

Review of APC report on the Assessment of Cumulative Severity and Lifetime Experience in Non Human Primates used in Neuroscience Research

Introduction

This document is submitted by Animal Aid, People for the Ethical Treatment of Animals Foundation (PETA) and the National Anti-Vivisection Society (NAVS) (hereafter the animal protection groups [APGs]) to the Animals in Science Committee (ASC) following a review of the report on 'The Assessment of Cumulative Severity and Lifetime Experience in Non-Human Primates used in Neuroscience Research', published by the Animal Procedures Committee (APC) in November 2013.

Summary of findings and recommendations

The APGs are extremely concerned by the APC review, as it provides some very disturbing insights, both into the suffering of non-human primates (NHPs) used in neuroscience experiments and into the attitudes of researchers, which seem to show a high level of desensitisation to animal suffering, coupled with a somewhat entrenched view of their research. The review draws conclusions that have very serious implications for the severity classification of experiments on NHPs, yet its methodology appears to be highly questionable and based largely on the subjective opinions of those involved directly in experiments involving NHPs. Our findings are too many to include in this submission as a summary, however, our primary concerns relate to i) how the review was researched and ii) the disturbing insights into the suffering of NHPs used in neuroscience research. We, therefore, strongly recommend that the ASC undertakes a comprehensive review of cumulative severity assessment and investigates the wider issues surrounding the use of NHPs in neuroscience research.

Review

Firstly, the credibility of the review is seriously undermined by its apparent preoccupation with how any findings might upset the current administrative system for severity classification and appears to be an attempt to 'cap' levels of severity categories. It states:

'It cannot be assumed that all procedures or events that cause a degree of suffering simply 'stack up' for evermore, with the result that severity would continually increase within a procedure. This would inflate the numbers of actual severity assessments deemed to be 'severe' or even 'above severe and requiring an application to invoke the safeguard clause'. Such an approach would obviously undermine the whole system of severity classification...' (P29, emphasis added). Also, with reference to *'it cannot be assumed that...procedures 'stack up''* it must also therefore be fair to say that it cannot be assumed that the effects of procedures **do not** stack up.

As one of its overall findings *'the Review found little evidence for additive effects between procedures, whether through incomplete recovery between events (additive stacking up) or potentiation of adverse effects and suffering by earlier procedures'* (P8). This leads to the general assertion that the overall severity assessment of an experiment involving multiple, repeated procedures should not normally be higher than that of the individual procedures.

This assumption is based on a highly subjective section of the questionnaire (P97), where respondents were asked if the welfare impact of certain procedures on individual NHPs increased, decreased or remained unchanged when performed repeatedly over a lengthy period of time, and to assess how procedures interacted with one another. Although the second part of the question required a written answer, the first appeared to be based primarily on a tick-box system (questionnaire P8), even if supporting data was welcomed.

As well as being extremely subjective, the data for the review was collected from individuals involved with NHP experiments on a daily basis, who are likely to experience a high degree of desensitisation, reducing their ability to perceive suffering. This was clearly evident in *'some cases where there had been an underestimation of severity by a minority of users,'* (P96), most notably when a *'non-human primate [who had undergone procedures] described as "Mild to Moderate" had experienced one major surgery for a chamber implant and ten further craniotomies requiring anaesthesia'* (P94). Describing such suffering as anything other than severe indicates a disturbingly high level of desensitisation. However, the researchers' overwhelming emphasis on the physical health of the NHPs and apparent disregard for cumulative psychological suffering suggests that this desensitisation goes far beyond the 'minority of users'. This attitude is further evidenced by the words of an 'experienced primatologist' and 'laboratory animal scientist' appointed to assess cumulative suffering in an EU establishment: *'the sum of the different procedures, their combination and their duration over many years do not result in additive effects with respect to pain, suffering or damage, because even after years of participation in the experiment, the animals show a very good health state with good general condition'* (P93). However, this claim is not consistent with numerous studies that have documented that the cumulative effect of repeated procedures—even seemingly innocuous procedures such as blood draws—have a profound effect on the psychological suffering of NHPs (Becker et al., 2008; Dettling, Feldon, & Pryce, 2002; Lutz, Chase, & Novak, 2000; Suomi, Harlow, & Domek, 1970).

