FORUM

THE CALVINIST CORTEX: PENETRATING EVOLUTIONARY PREDESTINATION COMMENTARY ON "CORTEX, COUNTERCURRENT CONTEXT, AND DIMENSIONAL INTEGRATION OF LIFETIME MEMORY" BY BJORN MERKER

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Theories of everything can expect to encounter a high rate of skepticism. The "everything" that includes evolution of the brain, the fundamental connectivity, physiology and expandability of the cortex and all of personal experience is certainly in that class, but Merker's "Cortex, countercurrent context, and dimensional integration of lifetime memory" counters skepticism surprisingly well. This paper opens up an organizational level of the brain to consideration in an evolutionary context in a way I have not seen before.

I will address my commentary principally to the first part of the paper, which discusses the proliferation of the cortex and to lesser extent the hippocampus; the correlation of relative cortex size with longevity, and the central notion of the cortex as the storage site of long-term memory. Merker concentrates on the cortex, and the utility of its pattern of connectivity in long term storage in terms of contextualized personal history. The complementary work of my colleagues and myself has focused on developmental structure in the pattern of brain size changes, and the push-pull relationship of the relative size of the limbic system and isocortex in primates. Primates have somewhat altered a highly-conserved mammalian developmental schedule in order to increase the relative size of the isocortex and decrease the size of the limbic system (principal contributors to limbic system in terms of reduced volume being olfactory bulb, cortex and hippocampus) (Clancy et al., 1999, 2001; Finlay and Darlington, 1995; Finlay et al., 2001; Kaskan and Finlay, 2001; Reep et al., unpublished). An attractive hypothesis to account for this evolutionary innovation is that primates are "longevity specialists" since the cortex is the structure that mediates the ability to store information gained over a long lifetime, an idea that Merker elaborates extensively and interestingly. The hippocampus, the structure involved in the immediate acquisition of contextual knowledge, need not change size as the length of the day in a primate life does not change, only their number. We have contrasted this argument with an earlier one by Jerison that primates reduce the size of the limbic system and increase their cortex, because as diurnal mammals, they have reduced their dependence on olfaction and increased their dependence on vision (Jerison, 1973).

There is a subtle and important problem with any argument invoked to give the reason for the increase in relative size of the cortex. This difficulty applies as much to our version of the argument as Merker's, but Merker's elaboration of the significance of the overall wiring pattern of the cortex could contain the solution. The trouble is teleology.

Since the ancestors of all mammals are thought to be relatively small-brained, nocturnal creatures, compared to the diversity of mammals present now, we can infer that their brains resembled in their general aspects the small marsupials, rodents and insectivores we may examine today. My colleagues and I have demonstrated that all of these current species share a highly conserved developmental program with each other (Finlay and Darlington, 1995; Finlay et al., 2001), and by the same inference, the "stem" mammal is likely to have the same program. Over and over in mammalian evolution, as animals with larger brains diverge in all the radiations, the same structures become disproportionately large: notably the cerebral cortex, and the cerebellum. These particular structures happen to have a high slope of relative increase of their size with respect to whole brain size: each neural structure has its characteristic slope, with negative, isometric or positive allometry with respect to the rest of the brain.

What predicts these slopes? Standard evolutionary argument is that disproportionate increases need to be accounted for, and the increased size of certain structures with their inherent extra cost, must indicate some particular adaptive value for that structure. It is thus interesting that the same structures, over and over again, become disproportionately large in mammalian evolution. It proves that what accounts for the conserved structure of evolutionary change is a conserved developmental schedule (Finlay and Darlington, 1995; Finlay et al., 2001). The structures that get disproportionately large when brain size increases are the structures that happen to cease neurogenesis last, and which get the benefit of extra cycles of cell division that increase the size of their precursor pools at some exponent greater than the rest of the brain. In the small-brained animals, the cortex is not the largest structure in the brain, but it overtakes and greatly exceeds the volume of all others due to its privileged embryological timing. Selected-for functions appear to be able to colonize areas of the brain where space is made available by developmental rule, genetically or epigenetically.

The trick is, though, that the cortex is the last-generated structure in the small-brained stem mammals, though its relative volume suggests no overwhelmingly central role. It seems improbable that the structure predestined to become disproportionately large, by virtue of its developmental position, also already contains the blueprints for the proper structuring of life-history information in long-lived, large-brained primates, as if the cortex somehow knew its intended fate.

So much is made of the commonality of cortical structure across mammals (and Merker does too) that the teleological conundrum described above has been overlooked. Two types of commonality are usually noted: first, the conservation of cell types, layers, columns, internal and external connectivity and fundamental sensory and motor areas across mammals, and second, the similarity of the cortical modules used for diverse functions in any one brain, from basic sensory functions, simple and complex motor control, and every aspect of cognitive organization and control, from life history to moral judgment. It is theoretically possible that in some way, the basic cortical structure of cognition is simpler than we think and all necessary rules for the organization of all knowledge are potentially available in the relatively few cortical columns of the stem mammal. Alternatively, something changes as brains enlarge.

