

Ontogenetic changes in the fractal geometry of the bronchial tree in *Rattus norvegicus*

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ABSTRACT

Respiration and metabolism change dramatically over the course of the development of vertebrates. In mammals these changes may be ascribed to organogenesis and differentiation of structures involved in gas exchange and transport and the increase in size. Since young as well as mature individuals must be well-designed if the species is to survive, the physiological changes during the development should be matched with geometrical or structural adjustments of the respiratory system. The aim of this study was to evaluate changes in the fractal geometry of the bronchial tree during the postnatal development of the rat.

The average fractal dimension of the bronchial tree of the rats was 1.587, but that of juveniles was larger than that of the adults. We found a significant negative correlation between age and fractal dimension. This correlation could be considered misleading because of the difficulty of separating age/body size effects. Nevertheless, because fractal dimensions of the bronchial tree of rabbits and humans are known to be similar, 1.58 and 1.57 respectively, the body size effect may be nil. To our knowledge, this is the first report of ontogenetic changes in the fractal dimension of the bronchial tree in mammals.

Key terms: Bronchial tree, Fractals, Ontogeny

Respiration and metabolism change dramatically over the course of the development of vertebrates. In mammals these changes may be ascribed to organogenesis and differentiation of structures involved in gas exchange and transport, as well as to the increase in size. This last factor affects both the metabolic rate and the relative importance of convection and diffusion in gas exchange and transport (3). Mammals continue their development after birth, changing their breathing dynamics, morphology and the mechanical properties of the respiratory system (2, 10, 15). Such changes include adjustments in minute ventilation, tidal volume, respiratory frequency, and passive and active compliance, thereby determine a minimum effort of breathing during the course of postnatal development (7).

Since young as well as mature individuals must be properly designed if the species is to survive, the physiological changes occurring during development should be matched with topological or structural adjustments of the respiratory system. Bartlett and Areson (2) showed changes in the allometric relationships between body weight and O₂ consumption and between alveolar surface and O₂ consumption in newborn mammals with respect to adults. Other reports have shown a two- to three-fold increase in the alveolar surface/O₂ consumption ratio during the postnatal development of the rat (4, 9, 21).

Mandelbrot (12) was the first to propose that the lung has a fractal geometry. Several other studies have subsequently shown fractal-like properties in the decrease of the diameter of the bronchia, the topology of the bronchial tree, the alveolar surface, and the pulmonary blood flow (5, 6, 8, 14, 17, 24). Although a large number of studies have evaluated the maturation of the respiratory system in several species, little information is available about the postnatal development (7) and, to our knowledge, no studies have been done on changes in the fractal morphology during postnatal development.

The aim of this study is to evaluate changes in the fractal geometry of the bronchial tree during the postnatal development of the *Rattus norvegicus* rat. We are also looking for the effects of the sex on the geometry. Following Taylor and Weibel (20), we expected to find that the developing respiratory system had made full morphological adjustments to its function. The physiological changes and the increase in size during development should be reflected in changes in the topology or complexity of the bronchial tree (i.e.: fractal dimension).

We dealt with four groups of a total of 23 individuals of albino rats (*Rattus norvegicus*): adult males (n = 7; 139.7 ± 8.7 days; 418.5 ± 48.7g), adult females (n = 6; 121.0 ± 1.5 days; 244.5 ± 22.9 g), young males (n = 5; 71.0 ± 1.3 days; 178.4 ± 8.0 g) and young females (n = 5; 85.2 ± 23.9 days; 238.9 ± 34.7 g). All animals were sacrificed, and a bronchograph of each individual was created. First, an 18g plastic catheter was introduced into the trachea and 1.5 ml of diluted barium sulfate was introduced. Next, air was introduced to displace the contrast medium and fill the finer airway. The entire process was performed under radiosopic visualization in the X-ray service of a public hospital in Chile (Hospital del Salvador). Radiographs were taken at a distance of 1 m, with 100 mA, 0.04 s and between 34 and 40 KV.

The bronchographs were digitalized in a standard format of 120 pixels from the clavicle plane to the distal bronchi. The images were studied using the PAINT SHOP PRO software to eliminate all structures except the bronchial tree. Each image was individually analyzed and its fractal dimension (D_f) computed by the box-counting method (16), with MFRAC v1.0 software.

The fractal dimensions of the four groups were compared using a two-way ANOVA with interaction, in which the sources of variation were the age and sex of the individuals. We also performed a regression analysis between the age and the fractal dimension. For comparative purposes, we included the fractal dimensions of human and rabbit bronchial tree from previous published data (5) as out-groups in the results, but not in the analyses.

The average fractal dimension of the bronchial tree of the rats was 1.587, with a median and a mode of 1.58 (Fig. 1). The 95% confidence interval was (1.569; 1.605).

