HHS Public Access

Author manuscript

Brain Behav Evol. Author manuscript; available in PMC 2015 July 01.

Published in final edited form as:

Brain Behav Evol. 2013 ; 81(3): 146–149. doi:10.1159/000348281.

You Are Who You Talk with – A Commentary on Dugas-Ford et al. PNAS, 2012

Anton Reiner

University of Tennessee Health Sciences Center, Department of Anatomy and Neurobiology, Memphis, Tenn., USA

Over the last decade, the intellectual reputation of birds has been greatly rehabilitated, notably by the studies of Nicky Clayton and coworkers on New Caledonian crows [Clayton, 2007] and the work of Irene Pepperberg and coworkers on African grey parrots [Pepperberg, 2002]. This realization stands quite in contrast to the prior and long-standing view that avian behavior, even the seemingly impressive vocal abilities of parrots for example, was merely driven by rote learning and hardwired stereotypical behavioral routines [Reiner et al., 2004]. This older view was reinforced by the other old notion that the avian telencephalon is largely hypertrophied basal ganglia and is nearly devoid of a neural region that could perform the cognitive operations carried out by the mammalian cerebral cortex [Reiner et al., 2004]. However, the work of Karten and Hodos [1970] beginning nearly 50 years ago, on the organization and function of the avian forebrain, had long shown that the avian telencephalon is not an overgrown basal ganglia, and that it possesses a large region that is functionally akin to the mammalian neocortex [Karten and Hodos, 1970; Karten et al., 1973]. Karten [1991] noted in his theoretical writings that this territory within the avian telencephalon, which encompasses the Wulst, dorsal ventricular ridge (DVR) and arcopallium, possesses the neuron types and connectivity characteristic of the mammalian neocortex, and can thus perform as the neural substrate for cognition. The Wulst, DVR and arcopallium, however, are arrayed as nuclei rather than as layers, which is why earlier neuroanatomists had thought that the nuclear avian telencephalon is largely equivalent to the nuclear basal ganglia of mammals.

How could two structures look so different yet perform such similar functions and possess hodologically similar neuron types? Early on in his work, Karten proposed that the similar neuron types are, in fact, homologous and coinherited from the stem reptile common ancestor (now called stem amniote common ancestor). The telencephalic region in which these similar neuron types reside has come to be called the pallium. He proposed that the pallial neurons of mammals and birds follow different migratory paths to lead to the differing adult cytoachitectures. He proposed that in the evolutionary lineage leading from stem amniotes to modern birds, the pallial neurons came to be accumulated in nuclear groups near their birthplace along the ventricle, with different neuron types in different nuclear groups. In the course of avian evolution, more of these neurons were born than in reptiles or in ancestral birds, enlarging the pallium and pushing the neurons farther from the

Anton J. Reiner, University of Tennessee Health Sciences Center, Department of Anatomy and Neurobiology, 855 Monroe Avenue, Memphis, TN 38163 (USA), areiner@uthsc.edu.

ventricle. In Karten's view, the homologous neurons in the mammalian lineage came to migrate away from the ventricle and organize into layers of type-specific neurons parallel to the pallial surface, and he, in particular, invoked this idea to explain the differing cytoarchitectures of the DVR-arcopallium compared to the temporal parts of neocortex.

An alternate view, however, has solidified more recently, which has proposed that while the Wulst may truly be homologous to the parts of neocortex medial to the temporal sulcus (including the primary visual, sensory and motor cortex), the DVR and arcopallium are homologous to parts of the claustroamygdaloid complex of the olfactory lobe of the telencephalon. This view, which has antecedents in the ideas of Holmgren [1925], is based on the similarly nuclear cytoarchitecture of DVR-arcopallium in birds and the claustroamygdaloid complex in mammals, their basal position in the pallium and the expression pattern of some developmental genes involved in establishing regional identity within the telencephalon (notably the presence of the ubiquitous pallial marker *emx2* but the absence of the pallial gene *emx1*) [Bruce and Neary, 1995; Striedter, 1997; Puelles et al., 2000]. The most detailed elaboration of this view has given the name ventral pallium to the pallial sector in mammals regarded as homologous to the ventral part of the DVR (i.e. the nidopallium), while the upper part of DVR (mesopallium) is regarded as homologous to the pallial sector termed the lateral pallium [Puelles et al., 2000]. Together, the lateral and ventral pallia are considered to give rise to different parts of the olfactory cortex and pallial amygdala in mammals, as well as the claustrum within the deep part of the insular cortex. In the claustroamygdaloid hypothesis, the hodological and functional resemblance of DVR and arcopallium to temporal neocortex is considered to be an example of convergent evolution, as the region from which DVR and arcopallium are said to derive in birds, instead gives rise in mammals to pallium devoted to emotional and autonomic functions. Thus, the claustroamygdaloid hypothesis appears to posit a transformation of an ancient autonomic and visceral pallial territory into a somatosensory and somatomotor territory in the avian lineage. The temporal neocortex is considered a new elaboration of the neocortex already present medial to the temporal sulcus.

