OPENNESS

IN ANIMAL RESEARCH

ANZCCART 2021 CONFERENCE PROCEEDINGS

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Public confidence in animal research depends on the scientific community taking part in an on-going conversation about why, and how animals are used. ANZCCART 2021 looked at animal research from different viewpoints and discussed transparency and the benefits or risks of openness, and what this looked like in practice. We also asked what cultural perspectives can teach us and explored what has and has not worked in other countries. As new approaches are adopted through the Three Rs and other means, ANZCCART 2021 shared the lessons learnt from these experiences.

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A tikanga approach

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Foreword

This paper was crafted building on an invited presentation to the 2021 ANZCCART 'Openness in animal Research' conference, held in Queenstown, July 2021. The invitation from ANZCCART, a standing committee of the Royal Society Te Apārangi, to present a paper on "doing research with animals from a different cultural perspective" reflects both the mission of the former to promote informed discussion about the care of animals in research and teaching, and the commitment of the latter to valuing diversity.

The invitation to present was accepted, on the understanding that as I haven't undertaken any research in this space, the contribution would be more generic, framed from a Māori worldview perspective. In addition, therefore, I need to acknowledge that there may already be work underway on the concepts I cover in this paper that I am unaware of.

Abstract

ANZCCART is the independent body established to provide a focus for consideration of the scientific, ethical and social issues associated with the use of animals in research and teaching. Increasingly, such institutions are recognising that other ways of knowing, being and doing can and should play an important role in their efforts. Mātauranga Māori is one such knowledge-belief-practice complex, comprising in addition to knowledge, Māori culture, values, practices and worldviews. A key component of mātauranga are tikanga, the customs, traditions and practices handed down through the passages of time. Derived from the root word tika – right, or correct, tikanga means 'doing the right thing'. In this paper we will detail what tikanga are and what they aim to achieve, and provide some examples of tikanga before posing some framing questions for ANZCCART to consider in its work.

Pepeha

Ko Waitomo te awa
Waitomo is the river

Ko Owhawhe te maunga
Owhawhe is the mountain

Ko Tokikapu te marae
Tokikapu is the marae

Ko Ngāti Uekaha te hapū
Ngāti Uekaha is the hapū

No Ngāti Maniapoto te iwi
Ngāti Maniapoto is the iwi

Ko Tainui me Te Arawa ngā waka
Tainui and Te Arawa are the canoes

Ko au he uri o Hoturoa me Tamatekapua
I am a descendant of Hoturoa and Tamatekapua

Ko Dan Hikuroa tōku ingoa
My name is Dan Hikuroa

In a Māori worldview we exist in a whakapapa kinship-based relationship with Te Taiao: the Earth, Universe and everything in it. Within this framing, waterways, mountains, animals and plants can be ancestors. The pepeha I shared above does more than identify me; it details my existence and wellbeing as inextricably interlocked with the existence and wellbeing of Te Taiao – the environment. Waitomo is the river, meaning I am the river, and the river is me; Owhawhe is the mountain – I am the mountain, and the mountain are me; and so on. Notably, although I have agency, as an individual I am the least important of all those I mentioned. Waitomo, Owhawhe, Tokikapu, Ngāti Uekaha, Ngāti Maniapoto, Tainui waka, Te Arawa waka, Hoturoa and Tamatekapua are all more important than I. There is a whakataukī, or proverb, "Toitu te whenua, whatungarongaro he tangata" – literally, the land endures, and people are fleeting. It means that I only exist because all of these other things existed before me, and they will exist beyond me. The iwi and hapū will live on, Owhawhe, Waitomo, Tokikapu will remain. Pepeha are small fragments of the whakapapa of an individual, part of the generative network of whakapapa of all that has existed.

Mātauranga Māori

Mātauranga Māori spans Māori knowledge, culture, values and worldview (Hikuroa, 2017), a continuum of distinct knowledge with Polynesian origins that grew in Aotearoa New Zealand (Clapcott et al., 2018), that further developed here along with the cultural and epistemological identities of iwi Māori (Mercier, 2018). Mātauranga Māori is rooted here and encompasses a wellspring of understanding of Aotearoa New Zealand ecosystems (Mercier, 2018), as well as actions, manifest as practices of interacting with other living and more-than-living things as part of the environment. Mātauranga Māori, te reo Māori (Māori language) and whakapapa (ancestral lineage) are used together to codify the Māori perspective and understand what an ecosystem is, how it works, and its components and functional units (Harmsworth & Awatere, 2003).

As Māori was not a written knowledge or language, much mātauranga Māori occurs in the spoken form, e.g. whakapapa, moteatea, pūrākau, waiata, pakiwaitara, whaikōrero and oriori. Additionally, mātauranga Māori was manifest in many other ways including maramataka; the design, construction materials, construction techniques and site selection for whare nui; hika ahi (fire-making) and rongoa (medicine and associated practices).

Worldview

We all possess a worldview. The dominant worldview in Aotearoa New Zealand is so pervasive it is almost invisible. The Reverent Māori Marsden, a highly respected tohunga describes worldview (Marsden in Royal, 2003):

"*Cultures pattern perceptions of reality into conceptualisations of what they perceive reality to be: of what is to be regarded as actual, probable, possible or impossible. These conceptualisations form what is termed the "world view" of a culture. The World View is the central systemisation of conceptions of reality to which members of its culture assent and from which stems their value system. The world view lies at the very heart of the culture, touching, interacting, with and strongly influencing every aspect of the culture*" (p. 56).

What does a different worldview look like? Remember when the world was flat? That used to be real. New observations have led to new realities; the world is now a sphere. Here's another, consider for example, a humpback whale. Its scientific name is *Megaptera novaeangliae* – Large-winged New Englander; large-winged on account of its pectoral fins being larger than its cousins in the whale family, and New Englander as it was first described, in a formal scientific way, on populations based in the coastal waters of New England. Some common Māori names for whale include ika moana, tohorā and parāoa. Both of these ways of knowing, relating to and making sense of the 'whale' or 'tohorā' reflect different worldviews. For some Māori there is a specific name for this whale – paikea, and furthermore Paikea is an eponymous ancestor for many of those people. Paikea the ancestor rode a humpback whale, a paikea, to Aotearoa New Zealand. Similarly, for some the tohorā is the southern right whale, and parāoa is the sperm whale. A key point to make here is that a mātauranga Māori approach accepts multiple versions to describe something – a whale, a maunga, a lizard. It does not seek to determine which version is right and which is wrong.

If you have ever found yourself saying or thinking 'I couldn't believe my eyes!' chances are it is because what you are seeing does not equate with what you believe to be real or possible. The power of your worldview is so strong it can cause you to doubt your eyes. I had a recent experience of this phenomenon. I was leading a fieldtrip and we were staying in a lodge on Ruapehu. One evening the sky was clear and I suggested we go and observe the night sky, and I urged the students to look for satellites. I told them they would recognise them as they look just like stars – same size, colour and shape, but they move across the sky as a group along one flight path. Some eager students had rushed ahead and started calling out excitedly saying "I see one, and another, and another, and another..." I recall thinking it was unusual to see so many at once, but I was not prepared for what I saw. Twenty-four satellites, all in row, travelling on the same flight path, same speed, as a group. In all my years of searching for satellites never had I seen anything like that. I can tell you for a few seconds, I could not believe my eyes. Of course my eyes were fine, it was just my worldview that needed updating – a quick internet search revealed they were a chain of Starlink satellites. Our worldview is powerful, and can operate

consciously or sub-consciously. Recognising that we all have one, and that others have one, that may be the same, or similar, or very different is a key step to beginning to understand mātauranga Māori and hence Māori ways of knowing (epistemology), being (ontology) and doing (axiology).

Whakapapa

In Te Ao Māori (the Māori world), people are simply one element in the relational networks known as whakapapa, linked with all other life forms through their shared descent from earth and sky (Salmond, 2014). Humans exist in a kinship-based relationship with Te Taiao – the earth, universe and everything within it (Hikuroa, 2017). Whakapapa is the central principle that orders Te Taiao – everything on Earth and in the sky, a relational schema (Brierley et al., 2018), wherein "We see ourselves as direct descendants of our earth mother and sky father and consequently not only 'of the land' but 'as the land'" (Te Aho, 2010, p. 285). People, sky, rivers, animals and ancestors overlap in Māori language (Salmond, 2014). Māori relational thinking might be understood to appreciate rivers as complex and emergent networks of plants, animals, land, water and people in a dynamic process of coevolution (Salmond, 2017).

So, just as the Linnaean system is a way to describe the world, whakapapa is a way to explain and make sense of the world, based on observations of the Taiao, within a Māori worldview. In another example, kauri is linked with whales – tohorā in some versions, and parāoa in others. Commonly, they are brothers, offspring of Tane Mahuta, deity of the forests. Tohorā/parāoa decides to live in the ocean. After failing to persuade kauri to join him in the ocean, tohorā/parāoa suggests they swap skins, and kauri agrees. This is the reason why kauri skin is so thin and is as full of resin as the whale is of oil, or why the kauri skin oozes resin like mīmiha – ambergris. A key point to make here is that although there is a clear distinction between what in a Linnaean system would be an animal (tohorā/parāoa) and a plant (kauri), there is nonetheless a whakapapa link between them. Thus, it is the relationship between animals and plants that is key. This is important to bear in mind when considering the scientific, ethical and social issues associated with the use of animals in research and teaching.

Mauri

Mauri is a prominent concept in Māori thinking, as it refers to the life force of an entity (Morgan, 2006), it is the attraction, or binding force, between the physical and the spiritual (Barlow, 1991) and is vital essence in the web of connections that sustains life (Hikuroa et al., 2018). Without this attraction, livings things die and inanimate entities (e.g. soil and water) lose their ability to support life (Morgan, 2006). It thus follows that mauri is important to protect, because without mauri, there is no life (Hikuroa et al., 2018).

One of the aims of kaitiakitanga is conceptualised as restoring or revitalising mauri (e.g. Hauraki Māori Trust Board, 2014; Hauraki Gulf Forum, 2014). Kaitiakitanga is the ethics and practices of managing our relationships with the Taiao, the environment of which we are a part and upon which we depend, derived from the guiding principle of maintaining intergenerational balance between the needs of people and those of the Taiao. It is an obligation to maintain the lands, forests, waters and their inhabitants to which Māori whakapapa and to which we are intrinsically joined.

In a practical sense, Māori of course caught and ate fish, birds and other animals, harvested wild and tended plants and crops in gardens. These activities were undertaken within a 'user-privileges' framing, not an 'ownership' model, and as soon as the privileges were entertained and exercised, there came with it consequent kaitiakitanga responsibilities. Mauri was a key consideration when it came to making decisions about working with anything, animals included.

Taonga species

In conservation work, much focus has been on 'keystone species', those with disproportionately large effect relative to their abundance (Power et al., 1996) or key indicators of ecological health, whose absence indicate poor health, e.g. torrentfish or our endemic Leiopelmid frogs. I have often heard taonga species used in discussions of keystone species and ecological health indicators, as a synonym for them both. If the similarity being drawn was 'importance', then it would be correct. However, I often hear taonga species being used interchangeably for keystone species and ecological health indicators, and I believe this is an incorrect use. A species is considered a taonga based on the relationship people have

with it, and the value they place on it. Accordingly, although taonga species can be keystone species, e.g. tui and their fertiliser coated seed dispersal or ecological health indicators, the criteria for being taonga is how valued a species is. Tuna are a taonga for my people in Waitomo, but are not necessarily good indicators of ecological health or even water quality, being able to withstand very poor quality water. In another example, we have taro in our maara kai at Waipapa Taumata Rau University of Auckland adjacent to Tanenuiarangi, our wharenui on Waipapa Marae. We consider this taro a taonga because it comes from the genetic stock from the garden at Aotea Harbour that was established by Whakaotirangi, wife of Hoturoa, captain of the Tainui waka. Although there is some overlap, in general, taonga species vary markedly between iwi. Thus, whether something is a taonga species is an important consideration for ANZCCART.

Tikanga

Tikanga Māori has become a common term in our world today, but understandings of what it means vary considerably (Mead, 2016). Simply put they are a Māori way of doing things, spanning correct procedure, custom, habit, lore, method, manner, rule, way, code, meaning, plan, practice, convention, protocol and are the customary system of values and practices that have developed over time and are deeply embedded in the social context (Māoridictionary.co.nz). Tikanga derives from the root word 'tika', meaning 'to be right' and thus tikanga focuses on the correct way of doing something, deals with right and wrong from a Māori worldview, firmly embedded in mātauranga Māori (Mead, 2016). Tikanga are acknowledged as Māori customary law, as a means of social control, the Māori ethic, a normative system, principled and pragmatic (Mead, 2016). Tikanga also encompass the reason, the motive, the intent, the purpose for doing something, focusing as much on the reason, as well as the things we do. Although tikanga can be prescriptive, they are always values-based; hence, whatever is prescribed is intended to uphold values. There can also be variability in how tikanga are practised, but with the same intent to uphold values, to 'do the right thing'. Hence, when we practise tikanga we do so because we want to 'do the right thing', not because of a fear of breaking rules or being caught.

Thus, when considering the scientific, ethical and social issues associated with the use of animals in research and teaching, I think the key questions to bear in mind are:

- Why are you doing it?/Why do you want to do it?
- What are you doing?/What do you want to do?
- What are the mauri implications?
- Are the animals taonga species? What is their whakapapa link to other animals and plants?

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Openness to difference in Māori philosophy

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Introduction

The term 'Māori philosophy' provokes how 'philosophy' is understood, just as the phrase 'Māori science' challenges key understandings of 'science' and demands an openness to fundamental or philosophical difference. The scholarly encounter between Māori and Western forms of knowledge has been dominated by the struggle to claim and disclaim 'Māori science' – a binary struggle, which, going by current debates, is arguably doing more harm than good (Stewart, 2021). Pairing a 'cultural' word such as 'Māori' with a strong knowledge noun like 'science' – so that the cultural term modifies the epistemological term – produces a two-word phrase that acts like a conceptual or philosophical provocation, or conundrum. Such a phrase works more like a thought experiment than a simple, natural or scientific concept or category.

One alternative to the intransigent 'Māori science' debate is to consider Māori knowledge as a local form of **philosophy**: a theorisation of Māori language and culture (Stewart, 2020b). To see Māori knowledge as a local form of philosophy takes the focus off 'scientific knowledge' and towards Māori values and concepts as a framework for right action based on cultural understandings of a Māori reality. This move reduces the relevance of the empirical knowledge base of science, and allows Māori knowledge and value concepts to provide a useful alternative to typical Western frameworks. A Te Ao Māori framework reflects a genealogical, dipolar cosmos, described below (Salmond, 1978).

I delineate Māori Philosophy as a contemporary, critical, Māori-centric approach to studying Māori knowledge (Stewart, 2020a). This approach calls out the influence of Agnotology (Proctor & Schiebinger, 2008) on dominant commonsense notions of what is factually and ethically correct. To stake a claim for Māori Philosophy is an assertion of difference that challenges the universalism of the academy and dominant views of knowledge. In creating New Zealand in Aotearoa, the British relied on distortions of science, e.g. Social Darwinism, and a handful of lies taught in schools for generations (Bell, 2004; Pearson, 1990). The 'truth' as Pākehā understand it is based on this 'handful of lies': that Māori wiped out the Moriori; that no 'full-blood Māori' have lived for many years; that Māori were lucky to be colonised; and that everything English/European is superior to all things Māori, which are inferior by definition. These ideological distortions of truth are like 'thought weapons'. British colonial intention was never to exterminate Māori but to assimilate Māori, which entailed a philosophical extermination.

A Māori Philosophy approach recognises and resists symbolic levels of Māori colonisation that operate by suppressing and appropriating Māori language and symbolic culture. Māori Philosophy is therefore a politically aware and activist Kaupapa Māori approach to studying Māori knowledge (Hoskins & Jones, 2017). Māori Philosophy asserts the philosophical rights of Māori people to think as Māori, with Māori cognitive resources. Māori Philosophy is a Kaupapa Māori form of philosophy of education (Stewart, 2017). The next section presents a synopsis of Te Ao Māori as a framework for understanding reality and ethics.

Te Ao Māori as a framework of philosophy and ethics

A sense of Māori Philosophy as a 'different' worldview (i.e. different from the normal mainstream) rests on, among other things, a Māori sense of the self, and a Māori conceptual model of reality/the world, so it makes sense to address these two big ideas. In terms of a Māori sense of the self, while 'tinana' is the dominant modern Māori word for body, 'waitahi' is an older word meaning the body that has fallen out of common usage. Wai literally means water and it seems relevant (in terms of psychic/environmental forces) that 'hau' or wind/air also has metaphysical meanings relating to the movement of spiritual energies. This word 'waitahi' for the physical body makes a complementary combination with 'wairua' (soul, spirit, astral body) and the use of 'wai' to refer to personal identity: *ko wai tō ingoa?* means what is your (singular) name? and *ko wai koe?* means who are you, singular? The idea emerges of a dual Māori sense of the self, consisting of the first or physical part, waitahi, and the second or metaphysical part, wairua, of a personal identity.

This binary identity concept maps well onto another recorded Māori tradition concerning the nature of the self: that the human being is conceived when te ira atua and te ira tangata collide in the body of the mother. Individuals who receive slightly more of te ira atua turn out to be male and those who receive slightly more of te ira tangata turn out to be female.

There are also two parts to Māori identity relating to the two aspects of the idea of 'te ao Māori' – either the pre-European world, frozen in time by the British invasion of Aotearoa, or the continuously changing post-contact Māori world, which co-exists with te ao whānui, the wider world. Pairs of Māori terms that express this binary are: 'te ao tawhito' (the ancient world) and 'te ao hurihuri' (or 'te ao hōu', the changing world, the new world); 'nō neherā' (from a long time ago) and 'nō nāianei' (these days); 'i mua/muri i te taenga mai o te Pākehā' (before/after the arrival of Pākehā).

Whakapapa is how Māori people introduce themselves to each other, and how they understand themselves and other people, a major topic of Māori conversation. Whakapapa is the master concept of a Māori worldview and ethics. Whakapapa is key to Māori views of both the self and the world, and for guiding right relationships between people, and between humans and other living and non-living things. In traditional Māori society, whakapapa knowledge was of both economic and social value as the basis of an individual's identity, rights, residence, status, occupation, companions and life partners. Whakapapa is like each person being a knot within a large and ever-expanding metaphorical fishing net of connections, in contrast with the modern economistic view of individuals as more like atoms of an inert gas, moving freely and randomly within the available physical limits.

The Māori creation stories or nature narratives operate as theories about reality and philosophies that give rise to ethics and values to guide behaviour (Alpers, 1996; Reed, 1967). The Māori nature narratives are not 'myths and legends' as they are known throughout scholarship and books written by Pākehā. The stories of the genealogical universe provide an underpinning theoretical framework for empirical Māori knowledge of the world and natural phenomena, taking the role played by scientific theories in modern culture.

As well as being based on a genealogical or whakapapa model of reality, te ao Māori is a world of binaries or polarities that operate at many different levels, from cosmic through to the everyday physical dimensions, to psychological, spiritual and philosophical levels. This binary nature of Māori reality is similar to concepts found in other Indigenous models, such as Yin Yang, the basic Taoist concept. The Māori world is profoundly metaphoric: in te reo Māori almost every lexical word can be used at many levels – literal, metaphorical and philosophical. The Māori cosmos is structured by foundational 'oppositions' or poles (pou), formed by pairs of attributes including ora/mate (life/death), tapu/noa (sacred/profane), ao/pō (day/night), and many others (Salmond, 1978). These pou are like the spokes of a spinning bicycle wheel, an image for the spiral nature of Māori time. Centred between the pou as represented by the hub of the bicycle wheel is the pae, described as "the threshold, liminal zone that mediates the main oppositions" (Salmond, 1978, pp. 15–16). The word 'pae' or 'paepae' has a range of literal meanings relating to 'edge' ideas including horizon, circumference, and horizontal beam. In the dipolar model of the Māori cosmos the pae is the zone of life, in which humans have moral agency to exercise will and act in the world.

Whakapapa is visually represented in Māori iconography by the double helix spiral motif seen in elaborate carved works such as the prow of a large ceremonial waka (canoe) or carved posts in the whare nui (large houses). There are two spiral forms in Māori art, and hence in Māori thought: the common koru, or simple spiral, inspired by the furled baby fern frond, signalling growth of all kinds; and the takarangi or double helix spiral, which represents whakapapa and also time, and therefore space-time, since the word wā was originally used for both, showing the unity of space and time in the Māori worldview. Each notch in the carved double spiral represents a generation; such carved items were used as physical mnemonics for teaching, learning and keeping whakapapa. Whakapapa is also a way of reckoning long periods of time, based on the inexact unit of a generation. The unusual double helix shape that represents whakapapa coincides with the shape of the DNA molecule in a remarkable convergence given DNA is the literal manifestation of whakapapa, in the sense of one's biological inheritance, and that which causes a person to resemble their forebears.

Whakapapa in its full range of meanings showcases the characteristic preference of Māori thought and discourse for spiral structures, rather than the typical linear structure favoured by Western notions of knowledge, particularly in logic, mathematics and science. The spiral shape and multi-layered concept of whakapapa are metaphors for the great family of Rangi and Papa. In other words, Māori bodies of knowledge take the form of whakapapa and its accompanying stories. Whakapapa in a general sense is also a concept, a value and a way of thinking, both a noun and a verb: "Māori use of whakapapa and narrative creates a 'metaphysical gestalt' or whole, integrated pattern, for the oral communication of knowledge" (Roberts *et al.*, 2004, p. 1). In this way, the concept of 'whakapapa' acts like a one-word synopsis, metonym and hologram of a complete indigenous worldview, comprising the cultural narratives that structure and keep in place all the related Māori concepts and values.

The rich indigenous concept of whakapapa is the key point of difference between Māori philosophy and Western philosophy, each understood on their own terms, that causes theoretical incommensurability or disparity between them. The concept of the relationship between humans and the natural world in Māori philosophy is whakapapa, as the above paragraphs have established. The corresponding Western concept is referred to in the Bible as humans having 'dominion over' animals and nature. In defining the essence of 'technology' Martin Heidegger (1999) describes a fundamental attitude of 'enframing' in Western culture towards nature; in other words, seeing the world in terms of our own needs and wants, and regarding natural resources as 'standing reserves' to use up at will. These attitudes are built into language, with the modern meanings of words including 'resource', 'interests', 'sustainability', 'management' and so on being tied to economic profit in economistic thinking.