The fractal dimension of the juveniles was larger than that of the adults ([Table I](#)). We did not find sexual differences in the fractal dimension, but we did find an interaction between sex and age. In this sense the changes in the fractal dimension with age of males were larger than those of the females. We found a significant negative correlation between age (a) and fractal dimension (Df) and also a negative slope in the regression: $Df = -0.0008 \cdot a + 1.6746$; $F_{1,21} = 11.79$, $p < 0.01$; $R^2 = 0.36$. Although weight could be a confounding factor, due to the greater body weight of adults and a negative correlation with the fractal dimension in our data ($r = -0.71$, $t_{20} = -4.5$, $p < 0.01$), we cannot attribute our changes in the fractal dimension to weight or body size. The fractal dimension of the bronchial tree, estimated by the same methods in 3 rabbits (3167 g) and in one human (female of about 60 Kg) were 1.58 ± 0.01 and 1.57, respectively ([5](#)). Neither of the ontogenetic differences in fractal dimensions can be caused by different fillings of the bronchial tree of the individuals, but with only one exception, all of the images of the bronchial tree were easily recognized up to the 12th generation of bronchi (numerated by the Horsfield's system ([8](#))).



Fig 1. Bronchial tree of a 247 g. adult male rat. The fractal dimension was $Df = 1.56$.

TABLE I
Fractal dimension of the bronchial tree of albino rat (*Rattus norvegicus*) by experimental groups and the effects of the sex, age and the interaction (sex x age).

	Juveniles		Adults		
	Df	S _E	Df	S _E	
Females	1.602	0.015	1.588	0.010	Sex :
					F _{1,20} = 0.97
Males	1.626	0.157	1.547	0.012	p > 0.05
		Age:			Sex x Age
		F _{1,20} = 13.19			: F _{1,20} = 6.24
		p < 0.01			p < 0.05

The design of the mammalian bronchial tree has been associated with the adjustment of their parts to the function of the respiratory system as a whole (20, 22), to an adequate flow of gases to the alveoli (19), to a minimum entropy production in the respiratory mechanics (25) and to minimum costs of energy and materials (22). The respiratory system must also solve the geometric problem of distributing a volume of blood and gases on a surface of exchange (alveolar surface) into a limited volume (thorax) (13). Several authors have shown that fractal geometry is a general feature in the respiratory system (5, 6, 8, 14, 17, 24), suggesting that it is a good solution to this geometric problem. For example, one of the consequences of the fractal geometry of the alveolar surface is an increase in the area/volume ratio, optimizing the gas exchange (13). Furthermore, the fractal geometry of the bronchial tree, with its branching pattern, allows the airway to reach the respiratory surface in a short distance (5). Other consequences are the heterogeneity of the blood flow in the lungs and the capacity of the bronchial tree to avoid developmental errors in the branching pattern (6, 19, 24). However, the fractal pattern must change during development with the changing volumes and changes in the physiological properties of the system.

Our results show a decrease of the fractal dimension during ontogeny. This change cannot be attributed to the change in volume for two reasons: 1) the change in the fractal dimension is small when compared with the change in weight, and 2) when comparing the fractal dimension of adult rats with those of rabbits and humans, they were similar. Nelson et al. 1990 (14) studied the fractal geometry of the diameter and length of the bronchi in four species (human, rat, dog and hamster) and found some differences in the bronchial scaling. However, in agreement with our results, the volume occupied by the lung by itself did not explain these differences. The bronchial scaling of the dog, hamster and rat were remarkably similar despite rather large differences in their lung volume and body size.

The decrease in the fractal dimension in our rats indicates a reduction in the complexity of the bronchial tree because the fractal dimension measures how much the airway exceeds its own topological dimension or how much it fills the space. We rejected the effect of the body size, one possible reason to expect a decreasing fractal dimension, because small animals have larger mass-specific metabolic rates than larger ones do. We therefore attribute the change to the structural and physiological

changes during maturation, either isolated from or in conjunction with changes in the fractal dimension of other attributes such as blood vessels. For several ontogenetic changes, such as increases in tidal or minute volume, and particularly for a two- or three-fold increase in the alveolar surface/O₂ consumption ratio in rats (4, 9, 21), we would expect an increase in the complexity of the bronchial tree. One possible explanation for the low alveolar surface/O₂ consumption ratio in small species with high metabolic rates is that to increase the alveolar surface under the constraint of constant lung volume, the animals would have to develop alveoli so small that they cannot be readily collapsed by surface forces (1). It is possible that similar physical constraints operate on a possible increase in the complexity of the bronchial tree because a more frequently branched tree is matched with a higher energetic cost in mass. Also, the small radii resulting from the branching process would yield a larger drag force acting on the lumen tissue. Another explanation, in agreement with our results, may be that the methods used to measure the alveolar surface have been unsatisfactory to account for the complexity of the alveolar surface. Rigaut (17) found increases in both the perimeter and the alveolar surface with an increasing resolution power, following a power law with fractal dimension from 1.06 to 1.15 for the perimeter, indicating a fractal dimension of 2.1 for the alveolar surface (13). In this sense we could consider the methods to measure the alveolar surface to be unsatisfactory for its implicit Euclidean geometry (23), and we should expect to find larger fractal dimensions of the alveolar surface in younger animals. If this were so, this fact would be in agreement with our results, but this remains to be elucidated.

It may be argued that our results are due to the loss of complexity as a consequence of aging. Lipsitz et al. (11) reported several examples of decreased complexity in advanced age, such as neuronal dendrites, bone trabeculae, heart rate etc. They also proposed that aging can be defined by a progressive loss of complexity in the dynamics of all physiological systems as a consequence of loss or impairment of functional components and/or altered non-linear coupling between those components. However, our comparisons were made with pre-pubescent and post pubescent rats, not adults, and thus the decrease in the complexity (fractal dimension) seems to be a consequence of the ontogenetical development rather than part of the aging process.

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