Theories exist about what changes, but to my mind these theories usually involve *ad-hoc* explanations for particular adaptations in particular species and ignore the systematic relationships of such central structure-function relationships as brain size and longevity. On the anatomical end, there are several claims of cell classes or gene expressions unique to particular areas in the large primate or human brain, though the significance of such observations is not known (for example Preuss and Coleman, 2002). Arguments about the origin of language and its association with the human brain often have implicit or explicit the argument that new circuitry must exist capable of representing symbolic operations, present at least in the language cortex (Pinker, 1994). The plasticity that cortex exhibits in representing sensory, motor and cognitive organization, both in normal learning, and after changed developmental trajectories due to early sensory loss or insult argues that localized changes in the cellular organization of particular areas of the cortex are a poor place to begin to understand the unusual capacities of large brains (for example, Pallas, 2001; Sadato et al., 1996). Merker's theory, however, gives me the first glimmering of what level of organization might be central to contrast in the cortical organization of animals with simple or complex life histories – the superordinate organization of the types described in his Figures 2-4. Understanding the accretion of this kind of superordinate structure, perhaps looking at differences in the organization of the cortex between animals whose cortices are the same size, but who differ in "encephalization", brain/body ratio, the variable that correlates with longevity, might be a way to begin.

A second place to use this general structure to understand evolutionary change might be in the respective functions of the hippocampus and cortex, asking whether they are different *ab initio* or whether they have systematically diverged in animals with longer life spans. Merker takes the contrast seen in primates between the temporally-limited functions of the hippocampus and the longer-term memory capacity of the cortex as essential properties of the two (and to be fair, much of the evidence demonstrating this distinction derives from rats, not primates (Wittenberg and Tsien, 2002)). How do we understand what limits the time window over which any structure might integrate? Is it a function of how easy it is to overwrite a memory trace at the level of the cell and synapse, at the level of the size of the buffer (the number of cells or equivalent information-carriers in a structure), or perhaps, at the level of the organization of connectivity between the two structures? It's not obvious: the duration of labile memory in humans, the type thought to be dependent on the hippocampus (Squire, 1992), exceeds the lifetime of rats, which would argue against fundamental synaptic properties being the basis of the difference. Perhaps, the original distinction between hippocampus and cortex is on task structure, and cortex's association with longevity is a secondary adaptation. Evolution does present us an interesting contrast where we might explore the "buffer" idea above – primates reduce the size of their hippocampus dramatically with respect to the rest of the brain compared to some reasonably close phylogenetic relatives, insectivores and rodents. Do primates incur any deficits on "hippocampal" tasks by this structural alteration?

In sum, I congratulate the author on a provocative paper that moves from known brain structure to cognitive structure in a new way. A framework able to distinguish the emerging cortical organization in larger brains that is implicit and predestined from the rules of smaller brains from adaptive alterations of the same structure must depend upon the development of theories that link overall brain structure to the integrative abilities that Merker describes.

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References

Clancy B, Darlington RB and Finlay BL. The course of human events: predicting the timing of primate neural development. *Developmental Science*, *3:* 57-66 1999.

Clancy B, Darlington RB and Finlay BL. Translating developmental time across mammalian species. *Neuroscience*, *105:* 7-17, 2001.

FINLAY BL and DARLINGTON RB. Linked regularities in the development and evolution of mammalian brains. *Science, 268:* 1578-1584, 1995.

FINLAY BL, DARLINGTON RB and NICASTRO N. Developmental structure in brain evolution. *Behavioral and Brain Sciences, 24:* 263-307, 2001.

JERISON HJ. *Evolution of the Brain and Intelligence.* New York: Academic Press, 1973.

KASKAN P and FINLAY BL. Encephalization and its developmental structure: how many ways can a brain get big? In T Sanderson (Ed), *Evolutionary Anatomy of the Primate Cerebral Cortex*. Cambridge: Cambridge University Press, 2001, pp. 14-29.

PALLAS SL. Intrinsic and extrinsic factors that shape neocortical specification. *Trends in Neurosciences, 24:* 417-423, 2001.

PINKER S. *The language instinct: How the mind creates language*. New York: William Morrow, 1994.

PREUSS TM and COLEMAN GQ. Human-specific organization of primary visual cortex: Alternating compartments of dense Cat-301 and calbindin immunoreactivity in layer 4A. *Cerebral Cortex, 12:* 671-691, 2002.

REEP R, DARLINGTON RB and FINLAY BL The limbic system in mammalian evolution. Submitted.

SADATO N, PASCUALLEONE A, GRAFMAN J, IBANEZ V, DEIBER MP, DOLD G and HALLET M. Activation of the primary visual cortex by Braille reading in blind subjects. *Nature, 380:* 526-528 1996.

SQUIRE L. Memory and the hippocampus – a synthesis of findings from rats, monkeys and humans. *Psychological Review, 99:* 195-231, 1992.

WITTENBERG GM and TSIEN JZ. An emerging molecular and cellular framework for memory processing by the hippocampus. *Trends in Neurosciences, 25:* 501-505, 2002.

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