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High Tail-Cuff Blood Pressure in Mice 1 Week After Shipping: The Need For Longer Acclimation

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Abstract

Background—For vendor-derived mice, an acclimation period of 1 week is usually recommended before blood pressure measurements are started. However, we observed hypertension in wild-type vendor-derived mice 1 week after shipping.

Methods—The index group (n = 12, BALB/c, age 3 months, weight 26-28 g) was shipped overnight (by truck, duration 13 h). Tail-cuff systolic blood pressures (SBPs) of the index group were compared to two control groups (n = 6/group), one acclimated for 3 weeks after shipping, and one derived from an in-house colony.

Results—One week after shipping, SBP in the index group was 141 ± 3 mm Hg. Because this was much higher than reported previously for this strain, acclimation was prolonged. Six weeks after shipping, SBP had fallen to 124 ± 3 mm Hg ($P < 0.005$). During this time, heart rate also fell from 721 ± 15 to 665 ± 13 bpm ($P < 0.01$). SBP in the two control groups was also lower than in the index group 1 week after shipping, including the group acclimated for 3 weeks (129 ± 3 vs. 141 ± 3 mm Hg, $P < 0.05$) and the in-house mice (124 ± 3 vs. 141 ± 3 mm Hg, $P < 0.005$).

Conclusions—Vendor-derived mice are hypertensive 1 week after shipping, become normotensive after 3 weeks, but do not return to levels of in-house mice until after 6 weeks. Acclimation periods of at least 3 weeks are required when measuring blood pressure in mice.

Many investigators involved in hypertension research routinely measure blood pressure in mice.1 Usually mice from in-house colonies are used, but occasionally the logistics of experiments require ordering mice from vendors. A general rule of thumb is to let these mice acclimate for 1 week after shipping, and this is also the advice of most institutional animal care committees.2 For rats, one study even suggested that 3 days of acclimation would be sufficient, as heart rate, body weight, and activity had returned to normal by this time.3 Here, however, we report our observation of finding higher blood pressures in wild-type mice that were acclimated for 1 week compared to mice that were acclimated for longer periods of time.

Methods

Animal studies. All studies were conducted in male BALB/c mice. The index group consisted of 12 mice (age 3 months, weight 26–28g). They were ordered from Charles River Labs (Hollister, CA) and were transported overnight by truck to Portland, OR (13h, 709 miles). Seven days after shipping, baseline noninvasive blood pressure measurements commenced. Blood pressure was also measured in two comparison groups including BALB/

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c mice of similar age and identical sex, which underwent the same procedure also for the first time. These groups consisted of a second set of vendor-derived mice (same vendor, same shipping route, different shipping date), which were allowed to acclimate for 3 weeks and a group of in-house mice. After the vendor-derived mice had arrived, four mice per cage were kept in the same day-and-night cycle and temperature controlled room, guaranteeing a quiet environment. During daily inspection, all mice appeared healthy, and no fighting or distress was observed.

Blood pressure measurements. Systolic blood pressures (SBPs) were measured using a validated tail-cuff method that relies on volume pressure recording technology (Coda 6; Kent Scientific Corporation, Torrington, CT).4 SBP was measured each day at the same time, by the same experienced operator. All mice were first acclimated to the SBP measurements for 3 days (these data were discarded) and then the baseline SBP was determined as the average of the subsequent 3 days. In addition, each day, ten acclimation cycles were followed by fifteen measurement cycles, which were averaged to obtain the average SBP of that mouse on that day. No decline in SBP was observed during the three measurement days, suggesting that no further acclimation occurred.

