

Comprehensive Assessment of Harms Caused by Experimental, Teaching and Testing Procedures on Live Animals

David J. Mellor

Animal Welfare Science & Bioethics Centre, Massey University, Palmerston North, New Zealand
E-mail: D.J.Mellor@massey.ac.nz

Summary — The comprehensiveness of assessments of experimental, teaching and testing harms, and the actions taken to minimise them, are measures of the scientist's acceptance of ethical responsibility for all features of each procedure that affect animals adversely. A system, refined from its original 1994 form, has been devised to assist in this process. Five "domains of potential animal welfare compromise" are identified. Domain 1 is *Water deprivation, food deprivation, malnutrition*; Domain 2 is *Environmental challenge*; Domain 3 is *Disease, injury, functional impairment*; Domain 4 is *Behavioural, interactive restriction*; and Domain 5 is *Anxiety, fear, pain, distress, thirst, hunger and boredom*. A proposal would be examined systematically in all these domains, and the degree of compromise in each rated on a five-step, non-numerical scale — O, A, B, C, X. Anxiety, fear, pain, distress, thirst, hunger and boredom arising from compromise in Domains 1–4, would be cumulated into Domain 5. The overall rating would commonly be that given to Domain 5, but if this were low or unknown, it would be given to the highest rating in the other domains. Each experimental group in a study would be rated so that compromise overall would neither be underestimated nor overestimated. Both the researcher and the animal ethics committee would rate each group in these terms.

Key words: *behaviour, environment, harm assessment, harm–benefit analysis, health, mental state, nutrition.*

Introduction

Harm–benefit analysis is a major feature of the review that institutional animal ethics committees undertake when they consider applications to conduct research, teaching and testing procedures on live animals. This is required because, if utilitarian ethical support for such animal use is to be credible, the sum of all the benefits must exceed the sum of all the harms by the greatest amount that can feasibly be achieved (1–3). Note that this is *strong* utilitarianism, where all the benefits must exceed all the harms by the *greatest* possible amount, and not *weak* utilitarianism, where the benefits merely need to be *greater* than the harms (1, 2). Therefore, an essential ethical step in this process, is the assessment of harm, such that the comprehensiveness of the assessment of harms and the actions taken to minimise them are measures of the scientist's acceptance of ethical responsibility for all features of each procedure that affect the animals adversely.

A System for Assessing Harms

A system — originally described in 1994 (4) and modified subsequently (5) — has been devised to permit the comprehensive ranking of harms caused

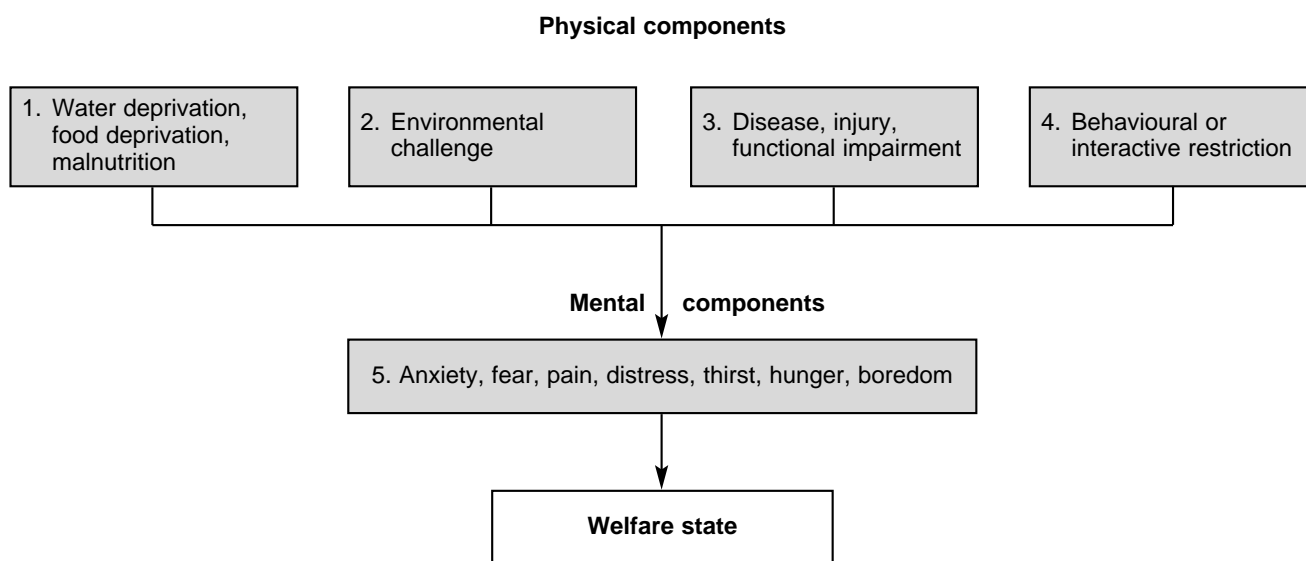
by experimental, teaching and testing procedures. It is based on the notion that an animal's welfare will be good when its nutritional, environmental, health, behavioural and mental needs are met (4). Accordingly, five domains of potential animal welfare compromise are recognised:

1. water deprivation, food deprivation, malnutrition — *nutrition*;
2. environmental challenge — *environment*;
3. disease, injury, functional impairment — *health*;
4. behavioural or interactive restriction — *behaviour*; and
5. anxiety, fear, pain, distress, thirst, hunger, boredom — *mental state/experience*.

