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Changes in intestinal lengths of 129S2/SvPasCrl mice from adulthood to agedness

MOU Lixian[Δ1,2] HU Pingdong[Δ2] CAO Xiao[1,2] HE Rongqiao[*1,2]

1 Basic College of Medicine, Southwest Medical University, Luzhou, Sichuan 646099, China
2 State Key Laboratory of Brain and Cognitive Science, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China

129S2/SvPasCrl 小鼠肠道在衰老过程中的变化

牟丽娴[Δ1,2] 胡平东[Δ2] 曹潇[1,2] 赫荣乔[*1,2]

1 西南医科大学基础医学院 四川 泸州 646099
2 中国科学院生物物理研究所脑与认知科学国家重点实验室 北京 100101

Dear Editor:

We would like to show "changes in intestinal lengths of 129S2/SvPasCrl mice from adulthood to agedness". The intestine functions not only in digestion, absorption and excretion, but also in the regulation of central nervous system through its microbiota so as called gut-brain axis[1]. As a tubular organ, the intestinal length is regarded as a significant morphological characteristic, which directly affects digestion and absorption[2]. Thus, clarifying changes in intestinal lengths at different ages is beneficial to understand the functions of the digestive system as well as the aging process.

Many laboratories have paid attentions to the development of intestinal length from birth to adult in animal and human. As early in 1974, McCance measured the intestinal lengths in pigs at different ages until adulthood. As compared with large intestine, small intestine grew rapidly in the first 35 days after birth, and attained the adult length in 164 days[3]. Analyzing 1 010 gut samples from unfixed necropsy specimens recorded in eight published reports, Weaver and colleagues indicated that the small intestinal length increased rapidly during early postnatal life, and then slowed down, but remained lengthening with the increasing age to adulthood[4]. The length of human small intestine was measured of 283.0 cm, 324.7 cm, and 356.0 cm at the mean ages of 0.58, 5.60 and 22.01 years old, respectively[5]. Wolczuk and Kobak observed the growth of small intestine in Siberian hamster from birth to about 3 months old, and emphasized the

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ΔThese authors equally contributed to this work
*Corresponding author: E-mail: herq@ibp.ac.cn
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*通信作者：E-mail：herq@ibp.ac.cn
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rapid lengthening in the first 14 days after birth, especially 0−3 days[6]. So far, however, few researches have been carried on the change in intestinal length from adult to agedness.

To measure the intestinal lengths in mice from the adult to agedness, 129S2/SvPasCrl mice (male and female) were obtained from Vital River Laboratory Animal Technology (Beijing, China). The “specific-pathogen free” (SPF) mice were housed in individually ventilated cages (330 mm×215 mm×200 mm, 2−5 mice in each cage) with the content of fodder in the Animal Center of China Astronaut Training Center until month 24. Mice were maintained in SPF environment with alternating 12-h light and dark cycles, and had access to food and water ad libitum. The growth and reproduction feed for rats and mice from Keao Xieli Feed Co., Ltd. (Beijing, China) was used. No abnormal behaviors were observed in mice. All experimental procedures were approved by the Animal Welfare and Research Ethics Committee of the Institute of Biophysics, Chinese Academy of Sciences (Permit Number: SYXK2019-06). According to the protocol (McCance, 1974)[3], mice were anaesthetized with 10% chloral hydrate. Then the whole intestinal tract below the diaphragm was removed, and the stomach was discarded. The whole intestine was dissected carefully without pulling or stretching, and the lengths of the small intestine (from the pylorus to the ileocecal valve) and the large intestine (colon, rectum, and anus inside the pelvic cavity) were measured with a ruler (scaled in 1 mm).

Here, we show changes in intestinal length of the male mouse at different months. As exhibited in Figure 1A, the whole intestinal lengths (small and large) of male mice significantly extended from month 2 to 24 (P=0.001 7) and month 4 to 24 (P=0.001 4), but not from month 2 to 4 (P=0.867 6). Then, we separated the whole intestine into small and large intestine and measured them. The small intestine significantly extended from month 2 to 24 (P=0.001 2) and from month 4 to 24 (P=0.000 4) in male mice, though marked growth was not observed from month 2 to 4 (P=0.999 5, Figure 1B). The large intestinal lengths distinctly increased from month 2 to 4 (P=0.018 7), but neither month 2 to 24 (P=0.726 0) nor month 4 to 24 (P=0.150 7, Figure 1C). These data suggest that the intestine, especially small intestine, extends from adulthood to agedness in male 129S2/SvPasCrl mice.

