FRACTAL ANALYSIS AS A TOOL FOR STUDYING SPECIALIZATION IN NEURONAL STRUCTURE: THE STUDY OF THE EVOLUTION OF THE PRIMATE CEREBRAL CORTEX AND HUMAN INTELLECT

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Received 17 March 2005

We review recent findings that, using fractal analysis, have demonstrated systematic regional and species differences in the branching complexity of neocortical pyramidal neurons. In particular, attention is focused on how fractal analysis is being applied to the study of specialization in pyramidal cell structure during the evolution of the primate cerebral cortex. These studies reveal variation in pyramidal cell phenotype that cannot be attributed solely to increasing brain volume. Moreover, the results of these studies suggest that the primate cerebral cortex is composed of neurons of different structural complexity. There is growing evidence to suggest that regional and species differences in neuronal structure influence function at both the cellular and circuit levels. These data challenge the prevailing dogma for cortical uniformity.

Keywords: Fractal; dilation; primate; cortex; visual; prefrontal; macaque; human; galago; marmoset.

1. Regional Differences in Pyramidal Cell Branching Structure in Neocortex

The analysis of large populations of pyramidal cells has revealed marked variation in pyramidal cell structure in different cortical areas in monkeys [9, 11, 13–17, 28, 30, 40]. However, Sholl analyses [48] have been employed in many of these studies, the results of which cannot easily be related to differences in brain size. Thus, it is not possible to speculate about how these specializations in dendritic branching structure may have evolved in the primate brain. Fractal analysis reduces the dendritic trees of individual neurons to a single number, making it an ideal tool for investigations into the relationships between cell structure and brain size [18]. Moreover, fractal analysis has been used to reveal aspects of neuron structure not detectable by other methods [1, 25, 45, 49] (see Refs. 1, 18 and 49 for reviews of fractal analysis). In a recent series of studies [12, 31, 32, 54], the dilation method was used to determine the fractal (D) values of the dendritic arbours of pyramidal cells in the
monkey visual cortex. It was demonstrated that the fractal values differ between large populations of neurons sampled in different cortical areas (Figs. 1 and 2). In the macaque monkey, the fractal values of pyramidal cells were found to differ quite dramatically between the primary (V1) and second (V2) visual areas and cytoarchitectonic areas TEO and TE (Fig. 1). Cells in areas TEO and TE, which process for global aspects of the visual scene, have more complex branching patterns than those in V1 and V2, which process for local features such as spectral signature, contrast and edge detection. The former cortical areas are often referred to as “high order” visual areas whereas those in V1 and V2 are often referred to as “low order” visual areas.
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**Fig. 2.** Frequency histograms of $D$ values of layer III pyramidal cells sampled from (top) the marmoset monkey and (bottom) the owl monkey. Data were sampled from the primary (V1), second (V2), and caudal and rostral inferotemporal visual cortex (ITc and ITr, respectively). Data taken from Refs. 12 and 32.
visual areas (see Refs. 19, 22, 23, 52, 53) for reviews). These data contradict widely held dogma that the cortex is comprised of repeated “canonical” circuits of similar computational power (e.g. Refs. 3, 4, 24, 38, 42, 51). Instead, pyramidal cells have specialized structure in different cortical areas, which is believed to subserve their functional requirements [5, 7, 29].

These initial findings in the visual cortex of the macaque monkey have since been confirmed in a number of other primate species (Fig. 2). In the marmoset monkey and owl monkey there is a tendency for increasing fractal value of neurons with anterior progression through occipitotemporal cortical areas involved in visual processing [12, 32]. As in the macaque monkey, neurons in these different cortical areas are characterized by different functional properties (i.e. local versus global features).

What also becomes apparent from these data is that the relative extent of the difference in fractal values of neurons between visual areas differs in these three species. This begs the question, why is the trend for an increase in branching complexity through these areas greater in the macaque monkey than in the marmoset and owl monkey? In order to investigate this observation further, the branching structure of pyramidal cells in different cortical regions in the brain has been compared between a more diverse selection of primates. Moreover, methodologies have been standardized to avoid potential methodological errors that could be introduced by differences in the algorithms and confidence levels used to determine the fractal values, and the size and resolution of the cell images they are based on [33].

