

T400-Series Technical Note

Experimental Design: Overview

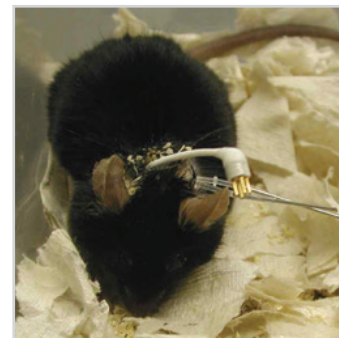
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Answers to experimental questions are developed according to results from experimental protocols. The challenge is to address a question so that the answer is valid. Analysis of these results must, therefore, take into account the experimental conditions under which they were obtained. Moreover, an interpretation of results is always limited to the confines of the experimental conditions. There are several approaches to experimental design to try to realize the most valid answers.

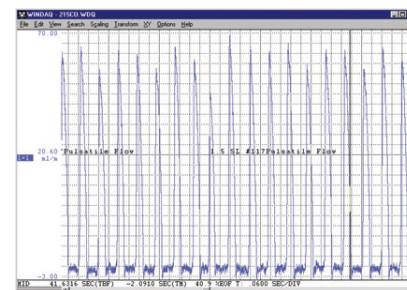
The simplest designs to execute are acute experiments in which all variables are controlled except for the variable under examination. In experiments with animals this usually means that anesthesia is used. If the experimental question involves the cardiovascular system, then the effects of anesthesia on cardiovascular parameters have to be taken into account.

Truly long-term, chronic experiments to study the cardiovascular system can be designed to examine the variables in question in intact conscious animals. These experiments can be elegant but there are many new variables which must now be controlled such as light/dark cycles, environmental stimuli such as temperature and noise, olfactory stimuli and potential long-term stressors such as cage bedding, social interactions and other behavioral factors. One can also quickly appreciate that in a design in which repetitive measures are made in each animal over time that loss of a data point in a specific animal can effectively remove that animal from the study, at a great expense in lost time.

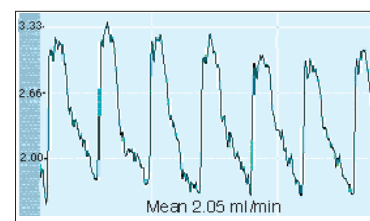
Acute experiments in chronically instrumented mice: These experiments take advantage of short-term observations but avoid anesthetics and acute surgical stress.



Flowprobe connector and catheter exit from C57BL6 Mouse. Courtesy, B. Janssen, University of Maastricht, Maastricht, the Netherlands



Chronic CO in the Mouse: 1.5PSL Probe on Ascending Aorta



Conscious Mouse renal arterial blood flow, day 4 after implant of 0.5PSL Flowprobe

Experimental Design: Overview Cont.

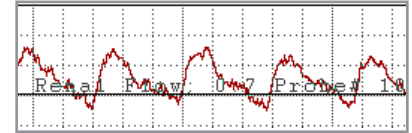
Approaches: Acute Versus Chronic Design

1. Acute Experiments:

- Simplest to execute but often the most difficult to design
- In the perfect design all variables are controlled except for the variable being examined
- In acute animal experiments, the design usually calls for the use of anesthesia which often leads to components of the experiment which are difficult to explain, because anesthesia can have powerful effects on the cardiovascular system.
- Ether, pentobarbital sodium and clorose urethane affect mean arterial pressure, cardiac output, heart rate and total peripheral resistance
- Anesthesia also has strain dependent effect, producing differing cardiovascular effects on different strains with different anesthetics
- Therefore, the challenge is to design an acute experiment so that anesthesia is less important

2. Chronic Experiments: An Alternative to Acute Experiments

- Instrument – 5-7 days recovery – follow over time
- 24-hour hemodynamic considerations such as diurnal variation which must be taken into account by monitoring lights and other environmental stimuli
- Primary consideration: how many days the experiment should last; although one can think of many elegant experiments, they can end up being costly if there is failure on day 5 or after.
- Perhaps the most practical type of experiment is one which performs acute observations on chronically instrumented animals. Chronic studies in mice necessitate the availability of instruments appropriately scaled for small implants.



This renal blood flow recording was made 1 day after implant in the conscious mouse.



Typical mouse chronic femoral artery flowtrace.



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