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Brief Communication

# Longitudinal Changes in Motor and Muscle Function in Senescence-Accelerated Mice

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SUMMARY

The purpose of this study was to verify longitudinal changes in motor and muscle function in senescence-accelerated mice using behavioral tests. Wire hanging tests (WHT) were performed on senescence-accelerated mouse prone 1 (SAMP1) and senescence-accelerated mouse resistant 1 (SAMR1), from the age of eight weeks to 44 weeks. In WHT, the hanging time of SAMP1 was lower than that of SAMR1 in eight-week-old to 44-week-old mice. The hanging time of SAMR1 decreased with age, however, this change was hardly observed in SAMP1. In addition, there was no difference in body weight between strains at each week. However, the weights of the soleus, plantaris, and gastrocnemius muscles in SAMP1 were lower than those in SAMR1 at 44 weeks of age. These results suggest that the motor and muscle function of SAMP1 is lower than that of SAMR1, and it is possible that the lower muscle weight contributes to lower motor and muscle function of SAMP1.



## 1. Introduction

Sarcopenia, the age-related loss of muscle mass, strength, and muscle function, impairs motor function and leads to fragility.[1,2] Therefore, it is necessary to elucidate the detailed mechanism by which aging reduces motor and muscle function and its prevention. However, as it takes time to prepare experimental animals for aging experiments, it is also necessary to develop an efficient experimental system.

The senescence-accelerated mouse prone 1 (SAMP1) strain shows early deficits in age-associated pathological features, such as senile amyloidosis and impaired immune response, compared to senescence-accelerated mouse resistant 1 (SAMR1) strain, which exhibits normal aging.[3] However, much is still unclear as to the motor and muscle function of SAMP1.

Here, we evaluated the longitudinal motor and muscle function of SAMP1 in comparison to SAMR1 using behavioral tests to investigate the suitability of SAMP1 as an aging model for motor function and muscle.

## 2. Materials and methods

### 2.1. Animals and ethics approval

Male SAMP1 (n = 18) and SAMR1 (n = 18) were obtained from Japan SLC (Shizuoka, Japan). Mice were bred between the ages of eight and 44 weeks in the present study. All animals were granted constant free access to food and water in standard clear plastic cages. The environmental conditions were maintained at 23 ± 2 °C and a 12 h:12 h light:dark cycle.

This study was approved by the Committee of Animal Care and Use of the Osaka University of Human Sciences (#2). All experimental procedures were conducted in accordance with the institutional guidelines for the use of experimental animals.

### 2.2. Wire hanging test

To evaluate motor and muscle function longitudinally in mice aged 8 to 44 weeks, the wire hanging test (WHT) with two or four limbs was performed according to a previous study.[3] Briefly, the mouse was hung on a single wire by two limbs or on a wire mesh by four limbs, and the time until the mouse fell to the soft floor was measured as the hanging time. In addition, since the hanging time of WHT is affected by the weight of the mouse, the body weight was measured at each WHT.

### 2.3. Sampling

The mice were sacrificed at 44 weeks of age using sodium pentobarbital. The soleus, plantaris, and gastrocnemius muscles were excised and weighed to evaluate the muscle weight that contributes to motor and muscle function.

### 2.4. Statistical analysis

All data are represented as mean ± SEM and were analyzed by two-way repeated measures ANOVA, followed by Bonferroni's post hoc test or unpaired Student's t-test. The level of significance was set at $p < 0.05$. Statistical Package for the Social Sciences (SPSS) version 22.0 was used for all statistical analyses (SPSS Inc., Chicago, IL, USA).

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## 3. Results

### 3.1. Changes in body weight

The body weights increased continuously in both SAMP1 and SAMR1 with age and no significant difference was observed between the strains (Table 1).

### 3.2. Changes of hanging time of two or four limbs WHT

The hanging time of two-limb WHT in SAMP1 was lower than that in SAMR1 at 8, 14, 20, and 44 weeks (Figure 1A). The hanging time of the four-limb WHT in SAMP1 was also lower than that in SAMR1 at 8, 14, and 20 weeks (Figure 1B). In the four-limb WHT, the hanging time of 20- and 44-week-old SAMR1 was decreased compared to that of 8- and 14-week-old SAMR1.

### 3.3. Muscle weight

The soleus, plantaris, and gastrocnemius muscle weights of 44-week-old SAMP1 were lower than those of SAMR1 (Table 2).

## 4. Discussion

This is the first study to report that the motor and muscle function of SAMP1 was lower than that of SAMR1 during aging and weight gain by longitudinal evaluation using WHT. In addition, the hanging time of SAMR1 decreased with age; however, this change was hardly observed in SAMP1 in the four-limb WHT. A previous study demonstrated that WHT could detect muscle weakness in mdx mice.[4] These results suggest that the skeletal muscles of SAMP1 are weakened and have different age-related changes compared to SAMR1.

