REPLY TO BARTON AND MONTGOMERY:
A case for preferential prefrontal cortical expansion

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In our article (1), we focus on prefrontal cortex (PFC) to (*i*) arrive at a surface-based delineation of PFC using modern architectonic and functional criteria; (*ii*) determine its absolute size in humans, macaques, and chimpanzees in terms of gray and white matter volumes analyzed using structural MRI data from many subjects; and (*iii*) compare PFC size across species both in absolute terms and relative to other brain regions. Barton and Montgomery (2) dispute neither our findings nor our conclusion that PFC is disproportionately larger in humans compared with nonhuman primates. They instead take issue with several matters of interpretation, particularly how relative size and preferential expansion are used in an evolutionary context.

We consider preferential expansion to indicate a region (e.g., PFC) having a larger size compared with other, more evolutionarily conserved regions (e.g., early sensory cortex) in one species (human) vs. others (nonhuman primates). In contrast, Barton and Montgomery (2) apparently consider preferential expansion and relative size in connection with divergence from allometry (e.g., lying above an allometric scaling line). They contend that that we "gloss over the distinction between proportional and relative size," yet using our definitions, we explicitly analyzed proportional sizes (e.g., PFC as a fraction of total cortical gray matter) and relative sizes (e.g., PFC vs. area V1 gray matter; our figure 4B). Regarding allometry, our data show human PFC to lie on the regression line with macaques and chimpanzees (humans were included in the regression), but our analysis was limited to three species and precluded a strong test of whether human PFC conforms to an allometric scaling relationship. Inclusion of more species might well show human divergence (3).

Even if humans do lie along the nonhuman primate allometric line, this would not preclude natural selection for increased PFC size in our species. This is because allometric plots are neutral with respect to cause of change; one could equally well argue that selection on brain size drives increases in PFC size or that selection on PFC size drives increases in brain size. However, we agree with Barton and Montgomery (2) that differential evolutionary expansion likely reflects differences in distributed cortical, subcortical, and cerebellar functional networks and are not confined to just PFC. We cited evidence for preferential expansion of other regions of association cortex—particularly lateral temporal and inferior parietal cortex—relative to early sensory regions (4, 5). In our view, association cortical relative (and absolute) expansion remains compatible with the idea that PFC may have specialized computational roles (e.g., mediating executive functions) related to its expanded size and lower neuronal density [larger dendritic arbors (6) and higher synaptic density], as well as its more complex interareal patterns of connectivity (7), consistent with an elevated proportion of white matter underlying PFC (1, 3). Definitions aside, evolution has endowed human PFC (and other association regions) with functional characteristics that apes and monkeys have to a lesser degree, if at all, including those related to language (8), numerical/symbolic manipulation (9), social cognition (10), and abstract relational reasoning (11).

1 Donahue CJ, Glasser MF, Preuss TM, Rilling JK, Van Essen DC (2018) Quantitative assessment of prefrontal cortex in humans relative to nonhuman primates. *Proc Natl Acad Sci USA* 115:E5183–E5192.

2 Barton RA, Montgomery SH (2019) Proportional versus relative size as metrics in human brain evolution. *Proc Natl Acad Sci USA* 116:3–4.

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