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Background

Migraine is a common neurological disorder that last on the order of hours to days and affects approximately 28 million people in the United States. Advances in molecular biology have greatly clarified the pathophysiology of migraine, though much research has yet to be done. Of particular importance to this research is the role of Calcitonin Gene Related Peptide (CGRP). CGRP is neuropeptide that when injected into migraineurs often causes migraines and migraine-like headaches to develop. The presence of CGRP alone is not enough; it must bind to the cell-surface molecule Receptor Activity Modifying Protein 1 (RAMP1). This triggers a signaling cascade in the cell, which is thought to eventually up-regulate CGRP expression, creating a positive feedback loop that is consistent with the observation that the duration of migraines can be quite sustained.

In an effort to create a model system in the mouse, a transgenic strain was generated through virus-mediated gene delivery and subsequent breeding programs. The gene introduced to the mice was the human RAMP1. This transgenic strain was engineered in such a way that the human RAMP1 gene is only expressed in the nervous system (see fig. 1).

A variety of experimental methods have been developed to assay the behavior of mice when treated with noxious stimuli normally associated with pain, such as heat, excessive light or mechanical pressure. Of interest to this study is the test of photophobia, or light-aversive behavior. The experiment was performed by putting a

mouse in a box that was well-lit on one half, and dark on the other half. The wall separating the two halves had a small hole through which the mouse could travel. The time spent in light was recorded in seconds, and the person testing the mice was blind to their genetic background.

Fig. 1 Introduction of the human RAMP1 gene into the mouse genome was engineered in such a way that a substantial quantity of protein is made and is present on the neural cell surface.

Questions

1) Do transgenic mice spend less time in the light than control mice?

2) Does gender have an influence on time in light between transgenics and controls?

Hypothesis

1) H_o: $x_c = x_t$

   H_a: $x_c > x_t$

2) H_o: $x_{tm} = x_{tf} = x_{cm} = x_{cf}$

   H_a: $x_{tm} \neq x_{tf} \neq x_{cm} \neq x_{cf}$

Statistical Tests

We defined our groups of mice as two independant samples. To determine whether transgenic mice spent significantly less time in the light compared to the control

mice, we used Student's t-test. We used ANOVA to test our second hypothesis to see if gender affects time spent in light. We performed a further ANOVA with the Bonferroni correction.

Results

Hypothesis 1:

---------- genotype=c ----------

The MEANS Procedure

Analysis Variable : count

N	Mean	Std Dev	Std Error	Lower 95% CL for Mean	Upper 95% CL for Mean
42	102.8333333	19.9167985	3.0732287	96.6268220	109.0398447

---------- genotype=t ----------

Analysis Variable : count

N	Mean	Std Dev	Std Error	Lower 95% CL for Mean	Upper 95% CL for Mean
35	74.8571429	40.1307736	6.7833388	61.0717398	88.6425459