Results

In the index group, SBP 1 week after shipping was found to be much higher than anticipated for this strain of mice (mean 141 ± s.e. 3mmHg, Figure 1).5 In addition, the mice did not gain weight during their first week after shipping (27.5 ± 0.2 to 27.2 ± 0.2g). Because we assumed that these observations could be attributable to the recent shipment, the acclimation period was prolonged. Interestingly, 6 weeks after shipping, SBP had fallen to 124 ± 3mmHg ($P < 0.005$ using paired T-test vs. the mean SBP at 1 week, Figure 1). Similarly, the mean heart rate in this period fell from 721 ± 15 to 665 ± 13bpm ($P < 0.01$ using paired T-test). Because one could argue that stress associated with the new procedure caused high blood pressure 1 week after shipping, the results were compared to two control groups. The mean SBP of the control group that was acclimated for 3 weeks was significantly lower than the mean SBP in the index group 1 week after shipping (129 ± 3 vs. 141 ± 3, $P < 0.05$ by independent T-test, Figure 1). Similarly, the mean SBP of the second control group derived from our in-house colony was also significantly lower compared to the SBP in the index group 1 week after shipping (124 ± 3 vs. 141 ± 3, $P < 0.005$ by independent T-test, Figure 1). Notably, in the vendor-derived mice, SBP was still slightly although not significantly higher 3 weeks after shipping compared to 6 weeks after shipping (129 ± 3 vs. 124 ± 3, $P = 0.3$).

Discussion

Blood pressures in vendor-derived wild-type mice were elevated for at least 1 week after shipping (Figure 1). Six weeks after shipping, SBP had declined and was similar to that of in-house mice. In a separate group of mice, which were acclimated for 3 weeks, SBP was still slightly, but not significantly higher than in the mice acclimated for 6 weeks after shipping (Figure 1). These observations were made in BALB/c mice, one of the most commonly used strains in animal research.

Although a direct effect of shipping appears as a plausible explanation for our findings, other factors should also be considered. For example, environmental changes associated with shipping or the assignment to group housing after shipping may have contributed to the elevated blood pressures. The mice from the index and control group were transported on different shipments. Therefore, the shipment of the index group may have been more stressful leading to higher blood pressures shortly after arrival. However, the observation

that SBP in a separately shipped group of mice was still higher after 3 weeks of acclimation, seems to suggest that decreasing blood pressure during acclimation is a phenomenon associated with shipping in general. This was the first time we observed this effect of shipping, because we normally only use mice from our in-house colony.

It is also important to consider possible effects of the method of blood pressure measurement. For example, blood pressure measurements using a different tail-cuff technique that relies on plethysmography suggested that a high fructose diet caused hypertension in rats, but this effect could not be corroborated with telemetry.6 However, our in-house mice, in which tail-cuff blood pressure was also measured for the first time, were not hypertensive (Figure 1); therefore, an effect of the method of blood pressure measurement seems less likely. Tail-cuff blood pressures were measured according to guidelines,1 including 3 days acclimation before starting “official” measurements. Also, the tail-cuff blood pressure measurement that we used relied on volume pressure recording, which appears more sensitive than the one relying on plethysmography.4 Finally, even if the method of blood pressure measurement contributed to increased blood pressure, it would still represent a change in the cardiovascular system with the potential to confound experiments making use of the tail-cuff procedure.

We were unable to find previous literature on the effects of shipping on blood pressure. A recent study, however, did show an increased stress response in vendor-derived BALB/c mice when compared to in-house mice.7 The vendor-derived mice had elevated glucocorticoid levels for up to 3 weeks after shipment, and increased monoaminergic activity.7 Although blood pressure was not measured in that particular study, it is quite conceivable that an activated neuroendocrine system contributes to higher blood pressure after shipping. Another study showed that white blood cells, electrolytes, and enzymes in rats directly after shipping were significantly different than in rats that were allowed to acclimate for 12 days;8 this suggests that shipping affects various physiological functions.

In summary, vendor-derived mice are hypertensive 1 week after shipping, become normotensive after 3 weeks, but do not return to levels of in-house mice until after 6 weeks. Thus, mice should be allowed to acclimate for at least 3 weeks after shipping. It remains to be seen whether this shipping-associated rise in blood pressure is also present in other strains of mice, and whether the same results are obtained when using a different blood pressure measurement technique, such as telemetry. Nevertheless, we believe this information is important for the hypertension research community when planning and performing experiments that include blood pressure measurements in mice.

