CASE STUDY

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Stress Induced Changes in Core Blood Pressure Using Tail-Cuff Methods

Introduction

In 2005, the American Heart Association (AHA) published recommendations for monitoring blood pressure in animal models. Their conclusion stated that overall, telemetry was the best method for collecting blood pressure in preclinical studies when compared to tail-cuff blood pressure collection. Tail-cuff is still a widely used method and from 2015 – 2019, over 350 studies published in AHA journals mention the use of tail-cuff in mice, whether used independent or in conjunction with telemetry. Due to a lack of consensus on reproducibility and reliability of the tail-cuff method, researchers sought to evaluate technical factors that influence stress response during tail-cuff use, as well as its accuracy of blood pressure measurements in mice.

Methods

Researchers used male and female C57Bl/6J mice aged 13 to 15 weeks and conducted three different experimental groups to evaluate handling and hemodynamics. Two subject groups were implanted with telemetry devices (PA-C10; Data Sciences International, Saint Paul, MN, USA) to monitor blood pressure, heart rate, and activity. The third group was implanted with telemetry devices (TA – F10, Data Sciences International, Saint Paul, MN, USA) to monitor temperature. Mice were housed in opaque polypropylene cages in a climate-controlled environment (22±2°C) and food and water were freely accessible. A tail-cuff plethysmography system (Kent Scientific, Torrington, CT, USA) was used to acquire non-invasive blood pressure measurements.

Study

Continuous and scheduled telemetry recordings were acquired throughout the study. Telemetry was measured simultaneously during tail-cuff readings. Tail-cuff measurements were performed for five consecutive days during three separate periods.

Three different handling techniques were used during transfer to tail-cuff systems: tube lifting, tail pick-up, and the tail and palm technique. Male and female handlers were both used. After the tail-cuff protocol acclimation period, mice who were being monitored for blood pressure were implanted with osmotic minipumps (1002 Alzet, Durect) and received a dose of 1.1 mg/kg per day of Angiotensin II (AngII) or vehicle for 14 days. This was performed to evaluate blood pressure reliability of tail-cuff versus telemetry.

Results

Habituation

Telemetry recordings showed that increased blood pressure and heart rate caused by restraint and tail-cuff measurements did not decrease over time with repeated assessment (Fig 1).

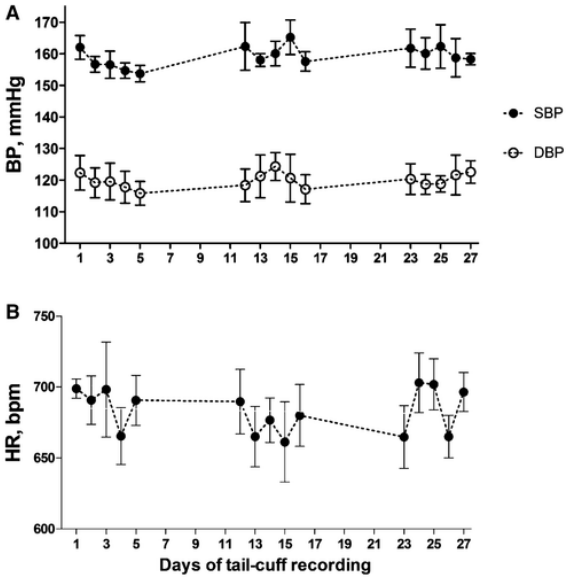

Figure 1. BP and HR telemetry recording (mean±SEM) of repeated tail-cuff exposure to 6 mice

Handling

The entry of the investigator into the room caused a slight increase in heart rate, while blood pressure was not affected. When the cage was moved across the room, both blood pressure and heart rate rose

significantly. All three handling techniques displayed similar increases in hemodynamic responses, while no substantial effect was noted based on the sex of the handler.

Restraint

Maximum hemodynamic levels were reached during restraining periods and cuff inflation, regardless of warming interventions. The effects did not decrease back to baseline until at least 1-hour after mice were returned to their home cage, following tail-cuff measurement. Increases in core body temperature were also observed, though slower to reach peak changes. Unlike blood pressure and heart rate, core body temperature did not return to normal for approximately 2 hours.

