Affective States and the Assessment of Laboratory-Induced Animal Welfare Impacts

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Summary

Animal welfare is increasingly understood in terms of a wide range of affective states or feelings animals may experience. Some of these can be assessed and others, as yet, cannot. Reference is made to a comprehensive system for ranking the impacts of scientific procedures on the affective states or feelings that can be assessed. To date, the predominant focus has been on pain and distress. It is argued that, in addition to these, other negative subjective and emotional experiences should be considered, including the following: thirst, hunger, nausea, breathlessness, dizziness, debility, weakness, sickness, anxiety, boredom, fear, frustration, helplessness, and loneliness. Moreover, negative impacts on positive emotional states or experiences – e.g., satiety, vitality, reward, contentment, curiosity, and playfulness – should also be evaluated, especially in light of the existence of cogent neuropsychological explanations of the sources of such states and their associated behaviors. A major purpose of this paper is to reinforce the principle that because animals may have bad or good experiences at our hands, we have an obligation to treat them considerately (at the very least). This translates into minimizing the harm we do to them and, importantly, maximizing the good. More effective harm minimization should result when the Three Rs are applied to mitigating a wider range of negative emotional experiences or affective states, and also when re-orientated refinement measures are adopted that will more strongly promote an extended range of specific positive emotional or affective states or the general wellbeing of animals. It is anticipated that this more comprehensive understanding of refinement will enhance caring and empathetic attitudes towards animals among investigators and members of Animal Ethics Committees or Animal Care and Use Committees.

Keywords: pain, distress, negative affective states, positive affective states

1 Introduction

When considering the impact of manipulating sentient animals for research, teaching, and testing (RTT) purposes, the predominant concern is the elicitation of negative experiences which, when extreme, may cause high levels of suffering (Mellor and Reid, 1994). The conscientious application of the Three Rs tenets of replacement, reduction and refinement, formulated by Russell and Burch (1959), has become the primary guide to minimizing such negative experiences. However, in order to fully realize the beneficial effects of Three Rs applications, it is necessary to recognize the wide range of possible negative experiences RTT activities may cause and to identify specifically which ones may be generated by particular manipulations. It is also important to consider the negative impacts of preventing positive experiences animals used in RTT may otherwise have.

2 A focus on pain

An early focus in conceptual and regulatory terms was the minimization of "pain and distress." The focus on pain had merit both because, by definition, pain has the potential to be exceptionally unpleasant and because it is commonly acknowledged to be among the most negative experiences people can have (Mellor, 2011). Once a connection has been made and accepted between the human experience of pain and the capacity of animals to experience it and suffer as a result (Mellor, 2008), this generates greater motivation to become proficient in dealing with the causes of animal pain and the methods of alleviating the pain that cannot be prevented. Moreover, an initial focus on pain and its management helps to address a wide range of factors that could cause welfare compromise (Mellor, 2011). This is because pain has many causes, including injuries of different types and numerous forms of disease-induced pathology. It has many manifestations, which may be acute, chronic, localized, generalized, physical, emotional, adaptive, or maladaptive – and more than one type of pain may be experienced at the same time (Gregory, 2004; Dolan and Nolan, 2008; Flecknell, 2008; Seksel, 2008). These considerations have direct relevance to the formulation of *refinement* strategies.

3 Giving more definition to distress

Early and current references to "distress" appear to be a means of expanding consideration of RTT impacts to a wider range of unpleasant experiences without specifying them. However, this

may have less merit than regulatory references to pain. Without some guidance, salient unpleasant experiences, apart from or in addition to pain, may be overlooked when prospective or retrospective evaluations of RTT impacts are being attempted. It follows, in addition, that under these circumstances the scope of potentially beneficial application of *refinements* would be significantly underestimated.

