

Absolute brain size: Did we throw the baby out with the bathwater?

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The recent study by Sherwood *et al.* (1) in this issue of PNAS is a study in irony. It is thus so because the authors used some of the most current and sophisticated histological and data-analytic tools to, in the end, unearth . . . a dinosaur. Now the authors did not do this in the literal sense. Rather, they laid bare an “extinct” measure of brain anatomy: that old fossil known as absolute brain size. Even as far back as the 1800s, Alexander Brandt (2) and, a bit later, Otto Snell (3) demonstrated the importance of scaling the brain to body size, signaling the impending demise of absolute brain size as a valid measure of brain capacity. The final death knell was struck in its most popular form by Harry Jerison, who reminded us once again that brain–body allometry plays a major role in the size of any species’ brain. He effectively argued that the brain, like any other organ, scales with body size, and the validity of the use of brain size as a measure of intelligence or information processing capacity rests upon the size of the brain relative to the size of the body. He introduced the encephalization quotient (EQ) as a proper measure of relative brain size across species (4). EQ is a number that essentially quantifies how much larger or smaller the average brain size of a given species is relative to the expected brain size based on body size. Likewise, the residual of a brain weight–body weight regression across a sample of species provides similar information. And, although different authors have different theoretical justifications for the parameters of the brain–body size relationship across species [see Deaner *et al.* (5) for review], all measures of relative brain size are based on the common assumption that it is only meaningful to consider brain size if body size, or some relative measure, is taken into account. Therefore, nowadays, absolute brain size as a measure of cognitive capacity is considered obsolete.

However, in the rush to abandon absolute brain size in favor of measures of relative brain size, have we been altogether too hasty? Well, no, not entirely. There are valid reasons for taking into account the allometric relationship between brain and body size when attempting to infer how much of any

species’ brain is devoted to cognitive processes. But could we have, at the very least, missed something important about absolute brain size in the process? Did we throw the baby out with the bathwater? The Sherwood *et al.* (1) study suggests that we might have.

Recent microarray studies have shown that neuronal signaling and energy production genes are up-regulated in the human neocortex compared with the great apes (6, 7). These findings suggest that there was selection for higher rates of energy expenditure in human neocortex compared with in other primates (8). One way to measure metabolic support

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for neurons is by examining the ratio of glia to neurons. The distribution densities of glia provide an indication of the metabolic demand of neighboring neurons. Sherwood *et al.* (1) investigated whether glial cell densities are relatively higher in human frontal cortex compared with other primates. They reasoned that significantly higher glia–neuron ratios in humans might exemplify the kind of unique trait that would provide a basis for human intelligence. However, the Sherwood *et al.* (1) study is much more than a study in cell densities, metabolism, and allometry. What makes this article so compelling is that it has profound implications for the question of neurobiological continuity across species, particularly across humans and our closest nonhuman relatives, the great apes. It addresses the general question of whether human brains should best be thought of as large hominoid brains, or, alternatively, as a singularly endowed product of evolution somewhat apart from the rest of primate brain evolution.

Sherwood *et al.* (1), did indeed find that the human frontal cortex displays a higher ratio of glia to neurons than in other primates. However, and importantly, this relative difference is pre-

dicted by the allometric scaling inherent in the enlargement of the human brain. In other words, Sherwood *et al.* (1) show that overall or absolute brain size constitutes a key factor in the ratio of glia to neurons. The authors suggest that the greater numbers of glia in the human neocortex may be due to the increased energetic costs of larger dendritic arbors and longer fiber projections within the context of the large human brain. The bottom line is that Sherwood *et al.* (1) show that the human brain conforms to the general mammalian pattern of higher glia–neuron ratios with larger brains.

Furthermore, Sherwood *et al.* (1) determined whether there were regional differences in glia–neuron ratios across humans and nonhuman primates in cortical regions associated with specific human abilities, such as area 44, a key area for language production, and area 32, which is active during theory-of-mind tasks in humans. Sherwood *et al.* (1) found no significant species differences in these critical areas and suggest that the energetics of frontal cortex, even in these regions, have been largely conserved over the past 25 million years of primate brain evolution. Their overall conclusion is striking: “. . . human cognitive and linguistic specializations have emerged by elaborating on higher-order executive functions of the prefrontal cortex . . . that evolved earlier in the primate lineage” (1).

Sherwood *et al.* (1) provide support for the idea that the human brain is more or less a large hominoid brain and can be understood in that context. However, these findings also engender many questions about the relationship between brain size and cognition. If human brains fall in line with generally expected patterns of relationship among overall size, neuron density, and glia–neuron ratios and yet possess a number of striking cognitive features, how should the absolute size of brains be interpreted? What happens to brains when they enlarge over time? How can

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these changes provide a substrate for changes in cognitive abilities?

When More Is More than Just More

When brains enlarge, they can do so in a couple of different ways. They may add more neurons or make existing neurons larger, or some combination of both. However, both of these changes pose design problems that need to be solved because larger neurons have longer axons and dendrite conduction times will be slower. When the number of neurons increases, it becomes more difficult for each individual neuron to maintain connectivity. Therefore, brains cannot enlarge (either by adding neurons or by making them bigger) without the organization of the brain changing. The main way most mammal brains have enlarged is by increasing modularity to accommodate increases in the number of neurons. Increased modularity increases the number of processing areas. Indeed, there is substantial evidence that mammals with more neocortex possess more cortical areas and more units of parcellation (e.g., columns, etc.) than smaller-brained mammals (9).

So enlarged brains can support increases in cognitive ability because they may be more highly segmented and differentiated, thereby possessing more complexity than their smaller counterparts. This is a case of more being more than just more. Enlarged brains not only have more neurons, they also have greater complexity, which is more than just more. Therefore, brain enlargement, and the increases in complexity that necessarily accompany it, may provide the substrate for enhanced cognitive abilities or even the emergence of new cognitive abilities. In this context, absolute brain size regains its value as a brain metric because it becomes a proxy for increased organizational complexity. So maybe it should be retrieved from the bathwater!

Implications for Neurobiological Continuity

The deep fundamental insight supported by Sherwood *et al.* (1) is that the human brain is not unique or anomalous. Rather, the human brain is a product of changes in brain anatomy that are well predicted by scaling expectations for any nonhuman anthropoid primate. The

study by Sherwood *et al.* (1) is a particularly elegant example of a growing body of evidence for this conclusion. For instance, several studies have shown that the human frontal cortex occupies the same proportion of total cortex in humans as it does in great apes (10, 11). Therefore, humans are typical primates with regard to the portion of their cortex devoted to frontal cortex. Similarly, the human brain possesses the degree of cortical gyrification expected for a primate of our brain size (12). These findings show that there are ways to obtain new or enhanced cognitive abilities in human brains that are perfectly consistent with the way brain evolution occurred in other primates. [To be fair, there is also evidence that the human brain might depart from certain allometric expectations (13).]

Regardless of which features of the human brain are typical of other primate brains, the more general point is that a consideration of absolute brain size provides insight into which features of the human brain are predictable and which are not. Therefore, absolute brain size has turned out to be an important variable in its own right for understanding mammalian brain evolution.

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