

Introduction for Special Topic, Part I

Extrinsic Environmental Variables: The Umwelt of Research Animals and the Implications for the 3Rs and Study Reproducibility

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In this issue of *Journal of the American Association for Laboratory Animal Science* (JAALAS), an initial set of articles are presented to review extrinsic factors having import to animal research. A later issue of JAALAS will extend this review of extrinsic factors with a second set of articles. It is hoped that these contributions will provoke thought and encourage discourse within the scientific community with respect to the need to consider, and attempt to mitigate, the impact of extrinsic factors on the reproducibility of research involving animal subjects. Estimates suggest that a staggering 70% to 90% of findings in biomedical research are not reproducible, accounting for a financial impact of many billions of US dollars spent annually on animal research findings that cannot be replicated.³ In addition to this financial loss, other important but less apparent losses are to animal life and delayed treatments and cures. This problem has produced a crisis in public confidence in biomedical research. Responding to this concern, an act of the US Congress (House Resolution 34 to 21st Century Cures Act) prompted the National Institutes of Health to impanel an Advisory Committee to the Director (ACD) to study the problem and suggest avenues for improving reproducibility and rigor of the research it supports. The 2021 report entitled “ACD Working Group on Enhancing Rigor, Transparency, and Translatability in Animal Research”¹ identified some key areas for improvement. Among the main recommendations from the report was to enhance researchers’ understanding of which extrinsic factors (such as light, noise, vibration, and many others) in an animal facility can influence research outcomes and therefore are critical to document, understand, and control. Except for temperature and humidity, most of the key extrinsic variables present in animal housing spaces and research laboratories are either not measured or are subjectively evaluated based on human senses and perception, which often do not accurately represent the way the animals experience these factors.

Critical to controlling (or controlling for) extrinsic variables is understanding how an animal’s perception of the sensory landscape differs from that of humans. Umwelt is a German word for environment and is often used broadly in ethology to describe the unique sensory experiences of an animal. Humans naturally tend

to take a very anthropomorphic view of what animals experience, using our senses and biases to judge the experience of a mouse or a fish in a cage or a tank. The disparity between the human and laboratory animal sensory umwelt is extensive, species dependent, largely unmeasured, and uncontrolled. For example, most research animals are rodents that have evolved to function in underground burrows/tunnels in which vibration can signal an imminent threat to life and where the use and value of sound and ultrasound can differ dramatically from the human experience.

This focus issue was devised as the result of AALAS Conference Special Topics Sessions from 2021 and 2023 on Extrinsic Variables led by the key contributing authors (Dauchy, Hankenson, Reynolds, and Turner) and championed by the Editor-in-Chief of the JAALAS journals at the time (Toth). The goal of this focus issue is to provide some essential context and background information on extraneous variables in animal facilities to guide stakeholders (facility administrators, veterinarians, researchers, and others) with respect to making decisions about why and how to control some of the critical extraneous environmental variables and personnel influences that add a layer of variability to animal-based research. This focus issue is not intended to include every extraneous variable that animals may experience in their environments. We hope that this information will promote additional awareness, research, and publications on this critical topic, thereby serving to truly promote animal welfare and the 3Rs goals and improve study reproducibility.

Note that one article intended for this issue (Suckow and Tirado-Muñiz)² on the topic of seasonal variation in animal physiology and behavior was published in advance of this issue. Please see that article for information on this important extrinsic variable.

References

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3. **Wilson E, Ramage FJ, Wever KE, Sena ES, Macleod MR, Currie GL.** 2023. Designing, conducting, and reporting reproducible animal experiments. *J Endocrinol* **258**:e220330. <https://doi.org/10.1530/JOE-22-0330>.

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