortex and DVR is the high similarity in their structural organization. For example, both DVR and temporal neocortex contain a secondary visual area and a primary auditory area, and it has been suggested that the thalamic and midbrain cell groups giving rise to these telencephalopetal pathways are so highly similar between mammals and sauropsids that it is unlikely that they evolved separately (Karten 1991; Luksh et al. 1998; Major et al. 2000; Reiner 1993; 1994; 2000). Moreover, the topological arrangement of the primary visual, tectothalamic visual, primary auditory, and primary somatosensory areas in living reptiles (spanning dorsal cortex and DVR) is nearly identical to that in neocortex of primitive mammals (Reiner 2000). This pattern could not have been inherited from the amphibian ancestors of stem amniotes because there is no evidence that modern amphibians possess them (Northcutt & Kicliter 1980). Therefore, the similarity between modern reptiles and mammals in the topology of these "cortical" sensory areas may be due to common inheritance from stem amniotes.

Aboitiz et al. present two main reasons for rejecting the connectional evidence favoring DVR and temporal neocortex homology. First, they allude to recent efforts to use region-specific markers to divide the thalamus into sectors. For example, Puelles and colleagues have proposed that the thalamus consists of three stacked sectors, and that the nucleus (lateral posterior/caudal pulvinar, LP/cPUL) conveying tectofugal visual input to mammalian temporal neocortex resides in a different sector from the nucleus (rotundus) conveying tectofugal visual input to sauropsid DVR (Davila et al. 2000; Redies et al. 2000). The evidence for such thalamic compartmentalization, however, is as yet sketchy, and the claim that hodologically comparable nuclei reside in different sectors in mammals from birds is currently conjecture. By contrast, Bruce et al. (2002) used the developmentally regulated marker ErbB4 to show that the primary auditory and tectofugal visual nuclei of thalamus in birds are highly similar to those in mammals.

Aboitiz et al., secondly, reject the hodological evidence for DVR and temporal neocortex homology based on the claims of Puelles and colleagues (Davila et al. 2000) that the layer of the superior colliculus projecting to the LP/cPUL develops at a different time in relation to the other collicular layers from the tectal layer projecting to nucleus rotundus. This claim is, however, based on an undue simplification of published data on the laminar histogenesis of mammalian superior colliculus. In brief, Davila et al. claimed that the published data of Altman and Bayer (1981) show that the neurons of the collicular layer projecting to LP/cPUL (in the deep superficial gray) are generated later in development than are neurons in deep colliculus, and that the tectal layer projecting to avian rotundus arises earlier than other tectal layers. The claim for deep colliculus in mammals is based, however, on only one early-born minority large neuron type in one collicular sublayer. In fact, neurons of the superficial gray layer in mammals otherwise have birthdates notably overlapping those of neurons in other layers. A proper developmental analysis of this issue requires that the birthdates of those specific neurons projecting to LP/cPUL and to rotundus be determined, and this has not yet been done. Even then it is uncertain to what extent relative birthdate information can be used to make inferences about neuronal or laminar homology.

Aboitiz et al. also suggest that recent homeobox gene mapping studies (Puelles et al. 2000; Smith-Fernandez et al. 1998) favor the independent evolution of mammalian temporal neocortex and sauropsid DVR. In particular, Aboitiz et al. note the claim of Puelles et al. (2000) that expression of *Emx1* in mammalian telencephalon is restricted to developing hippocampal cortex, neocortex, olfactory cortex, and dorsal claustrum, but is absent from ventral claustrum and much of basolateral/basomedial amygdala. Puelles et al. (2000) termed the *Emx1*-negative region the "ventral pallium," and suggested that it was a phyologenetically conserved pallial sector. The ventral DVR in turtles and birds also does not appear to express *Emx1* during development, and Puelles et al. (2000) suggested that this territory was the ventral pallial sector of sauropsid telencephalon, and that it was homologous to ventral claustrum and parts of basolateral/basomedial amygdala.

Two recent lines of evidence have somewhat unraveled these claims. First, Butler et al. (2002) have shown that monotremes lack a claustrum. This raises the possibility that the claustrum may have arisen with the common ancestor of placental and marsupial mammals. Under these circumstances, no part of the DVR of birds and reptiles could be homologous to claustrum. Second, the claim that the *Emx1*-negative territory in mammals gave rise to ventral claustrum and much of the pallial amygdala was not based on thorough fate-mapping studies. Recent sensitive fate-mapping studies have revealed that among the putative ventral pallial nuclei, only the ventralmost part of the ventral claustrum is entirely *Emx1*-negative (Gorski et al., 2002; Guo et al. 2000). In contrast, nearly all pallial amygdaloid nuclei are rich in *Emx1*-expressing neurons. Although quantitative studies are needed to ascertain the abundance of any *Emx1*-negative neurons in the various pallial amygdaloid nuclei, there clearly are no pallial amygdaloid nuclei that are entirely *Emx1*-negative. Thus, the evidence does not favor that a ventral pallial territory persists during development and gives rise to specific ventral pallial nuclei in mammals, rendering problematic the claims of homology for ventral DVR of birds and specific claustro-amygdaloid nuclei in mammals.

On that ground, I believe it is premature to take the positions that Aboitiz et al. have taken on the origins of neocortex.

Conserved functional organization of the amniote telencephalic pallium

Cosme Salas, Cristina Broglio, and Fernando Rodríguez

Laboratory of Psychobiology, University of Sevilla, Seville 41005, Spain.

cosme@us.es **cbroglio@us.es** **fernanr@us.es**

Abstract: The dorsal and medial pallial formations of mammals, birds, and reptiles show overall functional striking similarities. Most of these similarities have been frequently considered examples of convergent evolution. However, a considerable amount of neurobiological comparative evidence suggests the presence of a common basic pattern of vertebrate forebrain organization. This common pattern can support functional conservation.

Aboitiz et al. draw an integrated developmental and functional hypothesis to account for the evolutionary origin of the mammalian isocortex. This effort is valuable because interrelating artificially separated fields – such as evolutionary biology, neuroanatomy, and developmental and functional neuroscience – will stimulate a productive discussion on the most fundamental organizing principles of brain and function. To contribute to this discussion, we will point out some disagreements with Aboitiz et al.'s proposal and also offer alternative scenarios.

First, Aboitiz et al. found their hypothesis of isocortex emergence in a presumptive difference in the function of the hippocampus of sauropsids relative to mammals. But this claim is not backed by the available experimental comparative data, which suggest, instead, that the function of the hippocampal pallium re-