The two views are largely based on different types of evidence. The Karten idea is based on connectional data, and holds to the view that the hodology of a neuron type is a central part of its identity, irrespective of its dendritic morphology, location or cytoarchitectural disposition. The claustroamygdaloid view is based on developmental gene expression data and topological position, and regards neuronal identity as specified within a regionally unfolding developmental Bauplan. The recent study by Dugas-Ford et al. [2012] is welcome, therefore, as it provides data that bridge these forms of evidence – namely gene expression markers that are reflective of the hodological identity of neuron types. As their point of departure, the authors note that the Karten hypothesis about pallial homologies between birds and mammals makes specific predictions about which pallial regions in birds should express genes uniquely characteristic of layer 4 thalamorecipient neurons in mammals, and about which should express genes uniquely characteristic of layer 5 corticofugal neurons in mammals.

In short, they find that the predictions of the Karten hypothesis are met. Markers of mammalian cortical layer 4 neurons such as *eag2* (a potassium ion channel gene) and *Rorb*

(a transcription factor gene), as confirmed by their studies in mouse and ferret, are expressed by neurons in the major thalamorecipient nuclei of chicken telencephalon. For example, the interstitial part of the hyperpallium apicale of the Wulst (part of which receives visual input from the avian homologue of the dorsal lateral geniculate nucleus of the thalamus), the entopallium (which receives visual input from tectorecipient thalamus) and the L2 part of field L (which receives auditory thalamic input) all are enriched in *eag2* and *Rorb*. They also found that chicken orthologs of six different layer 5 markers (*ER81, FEZF2, CACNA1H, PCP4, SULF2* and *TMEM200A*) are strongly expressed in the chicken arcopallium, which gives rise to telencephalic projections to brainstem from the DVR [Zeier and Karten, 1971]. Similarly, four of these same layer 5 markers *(ER81, FEZF2, PCP4, and SULF2)* are intensely expressed in the hyperpallium apicale (HA), which gives rise to the descending projections of the Wulst to the brainstem [Karten et al., 1973].

The authors also examined the pallial expression of layer 4 and layer 5 genes in a reptilian group, turtles. They found that the layer 4 genes *eag2* and *Rorb* are expressed in the turtle homologue of the avian interstitial part of the hyperpallium apicale (IHA), namely within a rostrolateral part of the dorsal cortex, as well as by neurons of the turtle homologue of the avian entopallium. They also found expression of the layer 5 gene *ER81* in a rostral and lateral part of turtle dorsal cortex that is known to project to brainstem [Hall et al., 1977] and therefore corresponds to the avian HA.

These overall findings have several interesting implications. First, they are consistent with the Karten hypothesis that IHA, entopallium and field L (specifically L2) are all homologous to neurons in layer 4 of specific visual and auditory parts of the mammalian neocortex, and that arcopallium and HA contain neurons that are homologous to layer 5 neurons in specific parts of the visual, somatosensory and/or motor cortex. Secondly, the expression of *eag2* and *Rorb* in pallial thalamorecipient neurons and *ER81* in extratelencephalically projecting neurons in reptiles, birds and mammals, suggests that a subset of pallial neurons is fated to possess a thalamorecipient identity, and that another is fated to possess an extratelencephalic output neuron identity. Moreover, the results suggest that these genes play a role in establishing these hodological pallial identities.

