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COMMENT

Warning! Nearby Construction Can Profoundly Affect Your Experiments

Mary F. Dallman, Susan F. Akana, M. E. Bell, Seema Bhatnagar, SuJean Choi, Alan Chu, Francisca Gomez, Kevin Laugero, Liza Soriano, and Victor Viau

Department of Physiology, University of California San Francisco, San Francisco, CA

This is meant to alert people to potentially major effects of construction projects on research results. Because we study the effects of stress on regulation of ACTH and corticosterone secretion and of serotonin receptors and stress on energy balance, we serve as an early warning system when things go awry. Most of our experiments include taking daily, or twice daily, measurements of rat or mouse weights and food intake as well as stress hormone levels. We are highly sensitized to environmental disruption and we've shown previously the effects of construction on stress hormones *(1)*. However, we did not anticipate the change and disruption in energy balance that may occur in response to environmental perturbation. We provide two examples of these, below.

Key Words: Food intake; body weight; phenotypic expression; rhythms.

Introduction

Any successful university is bound to grow, and growth means new construction and/or renovation. People in our university try hard to proceed with as little nuisance as possible, and have much of the construction done at night and very early in the morning. The building in which our animals are housed is among the oldest and most outdated buildings in the complex. Many of the labs in the building are outmoded for research in the Y2K, and much of the infrastructure desperately needs bringing up to current state and city building codes. Therefore, the construction is highly beneficial for the well-being of all (staff, faculty, and animals) at the University, and is to be applauded.

However, construction means noise, vibration, power outages, and excursions in temperature and air-flow. Frequently, the construction-induced environmental changes are not taken into account in terms of their potential effects on animals housed within the complex being remodeled. The environmental upsets are not recognized as disruptive, because the investigators are not usually present when the construction is ongoing, although the animals are. Because those who use animals know that the personnel in the Animal Care Facility and their IACUC are all concerned with animal welfare, there is little investigator concern about ongoing construction projects that may impinge in any number of ways on the animals under study, or tissues collected from these animals.

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Author to whom all correspondence and reprint requests should be addressed: Mary F. Dallman, Department of Physiology, University of California, San Francisco, San Francisco, CA 94143-0444. E-mail: dallman@itsa.ucsf.edu

Delayed Emergence of Phenotype

We have reported that mice with a knockout of the 5HT2C receptor gene begin to eat more by 12 wk of age but don't gain more weight, compared to wild-type littermates, until considerably later in life *(2)*. This year we intended to do experiments to delineate the site at which these serotonin receptors act to reduce food intake and also to determine the mechanism by which the increased food intake in the knockouts is only reflected by increased body weight after a considerable lag. We housed mice in our usual animal rooms and found that they did not exhibit the hyperphagia typical of this KO at the time it was expected (by 12 wk; Fig. 1).

We continued to follow these mice and others in a different (no nearby construction) animal room and found that the mice in our room did not either eat as well or grow as well as those in the more protected room. The mice in our usual room exhibited the phenotype we had expected a full 6 wk later than the others studied subsequently in more protected animal rooms (Fig. 1). Although we were usually alerted to times of major construction, we were unaware of times at which "minor" construction was occurring in the vicinity of our animal rooms. The fact that the mouse food intake and growth rate was strikingly different in the two animal rooms, although the rooms were similar with respect to lighting, cleanliness, and diet, suggests strongly that it was the nearby construction that decreased food intake, growth

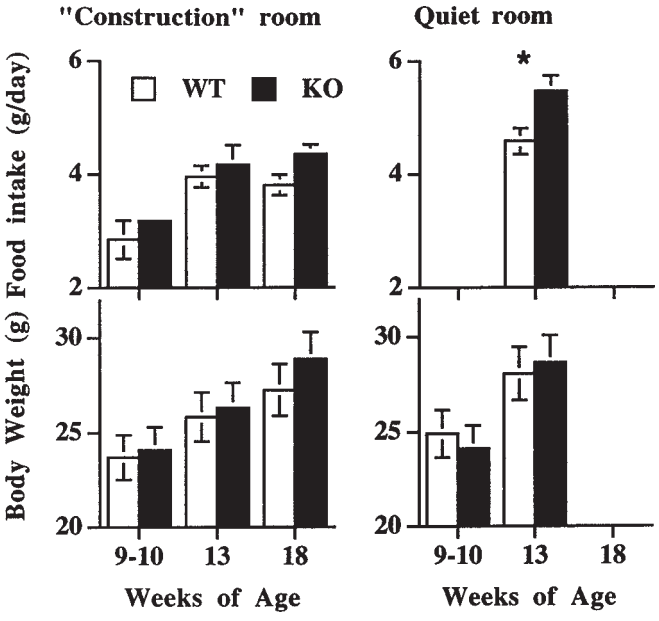

Fig. 1. Food intake and growth rates in wild-type (WT) and knockout (KO) mice housed in noisy (left) and quiet (right) rooms. The expected feeding phenotype is expressed at the expected time in mice in the quiet room, whereas the phenotype is barely expressed in the noisy room at 18 wk (top). Growth rate in the noisy room is much slower than in the quiet room (bottom).

