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Further evidence of running-based food avoidance in laboratory mice: An examination using C57BL strain mice

Takatoshi NAGAISHI, Sachi KIMURA, Kana KURAMOTO, You SUMIYAMA, & Daiki TAKESHIMA

Introduction

Conditioned taste aversion based on malaise induced by poisoning is considered as a kind of Pavlovian conditioning. Taste aversion can be produced by many other agents in addition to poison (see Riley and Freeman, 2004, for a database). Among them, running in an activity wheel has attracted much attention from researchers since the last decade (see Boakes and Nakajima, 2009, for a review).

Similar to poison-based taste aversion, running-based taste aversion in rats shares many qualitative features with traditional Pavlovian conditioning preparations. For example, running-based taste aversion learning follows the laws of unconditioned stimulus (US) strength (e.g., Masaki and Nakajima, 2006). Furthermore, there is evidence of CS-preexposure effect (e.g., Heth and Pierce, 2007), US-preexposure effect (e.g., Nakajima et al., 2006), and overshadowing effect (Nagaishi and Nakajima, 2010) in running-based taste aversion learning.

This learning paradigm has not been studied well in other species thus far. Recently, Nakajima (2019a) demonstrated running-based conditioned flavor avoidance (CFA) among laboratory mice (ICR strain mice) using flavored food. Moreover, Nakajima (2019b, 2021) reported the replicate of running-based CFA in ICR mice strain. This study examined whether running-based CFA can be observed in a different mice strain (C57BL mice strain).

Method

Subjects and Apparatus. The animals were eight experimentally naïve ten-week-old male C57BL mice, with a mean weight of 34.8 g (range: 34.1-35.8 g) at the start of the adaptation treatment. They were single housed in clear plastic cages because of the fear that interactions with conspecific mice in the home cages would reduce taste aversions (cf. Hishimura, 2015). Particularly, each of the two clear plastic home cages (AMC-N, GB: Pet Products, Aichi) was divided into four compartments using plastic cardboards, and the mice were individually housed in the compartments (13.9 cm wide, 17.7 cm long, 16.3 cm high); additionally, the floor was covered with 3 cm wood chip layer. The wood chip floor was changed once a week. The chow pellets (MF diet; Oriental Yeast, Tokyo) were placed in a ceramic container on top of the floor in each compartment. Fresh tap water was provided in each compartment from a bottle with a metal nozzle tube positioned 6.5 cm above the floor. The animals were adapted to this condition for a week, before beginning the adaptation treatment. Their body weights were maintained at 85% free feeding throughout the experiment. The vivarium was maintained on a light-dark cycle of 12-12 h (lights on at 0800 h) with controlled temperature (23° C) and humidity (60%). The experiment was conducted in a conventionally illuminated experimental room with four feeding cages (Pull out tall box, Inomata kagaku, Osaka; 11 cm wide, 13 cm long, 8.7 cm high) and four commercial wheels with a counter (15 cm wide, 38 cm in diameter).

Procedure. Prior to the conditioning phase, all the mice were placed in the feeding cages with a 7.5-g cubic piece of processed cheese (QBB Baby Cheese Original, Rokko Butter, Hyogo) for 30 min. Adaptation to the wheels was omitted from this experiment. The mice were then assigned to one of two groups of four mice each and matched for body weight on the adaptation treatment day.

In the following 7 days (conditioning phase), mice in Group Run were given a 30-min access to cheese in the feeding cages, immediately followed by a 45-min confinement to the wheels. Mice in Group No-Run were given 30-min access to cheese in the feeding cages followed by a 45-min holding in the home cages.

Ethical considerations. All treatments of this study were approved by the Animal Ethics Committee of Tezukayama University (Approval No. 2019-07).

Results

Cheese intake. Figure 1 depicted that both groups of mice initially consumed very little cheese, but the mice in Group No-Run gradually increased their consumption over the time lapse. The little or no increase in cheese consumption among the Group Run mice suggests that taste avoidance was established by wheel running. A 2 (group) × 7 (day) mixed-design ANOVA yielded significant main effects of the day (F (6, 36) = 3.13, p = 0.014), and, most importantly, the interaction term was also significant, $F(4, 56) = 4.17$, p = 0.002. Post-hoc simple main effect analysis of the interaction revealed a marginal group difference on the fifth day, $F(1, 42) = 5.68$, $p = 0.02$, the sixth day, $F(1, 42) = 4.45$, $p = 0.04$, and the seventh day, $F(1, 42) = 10.02$, $p = 0.002$. The simple day effect was significant only for Group No-Run only, ($F(6, 36) = 6.38$, $p = 0.001$), and not for Group Run ($F(6,36) = 0.93$, $p = 0.49$).

Wheel turns. The number of wheel turns gradually increased over the conditioning phase in Group Run mice: a one-way repeated ANOVA showed that the effect of the day was not significant, $F(6, 27) = 1.13$, $p = 0.383$. The averages (± standard errors) were 975 ± 275, 1591 ± 226, 1766 ± 135, 1834 ± 238, 1506 ± 234, 1872 ± 471, and 1882 ± 452 turns per day, in the time span of seven running days.

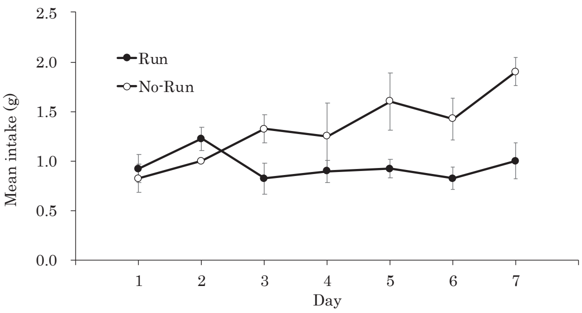

Figure 1. Mean intake of two groups (each n = 4) on the conditioning phase. Error bars indicate the standard errors of means.

Discussion

This study observed running-based conditioned flavor avoidance in C57BL mice. This result verifies the robustness and generality of previous studies (Nakajima, 2019a; Nakajima, 2019b; Nakajima, 2021) in running-based flavor avoidance preparations.

However, a primary limitation needs to be discussed. Because the control group in this study was the no-running group, the possibility of pseudo-conditioning could not be completely ruled out (Given the nature of the US, although this possibility is probably low). Therefore, future studies should set up a paired group and compare the effects again.

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