Māori concepts build on from the basic ground of whakapapa. Mana and tapu are two key philosophical Māori concepts, impossible to fully understand and hence prone to distortion, in the absence of an overall appreciation of the indigenous Māori worldview. Mana is approximated by power, authority or prestige, while tapu is equated to sacred, or set apart. These two words (or their cognates) are also found in related Pacific languages. Tapu (in Tongan, tabu) was appropriated into English as 'taboo' by James Cook after a voyage to Tonga, an example of how the Age of Discovery harvested cognitive as well as material/biological resources for extending European systems of knowledge. Today, both words, tapu and mana, are borrowed intact into New Zealand English.

The next level concepts are widely known as the triadic key Māori values of tika, pono and aroha (Stewart *et al.*, 2021). This formidable conceptual triad provides a useful ethical framework by which Māori society judges and is judged by its people. Tika is the basis of tikanga, or doing what is right according to a Māori worldview. Pono is being honest and truthful and seeking after truth, which is the central mission of science and a university. Aroha superintends both tika and pono; it is described as a 'supreme spiritual power' and the essence of a human/e response to reality/nature and the world/s in which we find ourselves as agentic ethical beings. Aroha is often translated by the single word 'love' or even 'compassion' but any one-word translation inevitably falls far short of capturing such an expansive concept.

The strength and vitality of the individual and group in relation these basic ethical dimensions is referred to as their mauri, hau, ihi, wehi, etc. The concept of 'utu' has been reduced to 'revenge' but actually means 'balance' in returning to the holistic complementary nature of the Māori cosmos. The point is that no big idea in Māori or any other cultural tradition can adequately be translated into one English word. To understand any Māori value, therefore, it is necessary to understand the nature of the overall Māori worldview.

Regardless of 'good intentions' any attempt to impose alien frameworks on Māori knowledge is bound to be deleterious to Māori interests. Unfortunately this 'imposing' approach is the major way in which scientists seek to engage with Māori people, knowledge, language and culture, as demonstrated by the recent *Listener* letter (Clements *et al.*, 2021; Stewart, 2021). This presentation includes a plea to mainstream science researchers to learn more about Māori knowledge, and how it has been consistently distorted in mainstream discourse, before jumping on the racist bandwagon represented by that letter.

Conclusion:
Staking a claim for Māori Philosophy

Māori Philosophy is a Kaupapa Māori way of thinking by Māori people who have no interest in becoming Pākehā, but rather in holding Pākehā scholarship and research to their own standards; parrying the ideological truth weapons embedded in Kiwi culture and the national imaginary of Pākehā New Zealand. Māori Philosophy is a protest and resistance against the sustained attack posed by colonisation on my philosophical rights to think Māori, to think as a Māori and to think with Māori cognitive resources. Māori Philosophy is a unifying meta-theme for considering how to add Māori ideas and examples into mainstream courses and programmes. Kia ora mai tātou katoa.

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Animal research: Time to talk

Kirk Leech
Executive Director, The European Animal Research Association

Global Changes in Communicating Animal Research

- There is global cultural change underway under which the Biomedical research community have adopted policies and practices to improve public understanding and acceptance of animal research.
- This cultural zeitgeist of **Openness and Transparency on animal research** stretches from Europe to the United States, and at this conference shows to New Zealand with Australia soon, involving both private and public research
- In my talk I want to show:

1. **Why these changes have occurred**
2. **What actual changes in policy and practice are taking place**
3. **How openness can help convince even those often reluctant to be associated with animal research to do so.**

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Modern Challenges

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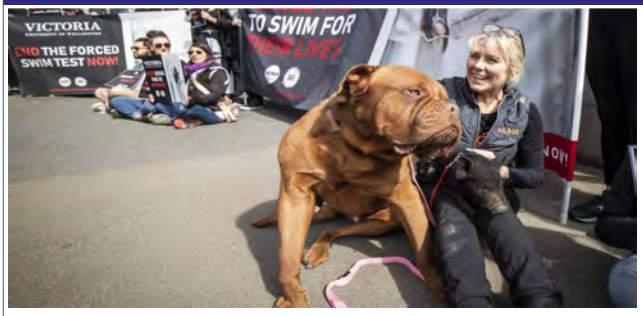
Communications & Campaigning



Professional organisations

Registered as NGOs and charities

Effective campaigners

Clear messaging

Animals Australia
the voice for animals

Cruelty Free INTERNATIONAL Donate

GAIA Voice of the Voiceless

PETA ANIMALS ARE NOT OURS
to eat, wear, experiment on, use for entertainment, or abuse in any other way.

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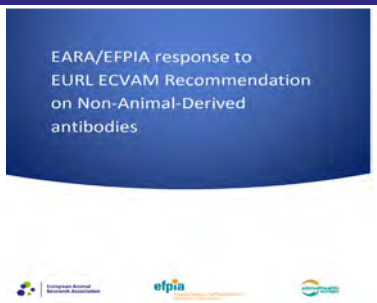
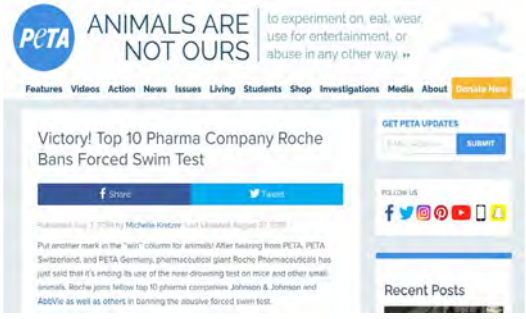
Communications & Campaigning

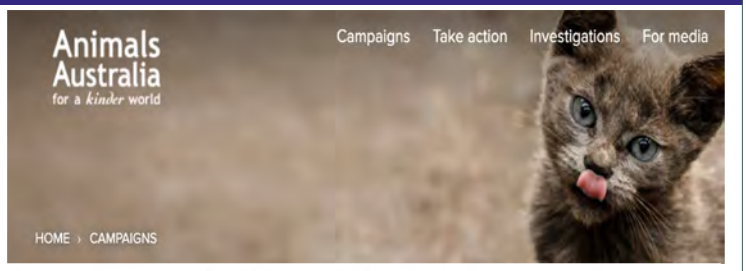
These are likely to be peaceful and will include:

- Activist groups **publicising the fact that animal research is taking place at your facility,** with statistics on the number and/or species used.
- **Online petitions or high-volume phone and mail campaigns** targeting individuals, criticising their animal research.
- Encouraged by activists the **media may seek your comment** on a story or a media release
- **Peaceful protests outside your facilities**,

Scientific and Regulatory Challenges







7 big secrets about primate experiments in Australia

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Reputational Challenges
Undercover films

European exposures

- Imperial College: **UK**
- Max Planck Society: **Germany**
- National Veterinary School: **France**
- Vrije Universiteit Brussel: **Belgium**
- Biomedical Primate Research Centre: **Holland**
- LPT: **Germany**
- Vivotecnia: **Spain**

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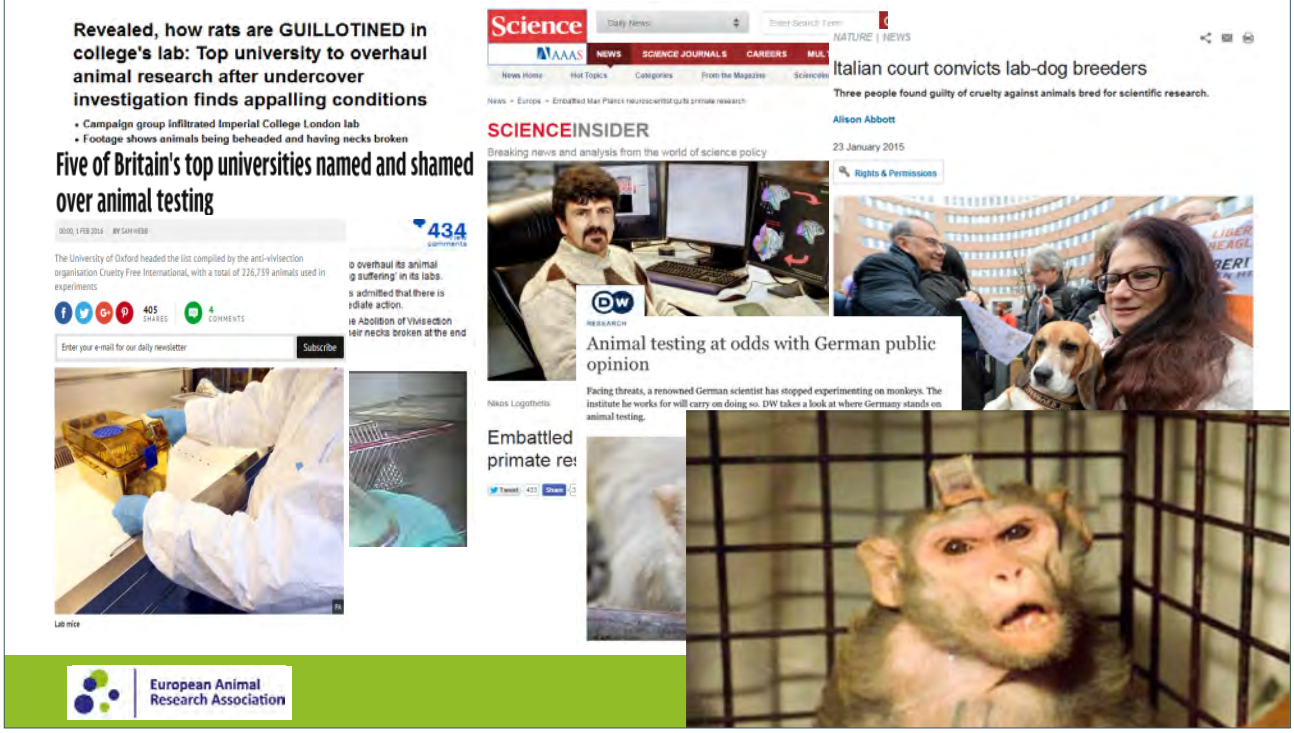
Trust Challenge

What the public sees



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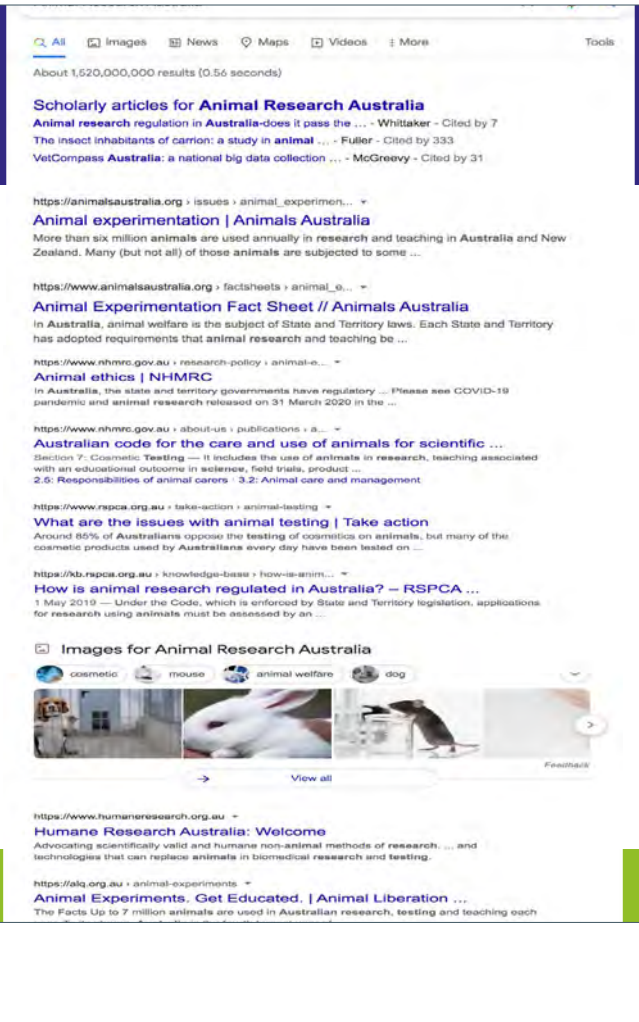

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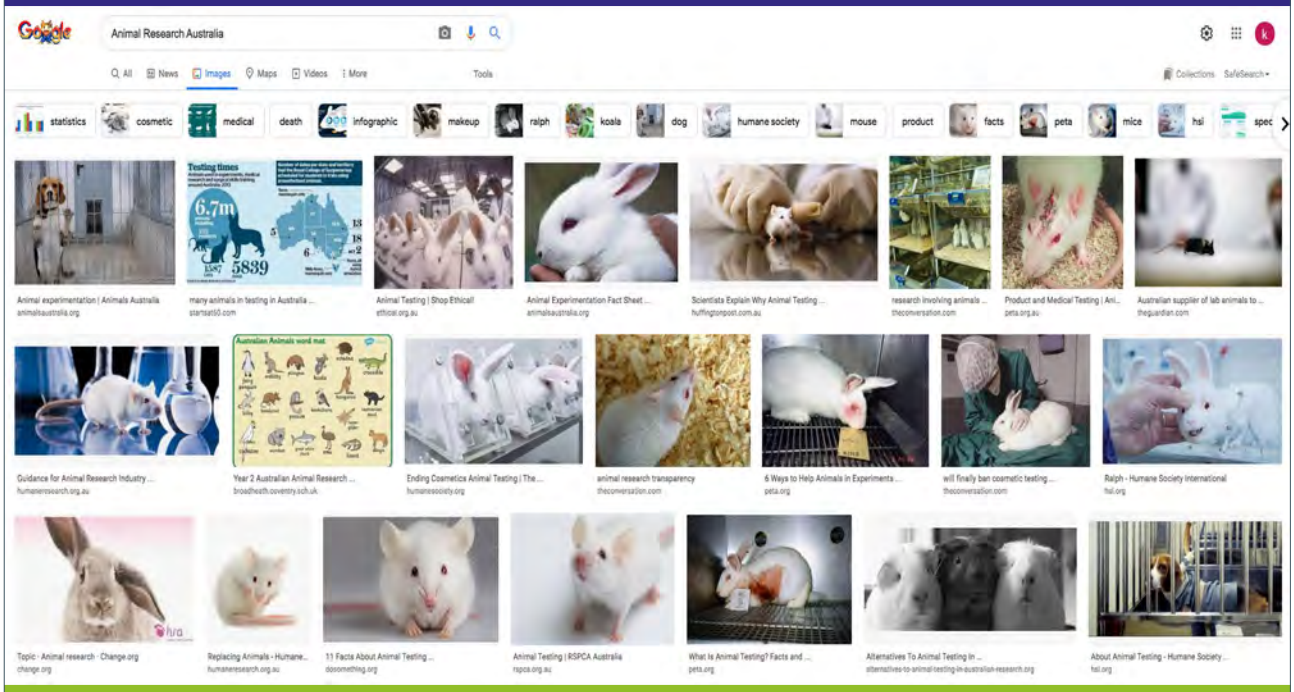
Images
Animal Research Australia



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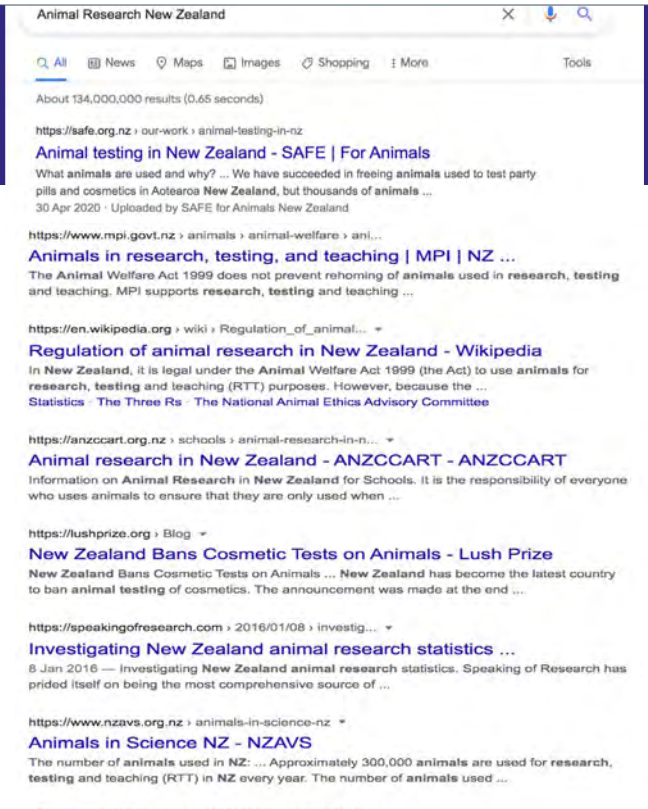

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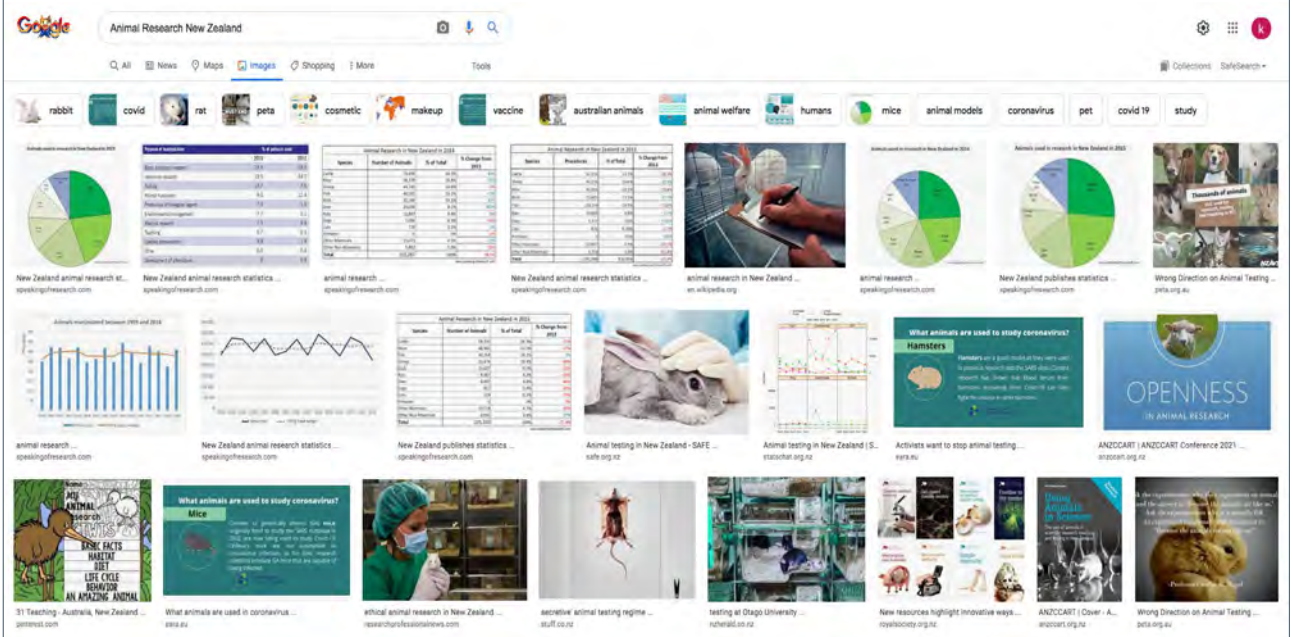
Images
Animal Research New Zealand



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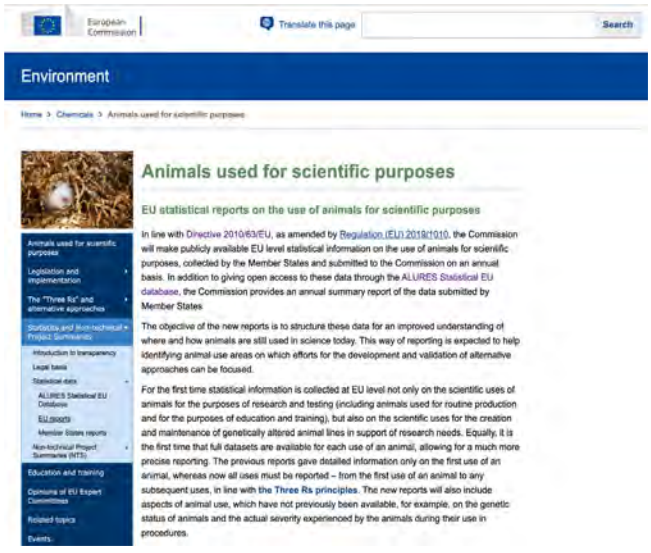
EU Commission Animal Use Statistical Reports 2021



- The European Commission was not traditionally proactive in disseminating animal use statistics
- EARA had long encouraged it to go beyond just publishing the reports, to take a more proactive communications approach.
- Last year they did, held a media briefing, and publishing a report that sets a high bar for openness, **species-> severity-> purpose**
- EARA supported these moves and we proactively communicated the statistics n ways to improve public understanding.
- Last week the Commission released the statistics for 2018 for the whole of the EU

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EARA Media Campaign on the 2021 EU animal use statistics

- EARA produced over **150 infographics** for use on social media.
- **Messaged in over 12 languages** explaining and contextualising the animal use statistics.
- Produced **case studies of animal research** from the countries which we knew have the largest animals use and those with EARA inspired Transparency Agreements.
- **Distributed media releases** to the top five science/health journalists in every European country.
- **This was a tremendously successful campaign**. The European biomedical research sector ensured that its messaging was heard first, before that of the activists who took **4 days to respond** to the statistics
- **We saw no negative media.**

