Rodent Little Brother: measurement of mouse activity, behaviour and interaction in the home cage

Rodent Little Brother aims to find innovative and creative solutions to:

- Integrate recording equipment into regular cage racking;
- Simultaneously record from two or more mice per cage;
- Collect data over long periods of time (months);
- Analyse large data sets including the development of innovative software tools required to differentiate between different types of activity;
- Integrate Chip ID monitoring with high quality video monitoring to record and delineate numerous specific behaviours.

BACKGROUND

Many common nervous system disorders, often the subject of intense research using laboratory animals, are associated with behavioural, locomotor and social deficits in humans. Several of these express multiple phenotypes that are currently assessed using batteries of mouse tests. For example, Huntington's disease models express locomotor and learning deficits whereas mouse mutants in genes associated with schizophrenia often exhibit hyperactivity with cognitive disturbances[1,2]. In order to measure these characteristics systematically and assess the validity of animal models a number of developments have led to a reassessment of how neurological and behavioural phenotyping are carried out. These include:

- Specialist cages for tracking activity;
- Phenotyping equipment allowing one to measure a range of behavioural and physical attributes e.g. social interactions, dominance, anxiety;
- Advanced software systems and algorithms for data interpretation.

Much of the sophisticated equipment and software which is available requires animals (mostly mice) to be placed in either a novel environment or single housing which may both compromise and confound model validation in addition to being detrimental to animal welfare.

Novel environment

Many current tests involve removing animals from their usual environment and placing them in a piece of equipment to monitor their activity e.g. the rotarod to measure locomotion. Recently, much publicity has been given to available 'home cage' systems. However, many of those available on the market are not the same as the caging animals are reared in. Mice have to be removed from their true home cage and are often placed in unfamiliar cages in different rooms, with different enrichment regimes and handlers.

Sponsor
MRC Harwell

Budget per project
Phase 1: Up to £100,000 inc. VAT where applicable

Phase 2: Up to £500,000 inc. VAT where applicable

Key words
Mice, welfare, home cage, tracking, social interaction, behaviour, neurodegeneration, RFID, activity

SBRI Government challenges. Ideas from business. Innovative solutions.

MRC Medical Research Council

Single housing

Almost none of the equipment available on the market allows the simultaneous tracking of multiple animals and requires mice to be singly housed for the period of the test. Social isolation (singly housing) has been reported to affect mouse behaviours[3]. Moreover, it is difficult, impractical and disruptive to rehouse male mice into groups after an experiment.

3Rs BENEFITS

The development of an automated, non-surgical system will impact on refinement and reduction of studies using mouse models of nervous system disorders. These are disease models where pain, suffering and lasting harm can be difficult to assess and where earlier humane endpoints and interventions are needed. Additionally, animals would not need to be moved to unfamiliar cages or be singly housed for testing. Fewer animals would be needed because less variable data would be obtained from individuals.

The caging system used by MRC Harwell, the sponsor of this Challenge, is the most common in the UK and represents large potential for uptake of the solution. More broadly, the technology could impact in other fields e.g. metabolism, where mechanisms leading to weight changes (altered activity or food intake) could be investigated.

NEED FOR COLLABORATION

To succeed in this Challenge a number of different specialist skills are required. Although MRC Harwell is well served in terms of scientific and experimental knowledge in mouse genetics, collaborations are required, possibly outside of the field of biological research, in order to deliver the full potential of this project. In order to develop an automated system which can record specific animal behaviours (e.g. grooming, climbing, etc) for long periods of time (months) it will be necessary to seek the assistance of electronics specialists, engineers (to enable devices to be incorporated into home-cage settings) and bioinformaticians to provide data analysis tools. Particular focus should be on the development of software tools that will enable automated assessment of numerous behaviours in the home cage. Moreover, an essential component in developing new systems such as these is feedback and communication amongst technical experts and scientists.

OVERALL AIM

To develop an automated, minimally-invasive or non-surgical system to assess activity, behaviour and interaction of at least two mice in the cages and setting the animals were reared in.

KEY DELIVERABLES

Phase 1

- Demonstrate technology to monitor remotely the position (x, y and z) of two or more mice per cage ensuring that their individual positions can be differentiated.
- Develop methodology that can be used in distinguishing animals that are in extreme close quarters (e.g. huddled together whilst sleeping).
- These deliverables must be compatible with the home caging system used at MRC Harwell.

Phase 2

It will be critically important to develop and validate algorithms and software systems to be able to detect and measure behaviours such as:

- Total activity (hyper/hypoactivity, repetitive movements);
- Social behaviours (such as interaction, grooming, juvenile play, nest building);
- Interactions with novel objects;
- Behaviours in the cage (time at hoppers, climbing);
- Pathological behaviours (tremors, seizures, fitting).

Final prototype

- Can be used to assess, optimise and validate the system for at least two mice in the home cage;
- When scaled up should deliver recordings for several, large unrelated studies in parallel;
- Can incorporate study design for behavioural studies e.g. novel object recognition where a novel object is associated with a known position (x, y, z coordinates) and time. Vicinity to the novel object could be assessed for two or more mice in the home cage.

BEHAVIOUR PRIORITIES

High priority behaviours (essential):

For all behaviours, it will be critical to obtain all data related to the time of day it was obtained. Most analysis will require simultaneous monitoring by video tracking from minutes to weeks.

- Activity: Total activity for two or more mice in the home cage over a period of time.
- Social interaction: Amount of time spent in close proximity to other mice (or objects) in the home cage over a period of time.
- Avoidance behaviours: Amount of time spent in isolation, not in proximity of other cage mates over a period of time.
- Aggressive behaviours: Behaviours that elicit a brisk response from cage-mates.
- Arousal: Proportion of time spent in an active state (moving around) and inactive state (not moving).
- Tremors and/or seizures.

Intermediate priority behaviours (desirable):

- Feeding/drinking: Amount of time spent at hoppers
- Stereotypies: Repetitive behaviours.
- Grooming, thigmotaxis (tendency to remain close to the wall)
- Nest building
- Mating behaviour
- Climbing, rearing
- Juvenile play

Low priority (ideal but not essential, would enhance interpretation of behaviours): direction of gaze, apparent changes in body size (e.g. when stretching), body temperature

IN-KIND CONTRIBUTIONS

Phase 1

- Advice and guidance as required i.e. on MRC Harwell cage setup and dimensions and behaviours to be monitored.
- Trialling of test systems to demonstrate differentiation between mice in the home cage.

Phase 2

MRC Harwell would run evaluation/optimisation/validation studies using mouse models of disease in their laboratories with a view to peer reviewed publication. MRC Harwell has extensive experience in mouse phenotyping and behaviour analysis and will contribute this expertise to the project. MRC Harwell also has active neuroscience programs which currently focus on many new and established models of the diseases this type of phenotyping equipment will be most widely used on.

REFERENCES

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