Thus, the pallial neuron thalamorecipient phenotype and the pallial neuron output phenotype are ancient amniote traits shared by living birds, reptiles and mammals. Neurons of cortical layers 2 and 3 also possess a unique hodological and functional phenotype, in that they receive input from layer 4 thalamorecipient neurons and project to layer 5 output neurons [Shepherd, 2009]. Interestingly, a recent study by Suzuki et al. [2012] reported that neurons of the avian mesopallium, which have the connectivity of cortical layers 2/3, express several genes that uniquely mark layers 2/3 in mammals, including *Satb2, Cux2, Mef2c* and *FOXP1*. Thus, it seems likely that the three main types of pallial neurons (thala morecipient, extratelencephalically projecting and intrapallially projecting) represent three ancient neuron types found in the common ancestor stem amniote pallium. These three neuron types then represent the building blocks from which similar circuits could be built in their descendents, irrespective of whether they came to be arrayed in a nuclear or laminar manner. Interestingly, the turtle homologues of the avian IHA and HA are cortical in organization, while the IHA and HA are largely nuclear. Thus, in the evolution of Wulst (to which IHA

and HA belong) from the reptilian dorsal cortex, a transformation from cortical to nuclear occurred. Overall, it seems that the avian pallium has embraced a more nuclear architecture than has the pallium in reptiles, as in some groups of reptiles the DVR is semi-laminated [Reiner and Northcutt, 2000].

But just because, for example, field L2 neurons of the nidopallium and layer 4 neurons of the primary auditory cortex are constructed from the same neuron type, how can we know this was not achieved independently from the same ancient pallial pool of thalamorecipient neurons? To answer this, we must ask, among other things, if claustroamygdala is also characterized by the presence of distinct sets of thalamorecipient neurons, intratelencephalically projecting neurons and extratelencephalically projecting neurons. As it turns out, according to the supplemental data of the authors and the Allen Brain Atlas, the basolateral amygdala (BLA) contains extratelencephalically projecting neurons that express layer 5 markers such as *ER81* , while the lateral anterior amygdala contains thalamorecipient neurons that express such thalamorecipient markers as *eag2* and *Rorb*. Given this, how can one know if the thalamorecipient and extratelencephalically projecting neurons of avian DVR are homologous to layers 4 and 5 of neocortex or to lateral amygdala (LA)/BLA? Several considerations argue that the thalamorecipient and extratelencephalically projecting neurons of avian DVR are not comparable to the LA/BLA. First, the thalamic neurons projecting to the LA do not correspond neurochemically or in terms of their own inputs to those projecting to the nidopallium of the DVR. For example, neurons in the shell of the auditory thalamus receive nontonotopic auditory input and project to the LA in mammals, while the homologous thalamic population in birds does not project to L2 [Brauth and Reiner, 1991; Bruce et al., 2002; Reiner et al., 2005]. Rather, as true for layer 4 of the primary auditory cortex, L2 receives its input from the tonotopically organized core of the auditory thalamus [Reiner et al., 2005]. Secondly, developmental gene expression in the LA/BLA does not fit the idea that these are comparable to avian DVR. For example, LA neurons express *dbx1* , but neither nidopallium nor layer 4 cortical neurons express the homeobox gene *dbx1* [Medina et al., 2004; Bielle et al., 2005]. Similarly, LA neurons express the LIM domain homeobox gene Lhx2 in mammals, but L2 and entopallium in birds do not [Abellán et al., 2009]. Moreover, the LIM domain transcription factor *Lmo4* is enriched in BLA/LA, but is poor in the L2 and entopallium in birds, as also true for the cerebral cortex in mammals [Abellán et al., 2009]. Finally, according to the claustroamygdaloid hypothesis, the BLA corresponds to the avian mesopallium [Puelles et al., 2000], yet mesopallium neurons express layer 2/3 markers and the BLA expresses layer 5 markers [Suzuki et al., 2012].