We also observed changes of intestine lengths in female virgin mice under the same conditions. The whole intestinal lengths significantly increased from month 2 to month 4 (P=0.020 7) and month 2 to month 24 (P=0.001 0), but not from month 4 to 24 (P=0.116 1, Figure 1E). The small intestine significantly from month 2 to 24 (P=0.000 6), and so was those from month 2 to 4 (P=0.037 6) and month 4 to 24 (P=0.038 7, Figure 1F). Large intestine increased from month 2 to month 4 (P=0.013 3) but neither month 4 to 24 (P=0.637 8) nor month 2 to 24 (P=0.144 2, Figure 1G). These results also indicate that the small intestine lengths of female mice extends from adulthood to agedness.

Intestines absorb nutrition and provide energy to animal body. Therefore, we analyzed the relationship between intestinal length and mouse body weight (Figure 1D, 1H). The whole intestinal lengths of male mice was correlated to their body weight (Figure 1I, r=0.550 3, P=0.014 6), and so is the small (Figure 1J, r=0.488 6, P=0.033 8) and large intestine (Figure 1K, r=0.508 8, P=0.026 1). For the female, the lengths of the whole (Figure 1L, r=0.742 0, P=0.000 2), small (Figure 1M, r=0.690 2, P=0.000 8) and large (Figure 1N, r=0.740 3, P=0.000 2) intestine were correlated with their body weights.

As we know, hormones affect female mouse growth, especially during the pregnant period. In our observations, 7 months old female mice who had given birth from month 2 to 7 showed a longer whole (P=0.003 8), small (P=0.007 2), and large (P=0.000 4) intestine than age-matched male mice. Note that body weights of male and female were similar at month 7 (P=0.155 2). We also compared the whole, small and large intestinal lengths between male and female mice at different ages as indicated in Figure 2.

We would consider that the intestinal length of the mouse is related to the body weight from adulthood to agedness. First, there are reports that small intestinal length increases as the direct proportion to body weight for growing pig, cattle and poultry[7-9] from born to adulthood though not to agedness. Second, our results showed the correlations between intestinal length and body weight in both male and female mice. Third, according to the other laboratory observations[7,10], intestinal morphology is extremely important for