Blood Pressure Values

Results showed that tail-cuff blood pressure recordings with and without AngII, were 39.3±16.1 mm Hg and 31.4±19.4 mm Hg (mean±SD) lower for systolic and diastolic blood pressure, respectively, than telemetry. Non-simultaneous recordings from tail-cuff data were similar to telemetry recordings collected when the mice were undisturbed without AngII (Fig 2). The addition of the AngII infusion raised overall blood pressure in the treatment group, but the difference of ≈40 mm Hg between simultaneous

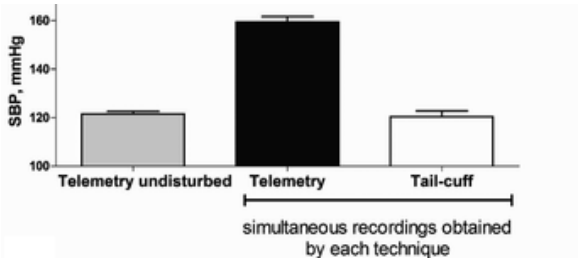

Figure 2. Baseline SBP without AngII in undisturbed mice using telemetry and simultaneously using telemetry and tail-cuff

telemetry and tail-cuff recordings remained the same (Fig 3). The study showed no difference in blood pressure between male and female mice.

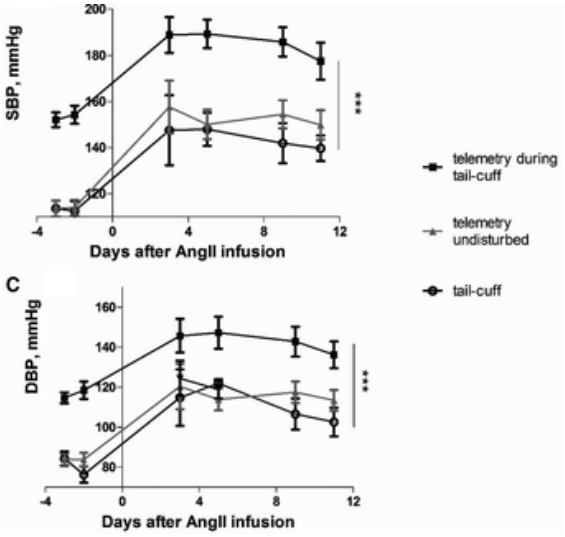

Figure 3. Baseline SBP without AngII in undisturbed mice using telemetry and simultaneously using telemetry and tail-cuff

The Successes

This is the first study to fully evaluate the way various handling techniques used in tail-cuff protocols affect hemodynamic and temperature responses in mouse models using telemetry. Overall, researchers found that factors associated with the tail-cuff technique resulted in significant changes to blood pressure, heart rate, and core body temperature, all biomarkers of animal stress. Restraint and inflation during tail-cuff measurements caused the most substantial physiological changes, which did not decrease after repeated restraint exposure. While telemetry was more accurate in overall blood pressure monitoring, tail-cuff was able to detect blood pressure changes, similar to telemetry, after AngII was administered. This study affirms the recommendation that tail-cuff plethysmography should only be used in animals to obtain blood pressure when high-throughput is necessary, for long-term studies. Telemetry remains the gold standard in hypertension research and is far more reliable for blood pressure monitoring.

DSI

Data Sciences International (DSI) offers complete systems that sense, transmit, acquire, and report physiologic data. To create a more robust study design, scientists rely on DSI and Harvard Bioscience technology to study specific targets as well as obtain a holistic view; allowing them to look at side effects that are upstream or downstream of the main pathology.

The DSI team ensures that researchers are equipped and prepared from the first minute of their study to the last, because your research is everything.

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References:

Wilde, E., Aubdool, A. A., Thakore, P., Baldissera, L., Alawi, K. M., Keeble, J., . . . Brain, S. D. (2017). Tail-Cuff Technique and Its Influence on Central Blood Pressure in the Mouse. Journal of the American Heart Association, 6(6). doi:10.1161/jaha.116.005204