Interestingly, during the last 20-30 years the range of specified unpleasant experiences which, when intense enough, may be included in the catchall term "distress" has broadened considerably (Green and Mellor, 2011). Thus, the five freedoms enumerated in 1979 by the Farm Animal Welfare Council in the UK referred to thirst, hunger, discomfort, and fear in addition to pain and distress (Webster, 1994; Anonymous, 2009). Today the list of such states that need to be considered includes at least thirst, hunger, weakness, debility, breathlessness, nausea, sickness, fear, anxiety, helplessness, and boredom, as well as pain and other unspecified forms of distress (Mellor et al., 2009; Green and Mellor, 2011). This expanded list has two benefits. First, it specifies areas that should be given explicit attention by those seeking to mitigate negative RTT impacts, and second, in being acknowledged as incomplete, this list also highlights the need for investigators to consider whether or not additional negative experiences may plausibly be generated by the RTT manipulations they are planning.

4 The five domains of potential animal welfare compromise

The five domains concept was originally formulated by Mellor and Reid (1994) and has been refined subsequently, most recently by Mellor et al. (2009). This concept is a major part of a comprehensive system for assessing the harms that may be caused by proposed RTT procedures, a system that in 1997 was incorporated into the formal regulatory framework for managing the scientific uses of sentient animal in New Zealand (Williams et al., 2006).

The five domains are: nutrition, environment, health, behavior, and mental state. The first four domains are predominantly physical/functional, and the last domain, mental state, represents the overall experience of the animal, i.e., its welfare status (Fig. 1). Conditions in the first four domains give rise to sensory inputs that may lead to perceived subjective experiences in the mental domain (Mellor et al., 2009). Examples of these include the following:

– *Nutrition domain:* water or food deprivation may lead to the subjective experience of thirst or hunger, respectively;
– *Environment domain:* extremes of cold or heat may lead to chilling-related debilitation or hyperthermic distress, respectively;
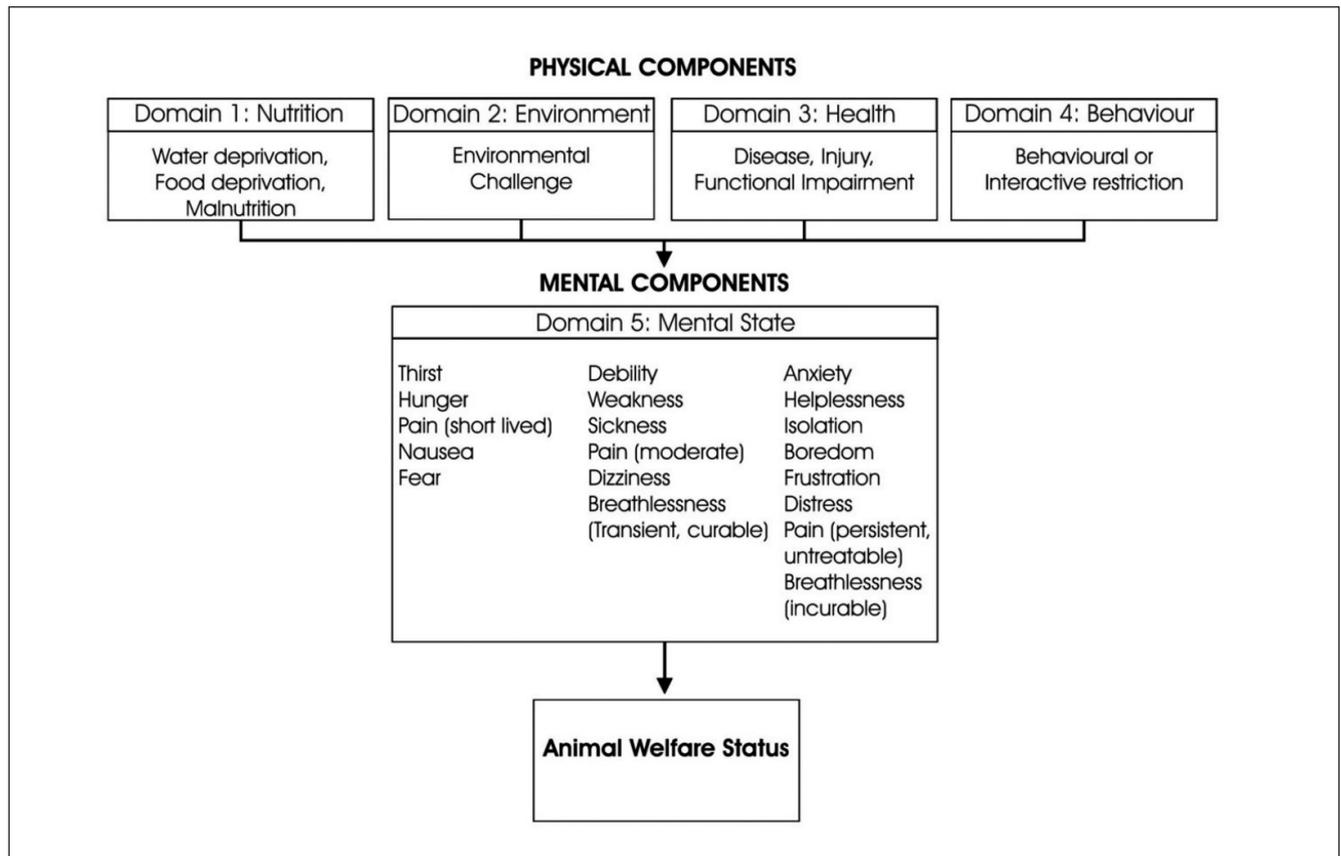– *Health domain:* disease or injury may lead to a number of