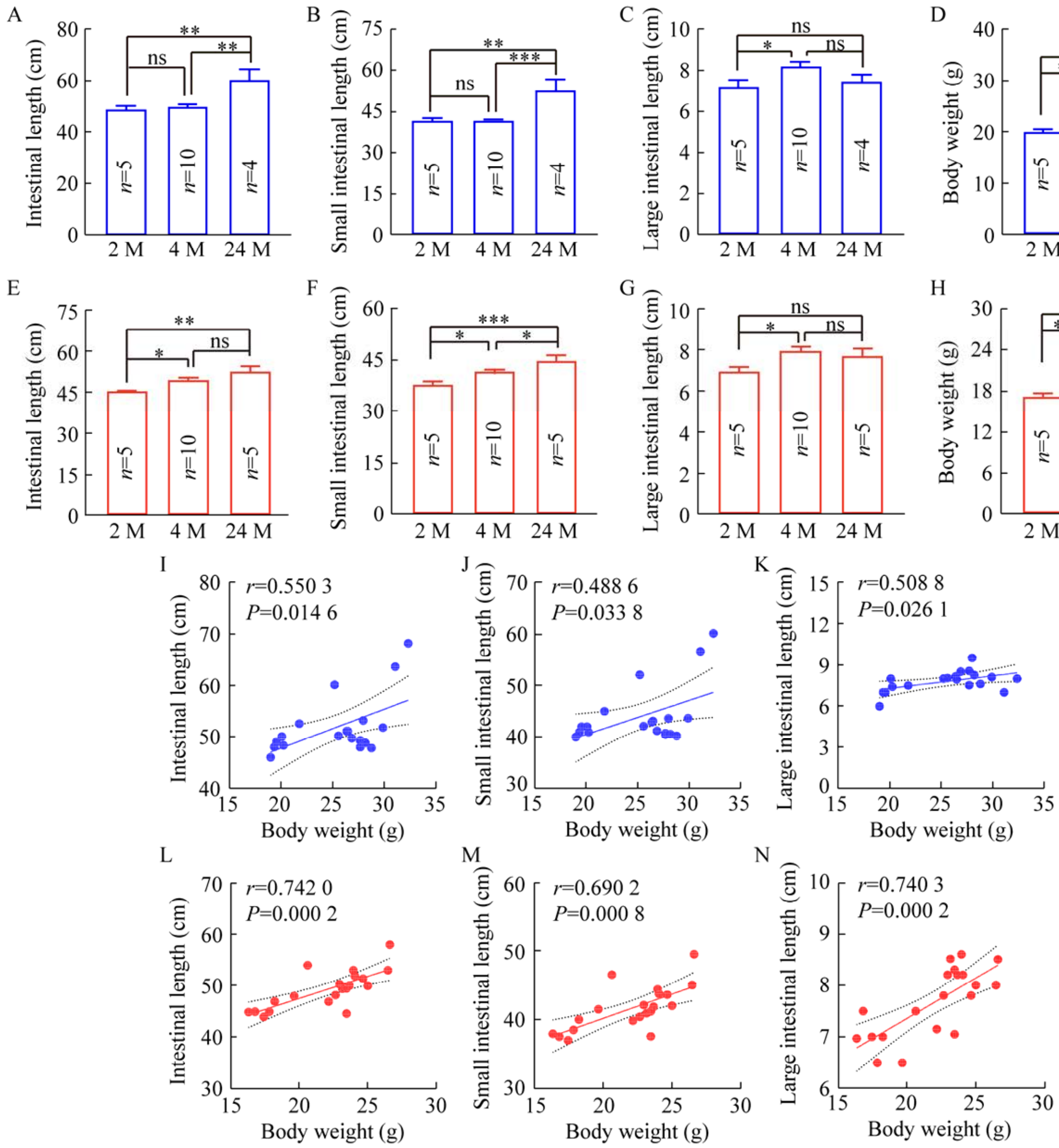

Figure 1 The intestinal lengths of 129S2/SvPasCrl mice at different ages

图 1 不同月龄 129S2/SvPasCrl 小鼠的肠道长度

Note: The lengths of the whole (A, E), small (B, F) and large (C, G) intestine of male (blue column) and female (red column) were measured, including body weight of 129S2/SvPasCrl mice (D, H). One-way ANOVA were employed to analyze the data in panel A–H. Pearson correlation was used to analyze the correlation between the intestinal length and body weight in male (I–K) and female (L–N) mice. Data were showed as mean±SE in A–H. *: $P<0.05$; **: $P<0.01$; ***: $P<0.001$; ****: $P<0.000\ 1$; ns: No significant. n is the number of mice examined

piglet to develop, and the influence even extends to adulthood. Finally, large body mass needs more resting energy expenditure to maintain the homeostasis of metabolism[11].

The whole intestine of 129S2/SvPasCrl mice, especially the small intestine, changes in lengths from month 2 to 24. The female mice showed their intestinal lengths increased at month 7 after pregnancy and lactation. As described previously[12-13], pregnancy can increase mouse intestinal length which will decrease but not return to prepregnancy values until 10 months after parturition. It appears

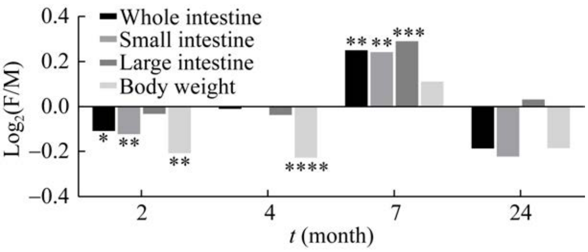

Figure 2 Comparison of the intestinal lengths between female and male 129S2/SvPasCrl mice at different ages

图 2 雌雄 129S2/SvPasCrl 小鼠在不同月龄的肠道长度比较

Note: Data of intestinal length and body weight from figure 1 and those at month 7 after parturition were used for logarithmic plotting. F/M showed the ratio of means in female and male mice. “*” indicates the significance of difference between female and male mice in the “whole intestine”, “small intestine”, “large intestine” and “body weight” at similar ages. The student’s *t*-test was employed to analyze the data. *: P<0.05; **: P<0.01; ***: P<0.001; ****: P<0.000 1

that the small intestine may feature in plasticity. Furthermore, it is interesting to study why the intestinal extension processes to agedness. To clarify the molecular events and mechanisms that regulate the intestinal extension from adulthood to agedness is meaningful to understand the nature of intestines as aging. Perhaps, there may be something in the relationship between intestinal length and gut microbiota, etc. All these ideas and whether human intestines also change and extend to agedness should be investigated in the future.

In conclusion, the intestine of 129S2/SvPasCrl mice may be characteristic in length changing from adulthood to agedness, especially the small intestine. The change of intestinal length seems to be associated with body weight. We have to say, our investigation is somewhat preliminary. Whether the correlation between intestinal length and body weight exists throughout life time needs further investigating in a larger sample size. This work may provide a new insight to the intestinal morphologies and functions in animal and even human life.

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