Husbandry refinements for rats, mice, dogs and non-human primates used in telemetry procedures

Seventh report of the BVAAWF/FRAME/RSPCA/UFAW Joint Working Group on Refinement, Part B

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1 Aims of this report

This article follows on from a report published in the last issue of *Laboratory Animals* (Morton *et al*. 2003). Both publications form a report that is intended to help scientists, animal technicians, veterinarians and members of ethics or animal care and use committees to refine all aspects of telemetry procedures, from the project planning stage through to reporting finished research. It is published in two sections; this part (B) which addresses the selection, housing and care of rats, mice, dogs and primates used in telemetry studies; and Part A (Morton *et al*. 2003), which focuses on refinements in telemetry procedures from the project planning stage through to reporting finished research. These include: factors that need to be considered when making decisions regarding the justification for individual projects; experimental design; choosing or designing a device; deciding on the method of attachment and device location; refinements in surgical implantation; the reuse of animals; removing devices and the potential for rehoming animals; issues associated specifically with telemetry studies using wild animals; writing up studies involving telemetry; and keeping informed about new technological developments.

It is strongly recommended that both reports are used together to ensure that suffering is minimized and welfare improved throughout the lives of animals used in telemetry studies. Guidance for ethics or animal care and use committees based on the recommendations in Parts A and B is also available at www.lal.org.uk/telemetry/.

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2 Implications of telemetry for animal husbandry

Rats, mice, dogs and non-human primates (hereafter referred to as primates) are social species that require group housing. From the animals' point of view, the ideal telemetry system would allow them to be housed in stable, compatible groups, would be minimally invasive and would not be interfered with by conspecifics. There is likely to be a degree of compromise in practice, however, and different systems have their own advantages and shortcomings in this respect. Table 1 sets these out with respect to their abilities to facilitate or preclude group housing only; it is essential to note that there are many other ethical and welfare issues that need to be carefully considered. For guidance on these, see Part A, Section 7.4.

In addition to technical limitations, animals who have had telemetry devices fitted often experience reduced levels of contact with humans and other animals, because of the belief that changes in physiological parameters caused by social contact would skew experimental data. There is no evidence for this and, furthermore, isolating animals accustomed to a high level of contact can cause serious welfare problems. For example, in the Working Group's experience more stereotypies are observed in individually-housed, telemetered dogs than those group-housed with no devices fitted, probably because they miss interacting with other dogs and humans. Telemetry has also been used to demonstrate that group-housed rats are less stressed by procedures (Sharp *et al*. 2002a,b). There is absolutely no need to segregate animals implanted with telemetry or data logging devices, to keep them quiet at all times, or to deny them a stimulating environment.

Telemetry can also have an impact on animal housing and care in that it can

Table 1 Implications of internally and externally mounted telemetry devices for group housing

	Can facilitate group housing because . . .	Can preclude group housing because . . .	Possible solutions
Fully implantable devices[a]	there are no externally mounted skin buttons or backpacks that could be damaged by conspecifics	commercially available devices all transmit at the same frequency, preventing simultaneous recording from more than one animal	the buddy system; using devices that can be switched on and off (Section 3)
Partly or wholly external devices	external data loggers can be used and frequently downloaded; a multi-frequency device is available[b]	pen- or cage-mates may interfere with and damage devices	ensuring that animals are thoroughly habituated to devices and trained to accept them (Part A, Section 7.4.2)

[a]Note that more invasive surgery is generally required to fit total implants. Guidance on the harm benefit assessment and welfare and ethical issues involved can be found in Part A to this report
[b]EMKA Technologies, see Section 3

provide measurements of physiological variables that are commonly used to predict levels of stress in animals, such as heart rate, blood pressure and body temperature. These can be used to evaluate the impact of different protocols for housing and care, as well as procedures (see Part A, Section 4.2, Duke *et al*. 2001, Harkin *et al*. 2002, Sharp *et al*. 2002a,b, Krohn *et al*. 2003, Kramer *et al*. in press). For example, telemetry has been used to demonstrate that C57BL/6N mice habituate after 2 weeks to disturbance in the form of humans entering the animal room, apart from the first entry at 09:30 h (Kramer *et al*. in press). This may be because the animals are less able to habituate to disturbance at the beginning of their rest period and so there may be a case for avoiding husbandry and experimental procedures at that time.

