Mouse Smart Hoppers (Moshers)

Overall aim

The overall aim of this Challenge is to develop an approach/device to accurately measure individual food intake (real time measurement or proxy) in group-housed mice (three to five mice). The approach/device should be affordable, compatible with all types of mouse caging (and maybe applicable to rat and other rodent caging), and data should be easy to collect, analyse and interpret.

Duration

Up to one year

Budget

Up to £100k

Sponsors

MRC Harwell Institute

Background

Measuring food intake in laboratory rodents can provide a vital indicator of general welfare, recovery from surgery and is an important experimental parameter for metabolic studies. However, accurately monitoring the individual feeding patterns of a mouse, especially in social housing is technically and logistically challenging.

Currently there are three main ways of measuring food intake:

- Weighing home cage food hoppers: Two or more mice of the same genotype are housed together and the food hopper is weighed daily. While mice remain in their home cage, this method has limited accuracy and sensitivity and the caging needs to be disturbed daily, which can affect animal behaviour and food intake. Many weeks of data collection is needed to measure a sustained change in food intake. It is not possible to measure consumption by individual mice by this method.

- Metabolic/calorimetry caging: Mice are singly housed on hard flooring (usually grids or plastic with holes) and specially designed hoppers are used to measure food intake. While this method gives accurate measurements of food intake, single housing of animals and the initial stress associated with changes in housing, reduces overall food intake. The food used often has to be a different formulation than the mice are reared on (e.g. ground diet or different pellets), the caging is expensive and requires specific racking, and is therefore not suitable for widespread use for routine welfare monitoring or for following developing phenotypes (Stechman MJ *et al*., 2010; Kalliokoshi O *et al*., 2013).

- In-cage hopper systems: Electronic, open source systems have been published which involve an in-cage pellet dispenser (Nguyen KP *et al*., 2016). While this provides accurate measurements from the home cage, it requires equipment to be installed inside the cage, reducing the floor space. Again, pellets will be a different formulation than mice are reared on, the analysis is not straightforward and crucially, individual animals cannot be identified. This, along with the cost, makes it unlikely to be suitable for all cage types and widespread use.

Mice typically eat 2 to 5g per day and in social housing, it is impossible to monitor individual food intake. Developing a system that can deliver basic and easy to understand data on food consumption for each individual mouse and be adapted to any caging system would be of benefit to many researchers using mouse models.

The Mary Lyon Centre houses up to 55k mice at any one time for hundreds of UK researchers with many of the mice undergoing regulated procedures. Currently welfare monitoring includes a range of measures such as weighing mice regularly. Due to the small size of a mouse, the accuracy of weighing very much depends upon the time of day, whether they have recently urinated, defecated or eaten. One-off weights can be inaccurate and therefore there is always a need for repeated handling and re-weighing. A rapid and accurate way of detecting decreases or increases in food intake in experimental stock would not only enhance phenotyping data but also provide an early warning system for health and welfare deterioration.

The metabolic research group at Harwell has carried out detailed energy balance studies in the mouse. However, accurate energy intake measurements remain a problem with single housing introducing changes in behaviour, which may be exacerbated in mice with anxiety and other traits, that alter food intake. Further, food intake data lacks granularity with averaging over time and over individuals. For example, the Harwell group has measured food intake in paired animals carrying a mutation in the Otp gene which is involved in mammalian energy homeostasis: when these mice are housed individually they frequently stop or significantly reduce their food intake (presumably due to stress) preventing accurate energy balance analysis. Given the importance of circadian rhythms in regulating metabolism there is also untapped potential in understanding how animals are feeding over the diurnal cycle. Continuous measurement of food intake, pattern of feeding and cyclical patterns in individual animals, intersecting with other metabolic data, would allow questions about “real life” metabolic regulation to be addressed.