2. Brain Size Versus Circuit Structure: What Happens to Cortical Neurons When the Brain Gets Bigger?

Mammalian brains vary considerably in their size. There is nearly a 10,000 fold difference in the surface area, and a 25,000-fold difference in the volume, of the cerebral cortex in the mammalian brain (see Refs. 26, 27, 34, 35, 37, 39, 43 for reviews). Modeling studies reveal how increasing brain size may influence patterns of connectivity in the brain (see Refs. 36 and 47 for reviews); however, there remain few quantitative data on how neuron structure and patterns of connectivity may differ in the mammalian cortex. Fractal analysis of large numbers of cells sampled from brains of differing size is beginning to reveal whether neurons in larger brains reflect species-specific specializations that occur irrespective of size, or whether they reflect scaling. Establishing which of these two possibilities has occurred is essential if we are to better understand the evolution of cortical circuitry and, thus, specializations in cortical function.

Studies of pyramidal cells in the cerebral cortex in a variety of primate species have revealed some interesting insights into how neuronal structure may vary in different sized brains, and how trends observed in one cortical region may not occur in another. For example, pyramidal cells in both V2 and IT of the human, baboon, macaque monkey, vervet monkey, owl monkey, marmoset monkey and the
galago have relatively similar fractal values (when scale, resolution and fractal method are standardized), despite their different sized brains (Figs. 3 and 4). However, data for the granular prefrontal cortex (gPFC), the region of cortex often associated with executive cortical functions such as memory, comprehension and thought [20, 21, 41], differ systematically between the various species (Fig. 4). There is a trend for progressively higher $D$ values with increasing size of gPFC.
Fig. 4. Frequency histograms of $D$ values of layer III pyramidal cells in the second visual area (V2), inferotemporal cortex (IT) and granular prefrontal cortex (gPFC) of the marmoset monkey, owl monkey, galago, vervet monkey, macaque monkey, baboon and human. Note there is no consistent trend for an increase or decrease in the average $D$ values (dashed line) with respect to brain size in either V2 or IT. In gPFC on the other hand, there is a trend for progressively greater $D$ values with increasing surface area of the granular prefrontal cortex. Mean ± SD included in brackets. Data for marmoset V2 and IT taken from Ref. 12; data for aotus taken from Ref. 32; data for macaque V2 and IT taken from Ref. 31; data for galago V2 and IT taken from Ref. 54.
Fig. 5. Plot of the fractal value (dilation method) versus the size of the dendritic trees of over 600 layer III pyramidal cells sampled from the primary and second visual areas (V1 and V2, respectively) and granular prefrontal cortex (gPFC) of human, baboon, macaque monkey, vervet monkey, owl monkey, marmoset monkey and galago. Note in particular the difference in fractal values in V2 with increase in brain size, and the disproportionate variation in the number of dendritic spines in gPFC ((c) and (d)). # p < 0.1, * p < 0.05. Data from (a), (c) and (d) taken from Ref. 10.

Relating these fractal data back to the size of the brains of each species reveals some dramatically different trends in neuron complexity in the visual cortex not observed in granular prefrontal cortex. For example, cells in V1 and gPFC tend to have a higher fractal value (i.e. are more complex) in larger brains whereas the opposite is true in V2 (Fig. 5). In addition, cells in the gPFC are disproportionately more spinous in larger brained primates than cells in either V1 or V2 (Fig. 5).

These differences in neuron structure detected by fractal analysis are likely to influence various aspects of neuronal function. For example, differences in the branching patterns of the cells and their space filling characteristics influence their functional capability and storage capacity, respectively [44, 50] (see Refs. 5–7, 29 for reviews). As each spine receives at least one excitatory synapse, differences in the number of dendritic spines reflect different numbers of inputs received by the neurons. In addition, these data reveal that cortical expansion does not necessarily occur through the addition of more of the same type of cells/circuits with the same computational power. Instead, expansion may occur through the addition of more cells, which have highly specialized morphology endowing them with different computational abilities. Moreover, the differences in the branching structure reportedly
influence the memory capacity of both individual neurons and the circuits they comprise. Neurons with more complex branching structure have a greater potential to compartmentalize processing within their dendritic trees than those with less complex branching structure, allowing for greater memory capacity (see Ref. 2 for a review).

These findings provide new insights into the evolution of executive functions performed by neurons in the prefrontal cortex in primates and their differing cognitive styles. In particular, the increasing complexity in neuron structure during the volumetric increase in the anthropoid brain may have been instrumental for the evolution of the human intellect. In addition to the wholesale upregulation of gene expression [46], and increase in volume [27], the evolution of human intellect may be closely linked to the disproportionate increase in the complexity of neurons in prefrontal cortex [8].

Acknowledgments

Funded by grants from the McDonnell Foundation and the National Health and Medical Research Council, Australia. Thanks go to Herbert Jelinek for assistance with earlier studies.

References


