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Research report

Challenges in quantifying food intake in rodents

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ABSTRACT

Feeding is a critical behavior that animals depend on for survival, and pathological alterations in food intake underlie disorders such as obesity and anorexia nervosa. To understand these disorders and their development in animal models, researchers must quantify food intake. Although conceptually straightforward, it remains a challenge to obtain accurate records of food intake in rodents. Several approaches have been used to accomplish this, each with benefits and drawbacks. In this article, we survey the four most common methods for measuring food intake in rodents: manual weighing of food, automated weighing scales, pellet dispensers, and video-based analyses. We highlight each method's benefits and drawbacks for use in feeding research, focusing on accuracy, potential sources of errors, affordability, and practical concerns relating to their use. Finally, we discuss the outlook for feeding devices and unmet challenges for measuring food intake in laboratory rodents.

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1. Introduction

Alterations in feeding underlie several diseases including obesity and anorexia nervosa. Such disorders are characterized by changes in food intake, and can be induced by specific diets, such as high-fat diet induced obesity in rodents. In rodent models of feeding disorders, researchers often relate food intake to weight gain or other changes in physiology. However, the explanatory power of these relationships depends on the ability to accurately quantify food intake. While measuring food intake is a simple concept, it remains technically challenging to achieve accurate measurements in research studies. In clinical studies, the difficulty in obtaining accurate food intake records has been termed the "fundamental flaw in obesity research" (Winkler, 2005), due to the difficulty in accounting for food intake in real-world conditions in humans.

In rodents, difficulties are caused mainly by technical challenges related to the relatively small amount of daily food intake, and the compounding effect that errors can have over time on variables such as body weight. Errors in this measurement may result in a misappropriation of caloric utilization, which is particularly problematic in studies that derive other metabolic measures from food intake records (Guo and Hall, 2009; Ravussin et al., 2013). In this review, we describe four common methods for quantifying food consumption in rodents: manual weighing, automated weighing, pellet dispensing, and video monitoring (Table 1). For each method, we highlight its strengths and weaknesses and discuss practical concerns related to their use. We conclude with potential future methods and a discussion of the unmet needs for measuring food intake in rodents.

2. Overview of methods

2.1. Manual weighing

The simplest method for quantifying food intake is manual weighing of a food dish before and after a feeding period. This approach does not have a high equipment cost, is easily scaled to dozens of cages, and can be accomplished in conventional vivarium caging racks. This approach can also be used for many different diets, and it is possible to put multiple dishes in a single cage to measure the relative intake of different diets. The main limitation of this approach is that it is both time and labor consuming to obtain each measurement. As a result, food intake records are often limited to one measurement every day or two. This produces data with a low temporal resolution, precluding analyzing temporal patterns of feeding, such as meal bouts. In addition, mice can create crumbs (Cameron and Speakman, 2010), and can defecate and urinate in the feeding dish, which reduces the accuracy of weight measurements. Liquid diets can also be assessed in home cages using graduated sipper tubes, which can be visually inspected or weighed. This is a cost-efficient method for measuring liquid

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Table 1
General description of the four major methods for quantifying feeding behavior, their accuracy, sources of errors, and home cage compatibility.

	Temporal precision	Caloric quantification	Accuracy	Sources of errors	Cage type compatibility
Manual Weighing	~daily	Yes	~100 mg	Spillage, animal feces and urine	Home cage compatible
Automated Weighing System	~seconds	Yes	~1mg	Load cell drifts, spillage	Requires specialized caging
Pellet Dispensers	~seconds	Yes	20–300 mg depending on pellet size	Hording pellets, crumbs, dispenser jamming	Home cage compatible
Video Recording	~sub-second	No	No quantification of amount of intake	Behavioral mis-classification, no measure of actual intake	Requires specialized caging

intake, but requires the animal to consume caloric sustenance through a liquid diet. Despite the low-tech nature of manual weighing, it is still commonly used, as it remains the only method that allows for high throughput measurements of food intake with little up-front equipment cost.