Recommendations:

- **Aim to facilitate group housing for rodents, dogs and primates wherever possible, paying due regard to all ethical, welfare and technical issues using parts A and B of this report.**
- **Make sure that animals on telemetry studies are not denied appropriate socialization and a stimulating environment.**
- **Consider using telemetry to assess and monitor animal well-being and to refine husbandry and procedures wherever possible.**

3 Facilitating group housing

Total implants should make group housing a possibility; but most commercially available devices currently transmit at the same frequency, and this could cause problems. An exception at the time of writing is a wholly external device that transmits ECG on 16 frequencies, but this is unfortunately only available for large animals such as dogs and primates (EMKA Technologies, http://www.emka.fr). Other potential solutions are the 'buddy' system (where animals are pair-housed and one individual is implanted) or the use of devices that can be switched on and off *in situ* and used one at a time in pair- or group-housed animals.

One form of remote monitoring that allows several animals to be monitored simultaneously involves data logging, whereby data are recorded on to a microchip and then downloaded at a later date once the microchip is retrieved from the animal. Data loggers may be either implanted or worn externally. Activity monitoring is an appropriate parameter for recording in this way, using sensors worn as neck tags on a chain in a similar manner to identity chains (Mann *et al*. 2001). Data using this type of technique are not available on-line and can only be retrieved after the period of study, so technical failure cannot be detected until devices have been removed.

Recommendations:

- **Avoid individually housing animals fitted with telemetry devices unless there is a strong likelihood of interference with external devices or there is veterinary justification for individual housing.**
- **Use the 'buddy' system or switchable devices if larger groups are not feasible.**
- **Consider the use of data loggers to facilitate the collection of data from multiple animals in a single arena.**

4 Selecting suitable animals and housing stable groups

It is the Working Group's experience that some individual animals are more suitable subjects for studies involving telemetry than others, and that it is often possible to select appropriate individuals before studies begin. It is essential to try to achieve a stable group of animals, well adapted to their environment and with appropriate temperaments, before any individuals are implanted. Subjecting unsuitable animals to surgical procedures so that only limited information can be gained from them would be unacceptable if appropriate screening procedures could have prevented this. It is also vital to ensure that health status is good, although the Working Group acknowledges that this can be problematic in the case of wild animals, and expert assistance may be necessary in the field.

Recommendations:

- **Always ensure that healthy animals of sound temperament are selected for each study wherever possible.**
- **Never operate on an animal unless every possible relevant screening procedure has been completed and s/he has passed them all.**

4.1 Rats and mice

Selection of the appropriate rodent species and strain to achieve experimental aims is a fundamental aspect of good experimental design. Specific characteristics or traits may be required, particularly when an investigator must ensure the validity of any comparisons between their current work and historical data. Rodent strains should always be selected on the basis of having suitable physical, physiological and behavioural (i.e. temperament) characteristics.

For pharmacological investigations in particular, all possible measures should be taken to minimize variability between individuals. Commercial breeders are usually able to guarantee comparable age, weight and health parameters and will provide certification of the health status and weight of a group of animals at the time of dispatch. Note, however, that it is essential to communicate requirements to breeders well before projects begin. It takes about 12 weeks to produce an 8-week-old mouse, yet UK breeders are generally given just 1–2 weeks notice by establishments (LASA 1999). This demand for 'off the shelf' animals leads to wastage and the death of those who are surplus to requirements, which is ethically unacceptable.

On arrival from the breeder, animals should be transferred to a suitably sized holding cage with appropriate environmental enrichment (see Table 2 and associated references). Pairing or group-housing the animals with cage-mates from the same batch should encourage socialization. Thereafter, a settling-in period of around one week should be allowed before individuals are subjected to any experimental or surgical procedures. This is a useful quarantine period that allows for necessary clinical

Table 2 Basic requirements of laboratory rats and mice

Housing in stable, compatible groups
Enough space for exercise, normal social behaviour and the provision of enrichment
Sufficient height to permit rearing (at least 30 cm for an adult rat)
Solid floors
Adequate depth of appropriate substrate
Something to gnaw
Shelter
Appropriate lighting levels
A varied diet and the ability to forage

This table is based on Jennings *et al.* (1998), Lawlor (2002) and Sherwin *et al.* (2002)

assessments, and also allows recovery from transport stress and orientation to new housing and social groups. It is also important for acclimatization to environmental changes, such as diet and nesting materials, the change in caretakers, and to previously unfamiliar sensory stimuli that may be present in the new environment. Where possible, the transition should be eased by liaising with the breeder to ensure that conditions are as consistent as possible between the breeder and user establishments; if there are differences, the aim should be to 'level up' and implement the better husbandry protocols.

