

Facts and demonstrations: Exploring the effects of enrichment on data quality

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There is widespread support for the concept that 'better welfare means better science', and good acceptance that environmental enrichment can improve welfare. However, many publications in the literature describe animals housed in 'standard' conditions without enrichment, and enrichment is still sometimes not provided for fear that this will have an adverse effect on data quality.

These concerns tend to relate to:

- the potential for the addition of another variable (i.e. enrichment) to affect the validity of the science within the project;
- the risk that data obtained from animals provided with enrichment will not be comparable with data obtained from animals in 'standard' conditions;
- increased variability could create a requirement for increases in animal numbers, which is the opposite of reduction.

It is essential to evaluate each of these concerns critically and objectively – hence the title of this webinar, which is taken from the quote by John Ruskin: '*the work of science is to substitute facts for appearances, and demonstrations for impressions*'.

A growing number of published studies have evaluated the effects of refinements, such as environmental enrichment, on animal physiology and experimental design. Some have reported significant effects, whereas others have not, but this presentation will argue that the interpretation of these results is not always straightforward, yet is crucially important for both animal welfare and scientific quality. The latter is of particular relevance given the current climate of reflection within the scientific community with respect to the translatability and validity of animal experiments.

If there are implications for data and/or animal numbers, a constructive approach is to try to accommodate these, for example by altering experimental design or statistical analysis, as opposed to simply not providing refinement. Good communication about practical refinement is also vital, not only for better science and welfare, but also due to increasing requirements for openness and accountability with respect to animal research and testing.

1. Studies and reviews looking at effects of refinement, including enrichment, on variability/standardisation

These are just a few examples, both 'classic' and recent; an online search using keywords such as 'environmental enrichment' + 'animal' + 'variability' will yield many more ...

- Baldwin AL (2012) Does lack of enrichment invalidate scientific data obtained from rodents by compromising their welfare? *Between the Species* 15: 2-23
- Baumans V et al. (2003) Environmental enrichment does not affect the variability of animal experimentation data in the Light/Dark test. *3R-Info-Bulletin* 22, download from http://www.forschung3r.ch/en/publications/bu22_print.html
- Bayne K (2005) Potential for unintended consequences of environmental enrichment for laboratory animals and research results. *ILAR Journal* 46: 129-139
- Castelhana-Carlos MJ & Baumans V (2009) The impact of light, noise, cage-cleaning and in-house transport on welfare and stress of laboratory rats. *Laboratory Animals* 43: 311-327
- Eskola S et al. (1999) Environmental enrichment may alter the number of rats needed to achieve statistical significance. *Scand J Anim Sci* 26: 134-144
- Hurst JL & West RS (2010) Taming anxiety in laboratory mice. *Nature Methods* 7: 825-826
- Hutchinson EK et al. (2012) Environmental enrichment during rearing alters corticosterone levels, thymocyte numbers, and aggression in female BALB/c mice. *JAALAS* 51: 18-24
- Mikkelsen LF et al. (2010) Clinical pathology and cardiovascular parameters are not influenced by housing rats under increased environmental complexity. *Animal Welfare* 19: 449-460
- Stam NC et al. (2008) Sex-specific behavioural effects of environmental enrichment in a transgenic mouse model of amyotrophic lateral sclerosis. *Eur J Neurosci* 28: 717-723
- Toth LA et al. (2011) Environmental enrichment of laboratory rodents: the answer depends on the question. *Comparative Medicine* 61: 314-321 (see also <http://enrichmentrecord.com/2012/01/22/viewpoints/>)
- Van de Weerd et al. (2002) Effects of environmental enrichment for mice: variation in experimental results. *JAAWS* 5: 87-109
- Wolfer et al. (2004) Cage enrichment and mouse behaviour: test responses by laboratory mice are unperturbed by more entertaining housing. *Nature* 432: 821-822
- Würbel H (2001) Ideal homes? Housing effects on rodent brain and behaviour. *TINS* 24: 207-211
- Würbel H (2005) Environmental enrichment does not disrupt standardization. *3R-Info-Bulletin* 30, ISSN 1421-6590
- Würbel H & Garner J (2007) Refinement of rodent research through environmental enrichment and systematic randomisation. Download from <http://www.nc3rs.org.uk/news.asp?id=395>

2. Useful enrichment-related books and online resources

The Enrichment Record is a free, quarterly online magazine that discusses and promotes enrichment for laboratory animals: <http://enrichmentrecord.com/>

The Animal Welfare Institute's Laboratory Animal Refinement & Enrichment Forum (LAREF) is a very useful and active online discussion forum which is open to animal technologists and care staff, students, veterinarians and researchers. There is also an occasional series of publications that reproduce some of the discussions; see <http://www.awionline.org/ht/d/sp/i/11589/pid/11589>

Young RJ (2003) *Environmental Enrichment for Captive Animals*. Blackwell Science: Oxford. ISBN 0-632-06407-2 One of a series of books produced by the UK Universities Federation for Animal Welfare (UFAW). It covers the reasons for enrichment and principles behind designing and evaluating it very well, including a chapter on designing and analysing enrichment studies.

Mellor DJ, Patterson-Kane E & Stafford KJ (2009) *The Sciences of Animal Welfare*. Wiley-Blackwell, Oxford. ISBN 978-1-4051-3495-8 Also in the UFAW series; an excellent and accessible background to animal welfare science with a chapter on enrichment.

