OPINION

Refinement: Lessons from the 2012 Olympics

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Until the day comes when animals are no longer needed for research, refinement *needs to be a priority for the scientific community*

British road and track cycling has gone though a major renaissance recently, with enormous success at the London Olympics and with Sir Bradley Wiggins winning the Tour de France. One of the reasons that British cycling is leading the world at the moment is the leadership of the head of UK cycling, Dave Brailsford, and in particular, his approach of 'aggregation of marginal gains'.

What does 'aggregation of marginal gains' mean in relation to professional cycle racing? If you wanted to surpass your opponents in terms of team performance, then you could invest your time in looking for the next big paradigm shift in technology (e.g. the Boardman bike), in order to overtake the rest of the field in a single step. Alternatively, you could break down all of the component parts that contribute to a successful cycling performance, and make every single one just a little bit better in a systematic, iterative way; e.g. slight changes to front fork, helmet, and suit design, and improvements to dietary, physiotherapy and psychological support to riders. The combination of a number of small improvements like these can lead to a significant improvement in performance for the elite, with the added benefit of raised standards for all of the team.

But what has this to do with *refinement* in relation to animal experimentation? In our view, 'aggregation of marginal gains' is a great principle that can also be applied to *refinement*.

The effective implementation of *refinement* requires the systematic breakdown of the lifetime experience of the animals involved into its component steps, in order to identify the potential for physical and psychological suffering and to put in place measures to eliminate or ameliorate this suffering. This process should begin during the planning stage of the experiment, and should then evolve as the project unfolds. *Refinement* has been represented as a 'loop',[1] and this is a good way to think about it. There should be an ongoing process of assessment of suffering, identification of *refinement* opportunities, implementation of *refinement*, then back to assessment of suffering and so on. Welfare science is a continually developing field, and thus a regular appraisal of the literature is essential to stay abreast of the current state of play with regard to optimising laboratory animal welfare.

Refinement practices, whilst apparently widespread (based on our interactions with the scientific community), are largely absent from the methodological sections of scientific research publications. One reason for this is that individual refinements are often small iterative changes that alone do not appear to be overly significant. However, refinements are not generally implemented in isolation, and the aggregated benefit of several small refinements can have a significant impact on the reduction of suffering and improvement of the welfare of animals used in research.

Efforts to reduce suffering are not simply a moral obligation or an exercise in sympathetic anthropomorphism. *Refinement* and improved welfare standards are broadly acknowledged to be essential for good quality science. This was well-articulated by Russell and Burch over 50 years ago: "It is widely recognised that the humanest possible treatment of experimental animals, far from being an obstacle, is actually a prerequisite for successful animal experiments",[2] and it has been repeated by many others since then.[1,3] Poor animal welfare can often be a confounding factor in an experiment, and will therefore increase variability and error,[4] yet some people still fail to understand this principle and fail to acknowledge the many factors that can affect welfare. Therefore, it is critical that all the sources of suffering that can occur in an experiment are identified and their impact is minimised.

Under the current UK legislation (the *Animals [Scientific Procedures] Act 1986*, as amended in December 2012 in compliance with EU *Directive 2010/63/EU*[5]), there are three categories of suffering that animals can experience, namely, Mild, Moderate and Severe. To date, there are no clear data on the proportion of the 3.7 million animals

used last year (or indeed any year before that) that underwent procedures that caused severe suffering. Thankfully, this is going to change, as, from January of this year, establishments are required to assess the actual level of suffering experienced by animals undergoing regulated procedures. This is good news, for three reasons. Firstly, it will give the general public a clear indication of the levels of suffering experienced by laboratory animals. Secondly, it will give establishments an opportunity to evaluate how successful their *refinement* programmes are in reducing suffering and to highlight areas where more work is needed. Finally, this new information will allow welfare organisations to focus their resources on areas of research where suffering is high and *refinement* is lacking, and to track the progress of Three Rs-related programmes targeted at ending this suffering.

All suffering is of concern, but procedures and models that have the potential to cause severe suffering are of particular concern to animal welfare organisations and to the general public. Annual opinion polls (conducted by Ipsos MORI) report that about 85% of the public are 'conditional acceptors' of animal research, i.e. that they are willing to accept animal research, as long as there is a clear medical benefit and as long as suffering is minimised, thus indicating that suffering is an important issue.

The RSPCA is committed to ending severe suffering in scientific research that uses animals, and has initiated a project comprising three parallel strands, in order to achieve that goal. The first of these is to identify refinements that have already been implemented to reduce suffering in severe models, and to encourage researchers and animal-care staff to promote their *refinement* approaches to the wider scientific community, in order to benefit as many animals as possible. The second strand is the establishment of working groups made up of researchers, animal-care staff, and veterinarians, who have expert knowledge of specific models and procedures that have the potential to cause severe suffering. These working groups will be tasked with establishing 'state-of-the-art' *refinement* principles for specific models or research areas, and with drawing up a set of recommendations for publication. We have already established two such groups, focusing on: a) procedures and models that involve seizures;[6] and b) experimental autoimmune encephalomyelitis (EAE).[7] Two further groups will be initiated in 2013, to look into refinements for models of rheumatoid arthritis and of sepsis. The third strand of our approach is called the 'stretch objective' — this is human resources jargon for a programme of work which, despite being challenging, is both achievable and worthwhile to strive for. The idea is to get establishments to think critically about their research programmes and to challenge the necessity and justification for severe procedures. We strongly believe that ending severe suffering is a desirable and achievable goal, and that *refinement* must play a key part in delivering it.

This brings us back to the 'aggregation of marginal gains'. An end to severe suffering could be achieved through a single large paradigm shift, i.e. by implementing an immediate UK ban on all severe procedures. This is unlikely to be achieved in the current scientific and political climate, and could result in under-reporting of actual severity and/or higher numbers of severe procedures being performed overseas. Alternatively, the many factors related to suffering could be systematically identified and addressed. This could take the form of pushes to achieve better welfare assessment, better housing and care, the implementation of humane endpoints, rigorous ethical review, better experimental design, greater sharing of *refinement* information, and a greater proportion of life science research funding going to research into alternatives. This could not only result in ending severe suffering, but it would also have the added effect of reducing the suffering of *all* animals used in research. This is because *refinement* principles can be applied to reduce the suffering of all animals used in research, and not only those who suffer most.

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