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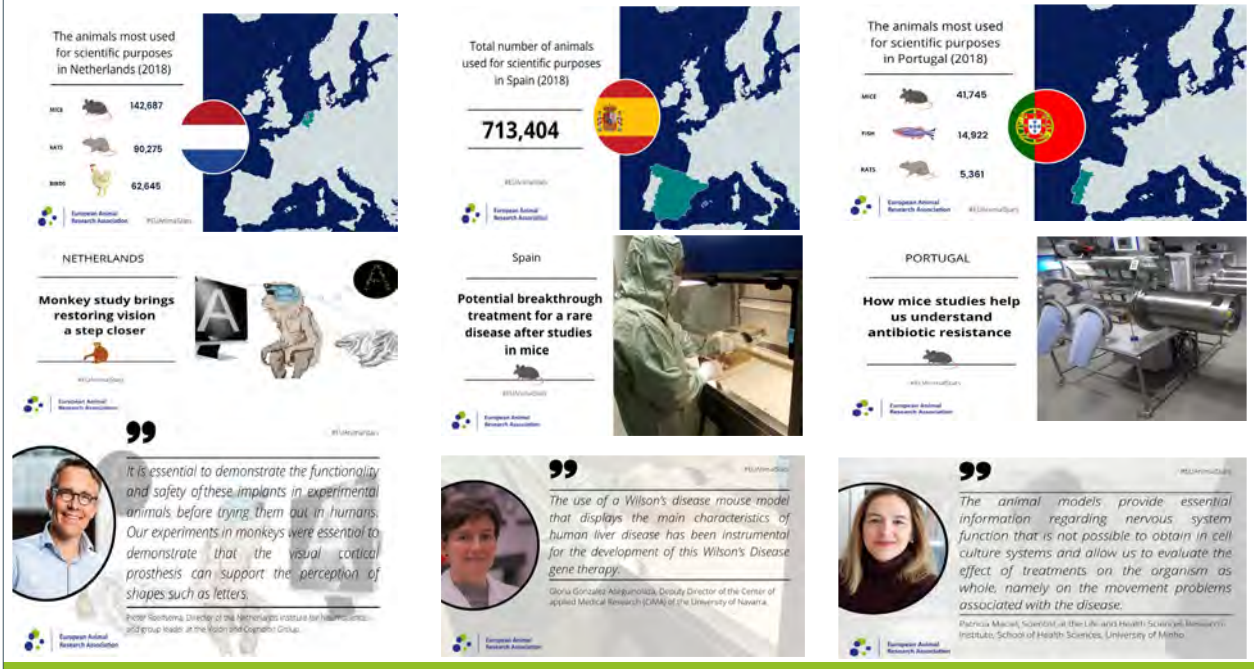
Country -> Case Study-> Quotes from a Named Researcher



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Turkey

Greece

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Media Releases

Key elements of a proactive communications approach to the public

1. **Transparency agreements** to promote greater public awareness about animal research
2. **Institutional website support** to help Institutions communicate their research effectively
3. **Social media platforms** to highlight the benefits of animal research and to counter fake news
4. **Media training for our members o**n communications strategies, crisis management and dealing with the media

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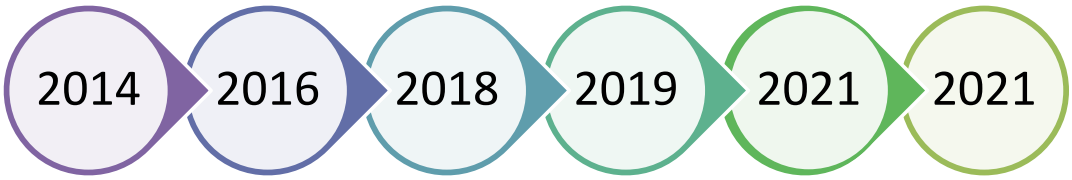
Existing Transparency Agreements



UK (127) **Spain (144)** **Portugal (18)** **Belgium (19)** **France (30)** **Germany (54)**

There are 392 European institutions covered by six national agreements

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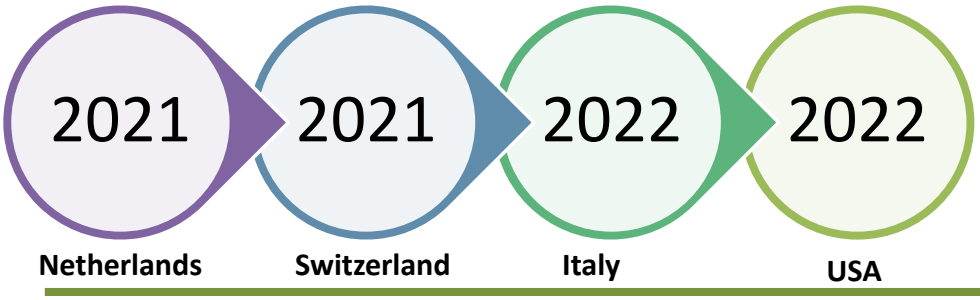
Future Transparency Agreements



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#BOARD21

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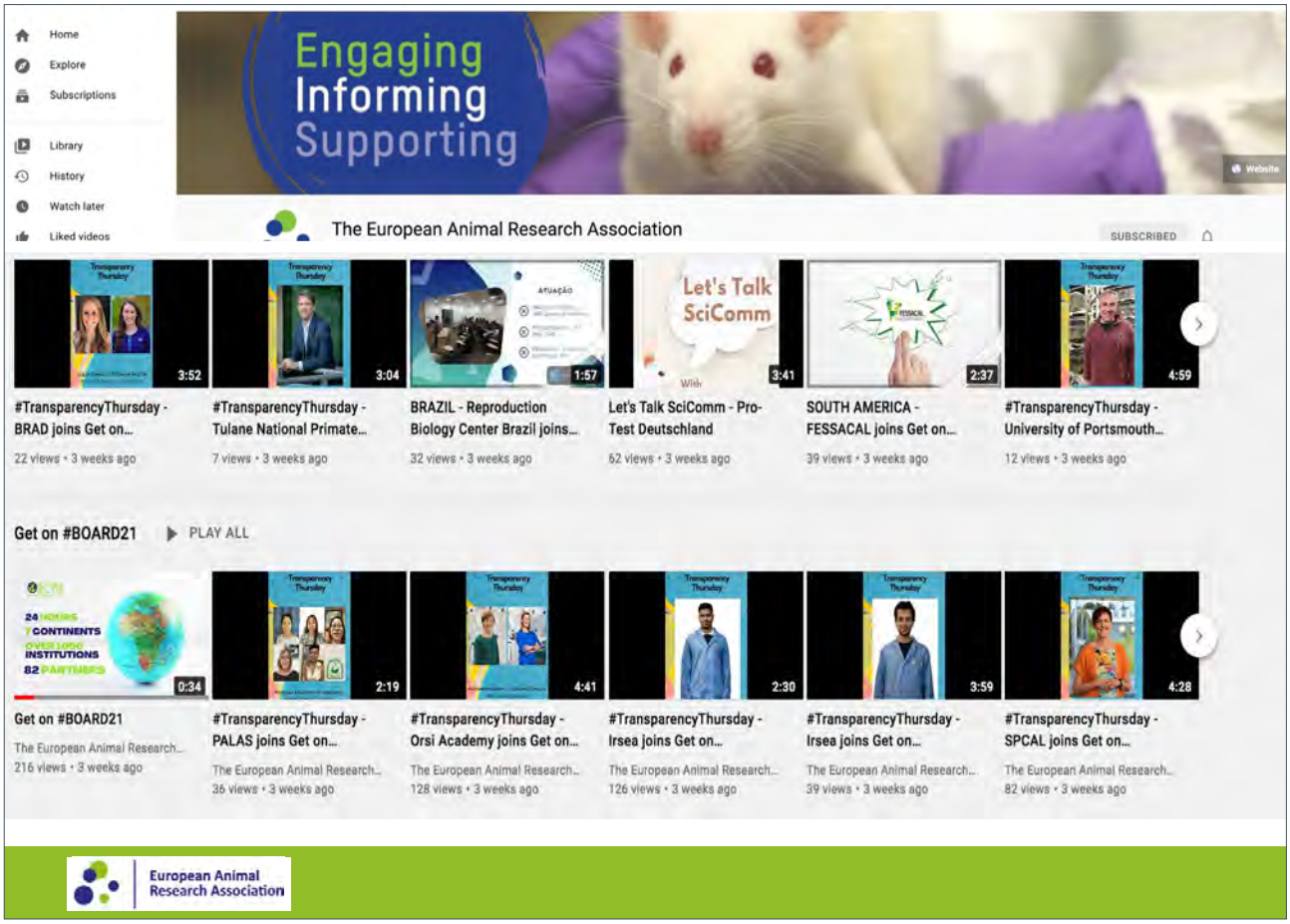
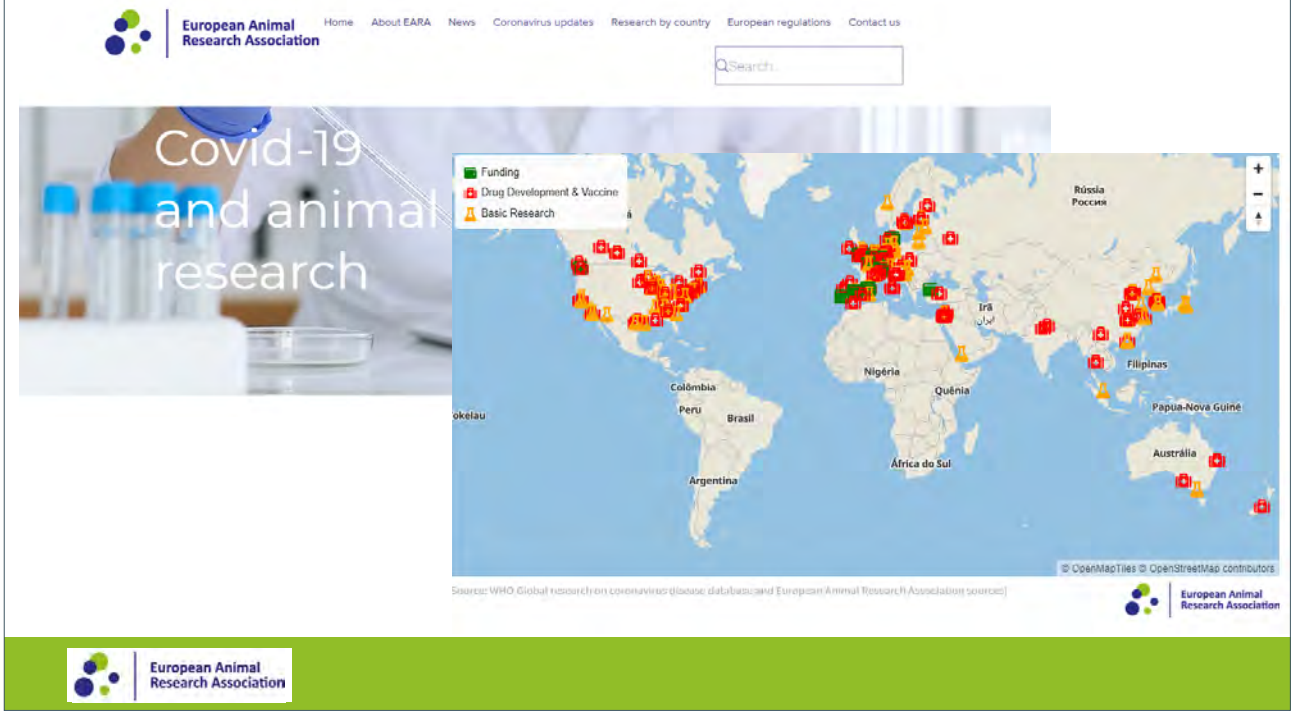


Covid-19 and Animal Research



Raising awareness
EARA News Digest

European Animal Research Association

EARA News Digest 2020 - Week 25

Welcome to your Monday morning update, from EARA, on the latest developments in biomedical science, policy and openness in animal research in Europe and around the world.

See EARA's Coronavirus updates

Research

Study uses three types of monkey to understand Covid-19 infection

US researchers have shown the effects of Covid-19 infection in three different species of monkey.

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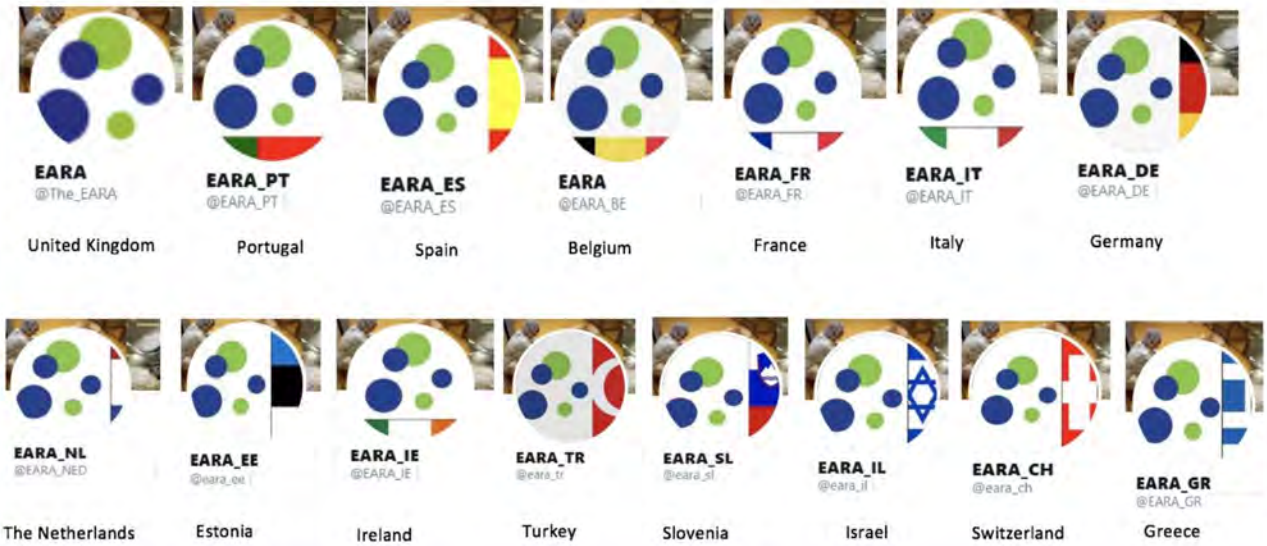
EARA Twitter



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Events and Workshops

Improving Openness in Animal Research

Media Training

Since 2019 we have 85 Events held across Europe

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EARA Institutional Website Support

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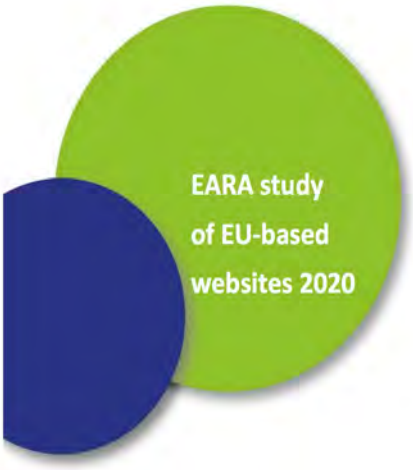

LETTRES SORBONNE UNIVERSITÉ

MAX-PLANCK-GESELLSCHAFT

THE UNIVERSITY OF CALIFORNIA 1868

UPPSALA UNIVERSITET

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The Key Elements of Effective Webpages

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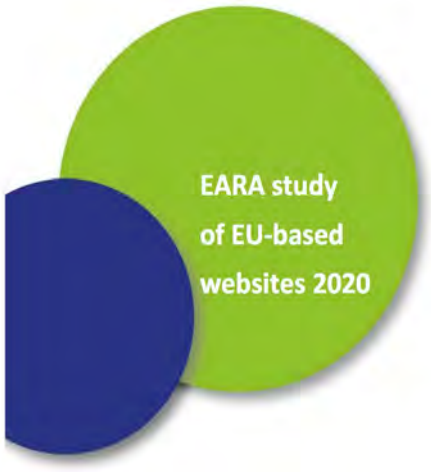

1. Recognisable statement on animal research
2. Statistics about animal use at your institution
3. Images and videos of your research and facilities
4. Case studies featuring the use of animal models
5. Additional information: (Frequently Asked Questions, further detail on animal welfare measures and the 3Rs, plus useful links to other information or organisations, such as EARA)
6. Prominence – how many clicks?

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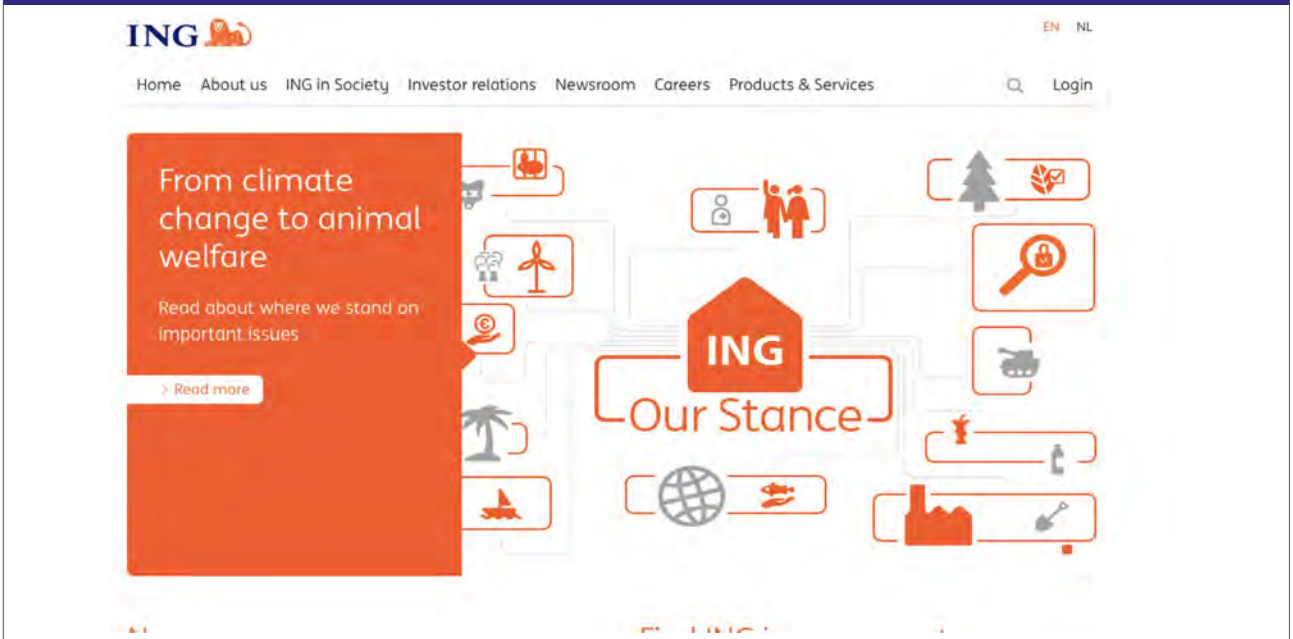
EARA Communications Handbook

Contents

ING Bank Boycott of Animal Research projects



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Dutch Biomedical Primate Research Centre

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China's ban on the export of NHPs for research

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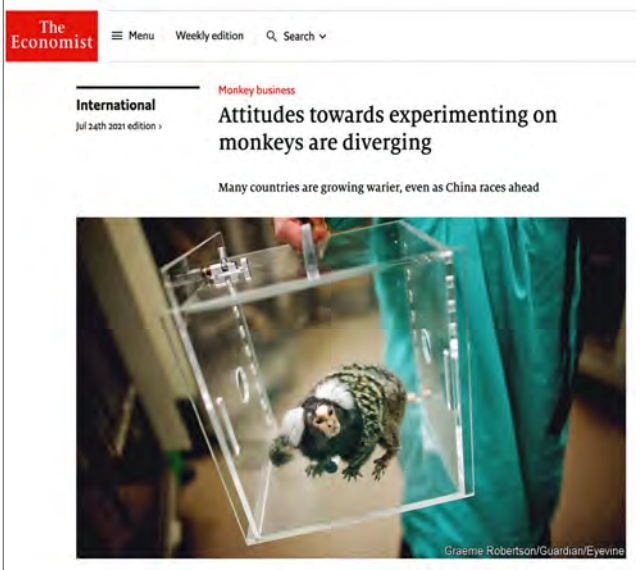
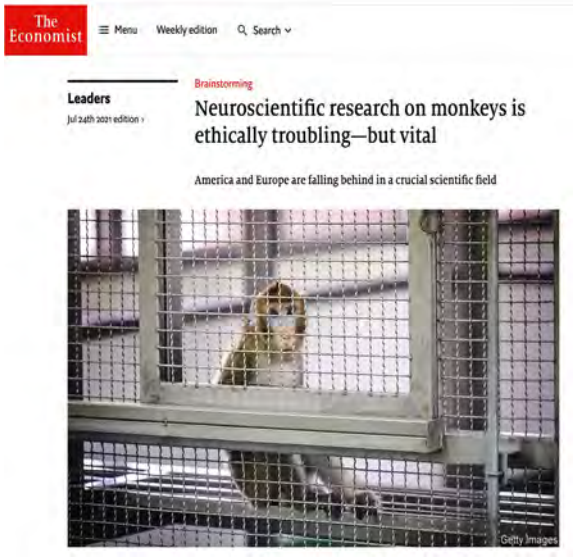
The role of NHPs in Scientific Research





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Collaborate with EARA

- EARA is a membership organisation
- We are open to collaboration with institution outside of Europe
- If your institution is interested in EARA membership
- Please contact EARA – kleech@eara.eu
- Follow EARA on Twitter @kirk_EARA @The_EARA

European Animal Research Association

Development of a transparency (or better said, openness?) agreement in Spain

Javier Guillén
AAALAC International, Pamplona, Spain

Introduction

Europe in general, and the European Union in particular, is the region with the strictest legislation on the protection of animals used for scientific purposes. Increasing transparency on the use of research animals was one of the main objectives declared by the European Commission when revising the legislation some years ago, which resulted in the current Directive 2010/63/EU (https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02010L0063-20190626&from=EN). However, in spite of this strict legal framework, there is a strong and active opposition to the use of animals in research, evidenced in part by the European Citizen´s Initiative "Stop Vivisection" that managed to go through the entire legal process to reach the European Parliament (one of the very few that have achieved this goal) after the publication of the Directive, with the intention of abrogating the Directive and promoting a paradigm shift in the way science is conducted (https://europa.eu/citizens-initiative/stop-vivisection_en). Important to note is that the Directive already states that "the final goal of full replacement of procedures on live animals for scientific and educational purposes", but this seems not to be enough for part of the society.

But in Europe there are also organisations that promote communication and awareness of the importance of animal research. At national level, Understanding Animal Research (UAR) in the UK promoted the first Openness Agreement (the Concordat on Openness on Animal Research in the UK) that was successfully launched in 2014 (https://concordatopenness.org.uk/). At European level, the European Animal Research Association (EARA) is promoting the development of similar agreements in other countries (https://www.eara.eu/transparency-agreements).