Thus, the study by Dugas-Ford et al. [2012] adds to the weight of evidence favoring the Karten hypothesis, and opposes the view that the DVR in birds and reptiles is a somatosensory-somatomotor-transformed version of what in mammals is a viscerolimbic territory. How then, in this case, did the Wulst-DVR come to look so different from the mammalian neocortex? There are three possible evolutionary scenarios: (1) the stem amniote common ancestor had a Wulst-DVR that was transformed into a neocortical pattern in the mammalian lineage, (2) the stem amniote common ancestor had a neocortex that was transformed into a Wulst-DVR in the lineage leading to birds or (3) the stem amniote

common ancestor had neither a Wulst-DVR nor a neocortex, but rather a region that was small and simple and could be transformed into either by further evolutionary change. Karten has appeared to argue for the first possibility [Karten, 1991]. However, the third is the most likely for several reasons [Reiner et al., 2005]. First, if the first possibility were true, there should be some developmental evidence that an incipient DVR forms in mammalian embryos, but there is not. The second possibility also seems unlikely because the cortical parts of the pallium and the DVR in reptiles lack obvious layer 2/3 neurons in their primary sensory and motor territories, and thus the putative stem amniote cortex was likely to as well. Endocasts of the brains of early cynodont members of the mammalian lineage compared to that of early extinct mammals also support the view that stem amniotes were unlikely to have possessed a 6-layered neocortex, in that the thin elongate shape of the cynodont cerebrum is more reminiscent of that in living amphibians than that in early mammals [Quiroga, 1980; Jerison, 1990]. Thus, the Wulst-DVR complex is unlikely to be a rearranged version of stem amniote neocortex. The DVR develops from the border region between the dorsal pallium (from which Wulst forms) and the striatum. The temporal cortex also develops from this region, which is called the corticostriatal angle. Of note, the DVR and temporal cortex are both relatively smaller in more primitive birds and mammals, respectively. The corticostriatal angle is also the source of the olfactory lobe and amygdala. Further study of the neuron specification and migration in this region, and of the differences in this regard between birds and mammals, should shed light on the respective evolution of the avian DVR versus the temporal pole of the mammalian cerebrum [Molnar and Butler, 2002]. As the study of Dugas-Ford et al. [2012] shows, the necessary tools for identifying and thus manipulating specific neuron types are becoming available for understanding this important branch point in evolution.

References

1. Abellán A, Legaz I, Vernier B, Rétaux S, Medina L. Olfactory and amygdalar structures of the chicken ventral pallium based on the combinatorial expression patterns of LIM and other developmental regulatory genes. J Comp Neurol. 2009; 516:166–186. [PubMed: 19598282]
2. Bielle F, Griveau A, Narboux-Nême N, Vigneau S, Sigrist M, Arber S, Wassef M, Pierani A. Multiple origins of Cajal-Retzius cells at the borders of the developing pallium. Nat Neurosci. 2005; 8:1002–1012. [PubMed: 16041369]
3. Brauth SE, Reiner A. Calcitonin-gene related peptide is an evolutionarily conserved marker within the amniote thalamo-telencephalic auditory pathway. J Comp Neurol. 1991; 313:239–279.
4. Bruce LL, Kornblum HI, Seroogy KB. Comparison of thalamic populations in mammals and birds: expression of ErbB4 mRNA. Brain Res Bull. 2002; 57:455–461. [PubMed: 11923010]
5. Bruce LL, Neary TJ. The limbic system of tetrapods: a comparative analysis of cortical and amygdalar populations. Brain Behav Evol. 1995; 46:224–234. [PubMed: 8564465]
6. Clayton N. Animal cognition: crows spontaneously solve a metatool task. Curr Biol. 2007; 17:R894–R895. [PubMed: 17956752]
7. Dugas-Ford J, Rowell JJ, Ragsdale CW. Cell-type homologies and the origins of the neocortex. Proc Natl Acad Sci USA. 2012; 109:16974–16979. [PubMed: 23027930]
8. Hall JA, Foster RE, Ebner FF, Hall WC. Visual cortex in a reptile, the turtle (*Pseudemys scripta* and *Chrysemys picta*). Brain Res. 1977; 130:197–216. [PubMed: 884523]
9. Holmgren N. Points of view concerning forebrain morphology in higher vertebrates. Acta Zool Stockh. 1925; 6:413–477.