Fig. 1: Domains of potential welfare compromise divided into physical and mental components the integrated effects of which give rise to the welfare status of the animal
Diagram modified from Mellor et al. (2009).

experiences including breathlessness, nausea, sickness, pain, fear, anxiety, or other forms of distress;

- *Behavior domain:* limitations on behavioral expression due to space restrictions, isolation, or barren environments may lead to feelings such as boredom, frustration, loneliness, or helplessness;
- *Mental state domain:* internally-derived sensory inputs arising from compromise in the other four domains, plus cognitive inputs and related mental activity arising from external environmental challenges that elicit fight-flight-fright" or other responses, may give rise to sensations of thirst, hunger, weakness, debility, breathlessness, nausea, sickness, pain, fear, anxiety, helplessness, boredom, and other forms of distress.

As described in detail elsewhere (Mellor and Reid, 1994; Mellor et al., 2009), the five domains system allows different levels of negative impact to be assessed and graded using a five-point, non-numerical scale. The different levels of compromise are designated in terms of grades A, B, C, D, and E (Mellor et al., 2009)[1], where A is the lowest severity and E the highest. Numbering the grades was specifically excluded to avoid the apparent precision of arithmetic assessments whereby arbitrary numerical thresholds assigned to impacts of RTT manipulations might be used as substitutes for reasoned judgment (Mellor and Reid, 1994). Key elements in assigning these different grades include the severity of functional disruption caused by each procedure, the duration of the disruption and its reversibility, and whether or not its noxious effects might need to be mitigated or ended by withdrawal of the animal from the study, treatment, and/or euthanasia (Mellor and Reid, 1994; Mellor et al., 1994).

5 Positive subjective experiences – an additional perspective on welfare compromise

Although the five domains system as originally conceived dealt almost entirely with negative impacts of RTT procedures on animals (Mellor and Reid, 1994), when generalized into a means of assessing the overall welfare status of animals on a spectrum from very poor to exceptionally good, it can also accommodate the existence of positive welfare states and the negative impacts of factors that may compromise positive states (Mellor et al., 2009; Green and Mellor, 2011). Accordingly, an animal's welfare may be said to be good when its nutritional, environmental, health, behavioral, and mental needs are met. Meeting these needs can be accomplished by managing animals in ways that both avoid negative mental states and promote positive ones (Mellor et al., 2009; Green and Mellor, 2011).

This characterization of animal welfare has recently been provided with additional support (Mellor, 2012). It has long been proposed and is now widely accepted that, in addition to negative subjective experiences such as those enumerated above, animals are likely to have positive emotional experiences or affective states (Duncan, 2005; Yeates and Main, 2008; Mendl

et al., 2010). Examples of positive experiences may include feelings of satiety, vitality, reward, contentment, curiosity, and playfulness (Mellor et al., 2009; Mellor, 2012). It follows that some forms of welfare compromise may result from an absence of such feelings so that the presence of some positive feelings might be considered to represent a "need" in the mental domain. It also follows that good animal welfare results both from an absence of negative experiences and the presence of positive emotional experiences or affective states (Kendrick, 2007; Yeates and Main, 2008; Mellor, 2012).