Throughout the review, there are also attempts to suggest a positive aspect to the use of NHPs in research, for example by use of the term cumulative 'experience' instead of 'severity' and suggestions that the lives of NHPs are somehow improved by their use in research, e.g. *'Many reports made the point that the trained task can be an enriching experience for the monkey'* (P86). The message of this report simply cannot be that NHPs are somehow 'better off' for being used in research and this conflicts entirely with the objective of the review. This is especially concerning given that the review also confirms that researchers find suffering difficult to assess; *'there is currently a poor understanding of the nature of suffering in any animal species'* (P41). If this is the case, how can the harm-benefit test be performed correctly? This is confirmed further by *'the concept and practical implementation of the harm-benefit analysis is still perceived to be rather nebulous'* (P19) and the alarming lack of clear medical benefit which is considered to have come from years of NHP research; *'In most cases however, little direct evidence was available of actual medical benefit in the form of changes in clinical practice or new treatments'* (P17).

Indeed, the review as a whole appears to rely heavily on physical health as evidence for an absence of cumulative suffering. For example, it is stated that fluid control was *'reported to be without clinical signs of adverse effects'* (P8), but this does not mean that

it was without psychological effects. Indeed, the review itself acknowledges: *'The psychological effects of fluid control regimes in nonhuman primates also merit further study'* (P85).

Further evidence of the heavy focus on the more obvious, physical signs of cumulative suffering is the awarding of NC3Rs funding for recognising facial expression of pain in macaques (P37). This is also a clear indicator of how any use of the 3Rs in NHP research appears to be restricted to refinement at best. (This is assuming that as stated, the facial pain scale would result in analgesia or anaesthesia being given, rather than incorporating pain recognition as a procedural objective.)

Another factor used as evidence of good welfare – and absence of cumulative suffering – is the NHPs' continued performance of the required tasks. However, the value of this particular indicator is severely undermined by the food and fluid 'control' protocols, which ensure, as stated in the review, that *'hunger or thirst becomes a key motivator for reliable performance'* (P79). Indeed, the study included at the end of the review (P126) indicates that a certain level of fluid restriction is needed before macaques will reliably perform the required tasks; they have to be sufficiently thirsty before they will do so.

The review strongly refutes the idea that compliant NHPs have entered a state of learned helplessness in which they have realised that their actions are without consequence. Whilst the NHPs' situations are not the same as those of rats subjected to inescapable electric shocks (and therefore do not fit the review's narrow definition of learned helplessness), this does not mean that they are not suffering as a result of the training and that the adverse effects of this are not cumulative. As discussed, it is clear that the NHPs are kept hungry or thirsty in order to motivate them to perform the tasks, and the use of force in training is still clearly in evidence, with over half the establishments still using the collar and pole (P86). Repeated subjection to stimuli such as hunger, thirst and force-based restraint can hardly have anything other than a negative psychological impact on the NHP. Indeed, the review acknowledges: *'Some chimpanzees have been shown to develop mental health problems after many years in the laboratory setting'* (P29). There is extensive evidence available to show that this applies to other species of NHP as well. For example, long-term effects of early-life stresses, such as social isolation, maternal deprivation, and fear-potentiated startle reflex in macaques and squirrel monkeys, are well documented (Levine & Mody, 2003; Lewis et al, 1990; Maestriperieri et al, 2006; Parr, Winslow & Davis, 2002).

Whilst the review argues against the existence of cumulative suffering in the majority of cases, it concedes that *'there were some nonhuman primates that could not cope and were removed from study'* (P8). This acknowledges that the repetition of procedures can have a negative impact on welfare, and some of the examples provided underline precisely how negative this impact was. One NHP had persistently self-mutilated for three years, one had *'severe behavioural pathology'* (P57) and one had *'persistent (whole of time on study) diarrhoea deemed to be a stress-related effect'* (P58).

In fact, the review contains many more disturbing examples of the suffering endured by NHPs used in neuroscience research. When macaques have been given brain lesions, they *'need support to maintain a sitting position, being fed by hand and receive intravenous fluid'* (P67), and epileptic seizures were reportedly seen in a number of

cases amongst brain-damaged animals (P71). One establishment admitted that a monkey '*might have got close to its physiological minimum*' (P80) during the initial period of a fluid control regime (appearing to indicate that the animal's health was put at serious risk).