During the immediate post-operative period it may be necessary to isolate rodents from their cage-mate(s). This causes distress, and so frequent human contact (where appropriate) and environmental enrichment are essential while animals are singly-housed. Once full recovery has been confirmed the animals should, where possible, be rehoused with one or more familiar cage-mate(s), using the 'buddy' system or devices that can be switched on *in situ* as appropriate.

Recommendations:

- **Ensure that variability between small animals is kept to a minimum.**
- **Allow sufficient time to recover from transport stress and acclimatize before implanting rodents.**
- **Closely monitor health status, particularly body mass, during the acclimatization period.**
- **Communicate effectively with breeders to avoid overbreeding and wastage.**
- **Aim to standardize housing and care protocols between breeders and user establishments, 'levelling up' where they differ.**
- **Avoid individual housing wherever possible.**

4.2 Dogs

New dogs arriving from external sources should be housed in compatible groups and allowed a period of at least 2 weeks for socialization and acclimatization before telemetry studies begin. A good quality and quantity of space is essential for dogs (Table 3; see also Hubrecht 2002 and Prescott *et al.* submitted) for refinement of their husbandry and care, and this must take into account considerations of long-term use.

Individual housing is highly undesirable for dogs and should be avoided at all costs. Dogs who cannot adjust to individual housing in their own holding pen should not undergo implantation surgery if they are to be individually-housed during procedures (see below). Note that animals who appear confident when pair-housed may not be able to tolerate individual housing. Where a jacket is to be worn, trials must be carried out to ensure that dogs tolerate these prior to surgery (e.g. for a one-month habituation period), possibly introducing dummy devices (see Part A, Section 7.4.2). It is useful to construct a checklist of events and criteria when selecting dogs, to record results of screening and ease of habituation and to review selection protocols.

If surgical implantation is required, dogs should initially be selected on the basis of sound physical conformation and clinical examination. In particular, care must be taken to exclude animals with signs of skin disease or fight wounds that could provide an entry for infection, as a distant focus of infection represents a potential source for a surgical wound or implant infection.

Table 3 Basic requirements of laboratory dogs

Housing in stable, compatible groups (pairs at least)
Enough space for exercise, a range of normal behaviours, suitable enrichment and to allow retreat to the back of the pen if anxious
Daily access to indoor or (preferably) outdoor runs
Solid floors
A warm, dry, draught-free resting area, at the least[a]
Variation in the standard diet different odours, flavours, tastes, textures
A platform for visibility and additional space
Toys and chews suspended from the ceiling by sprung chains if possible
Protection from excessive noise levels
Appropriate staffing levels for adequate socialization, habituation and training

This table is based on Hubrecht (2002) and Prescott *et al.* (in preparation)
[a]Beds with bedding material should be considered and are essential for old, young, sick or post-operative dogs and periparturient bitches

However, animals should not be rejected for superficial wounds or lesions, as overly stringent demands for 'perfect' animals can lead to unjustifiable wastage. Blood and urine samples should be taken for routine haematology and biochemistry. Haematology is an additional aid in the detection of possible subclinical infections. Inherent cardiac arrythmias occur in some beagles, and in 1% of dogs this is sufficient to render them unsuitable for studies. A manual ECG screen should always be carried out prior to surgery to check for this.

Only animals of sound, placid (not excitable) temperament should be selected, and the ability to remain quiet for a period of time in a Pavlov sling or similar restraint is desirable. A group of dogs can and should be pre-trained and formed into a stable group for easier reintroduction when the group is returned to group housing. It is very important to select animals who satisfy this requirement. Final selection and decision to proceed to surgery should be made by observing each dog's ease of acclimatization within the laboratory or procedure rooms where they will be used in procedures. Animals who do not adjust to these surroundings should not undergo surgery.

If individual dogs are found to have temperaments that make them unsuitable for implantation—for example, they may be unable to habituate to protocols or they may be too excitable—something will have to be done with them and decisions will have to be made about this. Options are training, rehoming, return to the breeder, use in other projects, or euthanasia for tissues. The relevant committee at each establishment should set out a clear decision-making process that can be immediately implemented should a dog prove to be unsuitable for surgery. Whatever the outcome in each case, it is essential to maintain good communication with the breeder, providing them with feedback about the problems that have been encountered and working with them to minimize the risk of inappropriate temperaments or behaviour in the future (see Prescott *et al*. submitted).