Genesis of the Spanish Agreement

In Spain, the initiative was taken by the Spanish Association for Laboratory Animal Science (SECAL), a member of EARA and of the Confederation of Spanish Scientific Societies (COSCE). SECAL was aware that to be successful, the project had to be led by the researchers, the animal user community. Therefore, SECAL promoted within COSCE, with the support of EARA, the creation of a Steering Committee in 2014, which, after the publication of an initial document highlighting the importance of animal research, launched the Spanish Agreement on Transparency on Animal Research. This cooperation between the laboratory animal science and researcher sectors was the key success factor of the Agreement.

The Spanish Agreement

The Agreement was launched in 2016 (https://cosce.org/acuerdo-de-transparencia/), and has basically the same four commitments as the UK Concordat:

1. Speak openly on when, how and why animals are used in research. This is the basic commitment that sustains the rest.
2. Provide adequate information to media and the public on the conditions and outcome of animal research. This refers to basic communication with media and public, trying to use all chances of contact to speak openly. It also includes the only 'tangible' requirement to be a signatory of the Agreement, which is to have a statement in the institutional public website explaining the performed use of animals in research.
3. Promote initiatives to enhance knowledge and understanding by the public. This refers to more active initiatives taken by the institution, such as visits to animal facilities, or talks at schools.
4. Inform on the progress and share openness practices. This refers to participation in the Annual Report.

The Agreement is open to all types of organisations involved in and supporting animal research from both the public and private sectors, including universities, pharmaceutical companies, foundations, contract research organisations, professional scientific organisations and even patient groups. Important to note is that members include organisations using animals and others that don't use them, but support the objectives. There are currently 147 members of the Spanish Agreement.

Process outcome and practical issues

Initially there were some fears and scepticism by institutions; however, the visible leadership of some important researchers overrode the issues and made the rest of the community feel more comfortable with the Agreement. Very likely the outcome would have been different if only the laboratory animal science community (veterinarians, animal care people, etc.) had been the face of it. As noted above, this was likely the key factor of success.

Having 147 institutions in the Agreement is a very successful outcome, but it creates some issues too. For example, there are very different levels of engagement with the Agreement: whereas some institutions are very active, others do the minimum, basically having the public statement in their website. Some even struggle to respond to the Annual Report. What can be done with these institutions? Several of these issues relate to administrative matters (e.g. losing contact with the changing contact persons at institutions) and the management structure of the Agreement, which makes an important difference between agreements developed in other countries. The best example is the UK Concordat, managed by UAR, a professional organisation with staff dedicated to this task. On the contrary, the Spanish Agreement is managed by the COSCE Steering Committee on a voluntary basis. COSCE hosts the Agreement website and the Steering Committee, but cannot provide staff or funds. This makes all administrative work fall on the shoulders of some already busy volunteers (researchers, veterinarians) who have to make extra effort to manage it effectively. Fortunately, EARA is helping every year with the Annual Report preparation and processing.

The participation of non-user organisations also creates the question of their level of engagement and how to evaluate it. For example, when gathering information for the Annual Report, the questionnaire will have to be different for this type of organisation that would not be able to comment on the use of animals or promote a certain type of openness on animal activities.

Overall, Annual Reports produced so far show a very positive outcome of the Spanish Agreement. We could have not believed, when the Agreement was launched in 2016, that a few years later there would be 147 public statements on the use of animals in research available in the respective members' websites. In the most recent EARA survey of European websites of animal research organisations (https://static.wixstatic.com/ugd/e7d918_4654e938dca647f79adf0e2a5a8a0414.pdf), Spain had the highest score with 81% of reviewed websites having a public statement.

There is a unanimous belief in the responses by research institutions that this Agreement has been an important step for the biomedical research community. The Annual Reports show many openness transparency activities that were not happening in the past, such as visits to animal facilities, talks at schools or publication of educational materials (https://cosce.org/informe-anual-2020-del-acuerdo-de-transparencia-sobre-el-uso-de-animales-en-experimentacion-cientifica-en-espana/).

Other practical questions

The terminology used in the Agreement may play an important role. Whereas the term 'openness' seems to be the most appropriate in the English language, its literal translation in other languages may not be the best option due to additional potential meanings and interpretations. Therefore, in Spain, the term 'transparency' is used. But this can also create the erroneous assumption that absolutely everything concerning animal research at a given institution must be known and accessible by the public. We all know that this is may not be the case, as animal facilities cannot work as public zoos for several obvious reasons (e.g. biosecurity and biosafety). Regardless of the term used, this is to be a step-by-step process to make animal research more understandable to the public to facilitate them to have an informed opinion.

Managing an agreement of this sort may be different also depending on the size and complexity of the country. Naturally, the potential issues will grow in relation to the size and complexity of the country and the number of members of the Agreement. There will be more different interpretations, levels of commitment and of course they will require a bigger administrative effort. For example, the initiative promoting an agreement in the US is being developed cautiously following a well-defined plan to encompass all views by stakeholders. Also, the existence in each country of organizations in favour and/or against animal research is a factor to be considered. The example of UAR in the UK is a very good example of how an organization can play a pivotal role in the successful development of such an Agreement in a country with high level of research.

Also, the existence in each country of organisations in favour and/or against animal research is a factor to be considered. The example of UAR in the UK is a very good example of how an organisation can play a pivotal role in the successful development of such an agreement in a country with a high level of research.

It is very difficult to evaluate the impact of the Agreement in the public perception of animal research. Private polls are extremely expensive, and those routinely performed by government authorities focus very little on this aspect.

Conclusions

The Transparency Agreement in Spain has made many institutions/investigators become aware of the importance of communicating animal research to the public thanks to the collaboration of laboratory animal science professionals and research animal users.

Already 147 Spanish organisations have posted a public statement on the use of animals in research on their websites.

Annual reports show a clear increase in openness activities that did not take place before the Agreement.

However, there is still a long way to go to reach the public effectively. Only a coordinated and convincing effort may yield positive results in the public opinion. Organisational matters have to be carefully considered to avoid problems during the implementation phase of an openness/transparency agreement.

How AAALAC accreditation might be integrated into New Zealand's oversight system for the use of animals in research, testing and teaching

Virginia Williams
Animal Welfare Consultant

What is AAALAC?

- Association for Assessment and Accreditation of Laboratory Animal Care International
- AAALAC International is a private, nonprofit organization that promotes the humane treatment of animals in science through voluntary accreditation and assessment programs.
- >1000 institutions in 49 countries accredited

Some history..

- In 2008, Dr David Bayvel of the then Ministry of Agriculture and Forestry – now MPI – supported a visit by AAALAC's Dr Kathryn Bayne, mainly because of a perception that, despite the quality and effectiveness of the New Zealand legislative framework controlling the use of animals in RTT, some institutions, particularly those with international connections, might wish to further their reputation for humane animal care – indeed, for those applying for NIH funding, accreditation with AAALAC provides a distinct advantage.

What are the differences?

- AAALAC – voluntary programme leading to an internationally recognised accreditation – seen as a peer review but doesn't have legal status

- New Zealand's oversight system is a statutory requirement under our animal welfare legislation.

Standards

- AAALAC
  - The *Guide for the Care and Use of Laboratory Animals*
  - The *Guide for the Care and Use of Agricultural Animals in Research and Teaching*; and
  - The European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes, Council of Europe (ETS 123).

- New Zealand
  - Animal Welfare Act 1999, [specifically Part 6 of the Act which relates solely to the use of animals in RTT] and Regulations
  - *Good Practice Guide for the use of animals in RTT*
  - *Codes of Ethical Conduct plus Guide*
  - *Animal use statistics*
  - *Approved codes of ethical conduct*

Frequency

Photo UAR

- Reviews in New Zealand are required every five years – a newly constituted organization is reviewed within two years
- AAALAC requires three yearly reviews

Perth 2019 3

Reviewers

Photo UAR

AAALAC

- Council member
- An *Ad Hoc* consultant
- Fees paid by AAALAC

New Zealand

- Five independent reviewers
- Four of the five are veterinarians; the fifth is a scientist
- Selected by institution being reviewed
- Reviewers negotiate payment and expenses with the relevant organisation

ANZCCART, 2021

So where are the similarities or conjunctions?

- Focus on the ethical and appropriate use of animals
- - and so - focus on the Three Rs
- Animal Care and Use Program = Code of Ethical Conduct and Checklist
- Appropriate oversight by the IACUC/Animal Ethics Committee

The pre-visit process

- AAALAC requires a detailed description of the Institutional Care and Use Program prior to the inspection
- This is reviewed by AAALAC prior to the visit
- In New Zealand, individual reviewers:
  - carry out a desktop audit of the Code of Ethical Conduct
  - review the AEC minutes from the previous five years, and
  - select up to 15 protocols of varying severity to examine closely

The visit

- Attend AEC meeting
- Meet with members, particularly external
- Meet selected researchers
- Meet animal care staff
- Visit selected facilities/farms/animal holding areas

Differences?

AAALAC

- Occupational Health and Safety of Personnel - more focus on this within AAALAC

New Zealand

- For work involving hazards, was the advice of the organisation's biohazards committee sought, and were appropriate procedures for containment, disposal and decontamination established?

- Photo Patrick Smith

Reporting - New Zealand

- Report from reviewer to code holder within 15 working days
  - Critical situations
  - Non compliances
  - Recommendations
  - Commendations
- Response from code holder within 15 working days
- Final report to code holder, NAEAC and Director-General within 5 working days

ANZCCART, 2021

Reporting AAALAC

- Site visit team prepares report which includes proposed accreditation status
- Report uploaded for review and discussion by assigned Council reviewers and two Council Officers
- Site visit team responds to reviewers' remarks, may seek additional information from Unit Contact, revises site visit report as needed
- Council convenes to deliberate on site visit report and formally votes on accreditation status of unit
- Accreditation letter is prepared and reviewed by President of Council before being sent

Advantages of accreditation

Particularly for those institutions with international connections, a greater degree of harmonisation in the quality of care provided to experimental animals and the animals' welfare status can be achieved.

Advantages of accreditation

- The resultant minimisation of variables and greater reproducibility of results and statistical significance of data, and hence greater comparability of studies, is important in an era when international collaborations are increasingly common in the scientific world, including the contracting in and out of projects and the greater number of multinational corporations.
- NIH funding

Not for every institution…

- New Zealand institutions reported an average of around 310,000 animals used for RTT in the last 3 years
- In 2019, 50 percent of these were farm animals, mostly cattle and sheep, 98% returning to their normal lives on farm
- 13 organisations used more than 10,000 animals in 2019
- 28 organisations used fewer than 100 animals
- In 2019, there were 28 animal ethics committees and a further 107 organisations that are "parented" by an AEC
- Medical research made up 14 per cent of all animals in 2019

So how might integration look?

- While the approach is somewhat different, there is much that is complementary between the two systems
- The main problems?
  - How to reconcile a five year gap with a three year gap?
  - Financial considerations – a combined system?
  - Most suitable for larger organisations with overseas links?
  - Time constraints

Where are we now?

- While positives can be seen, concerns have been raised about yet another layer of audit, raising the possibility of combining AAALAC audits with our own system in some way.
- Thirteen years on, one university (at least?) has accreditation on the radar

ANZCCART, 2021

Challenging the status quo: Openness in animal research and the use of annual animal statistics

Nicole Clark
Animal Ethics Manager, The University of Sydney

We acknowledge the tradition of custodianship and law of the Country on which the University of Sydney campuses stand. We pay our respects to those who have cared and continue to care for Country.

Challenging the status quo

openness in animal research and the use of annual animal statistics

THE UNIVERSITY OF SYDNEY

Why concern for animal statistics report?

Australian Regulation of Animal Use in Science and Education: A Critical Appraisal

Aaron C. Timoshanko, Helen Marston, and Brett A. Lidbury

Statement:

Australia was the fourth highest user

(of animals used for scientific purposes)…behind the United States, Japan and China

Globally, it is estimated that 126.9 million animals were used for scientific and educational purposes in 2005.

(2016)

The University of Sydney

Why concern for animal statistics report?

The Sydney Morning Herald: Millions of animals around Australia subjected to experiments and surgery

Statement:

More than six million animals including baboons, dogs, cats and native mammals are being used every year in Australia for medical research.

Nearly 6000 dogs and more than 1500 cats were also used and a NSW government report showed that some exotic zoo animals had been the subject of experiments that involved "minor pain".

(2016)

Why concern for animal statistics report?

The Guardian: Australian supplier of lab animals to close, sparking fresh debate about use of mice and rats in research

Statement: "Australia does not yet publish national animal research and teaching statistics. Humane Research Australia used to try to collate the data, but stopped doing so in 2018 because of a lack of reporting of this data by state and territory governments."

(2021)

But… What is the use in reporting animal research and teaching statistics, if:

1. **No one around the world reports in the same way?**
2. **Numbers are reported without simple definitions of what the data means?**

Definitions of what is being reported

1. Definition of a "protected animal"
2. Definition of a "procedure"
3. What is actually reported in way of animal usage report

Although a "protected animal" is defined, and a "procedure" is defined, this does not mean that these animals/procedure are reported on, it only means it is regulated.

Images sourced from Understanding Animal Research

Definition of an animal?

All living vertebrates except man

(or a variation of this wording in each country's legislation)

+ cephalopods

UK

– animals >⅓ through gestation or incubation period or able to feed independently

Australia

– Generally: animals >½ through gestation or incubation period

– NOTE: Victoria includes decapod crustaceans, SA excludes fish

US

– In short, only warm-blooded animals

– Excluding rats, mice, and birds (& other research, e.g. poultry & livestock where the use is for improving animal nutrition)

– Does not include – All living vertebrates except man

Definition of a procedure?

UK

– any test, experiment or other procedure which may cause them pain, suffering, distress or lasting harm which is equivalent to, or higher than, that caused by the introduction of a needle in accordance with good veterinary practice.

Australia

– all activities conducted with the aim of acquiring, developing or demonstrating knowledge or techniques in all areas of science, including teaching, field trials, environmental studies, research, diagnosis, product testing and the production of biological products.

US

What is & is not counted?

UK

(only count animals which may feel pain, suffering, distress or lasting harm)

– Animals are protected >⅓ through gestation or incubation period. But…

  – *If those animals are not born or hatched, then animals are not counted…*

Australia

(count all animals involved in any research or teaching)

– Animals are protected >½ through gestation or incubation period. So…

  – *Even if the animals are not born or hatched, then animals are counted…*

What is & is not counted?

UK

(only count animals which may feel pain, suffering, distress or lasting harm)

– Animals humanely killed with no procedure performed

(e.g. tissue collection/excess breeding stock)

– *No 'procedures performed' – animals are not counted…*

Australia

(count all animals involved in any research or teaching, even if pain, suffering, distress or lasting harm is not felt)

– Animal humanely killed with no procedure performed

(e.g. tissue collection/excess breeding stock)

– *No 'procedures performed' – animals are counted…*

What is & is not counted?

UK (now count per procedure, not per animals)

– Count an animal at the end of the procedure

– A study run October 2020 – December 2020:

– Counted once (in 2020)

– A study run November 2020 – January 2021:

– Counted once (in 2021)

Australia

– Animal counted each year it is alive in a project

– A study run October 2020 – December 2020:

– Counted once (in 2020)

– A study run November 2020 – January 2021:

– Counted twice (once in 2020 and once in 2021)

General observation

UK

- Focus on animals in biomedical research
- What reporting is there for wildlife field studies, observational studies, livestock nutritional, privately owned animals cats & dogs, poultry nutrition
- Although define an "animal" and "procedure" – do not report on all of these

Australia

- Focus on all research
- Report on wildlife field studies, observational studies, livestock nutritional, privately owned animals cats & dogs, poultry nutrition
- Define an "animal" and "procedure" AND report on all of these

Currently…

- We all aim for the same outcome:

  Open about animal research, reduce animals, improve animal welfare & robust science

  Good welfare = Good science

  = Benefit animals, humans & the environment

- Currently, it is difficult to compare across countries, and makes me hesitate to be open:
  - We all define differently:
    - Protected animal
    - Regulated procedure, manipulation
    - How we report animal numbers (what is and is not included)

I do not believe we should currently be reporting animal numbers involved in research until we define the use and value of this data

We need to consider our audience in openness! What questions are we trying to answer?

- Why are we gathering animal usage numbers and what message are we trying to convey with this data?

- We need to also consider:
  - Who is the audience? (the general public, community)

  - What do the public already know? (when they think of research, Biomedical research is all that comes to mind)

  - How can we provide this information that is clear and concise so it can not be misconstrued

How can we standardise this across countries? Follow the UK?

The University of Sydney

Nicole Clark, Animal Ethics Manager
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THE UNIVERSITY OF SYDNEY

Thank you

Perspectives on Australian animal and human research ethics frameworks

Tim Dyke
Chair, Animal Ethics Committee, La Trobe University; Chair, Animal Ethics Committee, The Walter and Eliza Hall Institute; Consultant, OmniAdvisory Consulting

Gordon McGurk
Chair Royal Brisbane and Women's Hospital Human Research Ethics Committee; Chair, Human Research Ethics Committee, University of Queensland; Director, OmniAdvisory Consulting

OUR EXPERIENCE

OmniAdvisory

LA TROBE UNIVERSITY

RBWH Royal Brisbane and Women's Hospital

NHMRC

WEHI brighter together

THE UNIVERSITY OF QUEENSLAND AUSTRALIA

OmniAdvisory

INTENTION

To show broad similarities between Australian ethical frameworks for human and animal research

To show differences between the ethical frameworks

To promote discussion about possible improvements to ethical frameworks

To be of interest to
- AEC members, particularly Category C and D members
- Research governance and ethics officers

KEY DOCUMENTS AND METHODOLOGY

SIMILARITIES

Both national documents that guide research in Australia
Ethical oversight across research life
Responsibilities of institutions, ethics committees, researchers (and animal carers – Code)
Independent decision making of ethics committees
- Each member and committee forms a view as to whether a research project is ethically acceptable and complies with the relevant standard

Principles guide design, review and conduct of research
- Respect
- Risk versus benefit
- Monitoring over research life cycle

Ethics-committee approved documents are single point of truth for how research will be conducted
Numerous supporting documents and guidelines e.g. GCP for therapeutic goods

RESPECT

Australian Code

Respect for animals must underpin all decisions and actions involving the care and use of animals for scientific purposes

National Statement

Respect is central…. each human being has value in himself or herself, and that this value must inform all interaction between people.

ETHICALLY - RISK / BENEFIT ANALYSIS

Australian Code

- Guiding principles include
  - Scientific integrity
  - Support wellbeing
  - Avoid or minimise harm, pain and distress
  - Replace, reduce and refine

National Statement

- Guiding principles include
  - Research merit and integrity, justice, beneficence, respect
  - Informed consent

LEGAL BASIS

Australian Code

Adopted *in toto* by State and Territory law including institutions, researchers and AECs

National Statement

Certain obligations of HRECs under Therapeutic Goods Act, Guardianship Acts, Privacy Acts

General obligations of individuals and organisations - guardianship, privacy

NON-COMPLIANCES

Australian Code

Institutions must have procedures for addressing non-compliance with Code

Notification of government regulators

National Statement

Protocol and GCP deviations to be reported to sponsor

If serious (affecting human subject protection or reliability of trial results) – root cause analysis, implement Corrective and Preventive Actions

CATEGORIES OF RESEARCH

Australian Code

- ‘One size fits all’
- No research exempted from review or involving no more than low risk

National Statement

- Some research exempt
- Some research (if no more than low risk) considered by mechanisms other than HREC

ETHICS COMMITTEE STRUCTURES AND PROCESSES

Australian Code – Animal Ethics Committees

- Requirements under State and Territory law
- 4 types of members (veterinarian, researcher, animal welfare focus, community)
- Meeting and decision-making quorom requirements

National Statement – Human Research Ethics Committees

- Requirements by NHMRC only
- 5 types of members (lay, professional care, community pastoral care, lawyer, researchers)
- Minimum membership attendance required but allows for views of absent members to be considered if not minimum membership attendance

COMPETENCE OF RESEARCHERS

Australian Code

2.1.8 Institutions must ensure that they …provide…certification of competence to the satisfaction of the AEC

2.4.4 Investigators must: ……. (v) undertake education and training, and competency assessment, in accordance with institutional and AEC policies and procedures (vi) ensure that procedures using animals are performed competently

2.4.8 Investigators must be satisfied that …..procedures are performed competently, by people competent for the procedures or under the direct supervision of a person competent to perform the procedures, and provisions are made for the education, training and supervision of people nominated on the application, as appropriate

National Statement –

Research that has merit is "by persons or teams with experience, qualifications and competence that are appropriate for the research"

POSSIBLE CODE IMPROVEMENTS BASED ON COMPARISONS

Consider 'no more than low risk' category e.g. observational studies

Better guidance for risk - benefit analysis

AEC membership requirements

Improved management of non-compliances

Getting out of the lab: The development of a free-range learning apparatus for pigeons (FLAP)

Damian Scarf
Department of Psychology, University of Otago

Acknowledgment

The development of FLAP was supported by a Ministry of Primary Industries (MPI) and ANZCCART (Australian and New Zealand Council for the Care of Animals in Research and Teaching) Aotearoa New Zealand Three 3Rs Award Research Grant. Information in the award can be found at: https://www.mpi.govt.nz/animals/animal-welfare/animals-research-testing-teaching/the-3rs/

Introduction

In simple terms, comparative cognition is the study of animal minds, with the aim of providing insight into the building blocks of the human mind. The first scholars of comparative cognition firmly believed in a *scala naturae*, according to which humans represent the apex of cognitive evolution. Non-human primates were thought to occupy the second rung on this 'intelligence' ladder, a position that was supported by neuroanatomical studies demonstrating that apes had relatively large brains. Not surprisingly, birds were several rungs down from primates, with a relatively small brain and an anatomical structure that looked very different to the primate brain. Over the last three decades, however, researchers have demonstrated that, although different in structure, the important areas of the primate brain (e.g., the prefrontal cortex) have a functional equivalent in the bird brain (Güntürkün, 2005; Jarvis *et al.*, 2005). Given this, scholars in comparative cognition raised the question: if the important areas of the primate brain have a functional equivalence in the bird brain, can birds display a comparable level of intelligence to primates?