The suffering is clearly not restricted to the procedures themselves. Despite the review stating that there 'were no major issues' with the conditions of NHPs arriving at establishments (P56), it refers to a macaque who arrived with a part-missing tail, and '*a female ex-breeder was deemed to be depressed / withdrawn due to intestinal neoplasia and was euthanized*'. In its section on housing, the review mentions numerous instances of aggression (arguably an indicator of psychological suffering in itself), for instance '*one animal managed to escape and attacked other animals, but was itself badly injured and had to be euthanized*' (P58). Further down the page, it reports '*12 animals were involved in fights that required surgical repair of wounds; a further animal sustained a severe tail de-gloving injury; 39 animals had several fights which may or may not have required suturing of / surgery to wounds.*'

Additional concerns of the APGs are noted briefly here:

- The report conveys a blasé attitude to direct welfare impacts of procedures, dismissing the suffering of the NHPs. For example, in response to high levels of skin infections around head implants, the report simply concludes that this '*probably reflects the open nature of the implant and the difficulty of keeping such implants clean*' (P73).
- Welfare impacts of single housing, repeated procedures, aggression and fighting injuries are referenced with conflicting information in the review. Although repeated examples are given of fighting, injury and aggressive behaviour in the laboratory (e.g. P58, 99, 106), the report absurdly states that '*the laboratory environment eliminates the many stressors that may be encountered by wild living primates (e.g. food scarcity, predation, **aggressive interactions**)*' (P40, emphasis added).
- The report highlights alarming complacency in the laboratory. For instance, when questioned on the issue of modifying head implants procedures, the response was '*why change a winning team?*'(P101), demonstrating total disregard for animal welfare.
- The report reveals that researchers' failure to grasp the discomfort and distress experienced by monkeys whose food or water has been 'controlled' results in the preposterous misinterpretation of a monkey's desperate thirst or hunger as 'willingness' to sit in a 'training chair'. Any water control, other than *ad libitum* access is deprivation, however it is termed.
- While the report purports to study the cumulative suffering of NHPs used in neuroscience research, it actually reveals the inability of laboratory workers to assess suffering associated with procedures over the shorter term, and indeed, exposes the resistance to performing the harm-benefit test on which all evaluations of laboratory protocols involving animals are ostensibly based.

- The report highlights lack of efforts in data sharing, e.g. in cataloguing of blood sample values (P11), which undermines reduction in animal use.
- The report exposes inconsistency in application of best practices and maximising welfare standards across establishments.

The report is based on subjective opinions about a relatively small number of NHPs who the researchers not only worked on but also selected to include in the review. This methodology is a major limitation of the report and any future review must ensure that independent assessments of cumulative severity and suffering are made on NHPs who have been selected randomly rather than chosen by the researcher.

The review outlines the two broad areas of NHP neuroscience research (P65). Given that thousands of NHPs have, for years, been used in both of these areas of research, a strict 'root and branch' review of what specific potential new information satisfies the harm-benefit analysis must be performed, each time yet another NHP undergoes surgery to implant a device or induce a lesion and then suffers even further in experimental procedures. This is a review we would like the ASC to incorporate into a future independent review on cumulative severity and use of NHPs in research.

Conclusion

Far from reassuring the public who – according to the review – are often '*uninformed about what really goes on in primate experiments*' (P114), the APC review actually provides compelling evidence for the urgent need to critically assess the ethical and scientific legitimacy of these – and other – animal experiments. As well as underlining the terrible suffering endured by NHPs used in neuroscience experiments, the review also highlights what appears to be a worryingly biased view of NHP researchers and most concerning of all, inconsistency, inability and reluctance to not only assess the suffering of NHPs used in research, but to adequately perform an analysis of the suffering against the proposed benefits of such research.

The APGs suggest that this is an urgent matter and strongly recommend that the ASC conducts a thorough and impartial investigation and reports, as soon as possible, its recommendations – one of which we believe would be the use of CCTV as an instruction and monitoring tool.

References

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