It is possible to train dogs to recognize when they are going to be used in procedures and have to be still and quiet, and when they have free periods for socialization and play (see Hubrecht 2002, Prescott *et al*. submitted). This is important for animal welfare and scientific reasons and should always be attempted.

Recommendations:

- **Examine dogs very carefully for skin diseases or wounds before selecting for surgery but *do not* reject individuals unless lesions are likely to cause problems following surgery.**
- **Ensure that dogs are temperamentally sound, appropriately screened for arrhythmias and able to acclimatize to procedure rooms and equipment before any surgery takes place.**
- **Make sure that a decision-making process has been set up to decide the future of individuals who are unsuitable for surgery.**
- **Monitor and record the screening process, regularly updating protocols as appropriate.**
- **Always house dogs in pairs or groups wherever possible.**
- **Regularly review new methods for training dogs to cooperate with procedures and set up a stable routine.**

4.3 Non-human primates

Primates intended for telemetry studies should always be housed at least in pairs and allowed sufficient time for socialization and acclimatization before screening for suitability, e.g. one month. Pairs should normally be formed in the housing where procedures will be conducted at least 4 weeks before surgery so that compatibility can be assessed. There will always be a dominant individual, which is acceptable provided that the subordinate is not excessively dominated and overwhelmed. Primate pairs must be housed in accommodation of sufficient height and with enrichment including perches and shelves so that animals can select their preferred level, which reduces stress and permits more natural behaviour and more effective observation (see Table 4, IPS 1993, National Research Council 1998,

Table 4 Basic requirements of laboratory primates

Housing in stable, compatible groups (pairs at least)
Enough space for exercise, a range of normal behaviours and suitable enrichment
Solid floors with substrate
Sufficient enclosure height to allow vertical flight if alarmed; no double tiers
Climbing structures to increase usable space perches, platforms, swings, ropes, ladders sufficient for all to occupy simultaneously
A varied diet appropriate for the species
The ability to forage, including appropriate artificial feeding devices and scatter feeding
Adequate light levels
Access to outdoors wherever possible
Nest boxes for species that use them, e.g. marmosets
Wood for gnawing and scent marking for species that use it, e.g. marmosets
Visual barriers for control over social interactions
Toys, chews, tactile materials, destructible materials, e.g. boxes
Novelty minor changes in furniture, feeding practices, toys
Adequate socialization, habituation to humans and training where appropriate

This table is based on IPS (1993), National Research Council (1998), Reinhardt (2002) and SCAHAW (2002)

Reinhardt 2002, SCAHAW 2002). If cages are used, it is good practice to interconnect top and bottom caging; then pairing should be reassessed if the subordinate is constantly restricted to the lower cage.

Health checks and evaluation for physiological suitability are essential (e.g. manual checking for arrhythmias in animals destined for cardiovascular monitoring), but are not sufficient to ensure that animals are suitable and welfare problems are minimized. Behavioural screening is also vital to ensure that primates are not used unless they are well balanced, calm and self-confident, with no apparent behavioural problems and little or no anxiety when separated from their cage-mate(s) if this cannot be avoided. Remote monitoring using video or viewing panels is advisable to detect behavioural abnormalities.

Stable pair bonds can be maintained and separation stress reduced by conducting implantation procedures on both monkeys on the same day and re-pairing them after surgery, having taken great care to ensure that stitches are well hidden and analgesia has been effectively administered (see below and Part A, Section 8). If periods of individual housing during subsequent procedures cannot be avoided, animals should be conditioned to separation (e.g. twice a week) and their activity and behaviour patterns observed. Individually-housed animals should be housed opposite one another to allow visual contact. If this is impractical, visual contact should be maintained using mirrors to enable them to see conspecifics. All primates should also have access to environmental stimulation devices at all times; and this is especially important during periods of separation.

Where projects require primates to perform cognitive tasks such as solving puzzles on video screens, the ability of each animal to learn and execute the desired task will be a major factor in deciding which animals should be selected for implantation. Trials with the experimental task should always be undertaken before any animals are implanted, to prevent animals undergoing surgical procedures unnecessarily. It is important to ensure that anaesthesia and surgery have not affected performance, so any tasks should be repeated post-surgery and before any other intervention.