With the above question in mind, one might be tempted to seek out corvids as experimental subjects. Indeed, comparative cognition research with corvids has rapidly grown in the past decade, with Emery (2006) noting that corvids had displayed abilities that "...are qualitatively and quantitatively more sophisticated than have been demonstrated by other birds, and in many domains comparable to monkeys and apes" (p. 23). Aotearoa New Zealand, however, is home to only one corvid species, the rook (*Corvus frugilegus*). Unfortunately, rooks very difficult to catch and, in Aotearoa New Zealand, they are considered a pest species, making the possibility of getting permission to breed the birds for research an unlikely prospect. The next obvious choice would be the kea (*Nestor notabilis*). However, comparative research is typically conducted in a tightly controlled laboratory setting and one that is not appropriate for a protected species. With rooks and kea ruled out, the humble pigeon tends to be bird of choice for comparative psychology in Aotearoa New Zealand.

Pigeon cognition

When working with pigeons, the first hurdle is demonstrating that they possess the potential to display cognitive abilities that are on par, or at the very least approximate, the cognitive abilities of primates and, by extension, humans. Two domains on which primates have demonstrated remarkable abilities, and which young children display an innate ability to acquire, are numeracy and literacy. With respect to numeracy, humans display competence across three concepts, quantity (i.e., cardinality), rank (i.e., ordinality), and counting (i.e., nominal/labelling). Obviously, in the absence of language, counting is beyond the grasp of non-human animals. Quantity and rank, however, can easily be tested in non-human animals and both abilities were initially demonstrated in only primates (Brannon & Terrace, 1998; Chen et al., 1997). Similarly, with respect to literacy, learning to read involves the acquisition of letter-sound relationships (i.e., decoding skills) and the ability to visually recognise words (i.e., orthographic knowledge). Much like counting, in the absence of language, decoding skills are human unique. In contrast, the ability to visually recognise words, and the statistical properties that underlie them, was recently demonstrated in non-human primates (Grainger et al., 2012).

Surprising to many, we have been able to demonstrate that the humble pigeon displays a comparable understanding of quantity and rank (Scarf & Colombo, 2011; Scarf et al., 2011) and orthographic processing (Scarf *et al.*, 2016) to non-human primates. Rather than a simple circus trick, in each study we were able to show that the performance of pigeons mirrored the intellectual signature of primates. For example, in distinguishing words (e.g., have) from gibberish (e.g., vhea), the performance of pigeons increased as the bigram frequency of the words increased (Vinckier et al., 2011). That is, the more frequently certain letter pairs were in the pigeons' vocabulary, the more accurate they were in responding to them. Second, the performance of pigeons on gibberish increased as their orthographic similarity to words increased. Orthographic similarity was measured by calculating each non-words' (Levenshtein, 1966), which is the number of changes (e.g., substituting letters in the non-word) required to turn a non-word into a word. For example, to change the non-word DMET into the word DONE, would require substituting letters M, E, and T, for letters, O, N, and E, respectively (i.e., three substitutions). Finally, the pigeons were presented with a transposed-letter test. The test consisted of presenting subjects with words in which the order of the internal letters was transposed (e.g., DONE transposed to DNOE), essentially turning them into non-words. Similar to humans, pigeons showed a tendency to misclassify transposed non-words as words. Thus, beyond discriminating between words and gibberish, pigeons displayed response properties that demonstrate they are utilising a similar orthographic-processing mechanism to non-human primates.

Tapping the limits of the pigeon's profound intelligence takes time. For example, in the study just described, pigeons required approximately a year and a half of training. Like most comparative cognition research, they were tested in laboratory setting, devoid of the social (e.g., pair bonding) and physical (e.g., flying) experiences that may be required for normal cognitive development. Although proving a high level of experimental control, a lab-based approach has two major downsides. First, with respect to animal welfare, it prevents pigeons from being able to display normal patterns of behaviour. Second, it may actually impair both learning and memory, making it difficult to get an accurate picture of their cognitive potential. Indeed, we have known for a long time that animals housed in complex and enriching environments display higher levels of cognitive than those housed in standard laboratory conditions (Fares *et al.*, 2013; Fischer, 2016).

Current approaches

With animal welfare, enrichment and efficiency in mind, a number of studies have investigated the efficacy of using automated testing systems (Clark, 2017; Cronin et al., 2017; Egelkamp & Ross, 2019; Washburn, 2015). Typically, these approaches have involved automated testing systems that, while reducing time investment required by the experimenter, still involve the animal being individually housed within a laboratory (Berger et al., 2018; Butler & Kennerley, 2019; Huber et al., 2015; Perdue et al., 2018). Further, studies that have investigated the efficacy of automated systems in a group living environment have exclusively used non-human primates as their experimental subjects (Fagot & Bonté, 2010; Fizet et al., 2017; Gazes et al., 2013).

The best example in this area is CNRS Primate Centre in France, which houses social groups of Guinea baboons (Claidière et al., 2017; Fagot & Bonté, 2010). As shown in Figure 1, the baboons are housed in a large outside area and have free access to 10 Automated Learning Devices for Monkeys (ALDM). The baboons access the devices through a narrow and short tunnel, such that is it difficult for any more than one baboon to access the device at a given time. The baboons view the

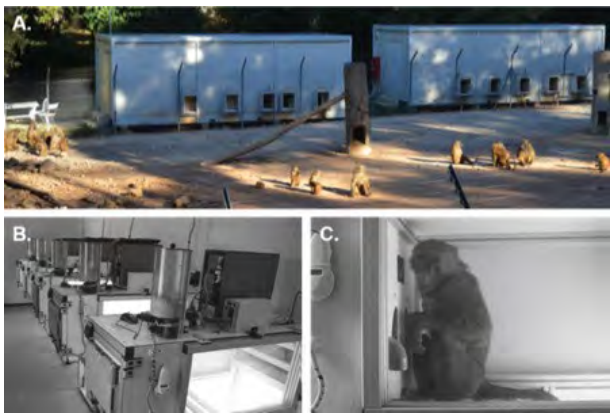

Figure 1. The social living environment at the CNRS Primate Centre (A), including the hardware behind each access port (B) and the individual testing context each port provides (C). Photo A is drawn from Claidière *et al.* (2017) and photos B and C are drawn from Fagot and Bonté (2010).

LCD display and touch screen through a small window, and access the screen by passing their arm through a small port. Each animal is identified by a radio-frequency identification (RFID) tag inserted in their wrist, with the arm port housing an RFID reader. Speaking to the potential of these approaches, the orthographic with non-human primates referenced above was conducted at the CNRS Primate Centre.

Using the CNRS Primate Centre as a model, the overall aim of the current project was to develop a Free-range Learning Apparatus for Pigeons (FLAP). In essence, FLAP allows comparative cognition research with pigeons to be conducted in a natural environment.

Development of a Free-range Learning Apparatus for Pigeons (FLAP)

The loft

The first step when developing FLAP was to create a free-range environment in which we could house pigeons. To this end, as shown in Figure 2, we built a pigeon loft. The loft consists of two areas, one in which the pigeons are housed, and a computer room in which we can house FLAP and the other equipment we use to monitor the birds. The pigeon housing area consists of a 3 by 4 housing grid, with 12 open-fronted boxes where the pigeons can perch, nest, and sleep. Pigeons exit the loft through an Omlet Autodoor™ (Omlet, 2021), which opens at 7am and closes at 7pm, allowing the pigeons to come and go freely during those hours. After 7pm, if the pigeons are still outside, they can enter the loft through a trap (i.e., one-way) door.

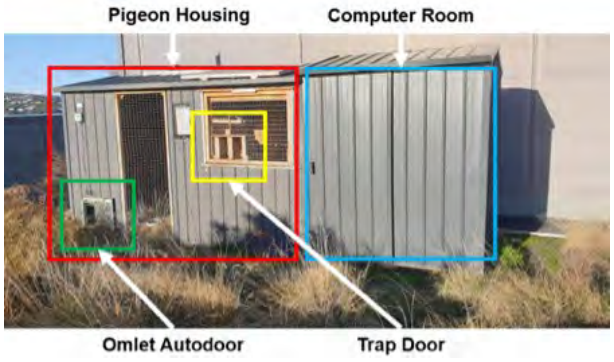

Figure 2. The free-range living environment pigeons are housed in, including the computer room that houses FLAP.

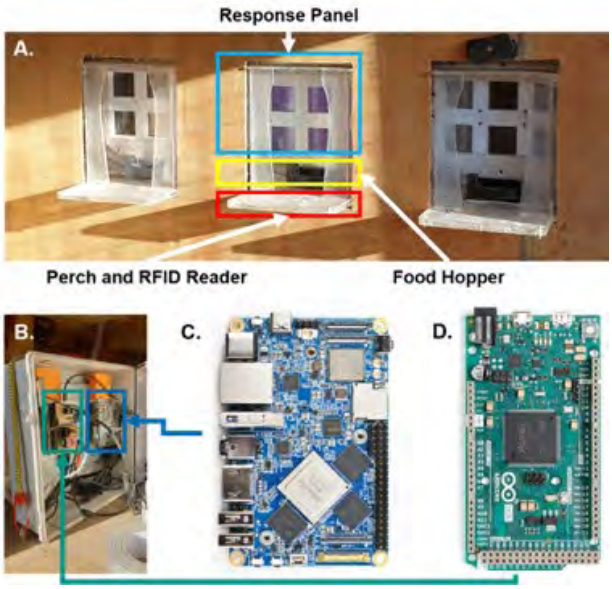

Figure 3. The response panels that face into the pigeon loft (A), behind the response panels is an LCD screen using to display stimuli (B), a NanoPC-T4 used to control the stimulus display (C) and an Arduino Due microcontroller that controls the administration of food (D).

Hardware

Pigeons access FLAP through three interfaces that face into the loft (Figure 3A). Specifically, each interface consists of a platform on which pigeons can perch, which contains an RFID aerial that is used to identify each bird through an RFID leg band. Food access is provided through a hopper using a modified PetSafe Treat and Train™ systems (Amazon, 2021), controlled by Arduino Due microcontrollers (Figure 2C, Arduino, 2021). The response panel consists of a 3 by 2 grid of response buttons. Each button houses several pressure sensors that are used to detect when the pigeon pecks. Stimuli are displayed on each button through a 12-inch LCD panel that is housed directly behind the response panel. The display is connected to a NanoPC-T4 (Figure 3C) that controls the stimulus display and is attached to the rear of the LCD screen (Figure 3B).

Software

The software was built in-house. FLAP is equipped with four pre-programmed tasks (outlined below), with each task including several variables that can be set manually.

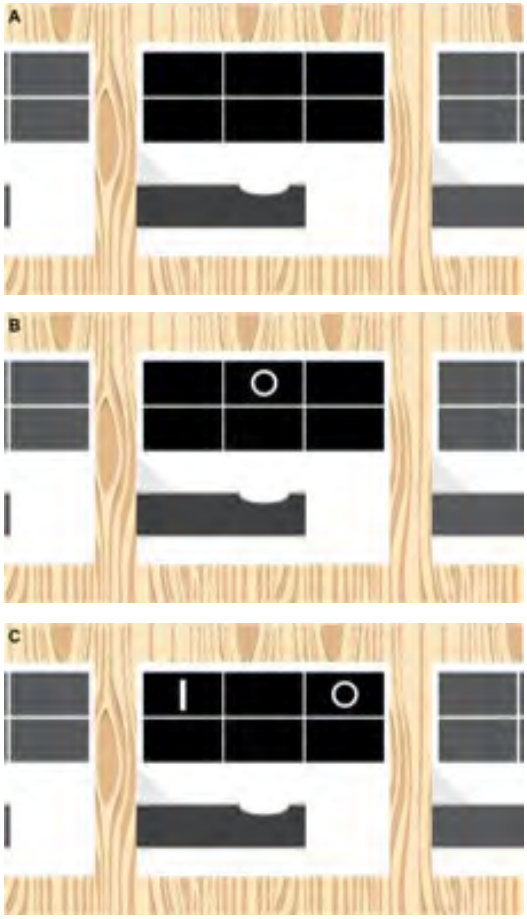

Figure 4. Flow of events in the matching-to-sample task. Specifically, the inter-trial interval (A), sample stimulus presentation (B) and the choice/comparison stimulus phase (C).

Matching-to-sample task

On this task, the animal is shown a sample stimulus, for example, either a circle or vertical line geometric form (Figure 4B). After responding to the sample stimulus two comparison stimuli appear on either side of the sample stimulus, one the same as the sample and the other different (Figure 4C). The animal must respond to the comparison stimulus that is the same as the sample stimulus. Within the programme, the delay between the sample and comparison phases can be manipulated, with longer delays placing more demands on the animal's memory.

Serial-order task

On this task, the animal is presented with a list consisting of *n* number of simultaneously displayed items. The list is trained using the successive phase method. Phase 1 consisted of only the first item (A) appearing, and the subjects are reinforced for responding to it (Figure 5A). In Phase 2, Items A

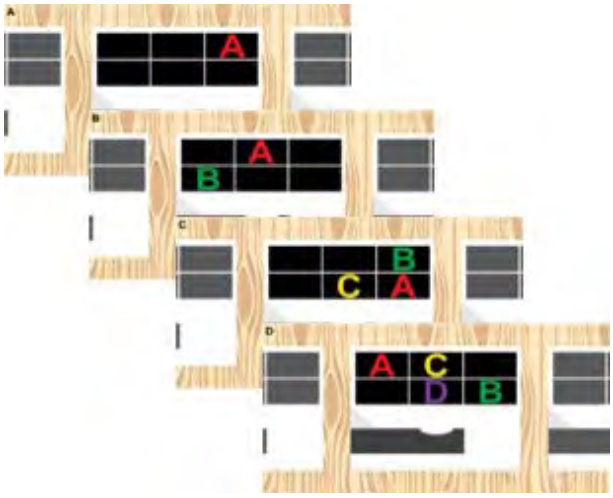

Figure 5. The standard training phases on the serial-order task. Specifically, Phase 1 (A), Phase 2 (B), Phase 3 (C) and Phase (4).

and B were presented simultaneously, and subjects were rewarded for responding to them in the order A > B (Figure 5B). After acquiring the A > B series, subjects are trained on the A > B > C series (Phase 3, Figure 5C) and the A > B > C > D series (Phase 4, Figure 4D). A correct response to an item produces a short tone and, when the entire list is completed correctly, the animal receives a food reward. The criterion between phases can be manually changed within the program. For example, you could set accuracy criterions of 80%, 75% and 50%, for Phases 2, 3 and 4, respectively. The length of the list can also be set between 2 and 6 items.

Discussion

The aim of the current project was to develop FLAP and create a 'lab' in which the pigeons are free range. This environment can be contrasted with the standard lab, in which pigeons are housed individually, food deprived and placed into an operant conditioning chamber to complete their daily training. As noted above, this approach has two major downsides. First, with respect to animal welfare, it prevents animals from being able to display normal patterns of behaviour, a requirement listed in Section 4(c) of the Animal Welfare Act. Second, it may actually impair both learning and memory (Cronin et al., 2017; Drea, 2006). For example, removing an animal's ability to interact with conspecifics may increase stress that, in turn, negatively influences cognitive performance (McEwen & Sapolsky, 1995; Newcomer et al., 1999).

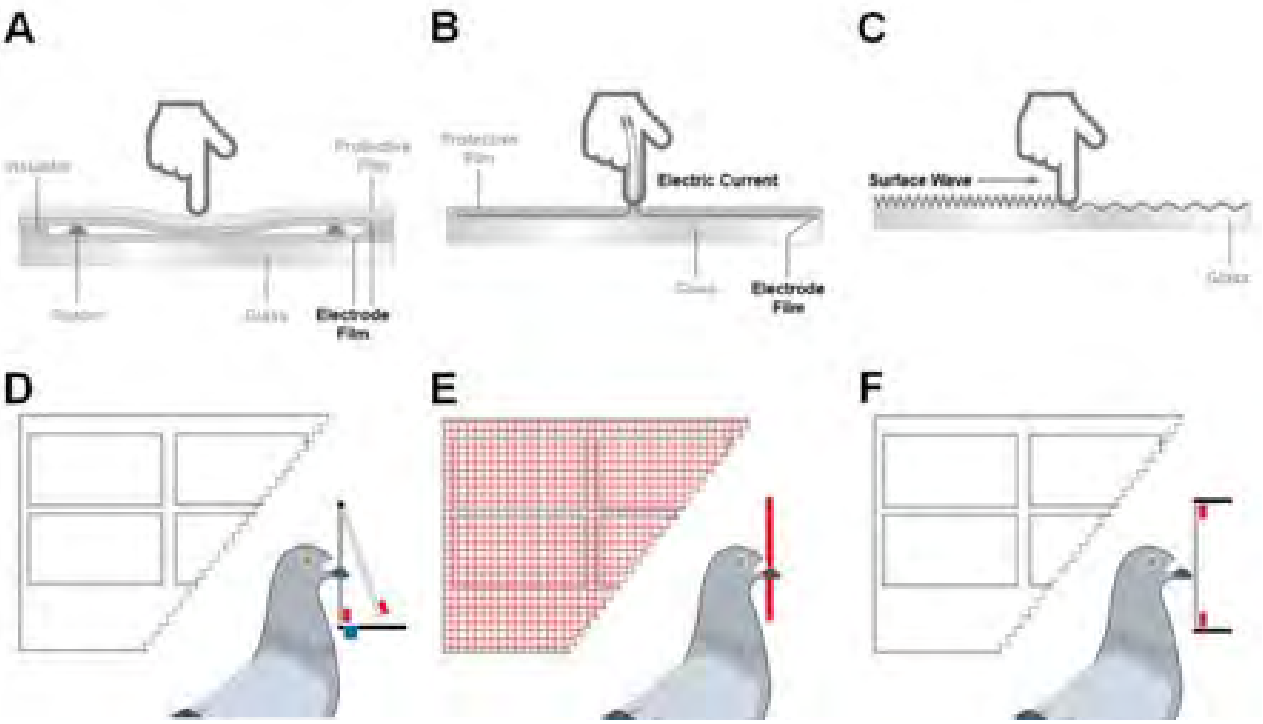

Figure 6. Resistive (A), capacitive (B), and acoustic wave touch screens (C). Flappy key (D), infra-red (E) and pressure sensitive (F) key setups.

Challenges with developing FLAP

Although the final version of FLAP is robust, its development was not without a number of challenges. The most significant challenge was developing the response panel. With non-human primates, the response panel typically consists of an off-the-shelf resistive (Figure 6A), capacitive (Figure 6B), or acoustic wave touch screen (Figure 6C). Unfortunately, these touch screens cannot be used with birds, as the beak does not have the surface area to be effective with resistive and acoustic screens, and does not have the conductance to work with capacitive screens. In a lab environment, pigeons' responses are detected using a key the pigeon pecks, with the key then swinging over a sensor (Figure 6D), or an infra-red beam the pigeon's beak can break (Figure 6E). In a free-range environment, however, these keys were not effective. Specifically, both key-types are vulnerable to material (e.g., food, bedding straw, etc.) becoming stuck and preventing the key from returning to the off position or blocking the infra-red beam. In addition, neither key is shower proof. To solve this issue, we developed a pressure sensitive key, with small force sensors placed on each corner of the key (Figure 6F). The sensitivity of the key can be set, making it flexible for use with different sizes or types of birds. Moreover, because the key relies on pressure rather than movement, the key can be sealed such that it is shower proof.

Conclusion

Although still undergoing testing in the loft environment, FLAP represents the first example of a free-range learning setup that can be used with pigeons. Beyond, pigeons, FLAP also represents a possible enrichment apparatus for captive birds. Indeed, with non-human primates, several zoos have employed touch-screen interfaces as enrichment devices (Egelkamp & Ross, 2019). In addition to enrichment, the devices have also been employed in zoo-based educational programmes, with observation of the animal using the touch screen combined with educational information regarding the cognitive abilities of animals.

In the context of Aotearoa New Zealand, a promising future direction is to deploy the devices with kea (*Nestor notabilis*) and kaka (*Nestor meridionalis*) that are part of captive breeding programmes. These animals are typically held captive for a number of years and, in addition to providing enrichment, the devices have the potential to reveal comparative insights into the building blocks of human cognition.

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Openness between researchers, animal welfare officers, veterinarians, and Home Office inspectors in the UK: Working with the NC3Rs to develop the IMPROVE guidelines

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Abstract

In 2014, the National Centre for the Replacement, Refinement & Reduction of Animals in Research (NC3Rs) in the United Kingdom (UK) convened a Working Group to develop best-practice guidelines for pre-clinical stroke research using animal models. The Working Group consisted of NC3Rs representatives, stroke researchers from both universities and industry, an animal welfare officer, a veterinarian and a Home Office inspector. In stroke research, it is well-documented that experimental drugs that are effective in animal models (mainly rats and mice) have not translated into clinical trial success. However, there is significant variability in how researchers perform their experiments using animal models of stroke, which could have led to this translational failure. Therefore, the Working Group's goal was to create a set of guidelines that stroke researchers could use that incorporated the latest information regarding both animal welfare issues and experimental design. Over six meetings throughout 2014–6, a consensus was reached and draft guidelines were developed. The guidelines were named the IMPROVE Guidelines (Ischaemia Models: Procedural Refinements Of in Vivo Experiments) and were published in 2017 in the *Journal of Cerebral Blood Flow & Metabolism*. These guidelines are now being taken up by pre-clinical stroke researchers across the world. The experience of forming these guidelines and working with people from all aspects of animal research was extremely valuable as consideration was given to differing perspectives and priorities. The openness and strong collaborative effort by all involved contributed substantially to this project's success.

Introduction

Throughout the world, ischaemic stroke is a major clinical and societal problem. Ischaemic stroke is characterised by an abrupt cessation of blood flow caused by a clot within a brain artery, leading to a damaging reduction in cerebral blood flow. Ischaemic stroke is highly prevalent, with 56,000 people in Australia having a stroke every year, and is currently the third leading cause of death in Australia, killing approximately one third of patients who suffer a stroke. Subsequently, another third of stroke patients suffer long-term disability requiring carer dependence. As a result, stroke costs the Australian economy approximately $5b per year (National Stroke Foundation, 2017). These terrifying statistics are not restricted to Australia, but are similar throughout the developed world.