10. Jerison, HJ. Fossil evidence on the evolution of the neocortex. In: Jones, EG.; Peters, A., editors. Cerebral Cortex, vol 8A, Comparative Structure and Evolution of the Cerebral Cortex, Part I. New York: Plenum Press; 1990. p. 285-309.
11. Karten HJ. Homology and evolutionary origins of the 'neocortex.'. Brain Behav Evol. 1991; 38:264–272. [PubMed: 1777808]
12. Karten HJ, Hodos W. Telencephalic projections of the nucleus rotundus in the pigeon *(Columba livia)*. J Comp Neurol. 1970; 140:35–51. [PubMed: 5459211]
13. Karten HJ, Hodos W, Nauta WJ, Revzin AM. Neural connections of the 'visual Wulst' of the avian telencephalon. Experimental studies in the pigeon *(Columba livia)* and owl *(Speotyto cunicularia)*. J Comp Neurol. 1973; 150:253–278. [PubMed: 4721779]
14. Medina L, Legaz I, Lez GG, De Castro F, Rubenstein JLR, Puelles L. Expression of Dbx1, Neurogenin 2, Semaphorin 5A, Cadherin 8, and Emx1 distinguish ventral and lateral pallial histogenetic divisions in the developing mouse claustroamygdaloid complex. J Comp Neurol. 2004; 474:504–523. [PubMed: 15174069]
15. Molnár Z, Butler AB. The corticostriatal junction: a crucial region for forebrain development and evolution. Bioessays. 2002; 24:530–541. [PubMed: 12111736]
16. Pepperberg IM. In search of King Solomon's ring: cognitive and communicative studies of Grey parrots *(Psittacus erithacus)*. Brain Behav Evol. 2002; 59:54–67. [PubMed: 12097860]
17. Puelles L, Kuwana E, Puelles E, Bulfone A, Shimamura K, Keleher J, Smiga S, Rubenstein JL. Pallial and subpallial derivatives in the embryonic chick and mouse telencephalon, traced by the expression of the genes Dlx-2, Emx-1, Nkx-2.1, Pax-6, and Tbr-1. J Comp Neurol. 2000; 424:409–438. [PubMed: 10906711]
18. Quiroga JC. The brain of the mammal-like reptile *Probainognathus jenseni (Therapsida, Cynodontia)*. A correlative paleo-neoneurological approach to the neocortex at the reptile-mammal transition. J Hirnforsch. 1980; 21:299–336. [PubMed: 7419907]
19. Reiner A, Northcutt RG. Succinic dehydrogenase histochemistry reveals the location of the putative primary visual and auditory areas within the dorsal ventricular ridge of *Sphenodon punctatus*. Brain Behav Evol. 2000; 55:26–36. [PubMed: 10773623]
20. Reiner A, Perkel DJ, Bruce LL, Butler AB, Csillag A, Kuenzel W, Medina L, Paxinos G, Shimizu T, Striedter G, Wild M, Ball GF, Durand S, Güntürkün O, Lee DW, Mello CV, Powers A, White SA, Hough G, Kubikova L, Smulders TV, Wada K, Dugas-Ford J, Husband S, Yamamoto K, Yu J, Siang C, Jarvis ED. Avian Brain Nomenclature Forum. Revised nomenclature for avian telencephalon and some related brainstem nuclei. J Comp Neurol. 2004; 473:377–414. [PubMed: 15116397]
21. Reiner A, Yamamoto K, Karten HJ. Organization and evolution of the avian forebrain. Anat Rec A Discov Mol Cell Evol Biol. 2005; 287:1080–1102. [PubMed: 16206213]
22. Shepherd GMG. Intracortical cartography in an agranular area. Front Neurosci. 2009; 3:337–343. [PubMed: 20198150]
23. Striedter GF. The telencephalon of tetrapods in evolution. Brain Behav Evol. 1997; 49:179–213. [PubMed: 9096908]
24. Suzuki IK, Kawasaki T, Gojobori T, Hirata T. The temporal sequence of the mammalian neocortical neurogenetic program drives mediolateral pattern in the chick pallium. Dev Cell. 2012; 22:863–870. [PubMed: 22424929]
25. Zeier H, Karten HJ. The archistriatum of the pigeon: organization of afferent and efferent connections. Brain Res. 1971; 31:313–326. [PubMed: 5569153]