



National Institutes of Health
Office of Research on Women's Health

Experimental Design, Methods and Data Analysis Techniques to Address Sex as a Biological Variable in Preclinical Research

NIH Campus, Porter Neuroscience Center
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Current efforts related to sex as a biological variable in preclinical research

- Multiple types of content on ORWH S4 website (<http://orwh.od.nih.gov/sexinscience/index.asp>)
 - Meeting summary
 - Interviews with experts
 - Meeting video
 - Content of speaker and moderator slides
- Significant trans-NIH promotion of the S4 website and SBV (sex as a biological variable) by ORWH staff and NIH leadership
- Significant public promotion of the concept of sex as a biological variable in scientific meetings, press/media, Advisory Councils
- NIH OD developed video training modules covering data reproducibility <http://www.nigms.nih.gov/training/pages/clearinghouse-for-training-modules-to-enhance-data-reproducibility.aspx>
- Development of policy related to rigor and transparency
- Workshops, meetings and conversations with publishers and editors; resulting in editorial changes to reporting results





Next steps...building on the momentum from the 'Methods Workshop'

- ***Develop materials that will help researchers make informed decisions about how to incorporate sex as a biological variable into preclinical research***
 - Methods and techniques to address the uniqueness of females (e.g., estrous) or males (e.g., aggression) in preclinical research; monitoring estrous, developing housing conditions that minimize costs
 - Experimental designs to incorporate sex as a biological variable; both to control for sex, analyze sex, and consider sex
 - Statistical techniques to account for the variability introduced by including both sexes through design and analyses (partitioning variance); control and analyze
- While materials will focus on sex as a biological variable, the same content could be widely applicable to other biological variables that need to be controlled or assessed for effect
 - Age, species/strain, genetic background





Nature and scope of effort

- Develop a learning module to address use of sex as a biological variable in preclinical research
- Incorporate the fundamental aspects of experimental design, methodology, and data analyses
- Demonstrate through examples how experimental design can increase the likelihood of a successful outcome and increase the discovery of new results when considered in advance of the execution
- Show the relationship between the research question hypothesis and the design





Background

- Learning module content based on a current, successful experimental design course taught at Texas A&M University Health Science Center (Graduate School of Biomedical Sciences)
 - Developed by Wei-Jung Chen, Ph.D. and Susan E. Maier, Ph.D.
 - Currently taught by Dr. Chen
- Experimental Design for Biomedical Scientists
- Course Outline and Goals: This course will explore many facets of experimental design including experimental control, hypothesis testing, and complex designs. The course will begin with a review of the basic principles of observation and developing a hypothesis, and subsequently lead to a critical analysis of how experiments may fail to achieve their goal due to flaws in experimental design. Although the principles of experimental design are straightforward and simple, a review of this material is essential for developing increasingly complex research designs and hypothesis testing. By knowing the foundation principles, students will be armed with the correct tools to perform their studies and to evaluate the results of studies based on their experimental designs.



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Methods to control systematic variation due to confounds for any experimental design

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Within Subjects Designs

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Evaluating the outcome: Accounting for inter and intra-group variability

- Three components of variation in an experiment
 - **Chance** variation
 - Non-systematic, random; difficult to control this type of variation
 - **Systematic** variation
 - Influence of the independent variable
 - **Systematic variation of confounds**
 - Due to confounding, uncontrolled variables; can control this variation



Correlation. Partitioning variance

- r^2 give one variable other
- r^2 & p
- Degree though be acc
- This c (regre

Alcohol and water maze learning

- Alcohol treated mice learn to find the hidden platform

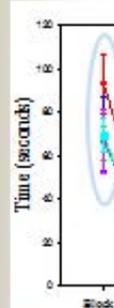
Redefine the dependent variable

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Scales of Measurement and Choice of Statistical Test

- Why do we need to pick the correct test to analyze our data?
- A statistician does not know the relevance of the numbers s/he analyzed and thus cannot interpret the data analysis
 - Statistics based on numbers, ranks of numbers, signs of numbers, etc.
 - Mathematical operations are applied to numbers, and can be applied regardless of the source of the numbers (ranks, ratios, Likert scale values, scaled scores=IQ, GRE, etc.)

Time (seconds)



- What these
- Rede mice

INTERPRETATION!



Considerations

- How will the learning module be developed and deployed?
 - What type of expertise will be needed?
- Should this learning module be incorporated into other ORWH-developed learning modules, e.g., *The Science of Sex and Gender in Human Health* (<https://sexandgendercourse.od.nih.gov/>)?
 - If yes, should the experimental design content be expanded to include human subjects studies?
- How can ORWH promote this type of content to improve the quality of the literature?
 - Quantity of articles in the literature will increase, but can or should we control the quality?
 - Is this the best method to influence quality?





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Please send suggestions, comments and
feedback ...

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