One of the major problems for the management of ischaemic stroke is the lack of treatment options available for patients. Currently, the only treatment strategy for ischaemic stroke is clot removal to restore blood flow back to the brain. The clot can be removed either pharmacologically (using thrombolytics such as recombinant tissue plasminogen activator (rtPA), which break down the blood clot), or surgically (using endovascular thrombectomy to physically remove the clot). Unfortunately, <10% of patients receive these treatments due to the limited time window for administration or the risk of intracerebral bleeding (Emberson et al., 2014). Of the patients who receive these treatments, 55% of patients do not experience improved outcomes (Lees et al., 2016). For the remaining 90% of patients who do not receive blood flow restoration therapy, therapeutic options that promote recovery are currently limited.

In order to develop novel therapeutic options for ischaemic stroke, rodent models of stroke are commonly employed. Over 1,000 drugs have been trialled experimentally for stroke, with many candidate agents showing strong neuroprotective actions in rodent models, but there remains only one approved pharmacological agent used for stroke (rtPA) (O'Collins et al., 2006). This suggests that there exists a translational roadblock for

successful stroke therapeutics to transition from rodent models to human stroke (Howells et al., 2010). Many reasons for this translational failure have been outlined, which include methodological differences between carrying out human clinical trials of stroke and pre-clinical studies with rodent models (Howells et al., 2014; Neuhaus et al., 2014; Sutherland et al., 2012). There are numerous types of stroke models used (Hoyte et al., 2017), but apart from the stroke-prone spontaneously hypertensive rat, all rodent models induce stroke mechanically or chemically, and so do not necessarily reflect how stroke occurs in humans. To induce stroke in these models, a level of surgery is required, which leads to the confounding effects of anaesthesia that are not present during human ischaemic stroke. In addition, various other factors such as species, ages and comorbidities may also account for differences in efficacy of pharmacological agents between rodent models and human stroke (Sutherland et al., 2012).

NC3Rs pre-clinical stroke Working Group

Rodent models of stroke are technically challenging, invasive and require careful monitoring of animals throughout the surgery and post-stroke period given the extensive injury to the brain. However, the monitoring of animal welfare parameters following stroke has been inconsistent between different research groups and institutions, even if the same pre-clinical stroke model has been used. Therefore, due to the variability in which researchers perform stroke experiments pre-clinically, inconsistent animal welfare constraints between groups as well as the lack of translational success with stroke therapeutics, a set of guidelines that incorporated best practice in both experimental design and animal welfare would provide the field with a consensus document to adhere to when carrying out experiments.

NC3Rs is a UK-based organisation that aims to work with the research community to change how animals are used for research and ensure that impacts are made that align with the 3Rs. In 2014, the NC3Rs convened a pre-clinical stroke Working Group that had the following aims: [1] to review the most commonly used rodent (mouse and rat) models of stroke; [2] to identify the animal welfare issues related to these models; [3] to recommend opportunities for refinement of these models; and [4] to publish the deliberations of the Working Group and promote its recommendations within the international stroke research community (Percie du Sert et al., 2017a). The Working Group was led by Dr Nathalie Percie du Sert from the NC3Rs and comprised members from throughout the UK who were involved in all levels of stroke research including academic and industry stroke researchers, veterinarians and animal welfare officers, a Home Office inspector and NC3Rs representatives.

The IMPROVE Guidelines

During the deliberations of the Working Group, numerous issues related to pre-clinical stroke research were discussed. The choice of optimal animal model for ischaemic stroke was raised but no recommendations were made due to the variability in the types of models used and the optimal model depends on the scientific question to be answered. Experimental design of animal stroke studies was discussed but no recommendations were made due to the dependence on the scientific question being answered and other tools that already exist that limit bias and improve quality of the experiments, such as the NC3Rs Experimental Design Assistant (Percie du Sert et al., 2017b). Reporting of animal stroke studies was discussed but similarly no recommendations were made due to this being extensively covered in the ARRIVE guidelines for reporting of all in vivo animal studies, widely adopted by numerous journals (Kilkenny et al., 2010; Percie du Sert et al., 2020). As a result, the Working Group focused on discussions around animal welfare and best-practice requirements for carrying out ischaemic stroke models in rodents. Therefore, the overall aim was to produce recommendations that might reduce the severity level experienced by animals undergoing common ischaemic stroke models, which was hoped to increase the value of the research being undertaken (Percie du Sert et al., 2017a).

Six meetings of the Working Group were held throughout 2014–6. At these meetings, deliberations led to a consensus being reached around key animal welfare requirements that researchers should consider when conducting rodent stroke models. This led to the drafting of the IMPROVE Guidelines (Ischaemia Models: Procedural Refinements Of in Vivo Experiments), a document that extensively outlines the best-practice requirements to maintain animal welfare and limit experimental variability while performing

models of ischaemic stroke in rodents. The IMPROVE Guidelines were published in 2017 in the *Journal of Cerebral Blood Flow & Metabolism*, a leading journal that publishes pre-clinical stroke research articles regularly (Percie du Sert et al., 2017a).

The IMPROVE Guidelines delivered 43 recommendations covering four different aspects of the experimental procedures related to rodent stroke models. The first 15 recommendations, related to the basic requirements before stroke surgery, provided guidance on parameters like acclimatisation pre-stroke, cage enrichment, bedding material, social housing, acclimatisation to post-stroke supplementary diet, food restriction pre-stroke and specific requirements for aged animals or comorbid animals. The next eight recommendations, related to the use of anaesthesia and analgesia while undertaking stroke modelling in rodents, provided considerations for the type of general anaesthetic (inhalational or injectable), the use of local anaesthetics at surgical sites (injectable or topical) and the use of analgesia post-stroke (opioids or non-steroidal anti-inflammatory agents), with indicative doses and routes of administration of common agents presented. The next 12 recommendations, related to considerations for the inter-operative care while performing surgery, provided guidance on aseptic surgical technique, the maintenance of core body temperature, requirements for cardiorespiratory and physiological monitoring, and fluid maintenance during surgery. The final eight recommendations, related to the care of rodents post-operatively, were focused on animal monitoring, assessment of pain and supplementary fluids and diets. These 43 recommendations were compiled onto a single A4 page for ease of display in laboratories that perform rodent stroke modelling (Percie du Sert et al., 2017a).

Post-operative monitoring is one of the key considerations for animal welfare in rodent stroke modelling. Consequently, the Working Group produced a traffic light system to aid researchers in deciding how to proceed while monitoring their animals. Under the traffic light system, green indicated animals that displayed expected signs of stroke should have their monitoring continued as planned. Amber indicated the presence of signs that would be considered worse than expected, and enhanced monitoring and potential intervention should be employed. Red indicated that signs were extremely severe or prolonged, and immediate euthanasia should be considered. This system is useful for researchers inexperienced in observing animals that have had a stroke, and provides a stepwise considered approach in terms of signs to look for and how to act. This provides the stroke community with another resource that is important for improving the health and wellbeing of animals that have had a stroke, ultimately reducing variability and enhancing experimental outcomes.

Conclusions

The NC3Rs convened a Working Group to develop best-practice guidelines for carrying out rodent models of stroke with a focus on animal welfare considerations. The IMPROVE Guidelines have provided experienced stroke labs with a resource to incorporate into their existing practices, while offering new stroke researchers the knowledge needed to ensure animal welfare is maintained while performing these invasive models. This project highlighted how people from all aspects of animal research (academic and industry researchers, veterinarians and animal welfare officers, government regulators and NC3Rs representatives) who bring differing perspectives and priorities can work cooperatively to develop a resource important for the pre-clinical stroke community. This collaborative effort and openness of the Working Group's deliberations contributed substantially to this project's success.

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Opportunities in funding and openness: A follow-up paper to the 2021 ANZCCART Conference

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When the New Zealand Anti-Vivisection Society (NZAVS) presented on funding at the ANZCCART conference, it sparked an interesting discussion. One member of an ethics committee asked a simple question – what if we got a bunch of great minds in a room and told them to work on an issue without using non-human animals. What sorts of new ideas and innovation might occur in that room?

This captures the essence of what NZAVS hopes to achieve by teaming up with the scientific industry. Combining our perspectives could spark innovation and lead to better outcomes for science and non-human animals alike.

The need to do better

Even in humans, it can be difficult to generalise results from one group to another. Māori and Pākehā can have important differences, such as allele frequency differences resulting in different reactions to medications such as fluoxetine and warfarin (Lea et al., 2008). In a study based on a (binary) gender analysis, it was found that women appear to have a significantly higher risk of developing adverse drug reactions (Rademaker, 2001).

So of course, when it comes to translating results from rats and dogs to humans, there is a growing consensus that the 'animal model' has some serious flaws. From studies looking at specific issues like side effects of drugs (Van Meer et al., 2012) to reproducibility of preclinical trials (Freedman et al., 2015), to studies looking at the big picture such as a meta-analysis of hundreds of studies (Kramer & Greek, 2018), a clear picture is emerging: nonhuman animals do not provide an adequate model for humans.

This creates a common ground between advocacy groups like NZAVS and scientific researchers – a growing desire for fully human-based and human-relevant research.

As technology advances, more and more areas of research will be able to eliminate the harmful use of animals entirely. This growing recognition is starting to develop into concrete changes. The American FDA Modernization Act (2021) would allow for new drugs to be approved without the use of nonhuman animals. If the American Food and Drug Administration begins to accept drugs without the use of animals, it will have implications for research all over the world. New Zealand needs to ensure it is keeping up with the advancing technologies of the 21st century.

Funding is a key driver that can help accelerate (or inhibit) this transition for New Zealand.

Footnotes

[1] Lea, R.A., Roberts, R.L., Green, M.R., Kennedy, M.A., Chambers, G.K. (2008). Allele frequency differences of cytochrome P450 polymorphisms in a sample of New Zealand Māori. The New Zealand Medical Journal, 121(1272), 33-37. PMID:18425152

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Funding as a driver of change

Funding is a core driver of change in science. Access to funding determines whether projects can get off the ground, whether scientists are offered the tools they need and in aggregate determines the overall direction of science for the country.

The aggregate effects of individual funding decisions are a key area of interest for NZAVS. It is the principle of non-summativity in action: the whole is greater than the sum of the parts. Even if every individual funding decision is made in a rigorous and robust way, that does not guarantee that the overall result will form a coherent whole. In short, a cohesive strategy is needed.

While new technologies that do not use animals are continuously being developed, New Zealand does not have a cohesive strategy for how we will transition to using these technologies. Through its Striking at the Source campaign, NZAVS is calling for forming a cohesive strategy. Among other things, this campaign calls for an emphasis on funding as a part of that strategy. Funding at every level can help drive change in a systematic, strategic way.

Funding at a committee level

Many individual projects receive funding by some discretionary body – whether that is a committee, a department head, or another decision maker that decides which projects to support. These decision-making bodies will often be working within a framework with its own limitations – for example, a body dedicated to funding health research will not approve a research project on veterinary care. Thus, the scope of change that a decision-making body can make is somewhat limited.

Nonetheless, there is always scope for improvement, and it can start at the level of these individual decisions.

NZAVS is encouraging funding bodies to:

- collect statistics on the frequency of funding non-animal-based research vs animal-based research
- actively discuss this balance of funding
- continuously question whether projects have adequately researched methods that do not use non-human animals.

By looking at the overall trends of project approvals, funding bodies can begin to paint a clearer picture of the direction of science.

Funding at an institutional level

While funding bodies tend to have more restrictions placed upon them about how they can allocate funds, institutions exist behind those bodies that set the rules of scientific progress.

From universities to government departments, some institutions are handling a large volume of funds and must set rules for how that money is used, rather than deciding on the individual project level.

At the institutional level, we are encouraging organisations to:

- establish an overarching policy to phase out the use of animals as technology permits
- actively assign funding to retrain scientists
- actively assign funding to providing the infrastructure for human-relevant, non-animal-based methods
- actively assign funding specifically for these types of projects
- in the long-term, consider creating departments or institutes dedicated solely to human-relevant, non-animal-based methods.

During the ANZCCART conference when NZAVS presented on funding, one of the points was raised that individual funding committees can only approve the projects that are put in front of them. Individual funding committees do not have the sort of system-wide influence that can drive change at the funding level.

That's why institutions such as universities are so important. They are big enough that they can set wider strategic direction. Scientists do not always apply to use modern human-relevant methods, but in many cases that may be for the simple reason that these methods are not accessible! Ensuring that retraining programmes are actively made available and that infrastructure costs such as equipment are addressed will open the door for scientists to make more applications to use this funding. As the saying goes: if you build it, they will come.

The ideal scenario of course would be to devote an entire institute or department to human-relevant, non-animal-based methods. That question at the conference really encapsulated what NZAVS would like to see: what if we put a bunch of smart people in a room, and told them to get to work without using animals?

Funding at the governmental level

Most of NZAVS's discussion with ANZCCART members focuses on things that ANZCCART members have control over. That is primarily the institutional and individual funding-level decisions. However, our wider campaign addresses the governmental level, which is of course of interest to ANZCCART members.

We have been working with and will continue to work with government officials to identify key areas that can be improved, but some already stand out. Government has a large role to play in setting an overall direction for widescale funding decisions, as well as helping coordinate efforts across a wide range of bodies. Examples of things NZAVS is investigating and may propose next year include:

- establishing a national database for animal-based research, to avoid unnecessary duplication of work
- establishing a national database for non-animal-based research, to greater increase cooperation in the field
- establishing a national institute dedicated to human-relevant, non-animal-based research methods
- when establishing funding policies, being sure to incorporate greater emphasis on human-relevant, non-animal-based research methods.

NZAVS will continue to be working on this project into 2022.

At every level, there is an opportunity to use funding to help drive a transition to technologies that do not rely on the animal model. Wherever possible, we encourage committees and organisations to strategically consider how their choices might help drive this change.

Transparency and openness

NZAVS is pleased to see that this is an issue that is already being progressed! It is a part of our Striking at the Source campaign and we look forward to seeing results from the Openness Agreement launched at ANZCCART.

To us, one of the gold standards of openness is if people could see exactly what is happening. For example, when experiments are filmed, those experiments can more easily be fully discussed. This also encourages researchers and ethics committees to fully scrutinise a project before they proceed with it.

Since the conference, NZAVS has experienced a much higher level of openness than ever before and we are pleased to see these steps forward. In 2022, we plan to take some proposals to the government to increase openness further, and we invite organisations to get in touch when we do. You can contact us at nzavs@nzavs.org.nz to get in touch.

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Animal Tissue Sharing website launched at Massey University

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Neil Ward
Animal Welfare Officer, Massey University

Researchers, technicians and teachers at Massey University's veterinary, animal science and agriculture schools have historically sourced animal tissues for their work by word of mouth within the institution. Occasionally, abattoirs have also been used, but this is becoming more difficult to organise. Neil Ward, a senior technician in the School of Veterinary Science, was part of this informal network and for many years saw value in developing a more formal system to comprehensively facilitate the sharing of animal tissues, over a wider group of people. In 2020, Neil sought support from Massey's Information Technology Services to develop a website database for this purpose. The project was approved, and a team of 21 people at Massey have contributed to the development of the website.

The sharing of animal tissues is a concept that is promoted by the National Animal Ethics Advisory Committee. 'The Good Practice Guide for the use of animals in research, testing and teaching' states, "Investigators and animal carers should ensure that, if practicable, tissue samples from animals that have died or been humanely killed are provided or made available to other investigators for their work or deposited in a tissue bank for subsequent distribution" (Section 7.4.9). The initiative applies the 3Rs principles of reduction and replacement. Our intent is that the site will increase the beneficial outcomes from these animals, with no additional cost to the animals themselves. We also hope that it will reduce the number of animals that are killed for research and teaching purposes.

The website is hosted by Massey. Initially, the site will be available only to Massey staff but it is anticipated that, with time, access to the site will be made available to people from other research and teaching organisations in New Zealand. Access is restricted to site members. Staff who can offer and/or who wish to receive animal tissues for research or teaching purposes are invited to apply to have access to the site. Massey's Animal Welfare Officer screens applicants to ensure they have a genuine interest in offering and/or receiving tissues, before accepting them as site members.

The Animal Welfare Officer will also moderate the site and help ensure it runs smoothly.

Members will be required to comply with some simple agreements, as follows:

1. Membership and access to the site is at the discretion of the site moderator. The moderator also reserves the right to suspend a member's access; for example, if the intent of the site is dishonoured.
2. Discussions between personnel offering and sourcing tissue are confidential, unless agreed otherwise by both parties.
3. After discussion, personnel offering tissue are not obliged to provide them to others if it is not practically feasible to do so.
4. The logistics, agreements and any costs associated with tissue sharing are determined by both parties, independently from the tissue sharing site.
5. Tissue received may only be used for research or teaching purposes.

Neither the identity of users, their institutions (when membership opens to external organisations), nor the nature of experiments, are revealed on the web site.

The availability of tissues following planned euthanasia are posted on the site in advance of the euthanasia. Basic information such as animal species, breed, sex, age, number, and specific details such as tissue type/s are included in the listing. Tissue banking is not required by the system. Other research and teaching personnel who may have a use for these tissues can express interest in discussing details relating to the tissues with the person offering. Clicking the 'request to use' button prompts the sending of an email to the person offering, notifying them of this person's interest. The requester can provide some information about their request, to help the tissue provider to know whether the offered tissues may be useful. The person offering the animal tissues can then contact the person requesting tissues; discussions will occur at the discretion of both parties and outside the website.

If a member wants a particular tissue that is not currently listed, the member can instruct the system to notify them (by email) if tissues from that species are subsequently offered. This eliminates the need to regularly monitor the site, looking for postings of this tissue type.

Each member can view their own personalised page, which displays a summary of their own offered tissues. This is accompanied by a list of respondents who have expressed interest in each listing. Similarly, the members' own requests to use tissues offered by others are also summarised. Members are asked to log successful shares into the web site to enable the usefulness of the system to be captured. Data on the number of tissue-offers and number of expressions of interest in receiving tissues will also be able to be extracted.

Our expectation at Massey is that the website will help teaching staff to access material for student practical classes. Obtaining material for cell cultures or other invitro testing, or organs for pilot investigations are other anticipated uses.

Extending membership to personnel in other research, testing and teaching institutions will likely facilitate wider collaborative relationships and make greater use of tissues obtained from euthanised animals.

Massey's animal ethics committee has given its support of utilising the tissue-sharing website and will encourage this use by requiring investigators who euthanise animals to post tissues that could be shared on the site. Animal ethics committee approval is needed to euthanise animals for the purpose of using cadavers for research and teaching purposes, so it can also be ensured that animals are not euthanised if tissues can otherwise be obtained (e.g. through the tissue share website).

The use of the Forced Swim Test to study depression

Bronwen Connor
Centre for Brain Research, Dept of Pharmacology
& Clinical Pharmacology, FMHS, University of Auckland.

Depression

- A leading cause of morbidity and mortality in the First World.
- NZ Mental Health Survey 2016/2017:
  - 1 in 5 adults had mild or greater depression symptoms.
  - Women suffer depression at twice the rate of men.

Old Man in Sorrow (On the Threshold of Eternity), 1890 Vincent van Gogh

What Causes Depression?

- Genetic factors may pre-dispose a person to develop depression.
  - No single gene is responsible.
- Chronic stressors, including early life stress, are implicated as vulnerability factors of anxiety and depression.
  - Major stressful events seem to precede depressive episodes early in disease course.
- ~50% of depressed patients exhibit increased release of the stress hormone corticosteroid.
- Clinical relapse is more likely to occur in individuals where increased corticosteroid persists.

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Current Treatments

- Selective serotonin reuptake inhibitors (SSRIs).
- Serotonin-Noradrenaline reuptake inhibitors (SNRIs).
- Not work for everyone.
  - 1/3 patients respond to first anti-depressant.
  - 1/3 patients not respond to any anti-depressants.
- Delayed clinical effect.
  - ~2-4 weeks.
  - Not due to immediate neurochemical effect.
  - Due to long-term cellular changes.
- Search for more rapid and effective treatments.

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How do we develop better treatments for depression?

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- Ideal model = humans.
  - Re-directed use.
  - New drugs.

- Cells in a dish / computer modelling.
  - Can't assess effect on mood.
  - Not a whole organism.

- Animal Research.

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What Does Depression Look Like in Animals?

- Depression is a “humanized trait”
- We can’t assess based on human clinical scale.
- Animals:
  - Anhedonia (decreased or loss of interest in pleasurable activities)
  - Changes in social interaction
  - Changes in sleep patterns
  - Stress / anxiety (causative).

- Assessed using behaviour tests



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Forced Swim Test

- Developed in 1970s to screen for potential anti-depressants.

- Rodent placed in cylinder of water.
- Measure how long until becomes immobile or until maximum time of test.

- Rats
  - Water temp = 25^{o}C. Cylinder = 40cm deep.
  - First trial 15 min. 24 hours later second trial of 5 min.

- Mice
  - Water temp = 23 ^{o}C. Cylinder = 25cm deep.
  - 6 min trial, immobility only measured last 4 min.

Different uses:

1. Used to induce “depression” to generate a model of depression.
2. Used for testing the effectiveness of new anti-depressants.

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Scientifically: Is This a Good Test?

1. Model of Depression:

- Forced swim test evaluates coping strategy and not behaviour despair / learned helplessness.

- Active vs passive coping strategies.
  - Swim or float?

- Anti-depressants reduce immobility in the test because they potentiate active coping strategies.

- Does passive coping reflect human depression?
  - There are no clinical symptoms directly related to coping.

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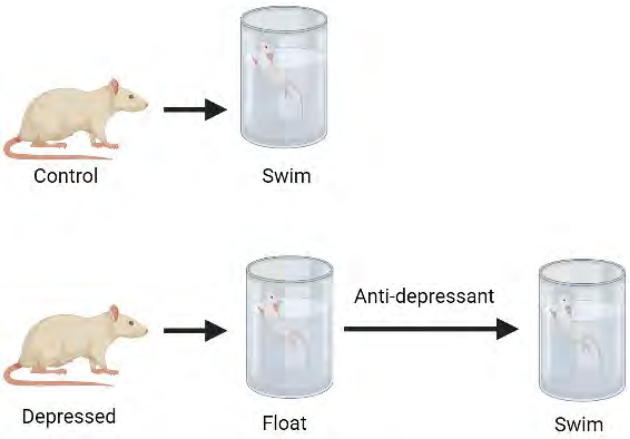
Scientifically: Is This a Good Test?