Recommendations:

- **Always house primates at least in pairs, with a good quality and quantity of space including adequate pen or cage height.**
- **Screen animals carefully for health, physiological suitability *and behavioural suitability* before surgery.**
- **If animals are to perform cognitive tasks, ensure that they are capable of doing them and do not implant devices if they are not.**
- **Minimize separation periods and maintain direct or indirect visual contact between pairs or groups.**

5 Regrouping animals following surgery

Groups of social animals should be re-established as soon as possible following surgery, provided that animals are fully able

to interact with conspecifics appropriately. For example, some centrally active analgesics such as some opioids have central nervous system depressant actions that could leave animals vulnerable to bullying. Judgements on reintroduction times should be made on a case-by-case basis, in consultation with the attending veterinarian and animal technician; in general, animals should not be group-housed during the first 24 h following surgery, to avoid harmful interference from others.

Subcutaneous suturing of wounds means that animals can be returned to the group or partner as soon as possible. In the Working Group's experience, marmosets can be kept as mixed sex pairs (with vasectomized males), so that once recovery has taken place familiar conspecifics can be placed in an adjacent cage to permit visual and vocal communication. They can then be returned to the holding room the following day and allowed to mix under supervision. Where animals are group-housed, reintroduction needs to wait until full recovery has taken place.

Each study plan should take account of the facts that it may take time for groups to re-establish, and that extra environmental stimulation should be supplied to encourage appropriate behaviour, reduce potential aggression and distract animals from any discomfort or pain that they may be experiencing. Adequate supervision is essential when groups are re-formed. There may be a greater risk of infection in group-housed animals, but this is not a reason to deny animals the company of their own kind. This potential harm should be weighed against the considerable benefits that accrue from housing social animals in groups.

Recommendations:

- **Regroup animals following surgery as soon as possible.**
- **Ensure that animals have fully recovered from any effects of surgery, anaesthesia or analgesia that could disadvantage them before regrouping.**
- **Investigate refinements in wound closure so that animals can be regrouped quickly.**
- **Consider any increased risk of infection in context with the welfare benefits of group housing.**

6 Long-term housing

Dogs and primates implanted with telemetry devices are frequently kept for comparatively long periods, especially in pharmaceutical and contract research establishments. Animals held for long periods will ultimately have to be rehomed or killed for scientific, technical, or welfare reasons. Technical reasons relate largely to the life of the batteries or the device, but this may not be the limiting factor, in which case decisions will have to be made regarding the upper limit at which it is deemed acceptable to maintain animals.

Indicators of poor health or changes from normality for that animal, such as weight loss, activity reduction or body temperature change, all necessitate immediate veterinary intervention, but the criteria for rehoming or euthanasia on welfare grounds are less easy to define because they cannot always be measured objectively. The Working Group believes that limits must be set on the length of time that individual animals live in the laboratory because this environment represents a conflict between animal and human needs. In particular, standard laboratory housing limits the expression of a range of normal (or desirable) behaviours, even when environmental stimulation is provided. However, the harms associated with housing an animal in the long term in the laboratory and reusing her or him in procedures (see Part A, Section 9) needs to be considered against the harms caused by obtaining a succession of naïve animals. All establishments should carefully consider and set out criteria for making decisions on rehoming and euthanasia, taking all of the above issues into account. For more on rehoming, see Part A, Section 10.

Recommendations:

- **Consider the impact that long-term housing in the laboratory will have on each animal from her/his point of view—consider whether animals risk becoming institutionalized and having an unacceptably poor quality of life.**
- **Think carefully about the criteria that would be considered as grounds for**

euthanasia, discuss these with the attending veterinarian, scientists and technicians concerned, and make sure that everyone responsible for monitoring animals is familiar with them.

- **Never reduce the number of animals used by holding individuals for prolonged periods if this will cause suffering such as behavioural problems.**

7 Conclusion

This report is intended to complement the existing literature on husbandry refinements for rats, mice, dogs and non-human primates by helping to minimize any potential conflicts between the use of telemetry and good practice in animal husbandry and care. The Working Group strongly recommends that it is used not only in conjunction with Part A, but also with the growing body of knowledge on animal behaviour and welfare, using the Appendix as a starting point.

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Appendix Husbandry refinements for laboratory rodents, dogs and primates

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