3Rs benefits

Development of a system to accurately measure individual food intake in group-housed mice offers the following 3Rs impacts:

- **Refinement**:
  - A non-invasive way of measuring food intake with no cost to the animal in terms of stress of physical confinement in novel surroundings.
  - Information that will be vital in refining the care and analgesia as animals recover from procedures such as surgery.
  - Food intake can be used as a proxy for well-being and as an earlier humane endpoint to weight loss (food intake is affected before an effect on weight is seen), allowing many types of studies and mouse models to be refined.
  - Databases of mouse feeding patterns could be utilised when designing experiments involving food restriction, weight monitoring, energy balance and/or metabolic mutants. This would allow refinements in experiments such as being able to restrict fasting periods to the minimum effective time needed for the physiological response required, avoiding prolonged periods of starvation.

- **Reduction**:

    - For diabetes, obesity and metabolism studies, the ability to take accurate, repeated and within animal measurements would improve the statistical power of the experiments, reducing the numbers of animals used. The added value of being able to track diurnal cycles in animals without any concomitant increase in welfare costs to the individual animal would also deliver significant scientific benefits.

- Compatibility with all cage types provides an opportunity to refine and reduce across a wide range of studies (e.g. welfare monitoring, recovery from surgery, metabolic studies, phenotyping, drug development, toxicology etc.).

Need for collaboration

To solve this Challenge expertise in the following areas will be required including, but not limited to:

- Electronics, engineering and wireless technologies (the final device should be portable and discern when individual animals are feeding e.g. use RFID or other technologies).

- Data analysis - expertise in analysing similar time-series data sets or experience in simplifying large datasets would be advantageous.

- Development of user-friendly software tools for data handling.

Key deliverables

Essential:

- Develop a device to individually monitor and accurately measure food intake which directly or indirectly (such as a derived calibrated value) will deliver data on the amount of food consumed by three to five mice housed together in a cage that:

    - Is compatible with all types of mouse caging and different feed-types.

    - Can discern when individual animals are feeding e.g. use of RFID or other types of technologies.

    - Has the potential to record number and duration of visits to the hopper.

    - Fits inside the mouse cage, but does not involve a permanent modification/addition to the home cage such as a pellet dispenser (e.g. no holes and screws etc. in the cage).

    - Is impervious to rodent chewing or other behaviours.

    - Does not require mice to be trained/an acclimatisation period.

    - Takes measurements at least every two to five seconds, providing high temporal resolution.

    - Runs for long periods of time without requiring manual intervention to refill or change batteries (at least seven days for 24 hours a day).

    - Is affordable and scalable to enable widespread use e.g. costs less than £50 per cage. Current systems are prohibitively expensive for widespread use in most facilities. Large facilities often house more than 10k cages, with at least 5% (~500) of caging under increased welfare monitoring.

    - Is portable and easy to install in regular cage racks.
    - Outputs results in understandable formats in excel.

- Validate and compare the device to commonly used alternatives (e.g. manual measurements, paired feeding, metabolic and calorimetry caging data) to ensure it provides accurate measurements of food intake.

- Develop a software system that displays and analyses data in a simple and intuitive format and has the potential for cloud-storage of data enabling easy open-sourcing.

Desirable:

- A device that is also compatible with rat and other rodent cages.

It is important to note that the CRACK IT Challenges competition is designed to support the development of new 3Rs technologies and approaches, which will improve business processes and/or lead to new marketable products. The application must include a plan to commercialise the results into a product or service. This should be taken into consideration when completing your application.

Sponsor in-kind contributions

The Sponsor will provide:

- Advice and ideas in device design.
- In-house testing of a prototype device.
- Data critique.
- In-house validation with wild type and mutant lines including a comparison of data from paired-feeding, metabolic and calorimetry caging data.
- Access to a wide network of mouse genetic researchers for advice/analysis and critique.

References

Kalliokoski O *et al*. (2013). Mice do not habituate to metabolism cage housing – a three week study of male BALB/c mice. *PLoS One* 8(3): e58460.

Nguyen KP *et al*. (2016). Feeding Experimentation Device (FED): A flexible open-source device for measuring feeding behavior. *J Neurosci Methods* 15;267: 108 – 114.

Stechman MJ *et al*. (2010). Establishing normal plasma and 24-hour urinary biochemistry ranges in C3H, BALB/c and C57BL/6J mice following acclimatization in metabolic cages. *Lab Anim* 44(3): 218 - 225.