

NEUROSCIENCE

Scaling of human brain size

Higher cognitive regions are preferentially expanded in individuals with larger brains

By David C. Van Essen

What makes humans unique as a species and as individuals? Our uniqueness stems from language, tool use, reasoning, and other cognitive abilities that are largely mediated by specialized regions of the cerebral cortex. These regions of higher cognitive function have expanded disproportionately during human evolution (compared with nonhuman primates) and during postnatal maturation, when cortical surface area expands threefold between infancy and adulthood (1). Our uniqueness as individuals reflects countless differences in brain structure, function, and connectivity. One basic anatomical difference between similarly aged individuals is a more than 1.5-fold variation in total brain size (and total cortical volume) (2). On page 1222 of this issue, Reardon *et al.* (3) bring this aspect of individual variability under the umbrella of “differential scaling” by showing that human brains of different sizes do not scale uniformly across all regions. Rather, larger brains show greater expansion in regions associated with higher cognition and less expansion in regions associated with sensory, motor, and limbic (emotion- and affect-related) functions.

A simple *a priori* hypothesis is that brains of different size might be linearly scaled versions of one another. However, there is already evidence against this hypothesis, insofar as the cerebral cortex is a mosaic of many cortical parcels (areas) that each show more than twofold individual variability in size (4, 5). But are individual differences in the size of various parcels correlated systematically, for example, according to function? Reardon *et al.* analyzed data from more than 3000 healthy individuals, drawn from three independent

cohorts: the Philadelphia Neurodevelopmental Cohort (PNC) and National Institutes of Health (NIH) cohort (each comprising children and young adults), as well as the Human Connectome Project (HCP) cohort (comprising young adults only). By using *in vivo* structural magnetic resonance imaging (MRI) scans of individual brains, surface models of the cerebral cortex were generated and aligned to a surface-based cortical atlas. Local cortical surface area was then expressed in relation to individual differences in total cortical surface area (see the figure). Notably, both age and sex were ruled out as confounding factors, even though average brain size differs by age and sex (2). Areal scaling maps show broad similarities across

the three cohorts in terms of which regions are expanded in larger brains (positive scaling) and which are less expanded in larger brains (negative scaling). However, there are many differences across the three cohorts, and regions that pass statistical significance for only one or two cohorts might not reflect genuine neuroanatomical effects. Given concerns about reproducibility (6), it is notable that Reardon *et al.* carried out what is effectively a multicohort reproducibility analysis.

The authors compared areal scaling maps to independent measures related to cortical evolution, development, function, and gene expression. They found modest correlations with maps of evolutionary expansion (compared to nonhuman primates) and postnatal developmental expansion (7). Comparisons with neuronal networks when at rest, mapped using functional MRI (7), reveal that the “default-mode” network (which is more active at rest) tends to show positive areal scaling, whereas the limbic network tends to show negative areal scaling. Comparisons with gene expression maps from postmortem human brains (8)

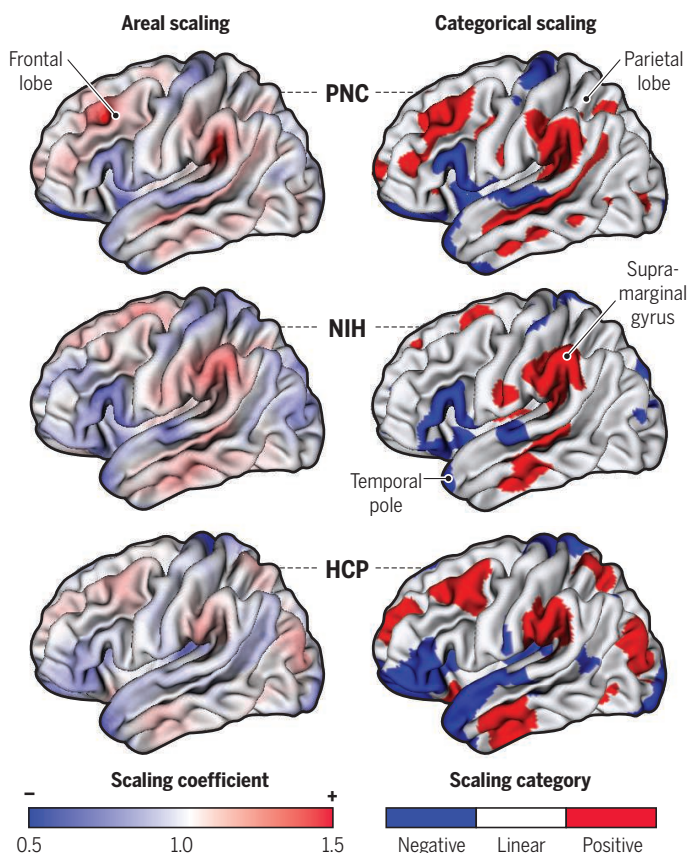
reveal that areal scaling is more positive in regions enriched in mitochondria-related genes and show high energy consumption at rest. These regions have lower myelin content within gray matter and greater synaptic plasticity (9) and have neurons with larger dendritic arbors and more dendritic spines (10).

Reardon *et al.* also examined other brain structures using a subcortical surface-based approach. They found positive- and negative-scaling regions within each structure, indicating that size-related differences are not restricted to the neocortex. For technical reasons, they excluded the cerebellum from their analysis, but this would be interesting to examine in the future, as the cerebellum is involved in cognition as well as coordination of movement (11).