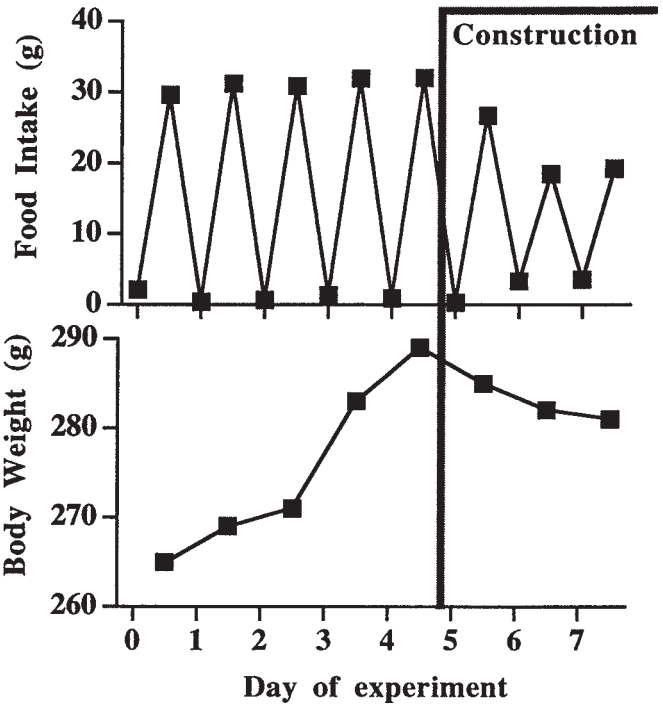

Fig. 2. When construction on the roof began on d 5 of the experiment, the sentinel rat abruptly decreased its food intake and lost weight. Characteristic of stressed rats *(3)*, he reduced his nocturnal and increased his diurnal food intake.

rates, and lack of the temporally normal phenotypic expression in our usual room. The experiment performed in our usual rooms led us to believe that we had lost the phenotype.

Construction and Energy Balance

The clearest example of the deleterious effects of nearby construction is shown by the results in a single rat that was used as a sentinel animal for an experiment that involved stress to three of six groups of manipulated rats. The sentinel rat was not operated on, nor was it treated in any fashion except for daily weighing and twice-daily food intake measures (Fig. 2). We found, *post hoc*, that there had been jackhammering on the roof above our animal rooms during the last 3 d of this experiment. This major construction had been performed during the evening and early morning hours so that people were not disturbed. However, the disruption to the sentinel rat is readily observed.

Problems associated with construction noises, vibration, temperature, light control, and air flow may be most readily determined by people who deal with their animals on a daily basis. However, it is very likely that the environmental disturbance also causes marked effects on the results of others who may collect tissue for measures of transcription factors or various other measures of specific gene activity.

Under conditions of stress (like nearby construction), animals respond with increased glucocorticoid and sympathetic neural secretion and decreased growth hormone, insulin, leptin, and gonadal hormone secretion *(4)*. These hormones have very widely dispersed receptors found in most cell types in the body *(5)*. Therefore, collecting tissue from animals that have been stressed by exposure to construction, would be expected to alter results of in vitro analyses of neural activity, receptor -, transcription factor-, and enzyme-expression. Thus, external factors (such as unknown construction variables) may contribute in a major way to the "biological variability" that is perceived in these disciplines.

We hope that our experience may help with your experiments. Our experience has suggested to us that under well-controlled conditions, biological variability is quite small, and that environmental variables, which may not be appreciated by some investigators, cause marked variance from day to day in otherwise tightly regulated and predictable systems.

There might be a happy outcome to this problem at UCSF. People in the Administration and Facilities Management were immediately active and concerned when we found and demonstrated the problem with construction. It was agreed that much more communication between FM and the Faculty about upcoming projects was essential. Policies may be put into place that will allow both controlled animal work and construction to proceed without undue interruption to either need.

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