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References

1. Kurtz TW, Griffin KA, Bidani AK, Davisson RL. Hall JESubcommittee of Professional and Public Education of the American Heart Association. Recommendations for blood pressure measurement in humans and experimental animals. Part 2: Blood pressure measurement in experimental animals: a statement for professionals from the subcommittee of professional and public education of the American Heart Association council on high blood pressure research. Hypertension. 2005; 45:299–310. [PubMed: 15611363]
2. Fox, JG.; Barthold, SW.; Davisson, MT.; Newcomer, CE.; Quimby, FW.; Smith, AL., editors. The mouse in biomedical research. Academic Press Publications, Elsevier; London: 2007.

3. Capdevila S, Giral M, Ruiz de la Torre JL, Russell RJ, Kramer K. Acclimatization of rats after ground transportation to a new animal facility. Lab Anim. 2007; 41:255–261. [PubMed: 17430625]

4. Feng M, Whitesall S, Zhang Y, Beibel M, D'Alecy L, DiPetrillo K. Validation of volume-pressure recording tail-cuff blood pressure measurements. Am J Hypertens. 2008; 21:1288–1291. [PubMed: 18846043]

5. Feng M, Deerhake ME, Keating R, Thaisz J, Xu L, Tsaih SW, Smith R, Ishige T, Sugiyama F, Churchill GA, DiPetrillo K. Genetic analysis of blood pressure in 8 mouse intercross populations. Hypertension. 2009; 54:802–809. [PubMed: 19652078]

6. D'Angelo G, Elmarakby AA, Pollock DM, Stepp DW. Fructose feeding increases insulin resistance but not blood pressure in Sprague-Dawley rats. Hypertension. 2005; 46:806–811. [PubMed: 16157789]

7. Olfe J, Domanska G, Schuett C, Kiank C. Different stress-related phenotypes of BALB/c mice from in-house or vendor: alterations of the sympathetic and HPA axis responsiveness. BMC Physiol. 2010; 10:2. [PubMed: 20214799]

8. Bean-Knudsen DE, Wagner JE. Effect of shipping stress on clincopathologic indicators in F344/N rats. Am J Vet Res. 1987; 48:306–308. [PubMed: 3826873]

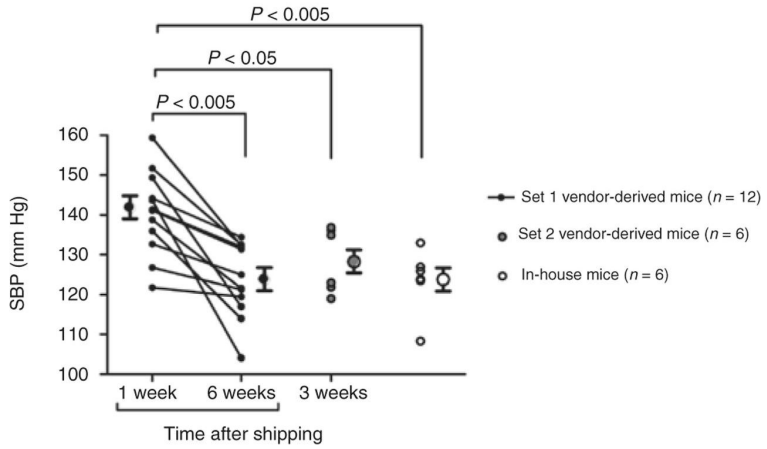

Figure 1.

Effect of shipping on blood pressure. Systolic blood pressure (SBP) is shown in (i) a first set of vendor-derived mice (the index group) 1 and 6 weeks after shipping (black symbols), (ii) a second set of vendor-derived mice 3 weeks after shipping (gray symbols), and (iii) in-house mice (white symbols). SBP of each individual mouse is shown as well as the group average ± s.e.m. All data points are considered to represent the average baseline SBP and were collected during 3 days. Statistics were calculated by paired and independent T-tests, as appropriate.