The first four domains largely represent physical elements of animal welfare, and the fifth domain mainly encompasses the mental element within which good or bad subjective experiences of the animal are expressed (5). Compromise in the first four domains will therefore usually be registered in welfare terms in the fifth domain, which includes the components of suffering (Figure 1).

It is difficult to envisage any feature of animal welfare compromise that could not be accommo-

Figure 1: Five domains of potential welfare compromise divided broadly into physical and mental components



Modified from (4) and derived from (5).

dated within these five domains, including even varieties of compromise that were not anticipated when this system was first devised. Accordingly, it appears to cover the breadth of possible compromise, but there remains the question of the severity of compromise and how it might be graded.

Grading the Severity of Animal Welfare Compromise

Allied to the five domains is a five-point, non-numerical scale that allows the severity of compromise to be graded (4). The levels of compromise are designated as grades O, A, B, C and X, where O is the lowest severity and X the highest. Numbering the grades was specifically excluded to avoid the apparent precision of arithmetic assessments whereby arbitrary numerical thresholds and manipulations might be used as substitutes for reasoned judgment.

An attempt has been made to link the different grades to 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 from the study, treatment and/or euthanasia.

The grades apply to each of the five domains and have the following general features in each domain (4).

Domain 1: nutrition

Grade O Water/fluid is available in quantities that satisfy thirst. Food of appropriate types and compositions for the species is made available in amounts that meet body maintenance requirements, plus any additional demands imposed by factors such as pregnancy, lactation, growth, exercise, thermal challenge or recuperation from illness or injury.

Grade A Water/fluid or food restrictions or excesses that cause minor, readily reversible effects on physiological state, body condition or performance.

Grade B Water/fluid or food restrictions or excesses that cause serious short-term or moderate long-term effects on physiological state, body condition or performance, but such effects remain within the capacity of the body to respond to nutritional variations and allow spontaneous recovery after the restoration of a good quality diet at the required intakes.

Grade C Water/fluid or food restrictions or excesses that lead to levels of debility where euthanasia would be used to avoid an inevitable further decline, because ther-

apy would either be ineffective or too protracted.

Grade X Water/fluid or food restrictions or excesses so severe that the predicted endpoint is death.

Domain 2: environment

Grade O Experiments involving outdoor or indoor environmental conditions that elicit body responses that remain inside the animals' capacity to react to external stimuli without recourse to adaptive physiological changes.

Grade A Experiments that cause body responses that remain within the homeostatic capacity of the animals to react, but that involve adaptive physiological responses.

Grade B Experiments that represent marked short-term or moderate long-term environmental challenges that elicit body responses beyond the physiological adaptive capacity of the animals, but where the untoward effects are readily reversed by restoration of benign conditions, with or without additional therapeutic intervention.

Grade C Experiments with extreme environmental challenges that lead to serious physiological compromise, where euthanasia would be used to prevent an inevitable further decline or because therapeutic procedures would be ineffective or too protracted.

Grade X Environmental experiments that cause protracted extreme physiological compromise or where the endpoint is death.

Domain 3: health

Grade O Experiments that use healthy animals and that do not cause or involve disease, injury or functional impairment.

Grade A Experiments that cause body responses that remain within the homeostatic capacity of the animals to react, with no or only minor debility or incapacity.

Grade B Experiments that cause marked short-term or moderate long-term functional changes associated with moderate debility or incapacity, but from which com-

plete recovery occurs spontaneously or can be readily effected therapeutically.

Grade C Experiments that cause marked debility or incapacity and serious physiological compromise, where euthanasia would be used to prevent an inevitable further decline, because therapeutic procedures would be ineffective or too protracted. Experiments that cause death unpredictably in a small proportion of animals, because a rapid deterioration in their state can occur with little or no warning.

Grade X Experiments in conscious animals that cause extreme debility or incapacity or where the predicted endpoint is an unpleasant death.

Domain 4: behaviour

Grade O Experiments that do not interfere with the behavioural needs of individuals or groups of animals (an animal's behavioural needs include those activities that, when thwarted, produce untoward physiological or psychological effects).

Grade A Experiments that cause minor interference with the behavioural needs of individuals or groups of animals.

Grade B Experiments that cause marked short-term or moderate long-term interference with the behavioural needs of individuals or groups of animals resulting in untoward physiological or psychological effects that are readily reversed by the restoration of benign conditions with or without additional therapeutic intervention.

Grade C Experiments that markedly interfere with the behavioural needs of individuals or groups of animals, leading to severe physiological or psychological compromise requiring restoration of benign conditions, with or without additional therapeutic intervention, or the use of euthanasia to limit the magnitude or duration, or both, of the imposed compromise.