2. Assessing New Anti-Depressants.

- Accurately predicts whether SSRIs and SNRIs are effective.
  - Inconsistent results with other anti-depressants.
  - Considered a "gold standard" test for assessing new anti-depressants with current treatments.



- Fast action of single dose of an anti-depressant in the forced swim test vs delay of 2-4 weeks for mood improvement in the clinic.
  - Immediate neurochemical effect
  - Not long-term cellular changes.

Factors Affecting Forced Swim Behaviour

Intrinsic to Test	Extrinsic to Test	Behavioural Traits
Number of exposures	Age	Coping style
Tank diameter	Sex	Activity
Water depth	Species / Strain	Novelty seeking
Water temperature	Prior stress	Anxiety
	Prior swim experience	Reward sensitivity
	Circadian rhythm	
	Circannual rhythm	

Armario A. 2021. The forced swim test: Historical, conceptual and methodological considerations and its relationship with individual behavior traits. Neuroscience and Biobehavioural Reviews, 128; 74-86.

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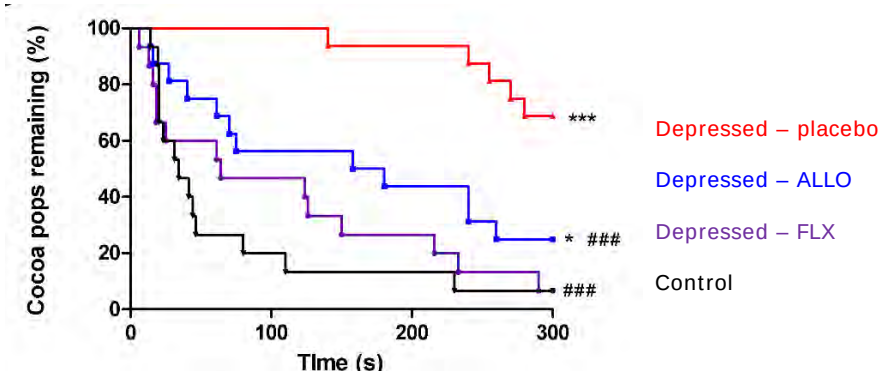
Alternative behaviour tests

- Anxiety-like Behaviour
  - Open-field test
  - Novelty suppressed feeding test
  - Elevated plus maze test
  - Light/dark box test
- Depression-like behaviour
  - Sucrose preference test



Evans, J., Sun, Y., McGregor, A., & Connor, B. 2012. *Neuropharmacology*, *63*(8), 1315-1326.

Scientifically, is the Forced Swim Test a model of depression?

- No.

Scientifically, is the Forced Swim Test useful for identifying potential new anti-depressants?

- Maybe

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Use of the Five Domains Model to assess the potential animal welfare impacts for a cost-benefit analysis of the test as a research tool

Ngaio Beausoleil

Co-Director, Animal Welfare Science and Bioethics Centre, Associate Professor (Applied Ethology and Animal Welfare Science, Massey University

What is it like to be the rat in the Forced Swim Test?

Assoc. Prof Ngaio Beausoleil

Co-Director

Animal Welfare Science and Bioethics Centre

Massey University

New Zealand

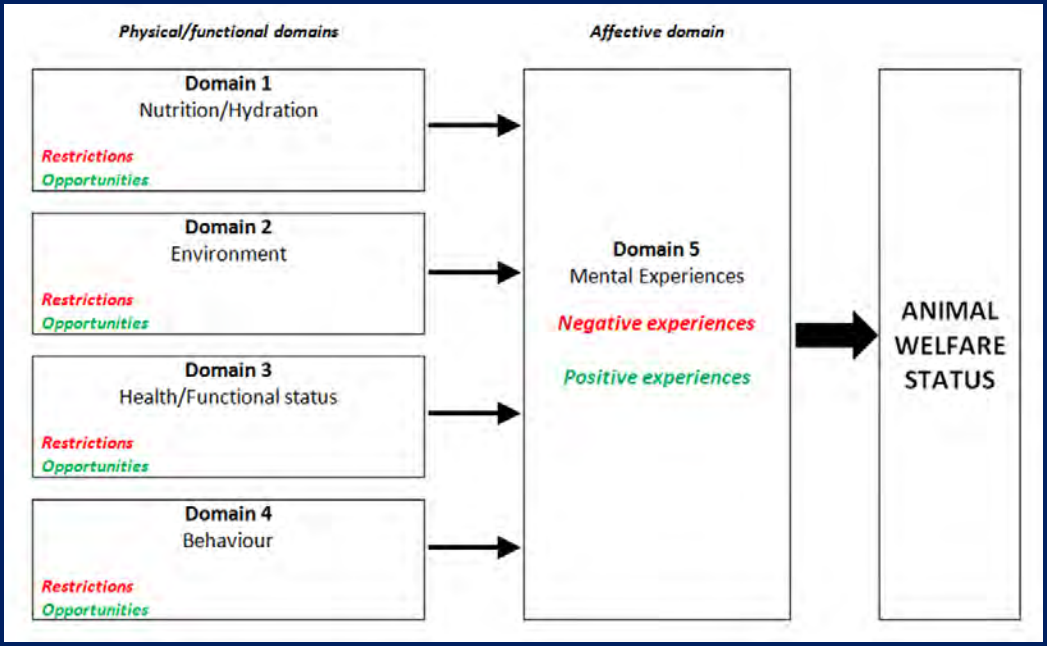
To be covered

1. **What is animal welfare?**
2. **How can we assess welfare state?**
3. **How does the FST impact on rat welfare?**
   - **Test as stressor**
   - **Test on background of chronic stress**
4. **Conclusions**

1. Animal welfare is….

- State within animal itself
- Integration of affective experiences arising from interpretation of sensory information
- Affective experiences = Mental experiences that matter to animal
  - *Negative experiences ↓ welfare*
  - *Positive experiences ↑ welfare*

2. Five Domains model for assessing welfare

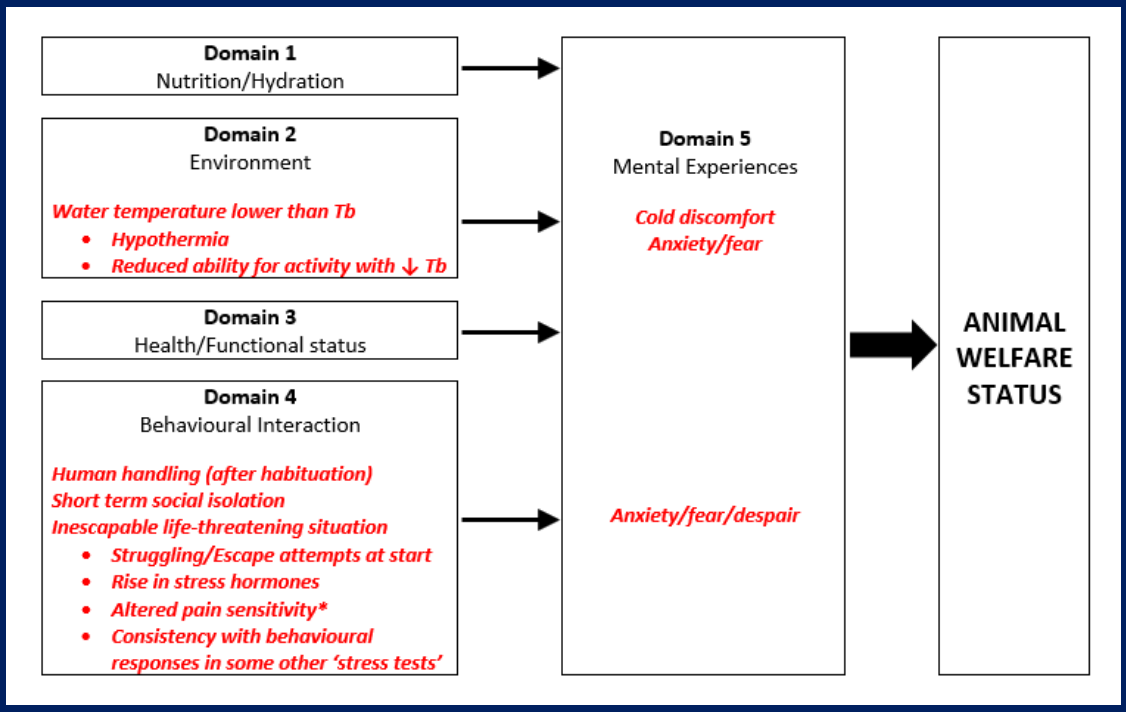


3. How does the FST impact rat welfare?

<u>Application 1:</u> Test itself as acute stressor

- Pre-test 15 min long (naïve animals)
- ~25°C water temperature
- Handling to introduce and remove
- Social isolation during test and drying
- Excluding:
  - Any impacts of applying treatments/controls
  - Test 5 min long @ 24 hours later

How does the acute FST impact rat welfare?



How does the acute FST impact rat welfare?

Domain 1 Water or food restriction, malnutrition				
No impact	Mild impact	Moderate impact	Severe impact	Extreme impact
Domain 2 Environmental challenge				
No impact	Mild impact	Moderate impact	Severe impact	Extreme impact
Domain 3 Injury, disease, functional impairement				
No impact	Mild impact	Moderate impact	Severe impact	Extreme impact
Domain 4 Behavioural or interactive restriction				
No impact	Mild impact	Moderate impact	Severe impact	Extreme impact
Domain 5 Anxiety/fear, cold discomfort				
No impact	Mild impact	Moderate impact	Severe impact	Extreme impact

Overall impact: Moderate impact for up to an hour

How does acute on chronic FSTs impact rat welfare?

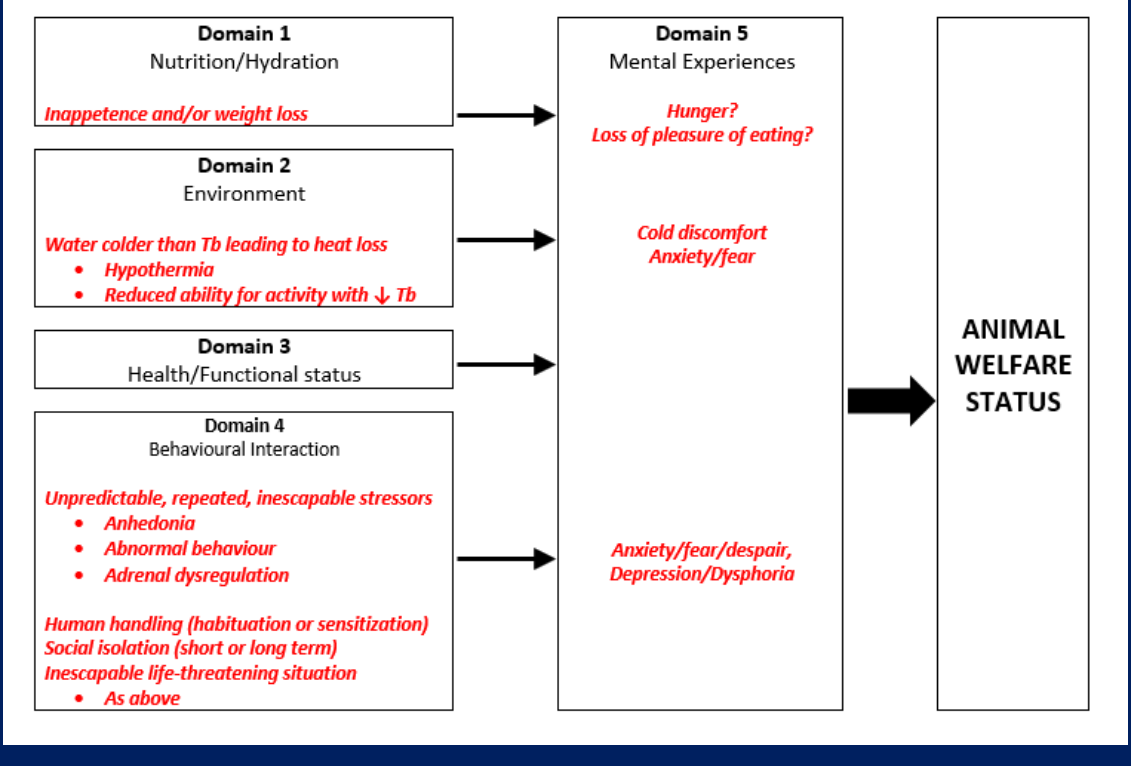
Application 2: Test as acute stressor on background of chronic stress

Test as above, following

Treatments designed to elicit depression-like states:

- Unpredictable (chronic intermittent) stress paradigms
- Repeated social stressors *e.g. defeat*
- Inescapable laboratory stressors *e.g. foot shocks, restraint*

How does the acute on chronic FST impact rat welfare?



How does the acute on chronic FST impact rat welfare?

Domain 1 Water or food restriction, malnutrition				
No impact	Mild impact	Moderate impact	Severe impact	Extreme impact
Domain 2 Environmental challenge				
No impact	Mild impact	Moderate impact	Severe impact	Extreme impact
Domain 3 Injury, disease, functional impairement				
No impact	Mild impact	Moderate impact	Severe impact	Extreme impact
Domain 4 Behavioural or interactive restriction				
No impact	Mild impact	Moderate impact	Severe impact	Extreme impact
Domain 5 Anxiety, fear, pain, thirst, hunger, breathlessness… (distress)				
No impact	Mild impact	Moderate impact	Severe impact	Extreme impact

Overall impact: Severe to extreme impact for weeks

Conclusions

- 5D Model allows holistic welfare assessment based on indicators
- FST elicits some negative experiences (mins) due to inescapability & cold
- Acute FST on Chronic Stress paradigm = significant impacts for weeks
- **Mainly impacts related to animal's perception of situation (D4) not impairment of it's physical state (D1-3)**
- Any test eliciting depression-like state → Compromise welfare state
- People's perception more important than science-based assessment (Big Pharma bans)

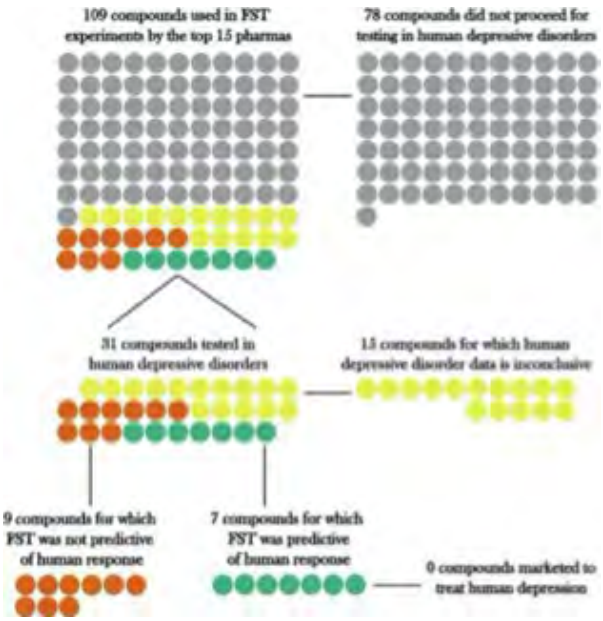
Progressing science means abandoning the Forced Swim Test

Tara Jackson
The New Zealand Anti-Vivisection Society

The New Zealand Anti-Vivisection Society (NZAVS) is leading a campaign to end the use of the Forced Swim Test (FST), also known as the Porsolt Swim Test in New Zealand.

This issue fits into the wider problem of translating results from non-human animals to humans. The evidence against the validity of the Forced Swim Test is particularly compelling, and so NZAVS is focusing on it as a stepping stone to opening up new ways of thinking about tackling human illness.

Acting on the Forced Swim Test will have wider ramifications for how science is conducted in New Zealand, resulting in positive advances for humans and non-humans alike.



This figure summarises the findings of the paper. For the compounds that were suspected to be of use for human depressive disorders, Forced Swim Test results ranged from inconclusive to contradicting the human response to predicting the human response. Ultimately, none of the compounds (that the authors were able to identify) that used the Forced Swim Test ever resulted in successfully treating humans.

The Forced Swim Test does not work.

A core theme of the discussion at the conference was centred on the idea that the Forced Swim Test does not meaningfully contribute to science or the understanding of human depression. One new aspect of the conversation around the efficacy of the FST during the conference was a paper that had not been published at the time. That paper is now published.

The paper, *The Forced Swim Test has poor accuracy for identifying novel antidepressants*, is a meta-analysis of a wide range of compounds that were tested using the Forced Swim Test.

This latest paper adds to the already existing body of evidence against the Forced Swim Test.

Time to End the Forced Swim Test

On ethical grounds alone, the case is clear: if a test does not work, it should not meet the ethical bar for being approved. Nonetheless, on occasion NZAVS has been able to identify cases of the Forced Swim Test continuing to be approved.

The continued use of the test damages the social license of the entire scientific community. Trust in the scientific community is more important than ever, but it is difficult to maintain that trust if tests that are acknowledged to have little scientific value continue to be conducted at the expense of nonhuman animals.

Projects involving the Forced Swim Test also siphon funds that could be allocated to other projects. With scientific funding in such short supply, it should not be wasted upon ineffective tests.

While most scientists have dropped the Forced Swim Test, a few have lagged behind and NZAVS has discovered a few instances of the test being conducted in recent years.

Footnotes

[1] 1 Emily R. Trunnell, Constança Carvalho. The forced swim test has poor accuracy for identifying novel antidepressants. Drug Discovery Today, 2021, ISSN 1359-6446, https://doi.org/10.1016/j.drudis.2021.08.003.

Action is Needed to End the Forced Swim Test

The Forced Swim Test has become a popular topic, and in many ways is acting as a litmus test for the scientific community's credibility. If such an obviously faulty test cannot be dealt with, then what else is the scientific community failing to address?

Some researchers have been able to secure approval for the Forced Swim Test. These gaps need to be closed.

NZAVS is calling for organisations and animal ethics committees to take formal stances against the Forced Swim Test. This would not only ensure that their own processes exclude the Forced Swim Test, but also help build a nation-wide message that the scientific community has advanced its position past the use of the test.

NZAVS is working with organisations on a case-by-case basis to identify what might be the most appropriate way for them to establish a formal policy or position. Some organisations have expressed interest in potentially adding it to their formal ethical codes of conduct. Others wish to simply add a sentence to their website.

Whatever the approach, NZAVS wishes to work with these organisations so we can help celebrate this positive step forward for science. We encourage anyone interested in advancing this goal to get in touch at nzavs@nzavs.org.nz.

References

Trunnell, E. R., & Carvalho, C. (2021). The forced swim test has poor accuracy for identifying novel antidepressants. *Drug Discovery Today*. https://doi.org/10.1016/j.drudis.2021.08.003.

Is the forced swim test a universal rodent model for antidepressant drug screening?

Greg Anderson
Department of Anatomy and Centre for Neuroendocrinology, University of Otago

From Gerhard et al 2018 “Rapid-Acting Antidepressants: Mechanistic Insights and Future Directions”

Major depressive disorder (MDD) is a chronic and debilitating neuropsychiatric illness that affects nearly 1/5 of the population and causes substantial social and economic consequences [1,2,3,4]. Depression affects nearly 300 million people worldwide, and rates of MDD are climbing, with an 18% increase in prevalence between 2005 and 2015 [5]. Traditionally, depression and closely related anxiety disorders have been treated using a combination of behavioural therapy and monoaminergic agents, notably, the selective serotonin reuptake inhibitors (SSRIs). However, one-third of patients will require a trial-and-error period before they find an appropriate treatment and another one-third of patients will not respond to multiple trials of antidepressants and are thus classified as having treatment resistant depression (TRD) [6]. Another serious limitation of SSRI medications is a time lag of weeks to months to be effective, and combined with the variable efficacy among MDD patients, pose significant constraints. In 2014 alone, suicide claimed the lives of more than 42,000 people, compared to 16,000 by homicide, and suicide rates are on the rise in the USA, with rates 24% higher in 2014 than 1999 [7, 8].

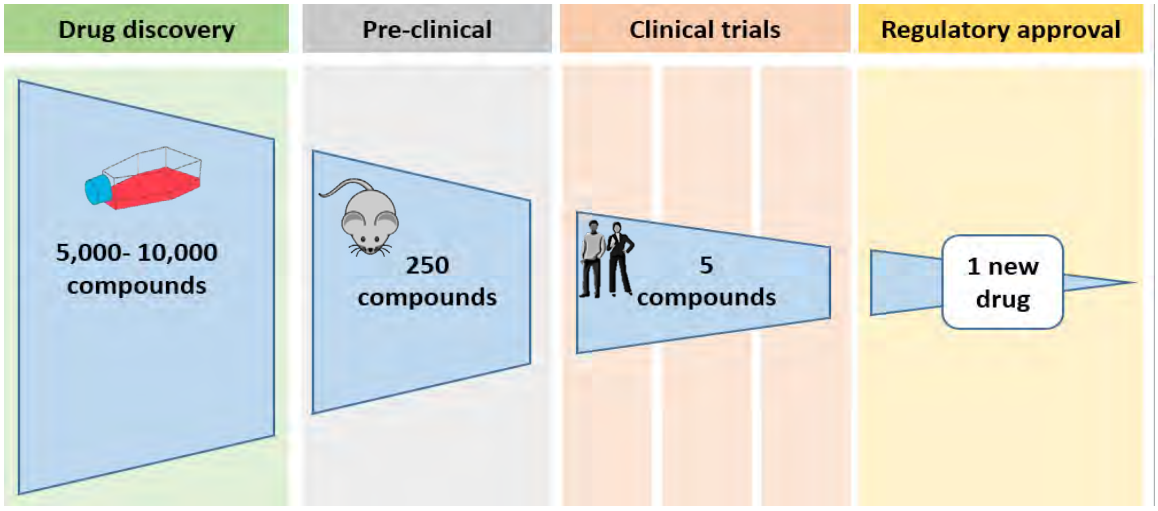
Depression is a recurrent and pervasive disease that can affect individuals throughout life. However, depression is approximately twofold more common in women than men. Although the exact biological cause for the observed differential diagnosis remains elusive, it is known that women suffer from specific forms of depression-related events during periods of hormonal fluctuations, namely puberty, peripartum periods, and menopause. However, prevalence of MDD in women is higher across the lifespan, independent of hormonal stage, suggesting other factors that place women at a higher risk [9]. Therefore, a thorough understanding of the underlying mechanisms driving the sex differences in depression is critical for developing better treatments.