The weights of the soleus, plantaris, and gastrocnemius muscles in SAMP1 were lower than those in SAMR1 at 44 weeks of age. The plantaris and gastrocnemius muscle weights in SAMP1 were already lower than those of SAMR1 at eight weeks.[5] Aging of skeletal muscle tends to occur in fast muscle fibers.[6] Therefore, it is possible that fast muscles, such as the plantaris and gastrocnemius muscles, tend to lose muscle weight in SAMP1.

In summary, SAMP1 had lower motor and muscle function and muscle weight than SAMR1. This suggests that SAMP1 can be used as a motor and muscle dysfunction model. Since SAMP1 has few age-related changes in motor and muscle function as shown by SAMR1, further studies are required for its utilization as a muscle aging model.

The present study did have some limitations. First, the cause of decreased motor and muscle function was not analyzed in the present study. A previous study reported that abnormal expression of tyrosine hydroxylase in cerebellar Purkinje cells is involved in impaired motor function in SAMP1.[7] In future, additional analysis including the nervous system and muscles is required. Second, longitudinal follow-up is up to 44 weeks of age, and further follow-up is needed.

**Table 1**
Change in body weight.

| Body weight (g) | 8-week-old | 14-week-old | 20-week-old | 44-week-old |
|---|---|---|---|---|
| SAMP1 (n = 18) | $27.2 \pm 0.5$ | $33.3 \pm 0.8^{\dagger}$ | $35.9 \pm 1.0^{\dagger\ddagger}$ | $38.2 \pm 1.5^{\dagger\ddagger\$}$ |
| SAMR1 (n = 18) | $28.0 \pm 0.4$ | $32.3 \pm 0.4^{\dagger}$ | $35.1 \pm 0.6^{\dagger\ddagger}$ | $40.1 \pm 0.9^{\dagger\ddagger\$}$ |

$^{\dagger}$ < 0.001 vs. 8-week-old of same strain; $^{\ddagger}$ < 0.001 vs. 14-week-old of same strain; $^{\$}$ < 0.001 vs. 20-week-old of same strain.

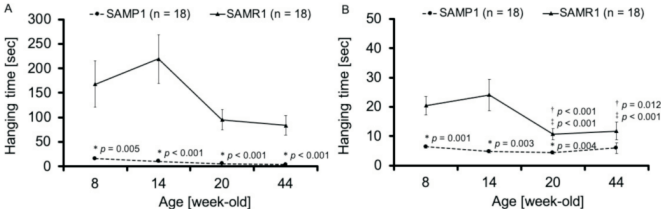


**Figure 1.** Change of hanging time in wire hanging test. The hanging time was measured in the two-limb WHT (A) and the four-limb WHT (B).* < 0.01 vs. same age SAMR1; $^{\dagger}$ < 0.05 vs. 8-week-old of same strain; $^{\ddagger}$ < 0.001 vs. 14-week-old of same strain.

**Table 2**
Muscle weight.

| Muscle weight (mg) | Soleus | Plantaris | Gastrocnemius |
|---|---|---|---|
| SAMP1 (44-week-old; n = 8) | $6.6 \pm 0.3$* | $14.4 \pm 0.6$* | $112.0 \pm 4.2$* |
| SAMR1 (44-week-old; n = 8) | $10.1 \pm 0.5$ | $20.5 \pm 0.5$ | $214.9 \pm 4.9$ |

* < 0.001 vs. SAMR1.

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## Declaration of interests

The authors have no conflicts of interest to disclose.

## References

1. Chao WC, Wang SY. Sarcopenia and frailty in elderly: Manifestations, impacts on diseases, and management. *Int J Gerontol.* 2020;14:2–5.
2. Tieland M, Trouwborst I, Clark BC. Skeletal muscle performance and ageing. *J Cachexia Sarcopenia Muscle*. 2018;9:3–19.
3. Takeda T, Higuchi K, Hosokawa M. Senescence-accelerated mouse (SAM): With special reference to development and pathobiological phenotypes. *ILAR J*. 1997;38:109–118.
4. Klein SM, Vykoukal J, Lechler P, et al. Noninvasive in vivo assessment of muscle impairment in the mdx mouse model--a comparison of two common wire hanging methods with two different results. *J Neurosci Methods*. 2012;203:292–297.
5. Haramizu S, Ota N, Hase T, et al. Aging-associated changes in physical performance and energy metabolism in the senescence-accelerated mouse. *J Gerontol A Biol Sci Med Sci*. 2011;66:646–655.
6. Nilwik R, Snijders T, Leenders M, et al. The decline in skeletal muscle mass with aging is mainly attributed to a reduction in type II muscle fiber size. *Exp Gerontol*. 2013;48:492–498.
7. Aoyama Y, Kim TY, Yoshimoto T, et al. Impaired motor function in senescence-accelerated mouse prone 1 (SAMP1). *Brain Res*. 2013;1515:48–54.