3. Journals that publish papers on laboratory animal science and welfare

- *Animal Technology and Welfare* - the journal of the UK Institute for Animal Technology (<http://www.iat.org.uk/journal.htm>)
- *Animal Welfare* - the journal of the Universities Federation for Animal Welfare, this covers all areas of human-animal interaction including laboratory animals (<http://www.ufaw.org.uk/journal/Animal%20welfare.htm>)
- *Applied Animal Behaviour Science* - the official journal of the International Society for Applied Ethology (ISAE). This reports mainly on farmed animal behaviour, but includes some papers on animals used in the laboratory or their wild equivalents (<http://www.applied-ethology.org/thejournalaabs.htm>)
- *Journal of Applied Animal Welfare Science (JAAWS)* - covers companion, farm, wild and laboratory animals (<http://www.psyeta.org/jaaws/>)
- *Lab Animal* - both the USA and European versions (<http://www.labanimal.com/>)
- *Laboratory Animals* - not to be confused with the journals above; this is the official journal of a number of bodies including the Federation of European Laboratory Animal Science Associations (<http://www.lal.org.uk/>)
- *Contemporary Topics in Laboratory Animal Science* - the journal of the American Association for Laboratory Animal Science (AALAS) (details in <http://www.aalas.org/>)

4. Relevant organisations

- The Animal Welfare Institute (AWI) searchable database on enrichment with summaries of many of the papers (http://www.awionline.org/lab_animals/index.htm)
- The Johns Hopkins Center for Alternatives to Animal Testing (CAAT) website includes details of news and events relating to refinement, as well as hosting Altweb, a Three Rs database (<http://caat.jhsph.edu/>)
- The RSPCA Research Animals Department series of sheets setting out good practice for the housing and care of commonly used species (<http://www.rspca.org.uk/sciencegroup/researchanimals/ethicalreview/housingandcare>)

- The UK National Centre for the Three Rs (NC3Rs) website includes an information portal that can be used to search for husbandry refinements and information on how to obtain NC3Rs funding for Three Rs studies such as enrichment evaluation (<http://www.nc3rs.org.uk/>)
- The *Shape of Enrichment* is mainly zoo animal oriented but its journal of the same name includes many interesting ideas and is cheap to subscribe to. It also organises an annual international conference on enrichment (<http://www.enrichment.org/>)

5. Articles cited in the presentation (in order of appearance)

- 1 Cudilo E, Al Naemi H, Marmorstein L, Baldwin AL (2007) Knockout Mice: Is It Just Genetics? Effect of Enriched Housing on Fibulin-4^{+/-} Mice. PLoS ONE 2(2):e229. doi:10.1371/journal.pone.0000229
- 2 Nachat-Kappes R, Pinel A, Combe K, Lamas B, Farges M-C, et al. (2012) Effects of Enriched Environment on COX-2, Leptin and Eicosanoids in a Mouse Model of Breast Cancer. PLoS ONE 7(12): e51525. doi:10.1371/journal.pone.0051525
- 3 Martin B et al. (2010) "Control" laboratory rodents are metabolically morbid: Why it matters. PNAS 107: 6127-6133
- 4 Montarolo F, Parolisi R, Hoxha E, Boda E, Tempia F (2013) Early Enriched Environment Exposure Protects Spatial Memory and Accelerates Amyloid Plaque Formation in APP^{Swe}/PS1^{L166P} Mice. PLoS ONE 8(7): e69381. doi:10.1371/journal.pone.0069381
- 5 Burrows EL & Hannan AJ (2013) Towards environmental construct validity in animal models of CNS disorders: optimizing translation of preclinical studies. CNS Neurol Disord Drug Targets 12: 587-592
- 6 Latham N & Mason G (2004) From mouse house to house mouse: the behavioural biology of free-living *Mus musculus* and its implications in the laboratory. Appl. Anim. Behav. Sci. 86: 261-289 (see also: Burn CC (2008) What is it like to be a rat? Rat sensory perception and its implications for experimental design and rat welfare. Appl. Anim. Behav. Sci. 112: 1-32)
- 7 Castelhana-Carlos MJ & Baumans V (2009) The impact of light, noise, cage-cleaning and in-house transport on welfare and stress of laboratory rats. Laboratory Animals 43: 311-327
- 8 Ratlife DVD: www.ratlife.org
- 9 Roedel A et al. (2005) Effects of light or dark phase testing on behavioural and cognitive performance in DBA mice. Laboratory Animals 40: 371-381
- 10 Maconochie M, Cadot S & Frenz D (2012) A novel method for retinoic acid administration reveals differential and dose-dependent downregulation of Fgf3 in the developing inner ear and anterior CNS. Developmental Dynamics 241: 741-758
- 11 Stereotypic Animal Behaviour website: <http://www.aps.uoguelph.ca/~gmason/StereotypicAnimalBehaviour/library.shtml>
- 12 Arras M et al. (2007) Assessment of post-laparotomy pain in laboratory mice by telemetric recording of heart rate and heart rate variability BMC Veterinary Research 2007, 3:16 doi:10.1186/1746-6148-3-16, open access at: <http://www.biomedcentral.com/1746-6148/3/16>
- 13 Deacon R (2012) Assessing burrowing, nest construction, and hoarding in mice. J. Vis. Exp. (JOVE) 59: e2607, doi:10.3791/2607, open access with video clips at: <http://www.jove.com/video/2607/assessing-burrowing-nest-construction-and-hoarding-in-mice>
- 14 Jirkof P et al. (2010) Burrowing Behavior as an Indicator of Post-Laparotomy Pain in Mice Front. Behav. Neurosci. 4:165. doi: 10.3389/fnbeh.2010.00165, open access at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2965018/>
- 15 www.NC3Rs/ARRIVE/

All URLs last viewed 4 September 2013.