One important issue is whether some of the underlying neuroanatomical scaling patterns are sharper than the relatively smooth gradations shown in their maps. Functionally corresponding regions were not consistently aligned between individuals because alignment was driven by cortical-folding patterns, which are variable and imperfectly correlated with cortical areal

Brain size variation

Maps of areal scaling relative to total brain size for the PNC, NIH, and HCP cohorts. The supramarginal gyrus is positively scaled and the temporal pole is negatively scaled in all three cohorts, but differences in scaling between the cohorts also exist. IQ correlates with overall cortical surface area.



Washington University, St. Louis, MO, USA.
Email: vanessen@wustl.edu

boundaries (4, 5, 12); in addition, the authors extensively smoothed the data for methodological reasons. The HCP dataset is well suited for further exploration because it was aligned using areal features rather than only cortical folding (5, 13) and it also includes a 180-area-per-hemisphere multimodal cortical parcellation that has been accurately delineated in individuals and as a group average (5). This should enable analysis of scaling relationships determined for each cortical parcel, which would circumvent the confounds of imperfect intersubject registration.

Another issue is the possible relationship between the size of different brain regions and behavior. Reardon *et al.* found that the intelligence quotient (IQ) significantly correlates with overall cortical surface area (higher IQ is observed in individuals with more cortex, after factoring out age and sex). Others have reported that variability in “functional connectivity” in individuals at rest appears to be greatest in regions of higher cognitive function, including those associated with personality, intelligence, visual perception, and memory performance (14). Intersubject variations in behavior and lifestyle that are predictable from functional connectivity may largely reflect individual differences in the spatial arrangement of functional regions, perhaps including their size, particularly in regions of higher cognitive function (15).

Questions of how areal scaling emerges during brain development and maturation are also intriguing to consider. Are areal-scaling differences driven by genetic factors and/or influenced by environmental factors? Do regions that are larger in some individuals have a greater number of neurons and/or a larger fraction of neuropil (dendritic, axonal, synaptic, and glial arborizations)? These questions are amenable to analysis through large-scale human neuroimaging projects combined with advances in postmortem and in vivo anatomical methods. ■

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ECOLOGY

Animals feel safer from humans in the dark

Mammals shift their activities to twilight and night hours in response to human disturbance

By Ana Benítez-López

About 75% of Earth's land surface is currently modified by human activities (1). The expanding footprint of human activities is not only causing the loss of habitat and biodiversity but also affecting the dynamics of wildlife populations. Researchers have long examined human-induced spatial shifts in the distribution of wildlife, but temporal adjustments in animal activity have received less attention. On page 1232 of this issue, Gaynor *et al.* (2) present a comprehensive meta-analysis to quantify the increase in wildlife nocturnality due to human disturbance.

About 50 years ago, Walther suggested that animals perceive human disturbance similarly to predation risk (3). According to this risk-disturbance hypothesis, animal responses to predation risk and anthropogenic disturbance stimuli create similar trade-offs between avoiding perceived risk and pursuing other fitness-enhancing activities, including feeding, parental care, or mating displays (4). Although these responses allow human-wildlife coexistence, they may have important effects on animal fitness through indirect effects on survival and reproduction.

Humans, as day-active (diurnal) apex “superpredators” (5), instill fear in other wildlife like no other predatory species. Animals usually respond by reducing movement rates (6) and spatially avoiding anthropogenic activities (7). However, as wilderness areas disappear, there is little opportunity for animals to spatially avoid humans. In highly disturbed areas, animals may substitute spatial refuges by temporal refuges, with animals shifting daytime activities to the twilight or night hours (see the figure). Such temporal partitioning is a common response in animal communities that allows coexistence between competitive species and shapes predator-prey dynamics. However, until recently, the effect of human disturbance on animal temporal activities

has been difficult to assess, particularly in secretive wildlife.

In recent decades, the advent of technologies, such as satellite and global positioning system (GPS) telemetry or camera traps, has made it possible to monitor wildlife activity more accurately. Gaynor *et al.* have now collated data from 76 studies of 62 mammal species from different locations across the world and have quantified the effects of several forms of human disturbance on wildlife. They conclude that nocturnality is a universal behavioral adaptation of wildlife in response to humans.

In their analysis, the authors compared activity patterns of mammals in areas with high and low human disturbance. They report that mammals increased their nocturnality by a factor of 1.36 across continents, habitats, taxa, and human activities. This means an increase of ~20% in nocturnality on average. Furthermore, out of 141 identified mammal responses to human disturbance, 83% corresponded to an increase in nocturnality; larger mammals exhibited a slightly stronger response than smaller mammals, either because they are more likely to be hunted (8) or as a result of an increased chance of human encounter. Lethal (hunting) and nonlethal activities had comparable effects on mammal activity, supporting Walther's seminal idea on the similarity in animal perception of predation risk and human disturbance (3, 4).

The consequences of human-altered patterns in the activity of wildlife are manifold and are not necessarily limited to the disturbed species or population. The diminished ability of apex predators to hunt at night may impair their role as top-down regulators, and predator-prey interactions may change drastically, whereas prey species that become more nocturnal to avoid humans may be more susceptible to predation by nocturnal predators. Further, human impacts may constrain the temporal partitioning of carnivores exploiting the same prey communities, thus altering competitive dynamics among carnivores by increasing temporal overlap while hunting. Human-altered interspecific competition dynamics may in turn enable human-tol-

Department of Environmental Science, Institute for Water and Wetland Research, Radboud University, 6525 HP Nijmegen, Netherlands. Email: a.benitez@science.ru.nl

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