Grade X Experiments that cause severe interference with the behavioural needs of individuals or groups of animals leading to psychotic-like behaviour or to agonistic interactions that result in severe injury or death.

Domain 5: mental state/experience

Grade O Experiments that do not cause anxiety, fear, pain, distress or significant thirst, hunger or boredom, such as non-invasive observation of animals in benign circumstances.

Grade A Experiments that cause minor discomfort or low-level anxiety or apprehension or

mild thirst, hunger or boredom for short periods.

Grade B Experiments that cause moderate anxiety, fear, pain, distress, thirst, hunger or boredom for short periods or minor discomfort, distress, thirst, hunger or boredom for long periods.

Table 1: Examples of grading the severity of animal welfare compromise during experiments (from 4)

Domain	Grade
Operant conditioning with positive reinforcement using animals accustomed to the experimental environment and apparatus	
1. Fluid/food intake unaffected	O
2. Thermoneutral environment	O
3. Healthy, uninjured animals	O
4. Minor behavioural restriction	A
5. No suffering	O
	Overall grade: A
Studies of limited gut resection (removal) and its consequences	
1. Fluid/food intake affected slightly	A
2. Thermoneutral environment	O
3. Anaesthesia plus surgery with effective analgesia	B
4. Minor behavioural restriction (indoor individual pen)	A
5. Moderate pain/distress (mainly with surgery)	B
	Overall grade: B
Blood sampling of recently confined and untamed free-range domesticated animals with strong flight responses	
1. Fluid/food intake affected slightly (reduced for first 48 hours)	A
2. Thermoneutral environment	O
3. Simple venipuncture of healthy uninjured animals	A
4. Mild behavioural restriction (handling, large indoor pen)	A
5. Marked fear/distress (mainly from handling/restraint)	C
	Overall grade: C
Studies of usually fatal viral diarrhoea in hand-reared newborn animals	
1. Fluid/food intake moderately affected	B
2. Thermoneutral environment	O
3. Extreme debility or functional compromise	X
4. Minor behavioural restriction	A
5. Severe pain/distress (mainly from gut effects)	X
	Overall grade: X
Studies of underfed animals exposed to severe cold for a short period (24 hours)	
1. Food intake restricted to cause weight loss of 20%	B
2. Cold challenge at the limit of animal's adaptive response	B
3. Mild functional impairment	A
4. Mild behavioural restriction (indoor individual pen)	A
5. Marked overall distress (from underfeeding and cold)	C
	Overall grade: C

Grade C Experiments that cause marked anxiety, fear, pain, distress, thirst or hunger, where any suffering caused is ended by euthanasia or by therapeutic or other interventions before it becomes excessive, or where the suffering is short-lived and complete recovery can occur. Experiments that cause moderate anxiety, fear, pain, distress, thirst or hunger for long periods.

Grade X Experiments that cause severe, inescapable, or unrelieved anxiety, fear, pain, distress, thirst or hunger, where the intensity or duration, or both, of the induced suffering are at or beyond the limits of reasonable endurance.

A detailed list of examples for each grade within each domain is provided by Mellor & Reid (4).

When using the grading system, each experiment must be graded in all five domains of potential welfare compromise. The overall grading of an experiment would usually be that assigned to Domain 5 — mental state. However, the combined use of all five domains is necessary to help ensure that all factors that can contribute to suffering of different kinds have been assessed. When assessing compromise in each domain, care must be taken to avoid inclusion of compromise to the features of welfare dealt with in the other domains. The greatest anticipated compromise specific to each domain should be used when assigning the grade within each domain. When compromise in two or more domains contributes to suffering, assigning an appropriately higher grade to Domain 5 — mental state — should be considered. The process of determining the overall grade is illustrated by the five examples in Table 1. The first shows that in the absence of suffering — graded O in Domain 5 — the highest grade in one of the other domains becomes the overall grade. In the next three examples, the overall grade is the same as that assigned to Domain 5, and in the last example, the grade in Domain 5 is greater than any of the individual grades because compromise in two other domains magnifies distress.

Each experimental group in a study needs to be graded to ensure that the grade assigned to animals receiving the most severe treatment (e.g. induction of a distressing disease) is not assigned to groups that are treated more benignly (e.g. non-diseased control groups). This helps to ensure that the severity of compromise imposed on all animals in an experiment is neither underestimated nor overesti-

mated. Both the researcher and the animal ethics committee would rate the groups in these terms.

Harm–Benefit Analysis

As noted above, assessing the level of harm is just the first step in conducting a harm–benefit analysis on proposed procedures that will involve the use of live animals. Although it is not the purpose of this paper to consider harm–benefit analyses in detail, suffice it to say here that the comprehensive assessment of harm that use of this system allows will have major implications for the outcome of harm–benefit analyses. That is because the greater the harm done to the animals the greater the anticipated benefit must be before a procedure can be approved. The level of harm, as it were, sets the threshold of realistically anticipated benefit that must be reached before approval can be granted. This matter is discussed in more detail by Mellor & Reid (4).

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