

RAT'S AGE VERSUS HUMAN'S AGE: WHAT IS THE RELATIONSHIP?

Idade do rato versus idade humana: qual é a relação?

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ABSTRACT - Background - Millions of mice are used annually in research and teaching. The exact relationship between age of the animals compared with the age of humans is still subject to discussion and controversy. **Objective** - Literature review analyzing the age of rats in comparison with men age. **Methods** - Were reviewed the existing publications on the subject contained in Medline / Pubmed, Scielo, The Cochrane Database of Systematic Reviews and Lilacs crossing the headings rats, experimental surgery and physiology. **Results** - Rats rapidly develop during childhood and become sexually mature at about six weeks old, but reach social maturity five to six months later. In adulthood, every month of the animal is approximately equivalent to 2.5 human years. Several authors performed experimental studies in rats and estimated 30 days of human life for every day life of the animal. **Conclusion** - The differences in anatomy, physiology, development and biological phenomena must be taken into consideration when analyzing the results of any research in rats when age is a crucial factor. Special care is necessary to be taken when the intention is to produce correlation with human life. For this, special attention is needed to verify the phase in days of the animal and its correlation with age in years of humans

HEADINGS - Rats. Experimental surgery. Physiology.

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Financial source: none
Conflicts of interest: none

Received for publication:
Accepted for publication:

DESCRITORES - Ratos. Cirurgia experimental. Fisiologia.

RESUMO - Racional - Milhões de ratos são empregados anualmente em pesquisas e no ensino. A exata relação entre a idade dos ratos, comparada com a idade dos humanos ainda é assunto de discussão e controvérsias. **Objetivo** - É revisar a literatura, analisando a idade dos ratos em comparação com a idade dos homens. **Métodos** - Foram revisadas as publicações existentes sobre o assunto contidas nas bases Medline/Pubmed, Scielo, Biblioteca Cochrane e Lilacs cruzando os descritores ratos, cirurgia experimental e fisiologia. **Resultados** - Ratos desenvolvem rapidamente durante a infância e se tornam sexualmente maduros com cerca de seis semanas de idade, mas atingem a maturidade social cinco a seis meses mais tarde. Na idade adulta, a cada mês do animal é aproximadamente equivalente a 2,5 anos humanos. Vários autores realizaram trabalhos experimentais em ratos e afirmaram existir Correspondence de 30 dias de vida do homem para cada dia de vida do rato. **Conclusão** - As diferenças na anatomia, fisiologia, desenvolvimento e fenômenos biológicos devem ser levados em consideração quando são analisados os resultados de qualquer pesquisa em ratos em que a idade é um fator crucial. Cuidado especial é necessário ser tomado quando os estudos efetuados pretendem produzir correlação com a vida humana. Para isso, atenção especial é necessária para verificar a fase em dias do animal e sua correlação com os anos em humanos.

INTRODUCTION

Currently is difficult to evaluate the number of animals employed in scientific experiments or in teaching. An estimation suggests some dozens of millions for year, being 15 millions in the United States, 11 millions in Europe, five millions in Japan, two millions in Canada and less than one million in Australia. In Brazil, the number is unknown, but insignificant in comparison with the world totals. It can be said that 80% of the experimental animals are rodents - mice, rats and guinea pigs -, and that others 10% are fish, amphibians, reptiles and birds. A third group includes rabbits, goats, bulls, pigs and in smaller amount, dogs, cats and some species of primates. They substitute the human being as experimentation object in scientific researches, in the preparation and quality control of

medicines and in teaching¹.

Fagundes and Taha³ looked for database information in Medline (National Library of Medicine-USA), Lilacs (Latin-American Literature and of Caribbean in Sciences of the Health), Scielo (Scientific Eletronic Library Online) and Library Cochrane (The Cochrane Database of Systematic Reviews) about the six animals species more commonly mentioned, in a period of four years. This survey showed that the rats were the animals more used in research, followed by mouse, rabbit, dog, pig and primate. About 85% of the articles in Medline and 70,5% of the articles in Lilacs employed rats and mice.

Many questions often arise when animals are being used as models of human diseases and biology: When are these animals considered aged? Which is the relationship of the age of the rat with the human age? How many rat days are equal to one human year? The number of existing publications and focusing on the issue in depth is very limited.

