RATURN™

The **What** and **Why** of BASi's Movement Responsive Caging

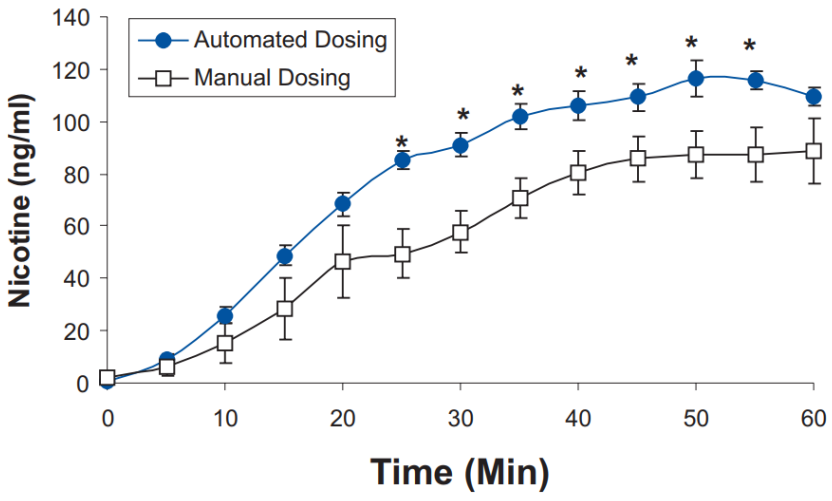
Novel environments and handling cause stress in research animals[1]. Minimizing and overcoming stress is key to generating accurate data and improving animal welfare. BASi's Raturn™ is a movement responsive cage that acts as a home cage for rodents during tether-based studies. The Pigturn is a similar system designed for use in large animal models. Both the Raturn and the Pigturn interactively respond to animal movement to keep wires, tubing, fluid lines and optic and electrical cable connections from twisting. Paired with automated sampling devices such as the Culex® Automated Blood Sampling System, the Raturn (and Pigturn) reduce the number of human interactions to keep stress levels at a minimum.

BASi's Movement Responsive Caging generates a buzz of conversation around its functionality and purpose, and it raises some questions for researchers. We all want the best for our research animals, and we want to make sure that we are gathering the best possible data from the fewest number of animals. Read on for answers about how we know the Raturn is a low stress system, and how it can improve study outcomes.

Is movement-responsive caging a worthwhile improvement over traditional handling and restraint?

Traditional handling and restraint methods for rodents include restraint by hand, or use of commercially available restraining devices. Both of these options are regularly used in the lab setting, and both of them can cause distress in the animals being sampled. In addition to the handling or device, we often use methods such as warming lights to encourage vasodilation, and then we must use needle sticks to dose or sample from the restrained animals. It is probably not a surprise that all of this activity can cause changes in respiration, cardiovascular output and stress-hormone release. So the question is not whether we cause stress to animals, it is whether we can introduce a system that reduces the stress and improves the data. BASi explored this question in a comparative study that looked at automated vs manual dosing in rats on the Raturn System.

Male Sprague Dawley rats were implanted with blood sampling and gastric dosing catheters. In this crossover design, the automated dosing group received their dose through a programmable syringe pump- no humans were present in the room. The manual dosing group received their dose through manual restraint and gavage needle delivery. Both groups had blood collections performed with an automated blood sampling system (no humans present). After a washout, the treatment groups were reversed.This change in technique resulted in a change to the PK curve. For some timepoints, this difference was statistically significant. Also of interest in this study is that the data for the automated dosing group was less variable than the manual group. This is a strong example of the effect that human handling and restraint can have on research animals, and why method matters.