As the principal indices for monitoring such positive states are likely to be behavioral (Knierim et al., 2001; Duncan, 2005; Fraser, 2008), this raises concerns among some scientists who have mostly used quantitative functional indices to assess welfare (Mellor, 2012). Affective states of this type appear difficult to define rigorously, and the neurological links between them and their assigned behavioral indices also appear to be poorly defined. However, perusal of the neuropsychological literature, in particular that of Panksepp and colleagues (see Panksepp, 2005), reveals an increasingly secure scientific understanding of the neurological foundations of affective states and the motivational drives that energize and direct their associated behaviors. However, apart from some brief references to this new understanding (Knierim et al., 2001; Mendl et al., 2010), apparently, no significant attempts were made to import these concepts into animal welfare science thinking until very recently (Mellor, 2012).

As outlined by Mellor (2012), Panksepp proposed the existence of several genetically programmed action-orientated systems or state functions. These were conceived in psycho-ethological terms that envisage the apparent purposefulness of specific behavior patterns in animals as indicating different forms of embedded and compelling intentionality experienced emotionally in negative or positive terms (Panksepp, 2005; Panksepp et al., 2011). This represents an active organism perspective focused on what the animal's behavior suggests it is aspiring to achieve, as opposed to the previously more common view that the animal is a reactive or passive receiver guided predominantly by stimuli that have impinged on it in the past. Mellor (2012) argued that the evidence advanced by Panksepp and his colleagues extends understanding of the interactivity between neural-cognitive processing, affective states and behavioral expression in ways that strongly support both the principle of promoting positive welfare states in animals and the practical measures recommended for achieving that. This evidence, reported in detail by Nelson and Panksepp (1998), Panksepp (1998), Panksepp and Zellner (2004), Panksepp (2005) and Panksepp et al. (2011), has been summarized by Mellor (2012). Accordingly, only a very brief description of each system is provided here.

The action-orientated systems or state functions are designated as SEEKING, FEAR, RAGE-ASSERTIVENESS[2], BONDING[3], CARE, PLAY and LUST. The capitalization of the names was adopted by Panksepp to emphasise that each one represents an entire action-orientated system, including its neural foundations,

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[1] Originally these grades were designated O, A, B, C and X (Mellor and Reid, 1994).

[2] This was originally named the RAGE system by Panksepp (1998) and renamed by Mellor (2012).

[3] This was originally named the PANIC system by Panksepp (1998) and renamed by Mellor (2012).

and not a single emotional or behavioral element associated with the operation of the system.

The embedded emotional content of the SEEKING system includes compelling exploratory urges involving wanting and expectancy leading to engaged aliveness and excitement, which are expressed behaviorally as goal-directed, energized investigation of and interaction with the environment. The neural circuits are those associated with positive affect or reward.

The FEAR system generates the negative affects of anxiety, a sense of threat and fear expressed behaviorally as nervous vigilance, freezing or flight, and involving neural circuits for threat recognition linked to others for behavioral evasion of threat.

The RAGE-ASSERTIVENESS system has two major manifestations. The first is characterized by the strongly negative affects of anger, rage, and a highly aroused urge to defeat, dominate, or defend, expressed as species-typical offensive or defensive enraged attack behaviors. These emotions and behaviors arise from the operation of neural circuits specific for the expression of rage linked to circuits for threat recognition and to the FEAR circuits. The second manifestation relates to predominantly positive affects of energized, goal-directed wanting and expectancy driven by appetitive and consummatory urges expressed behaviorally as highly focused predatory stalking and attack or focused and engaged foraging. The specific circuits involved are merged with those of the SEEKING system that engender positive affect and a sense of reward.