The objective of this review is to evaluate these issues on the existing literature.

METHOD

Were reviewed the existing publications on the subject contained in Medline / Pubmed, Scielo, The Cochrane Database of Systematic Reviews and Lilacs crossing the headings rats, experimental surgery and physiology.

The *R. norvegicus* and the black rat (*R. rattus*) belong to the murine family (the same that originated the mice and hamsters) and came from Asia to America and Europe traveling with humans. Today there are 51 known species of the *Rattus*. Norway rats originated in the Asia, probably in northern China and Mongolia are wild living rats. The albino rats were used in laboratories for physiology studies in the early 19th century, and the white rats were brought from Europe to America from 1856. The Wistar rats were created by Helen Dean King, Philadelphia (USA) in 1909. Currently Wistar rats and Sprague-Dawley rats are gradually becoming the most used worldwide in laboratory^{5,8,13}.

Compared to humans, rats have a brief and accelerated childhood. Rats develop rapidly during infancy and become sexually mature at about six weeks of age. Humans, on the other hand, develop slowly and don't hit puberty until about age 12 to 13 years (8 to 16). Social maturity is obtained in five to six months of age. In adulthood, each rat month is roughly equivalent to 2.5 human years. Female rats enter menopause between ages 15 and 18 months, while humans between 48 and 55 years¹¹.

Domestic rats live about two to 3.5 years¹¹. In agreement with Quinn the average laboratory rat lives approximately three years¹⁰. In a survey, rat

lifespan in the UK was 21.6 months, and 95% percent had died by age of three years. In contrast, 95% of rats living wildly tend to live less than one year¹¹.

The worldwide human life expectancy is about 70 years, with differences among countries. Human lifespan tends to correlate with economic development. Quinn estimates that humans can live approximately 80 years¹⁰. Table 1 tries to estimate the relative age of the rat in relationship to the human.

TABLE 1 - The rat's age in months and its relationship in years with human being in social maturity phase¹¹

Rat's age in months	Human's age in years
6 months	18 years
12 months	30 years
18 months	45 years
24 months	60 years
30 months	75 years
36 months	90 years
42 months	105 years
45 months	113 years
48 months	120 years

Several authors accomplished experimental studies in rats and they demonstrated a correspondence of 30 days of the man's life to every day of life of the rat^{4,6,7,9}.

Quinn¹⁰ mentioned that there is no simple answer on making age comparisons between humans and animals. So, considering all the analysis and using the birth as a starting point for both species, the conversion rate is shown in Figure 1.

Total lifespan:	13.8 rat days	= 1 human year
Nursing period:	42.4 rat days	= 1 human year
Prepubescent period:	4.3 rats days	= 1 human year
Adolescent period:	10.5 rat days	= 1 human year
Adult phase:	11.8 rat days	= 1 human year
Aged phase:	17.1 rat days	= 1 human year
Average:	16.7 rat days	= 1 human year

FIGURE 1 - Correlation days / year of age of mice against human

The most important concept is that the results are different depending on how old are rat/man and what factors are being analyzed. If you are making comparisons in the very early stages of life, will be drastically different compared with adulthood^{4,6,7,9,10}. For example, if you are using an obese rat model to study neurobiological changes associated with bariatric surgery and you are looking at changes in 10 to 12 week old animals, a conversion rate of approximately 10 to 12 rat days per human year would probably be appropriate¹². In contrast, if you are studying mammary gland developmental changes in association with diet and you are looking at gland development from three to seven week of

age, then a conversion of approximately four rat days per human year would probably be more relevant².

Rats and animal models in research in general can be very important and useful. The results can be applied to humans with precaution. They can not be interpreted as miniature people. Just because the rat's lifespan is three years does not mean it lives a miniature human lifetime within those three years^{8,9,10,11}.

CONCLUSION

The differences in anatomy, physiology, development and biological phenomena must be taken into consideration when analyzing the results of any research in rats when age is a crucial factor. Special care is necessary to be taken when the intention is to produce correlation with human life. For this, special attention is needed to verify the phase in days of the animal and its correlation with age in years of humans.

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