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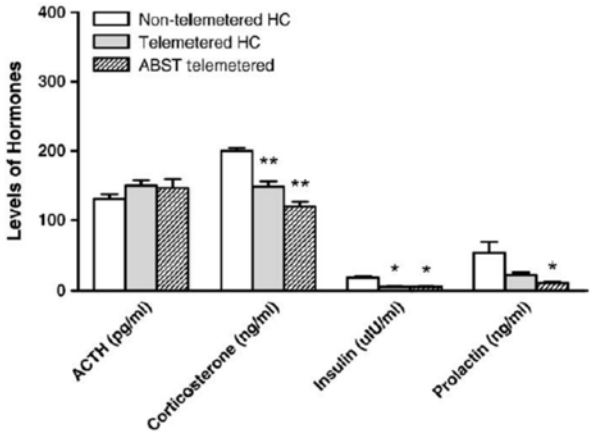
Does restraint-free animal research reduce stress?

Rodent physiology is affected by human presence. To reduce confounding effects of experimenter interaction on rodent physiology, efforts must be made to remove the human factor from the equation. This is achieved through fully automated sampling and data collection.

Kamendi et al. (2010) stress hormone levels in rats using three types of sample collection methods:

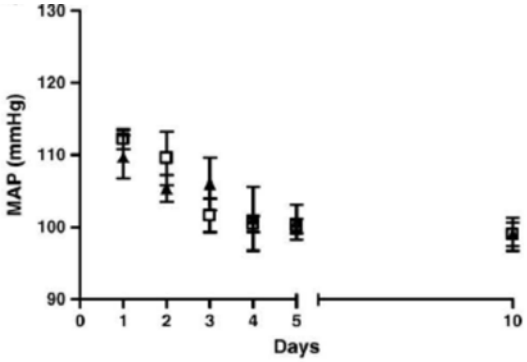
Non-telemetered HC: rats without telemetery implants, house in a home cage and restrained during tail vein blood sampling
Telemetered HC: rats with telemetery implants and jugular vein catheters, unrestrained, samples are collected by a human (sans animal handling)
ABST telemetered: rats with telemetery implants and jugular vein catheters, unrestrained, samples are collected from Automated Blood Sampling System (Raturn, Culex; without humans in the room)

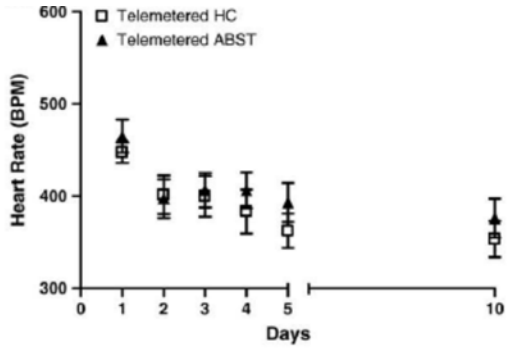


Telemetered HC and ABST telemetered groups were not physically handled during sampling. Corticosterone, insulin, and prolactin were lower in both of the "hands-free" sample collection methods compared to rats that were physically restrained during sampling. Corticosterone and prolactin levels were lower in the ABST telemetered group compared to the telemetered hc group. These results suggest that manual restraint and human presence increase stress during sampling which ultimately effects data. Similar results have also been reported in large animal models when comparing restrained versus automated sampling[2].

How does placing an animal in the Raturn cage compare with a traditional cage change?

Similar to humans, rodents need a certain amount of time to adjust to their environment. Over the course of one week, a rodent's home cage might be changed up to four times. Each cage change represents a novel environment and requires time for acclimation. In addition to the stress hormones mentioned above, Kamendi et al., (2010) also compared physiological changes that occurred after introducing a rat to a new home cage versus a Raturn cage. Mean Arterial Pressure (MAP, below left), Systolic and Diastolic Pressure (data not shown) Heart Rate (below right) and Body Temperature (data not shown) were measured over 10-days. Data suggests that both types of cage changes require approximately 4-days before a rat's vital signs return to baseline.