2.2. Automated weighing scales

A modern version of the manual method is the Automated Weighing Scales (AWS). Here, a load cell or a strain gauge continuously weighs a food source (Hulsey and Martin, 1991; Meguid et al., 1990; Minematsu et al., 1991). A computer analyzes changes in weight and outputs data on food intake with high temporal precision. These systems produce high-resolution food intake data with minimal human involvement, allowing for analysis of meal patterns (Farley et al., 2003). These systems can also be used to measure liquid diets, with slight modification to the food hopper or weighing compartment. Some AWS systems also include a functioning door that blocks mice from the feeding/drinking port, giving researchers control over time or caloric based scheduling restrictions. However, there are limitations to AWS: the signal from a load cell has a tendency to "drift". This requires calibration and correction, and can introduce errors if not properly calibrated over long time durations. In addition, AWS' are costly and require specialized experimental cages, as well as dedicated space to deploy these cages. Mice can also gnaw on food until the pellet is small enough to fall though the rack, creating a large sudden weight change that may not be consumed by the mouse (Moran, 2003). Some systems include a crumb collector to minimize this effect. Finally, some AWS systems are designed for specific food sources such as powdered food (Miller, 1990), and may not be usable with a variety of diets. AWS are best utilized in small-scale feeding studies that require measurements of caloric intake with high accuracy and temporal precision.

2.3. Pellet dispensers

Pellet dispensers can be used to dispense compressed pellets of a known mass (Gill et al., 1989). Most often, these have been used in an operant conditioning context, where mice learn an operant task (pressing lever or nose poking) to receive a pellet. However, pellet dispensers can also be used to measure adlib feeding (Aponte et al., 2011). A sensing mechanism such as an infrared beam, detects pellet retrieval events, which triggers the dispenser to release another pellet. Time-stamp analyses of pellet retrieval events allow for calculation of caloric intake with high temporal precision. Pellet dispensing devices can be small enough to be placed in standard vivarium housing, and open source versions exist that are cheap to build (Nguyen et al., 2016, 2017; Oh et al., 2017). Dispensers can be programmed to restrict food based on caloric or temporal requirements (Acosta-Rodriguez et al., 2017), or based on the animal performing an operant task (Rainwater et al., 2017). Finally, pellet dispensers provide high temporal resolution records of food intake, allowing for analysis of meal patterns. However, there are drawbacks associated with using pellet dispensers to measure food intake. Pellet dispensers are mechanical devices, which can be prone to jamming. A jammed pellet dispenser will deprive the experimental animal of food, and therefore these devices require routine monitoring. Animals can also remove but not eat pellets, which is known as "hoarding". This reduces the accuracy of both caloric intake and meal analysis. Finally, pellet dispensers require specialized food pellets that have a preset size, composition, and caloric content. As a result, soft diets (such as those high in animal fats) are not compatible with pellet dispensers. As a somewhat analogous system, fluids can be dispensed in discrete quantities using an infusion pump that delivers a set volume of the intended liquid. Infusion pumps are available commercially and several open-source devices have also been designed (Longley et al., 2017; Wijnen et al., 2014). Overall, pellet or liquid dispensers are a good option for experiments that require precise control over the timing and quantity of food availability. The compatibility of some of these designs with home-cages also opens up the possibility of high-throughput investigations of food intake without requiring additional laboratory space.

2.4. Video based systems

With the advancement of statistical modeling and machine learning algorithms, computer vision methods have been developed for classifying feeding behavior. The approach is non-invasive, and allows animals to interact with a standard home-cage food hopper. It returns data with high temporal resolution, and can be used to quantify other behaviors concurrently. However, there are several drawbacks to video-based detection of feeding. By visually analyzing feeding behavior, the approach is limited to quantifying "interactions with" food, but cannot measure the actual amount of food removed from the hopper. While it may be possible to calibrate video-based feeding behavior with caloric consumption, this has not yet been attempted. Videos systems can be used in home-cages (Jhuang et al., 2010; Salem et al., 2015), but this requires some modification to fix the camera position and light levels. Video based classification systems also need to be "trained" on a specific cage, and cannot be easily adapted to different caging without re-training the vision algorithms. Finally, these systems are computationally expensive and require substantial memory to process and store video data. Despite this limitation, video is a unique tool for investigators examining behavioral analysis that includes feeding as a subcategory (Noldus et al., 2001; Spink et al., 2001). In a simpler use of video, "food interaction zones" can be defined in a video image, and used to determine the frequency or length of time that an animal interacts with food (Burnett et al., 2016). And finally, video has long been used with human observers scoring the time interacting with food (Ishii et al., 2003), although this is time consuming and not suitable to large experiments.

3. Future directions

Many questions in feeding research are influenced by individual heterogeneity and require large sample sizes to tease out small