The BONDING system gives rise to a drive to attain and retain the comfortable and comforting affects of affectionate companionship or protection expressed behaviorally through initiation of and responsiveness to species-typical prosocial or affiliative interactions. It also gives rise to the drive to avoid separation-induced anxiety or panic, or isolation-induced loneliness, expressed as behavioral attempts to reunite with bonded others or as depressive inactivity, respectively. The neural circuits involve neuroactive agents such as endogenous opioids, oxytocin, vasopressin, and noradrenaline, as well as circuits for detecting thermotactile and odor cues.

Finally, the CARE, PLAY, and LUST systems also manifest positive affects through protective and empathetic maternal care, the joyfulness of play, and the appetitive eroticism and orgasmic pleasures of lust, where each positive affect is indicated by specific and explicit behaviors and is derived from the operation of neural circuits, neurochemicals and neuroactive hormones that underlie these particular prosocial and affiliative emotions and behaviors.

Thus, manipulation of these action-orientated systems offers the opportunity to replace some of the negative emotions they may generate with positive ones (Mellor 2012), for example, by environmental enrichment (Young, 2003; Fraser, 2008; Mellor et al., 2009). It is acknowledged that most enrichment strategies devised to date have been informed by behavior-based assessments of how motivated animals are to satisfy their needs, wants, or preferences (Hughes and Duncan, 1988; Hurnik and Lehman, 1988; Kirkden and Pajor, 2006; Dawkins, 2008). However, Panksepp's concepts and their detailed neuropsychological support have the capacity to strongly reinforce the predominant behavioral basis for most such initiatives taken to date, and, in addition,

they have the potential to boost the drive for further beneficial developments of this type (Mellor, 2012).

6 Strategies to replace negative with positive affective states

The following strategies for enhancing the emotional or affective states experienced by animals used for RTT have been paraphrased from those outlined by Mellor (2012) for non-laboratory animal welfare codes. Thus, anxiety, fear, and nervous vigilance, which are associated with operation of the FEAR system, may be replaced by calmness and harmonious interactions with other animals and human beings by implementing laboratory standards that minimize visual, auditory, olfactory, environmental, handling, and other cues that may engender a sense of threat. Such standards may encourage animals that would otherwise be fearful to experience the enlivening rewards of exploratory and appetitive behavior generated by the SEEKING system. Moreover, the positive operation of the SEEKING system could be the focus of species-specific laboratory approaches that would improve the levels of environmental complexity and variety available for the animals. Such enlivening variety and rewarding appetitive occupation may likewise be expected to replace boredom. Animal management practices centered on the BONDING system would have benefits, as they are designed to ensure that animals have the company of others of their own kind or an appropriate alternative species (including human beings) and thereby encourage affiliative interactions and minimize the separation of bonded animals. This is because such practices would tend to replace loneliness, isolation, helplessness, separation distress, and feelings of abandonment with feelings of affectionate companionability and of being secure and protected. Such positive emotions could be reinforced if additional laboratory animal management practices were to be directed towards the CARE and PLAY systems and, probably limited to breeding animals, the LUST system. Finally, frustration accompanied by anger arising through the operation of the RAGE-ASSERTIVENESS system may be replaced by positive emotions resulting from a combination of all of the above initiatives, and these benefits might be reinforced by implementing breeding and culling programs that target temperament and, as occurs already, by keeping only mutually compatible animals together in groups. Overall, these approaches would minimize aggressive hierarchical interactions that give rise to strongly negative affects through activation of the RAGE-ASSERTIVENESS and FEAR systems.

7 Concluding remarks

A major purpose of this paper is to reinforce the principle that, because animals may have bad or good experiences at our hands, we have an obligation to treat them considerately (at the very least). This translates into minimizing the harm we do to them and, importantly, maximizing the good. More effective harm minimization should result when the Three Rs are applied to mitigating the wider range of negative emotional experiences or affective states outlined here, and also when re-orientated *refine-*

ment measures are adopted that will more strongly promote an extended range of specific positive emotional or affective states or the general wellbeing of the animals. It is anticipated that this more comprehensive understanding of *refinement* will enhance caring and empathetic attitudes towards animals among investigators and members of Animal Ethics Committees or Animal Care and Use Committees.

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