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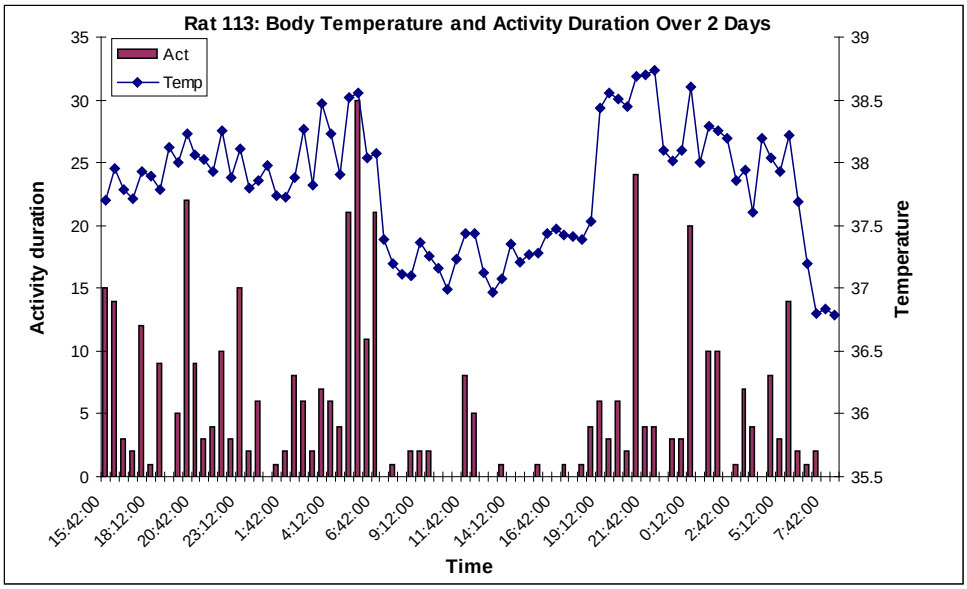
The Raturn prevents fluid and cable connection tangling. What other functions does it have?

The Raturn™ Activity Monitor is an accessory to the Raturn that collects information on animal movement when an animal is tethered in a Raturn Movement Responsive Cage. This addition generates comparable data to traditional beam-break systems[5] and allows for correlation of temporal profile of drug-induced neurochemical and behavioral changes[5,6] – without the confounding effects of human interaction during sampling.

With the Raturn™ Activity Monitor, it is possible to explore changes in diurnal variation, as shown below, and also to establish acclimation the caging system.



BASi will continue to explore and verify that our instruments are holding up to their claims. We are committed to making a positive impact on lab animals and we value their contribution to the advancement of science.

1 Balcombe JP, Barnard ND, Sandusky C. Laboratory routines cause animal stress. Contemp Top Lab Anim Sci. 2004 Nov;43(6):42-51.

2. Woods, JE, et al. Comparison of Automated and Manual Oral Dosing on the Absorption, Conversion, and Locomotor Activating Effects of Nicotine http://www.currentseparations.com/issues/22-1/CS22-1f.pdf

3. Marchant Forde, J.N., Matthews, D.L., Poletto, R. et al., (2012) Plasma Cortisol and Noradrenalin Concentrations in Pigs: Automated Sampling of Freely Moving Pigs Housed in PigTurn vs. Manually Sampled and Retrained Pigs. Animal Welfare. 21: 197-205.

4. Kamendi, H.W., et al., Combining radio telemetry and automated blood sampling: A novel approach for integrative pharmacology and toxicology studies. Journal of Pharmacological and Toxicological Methods (2010).

5. Heal DJ *et al.* Demonstration of the relationship between the in vivo dopamine efflux, behaviour and drug pharmacokinetics. Poster at a College on the Problems of Drug Dependence (CPDD) Meeting, Washington, DC, USA, 27th-28th October 2008.

6. Heal D.J., A microdialysis and behavioural comparison of lisdexamfetamine, methylphenidate and modafinil in freely-moving rats. Presented at British Association for Psychopharmacology Meeting, Harrogate, UK 22-25 July 2012.