Given the extensive personal and economic consequences and anticipated rise in rates of MDD, more efficacious and faster acting treatments are sorely needed. Current pharmacological treatments, while effective for some, are largely inadequate and are associated with undesirable side effects. One logical step towards the development of effectual treatments is to better understand the etiology of the disease. Much of the work has focused on deficits in monoamine neurotransmitter systems, including serotonin and norepinephrine, and is based largely on the discovery that drugs that block the metabolism or reuptake of monoamines have clinical efficacy for some [10]. However, the therapeutic limitations of these agents, combined with a lack of evidence to support a monoamine deficiency hypothesis, have led to new avenues
of investigation.

https://www.eara.eu/post/depression-swimming-mice

~30% of depressive patients don’t respond to any antidepressants...these are the people likely to end up receiving electroconvulsive shock therapy out of desperation.

The therapeutic drug development pipeline



Proteomes 2016, 4, 28; doi:10.3390/proteomes4030028

Antidepressant tests you can only really do in animal models

- Test for mechanism of action and correlate with anatomical changes
- Screen many drug candidates (different subtypes, doses, formulations)
- Blinded testing of hallucinogens and psychoactives

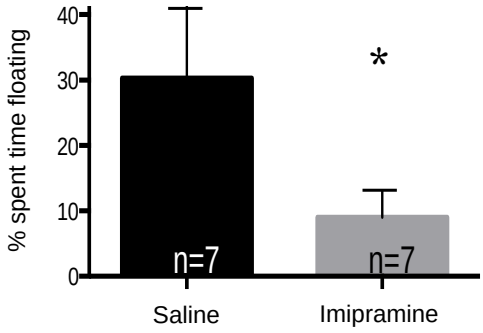
Antidepressant tests you can only really do in human studies

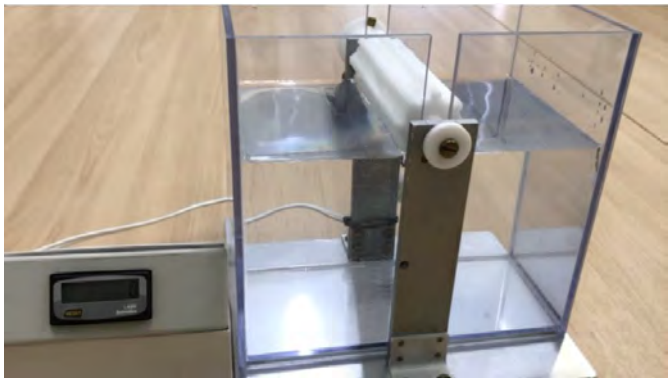
- Test effectiveness in humans
- Assess thoughts (e.g. suicidal thoughts)

- Test for mechanism of action and correlate with anatomical changes (e.g. modulation of 5-HT or NMDA receptors, TrkB and mTOR signalling, synapse density in hippocampus and medial prefrontal cortex)

Some common antidepressants supported by the FST

Antidepressant	Onset	Duration	Mouse FST	Rat FST	Target	References
Imipramine	Slow-acting	Short-term	+	+	Dopamine receptors, serotonin, noradrenaline	Kara 2018, Nguyen 2016, Paul 1990





Imipramine, sold under the brand name Tofranil, among others, is a tricyclic antidepressant (TCA) mainly used in the treatment of depression. It is also effective in treating anxiety and panic disorder. The drug is also used to treat bedwetting. Imipramine is taken by mouth.

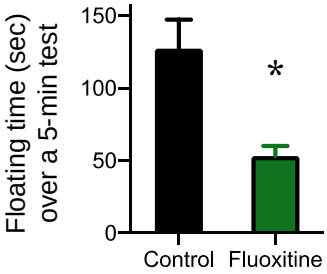
Common side effects of imipramine include dry mouth, drowsiness, dizziness, low blood pressure, rapid heart rate, urinary retention, and electrocardiogram changes. Overdose of the medication can result in death. Imipramine appears to work by increasing levels of serotonin and norepinephrine and by blocking certain serotonin, adrenergic, histamine, and cholinergic receptors.

Imipramine was discovered in 1951 and was introduced for medical use in 1957. It was the first TCA to be marketed. Imipramine and the other TCAs have decreased in use in recent decades, due to the introduction of the selective serotonin reuptake inhibitors (SSRIs), which have fewer side effects and are safer in overdose.

Nomura water wheel. Nomura et al (1982). A new behavioural test for antidepressant drugs. European Journal of Pharmacology 83: 171-175.

Antidepressants supported by the FST

Antidepressant	Onset	Duration	Mouse FST	Rat FST	Target	References
Imipramine	Slow-acting	Short-term	+	+	Dopamine receptors, serotonin, noradrenaline	Kara 2018, Nguyen 2016, Paul 1990
Fluoxetine	Slow-acting	Short-term	+	+/-	Serotonin	Kara 2018, Detke 1995, Cryan 2005, Moskal 2017



Moskal et al (2017) *Current Neuropharmacology* 15: 47-56

The antidepressant-like effects of fluoxitine (3 mg/kg, IV) in the rat forced swim test measured 1 hr after dosing (Moskal et al)

Fluoxetine, sold under the brand names **Prozac** and **Sarafem** among others, is an antidepressant of the selective serotonin reuptake inhibitor (SSRI) class.[2] It is used for the treatment of major depressive disorder, obsessive–compulsive disorder (OCD), bulimia nervosa, panic disorder, and premenstrual dysphoric disorder.[2] It is also approved for treatment of major depressive disorder in adolescents and children 8 years of age and over.[6] It has also been used to treat premature ejaculation.[2] Fluoxetine is taken by mouth.[2]

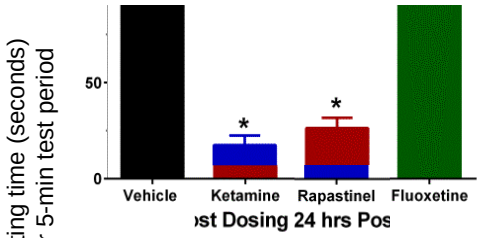
Common side effects include indigestion, trouble sleeping, sexual dysfunction, loss of appetite, dry mouth, and rash. Serious side effects include serotonin syndrome, mania, seizures, an increased risk of suicidal behavior in people under 25 years old, and an increased risk of bleeding.[2] Discontinuation syndrome is less likely to occur with fluoxetine than with other antidepressants, but it still happens in many cases. Fluoxetine taken during pregnancy is associated with significant increase in congenital heart defects in the newborns.[7][8] It has been suggested that fluoxetine therapy may be continued during breastfeeding if it was used during pregnancy or if other antidepressants were ineffective.[9] Its mechanism of action is unknown, but some hypothesize that it is related to serotonin activity in the brain.

Fluoxetine was discovered by Eli Lilly and Company in 1972, and entered medical use in 1986.[10] It is on the World Health Organization's List of Essential Medicines.[11] It is available as a generic medication.[2] In 2018, it was the 23rd most commonly prescribed medication in the United States, with more than 25 million prescriptions.[12][13]

From Porsolt European Journal of Pharmacology, 57 (1979) 201—210 (a rat paper involving 2 doses over 24 h) "Some 5-HT uptake blockers, chlorimipramine (Carlsson *et al.*, 1969d), citalopram (Hyttel, 1977) or pirandamine (Lippmann and Pugsley, 1976) had no effect whereas others, femoxetine (Buus Lassen *et al.*, 1975), fluoxetine (Fuller and Wong, 1977) or LM 5008 (Le Fur and Uzan, 1977} reduced immobility only at relatively high doses where the specificity of their action may be doubted."

Antidepressants supported by the FST

Antidepressant	Onset	Duration	Mouse FST	Rat FST	Target	References
Ketamine	Fast-acting	Medium-term	+	+	NMDA receptor	Nguyen 2016, Moskal 2017, Lu 2014, Hibicke 2020
Rapastinel	Fast-acting	Long-term	+	+	NMDA receptors	Moskal 2017, Lu 2014



Moskal et al (2017) *Current Neuropharmacology* 15: 47-56

Why go back to animal studies? Mechanism of action...From Gerhard et al: Stress and depression cause neuronal atrophy

MDD has been characterized by reduced blood flow and glucose metabolism, a proxy for neural activity, in the PFC, and is attributed to the episode-dependent reductions in volume in depressed patients [17, 18]. Furthermore, rodent models of stress and depression and post-mortem MDD studies report decreased synapse numbers in the PFC [16, 17]. Synapses are the key connections linking neurons, and reductions in synaptic number can decrease neural communication. Reduced activity and connectivity in the PFC is believed to underlie impairments in executive function observed in patients with MDD [14], and could also lead to loss of top down control of other brain regions, such as the amygdala and NAc that underlie anxiety, emotion, motivation, and reward.

The finding of ketamine's rapid-acting antidepressant effects is possibly the most important discovery in depression research in the past 60 years. Despite ketamine's efficacy, especially for TRD and suicidality [89], it also has negative or undesirable side effects and has the potential for abuse. Furthermore, for most patients, the antidepressant effects are short-lived following infusions. This necessitates further investigation into ketamine's mechanism of action to guide the development of more selective treatments that lack these effects and are safe for chronic use.

Importantly, rodent studies demonstrate that ketamine rapidly increases synaptic connections in the prefrontal cortex (PFC) and reverses the deficits caused by chronic stress [15, 16].

Phase II trials in depressed patients have also demonstrated that GLYX-13 produces rapid antidepressant action, but without the dissociative and psychotomimetic effects of ketamine [55•]. Preliminary, but unpublished, research on NRX-1074 (Naurex, Inc.), report rapid and robust antidepressant effects following a single infusion [unpublished data available at: www.naurex.com/pipeline/nrx-1074]. Furthermore, an orally bioavailable analogue of GLYX-13 underwent Phase I trials, but data has yet to be published on the safety and tolerability of the drug candidate [ClinicalTrials.gov Identifier: NCT02366364].

From Wikipedia July 2021: On March 6, 2019, Allergan announced rapastinel failed to differentiate from placebo during phase III trials. [13] Its development has since been discontinued. [14]

Apimostinel (NRX-1074), an analogue of rapastinel with the same mechanism of action but greatly improved potency, is being developed by the same company as a follow-on compound to rapastinel. Its mechanism of action and effects are similar to those of rapastinel (GLYX-13), which is under development as an adjunctive therapy for treatment-resistant depression also

by Naurex. However, apimostinel is 100-1000 fold more potent by weight and, whereas rapastinel must be administered via intravenous injection, is orally-active.[3] Apimostinel is intended by Naurex as an improved, follow-up drug to rapastinel. Similarly to rapastinel, apimostinel is an amidated tetrapeptide, and has almost an identical chemical structure to rapastinel, but has been structurally modified via the addition of a benzyl group. The drug has shown rapid antidepressant effects in pre-clinical models of depression.[3]

Home » Harvard Health Blog » Ketamine for major depression: New tool, new questions – Harvard Health Blog

Ketamine for major depression: New tool, new questions

Posted May 22, 2019, 10:30 am

Robert C. Meisner, MDContributor

Ketamine was once used mainly as an anesthetic on battlefields and in operating rooms. Now this medication is gaining ground as a promising treatment for some cases of major depression, which is the leading cause of disability worldwide. In the US, recent estimates show 16 million adults had an episode of major depression in the course of a year. Suicide rates rose substantially between 1999 and 2016, increasing by more than 30% in 25 states. Because of its rapid action, ketamine could have a role to play in helping to prevent suicide.

Why is ketamine exciting for treating depression?

If a person responds to ketamine, it can rapidly reduce suicidality (life-threatening thoughts and acts) and relieve other serious symptoms of depression. Ketamine also can be effective for treating depression combined with anxiety.

Other treatments for suicidal thoughts and depression often take weeks or even months to take effect, and some people need to try several medications or approaches to gain relief. This is true for talk therapies, antidepressant medicines, transcranial magnetic stimulation (TMS), and electroconvulsive therapy (ECT), which is currently the most effective treatment for major depression that fails to respond to other therapies.

Are there different types of ketamine?

Two main types of ketamine are used to treat major depression that hasn't responded to two or more medications (treatment-resistant depression).

Racemic ketamine, which is most often given as an infusion into the bloodstream. This is sometimes called intravenous, or IV, ketamine. It is a mixture of two mirror-image molecules: "R" and "S" ketamine. While it was approved decades ago as an anesthetic by the FDA, it is used off-label to treat depression.

Esketamine (Spravato), which the FDA approved in March, is given as a nasal spray. It uses only the "S" molecule.

Thus far, most research has been on ketamine infusions.

The two forms of ketamine interact differently with receptors in the brain. The delivery of ketamine and the type given affect drug effectiveness and side effects. We don't yet know which type is more effective or how much side effects may differ. Further research comparing effectiveness and side effects is needed.

How does ketamine work?

It's not entirely clear how ketamine works. Because it exerts an antidepressant effect through a new mechanism, ketamine may be able to help people successfully manage depression when other treatments have not worked.

One likely target for ketamine is NMDA receptors in the brain. By binding to these receptors, ketamine appears to increase the amount of a neurotransmitter called glutamate in the spaces between neurons. Glutamate then activates connections in another receptor, called the AMPA receptor. Together, the initial blockade of NMDA receptors and activation of AMPA receptors lead to the release of other molecules that help neurons communicate with each other along new pathways. Known as synaptogenesis, this process likely affects mood, thought patterns, and cognition.

Ketamine also may influence depression in other ways. For example, it might reduce signals involved in inflammation, which has been linked to mood disorders, or facilitate communication within specific areas in the brain. Most likely, ketamine works in several ways at the same time, many of which are being studied.

What are the possible side effects of ketamine?

All drugs have side effects. When someone is suicidal or severely depressed, possible benefits may outweigh possible risks.

Ketamine given by infusion may cause:

- high blood pressure
- nausea and vomiting

perceptual disturbances (time appearing to speed up or slow down; colours, textures, and noises that seem especially stimulating; blurry vision)

dissociation (sometimes called out-of-body experiences); rarely, a person may feel as if they are looking down on their body, for example.

Generally, any changes in perception or dissociation are most noticeable during the first infusion and end very quickly afterward.

Esketamine nasal spray may cause the same side effects. However, the timing and intensity of those effects is different.

Long-term or frequent use of ketamine may have additional side effects. More research on this is needed.

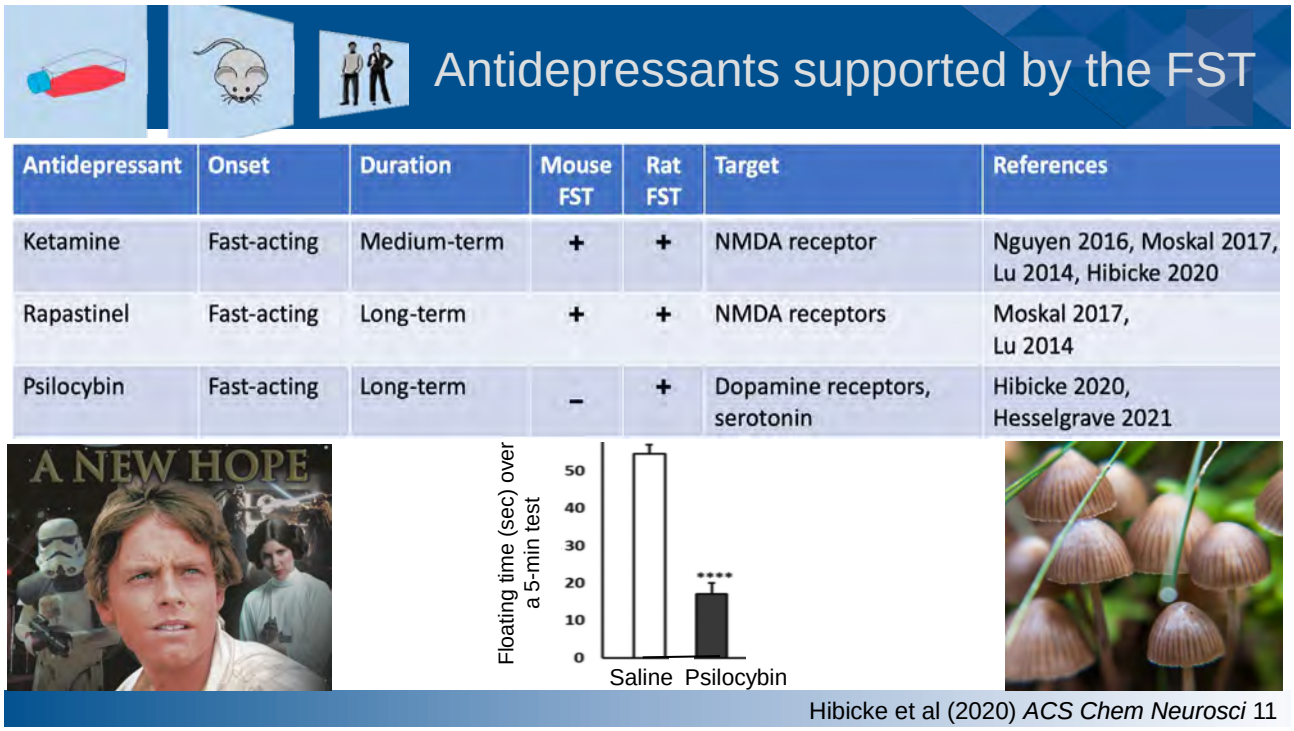
What else should you know about ketamine?

A much lower dose of ketamine is given for depression compared with the dose necessary for anesthesia.

Like opioids, ketamine has addictive properties. It's important to understand this when weighing risks and benefits. If you have a history of substance abuse –– such as alcohol or drugs –– it's especially important for you and your doctor to consider whether ketamine is a good option for you.

When IV (racemic) ketamine works, people usually respond to it within one to three infusions. If a person has no response at all, further infusions are unlikely to help. Instead, it's probably best to try other treatments for depression.

People who experience some relief from depression within one to three ketamine treatments are probably likely to extend these positive effects if the treatment is repeated several more times. The subsequent sessions may help prolong the effects of ketamine, rather than achieving further dramatic relief of symptoms. There are no standard guidelines for this. Many studies offer eight treatments initially (acute phase). After this, patient and doctor decide whether to taper or stop ketamine treatments, or continue treatments at longer intervals.



Graph shows effect of psilocybin **35 days after administration**. The FST enables this type of assessment at various time points.

Psilocybin, a psychedelic prodrug long excluded from biomedical research due to legal restrictions and social stigma, has been shown in multiple clinical trials to have rapid, long lasting antidepressant(22,23) and anxiolytic(22,24,25) effects in humans after only one or two acute treatment sessions. These trials included strictly controlled and highly supervised sensory environments incorporating several psychotherapy sessions post drug administration to "integrate" the subjective experience. There has been significant debate in the field as to whether the therapeutic effects of psilocybin to treat depression and anxiety are purely dependent on the individuals' subjective "peak" experience,(26,27) or are physiological in nature with the peak experience merely serving as a biomarker for antidepressant efficacy.(28)

With psilocybin recently achieving Breakthrough Status by the FDA for human Phase III clinical trials in the United States, it is imperative that we gain a better understanding of the mechanisms through which psychedelics can, after only one or two treatments, produce positive and long lasting antidepressant and anxiolytic effects persisting for six or more months in patient populations.

Recommendations for use of the FST

- Beware of false positives from stimulants (e.g. caffeine, amphetamine). Check locomotor activity.
- Test duration should be limited to 5 or 6 minutes.
- Don’t rely on the FST as an ’readout of depression’.

- When combined with other tests (e.g. sucrose preference, social interaction or open field tests), the FST is a useful predictor of clinical antidepressant efficacy.

  Ferreira MF (2018) Depression assessment in clinical trials and pre-clinical tests: a critical review. *Current Topics in Medicinal Chemistry* 18: 1677-1703

Decontextualized use of scientific data breeds hysteria.

Gene drives for pest control: Panacea or painful problem?

Professor Peter Dearden
School of Biomedical Sciences Te Kura Mātai Rongoā-Koiora,
University of Otago Te Whare Wānanga o Otāgo

Who am I? What do I do?

- Geneticist- mainly of insects
- Research fundamental questions about the evolution of embryos
- Research the mechanisms controlling phenotypic plasticity
- Carry our research to support looking after bees and the beekeeping industry
- Research into novel methods of pest control.

Why pest control?

Because I want to help

- NZ's natural environments, production environment and marine environments are challenged by introduced pests and weeds.
- About 10% of our conservation estate has active pest control.
- Invasive pests kill our native species, cost our primary production sector and lead to the wide-spread use of toxins

We are not winning…

Almost 4,000 of our native species are currently threatened with or at risk of extinction.
(Environment Aotearoa 2019, MFE and StatsNZ)

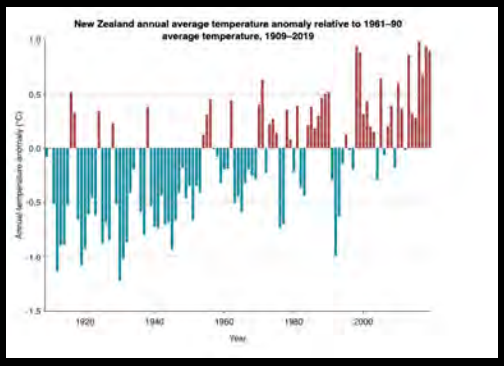
Non-native plant species now outnumber natives here, and stoats, possums, and rats were present on more than 94 percent of New Zealand land in 2014.
(Environment Aotearoa 2019, MFE and StatsNZ)

In 2011, 799 indigenous plant and animal species were identified as being threatened with extinction.
Between 2005 and 2008–11, the conservation status changed for 71 of the 799 threatened indigenous species (8.9 percent).
12 species (1.5 percent) genuinely improved, and their risk of extinction reduced.
59 species (7.4 percent) genuinely worsened, and their risk of extinction increased.
Species with increased risk of extinction are found in freshwater, land, and marine environments.
(Environment Aotearoa 2019, MFE and StatsNZ)

Climate change is already impacting some species by changing where they are found or creating conditions where invasive pests like wasps can live (Environment Aotearoa 2019, MFE and StatsNZ)

Not only but also…

- NZs ecoclimatic zones are changing with global warming
- This is/will happen faster than adaption can occur
- Only pre-adapted species will cope well- those with broad tolerance and broad range- often invasive pests
- Primary production and conservation
- How do we manage that? What tools do we have?



In the 22 years to 2019, New Zealand had its five warmest years on record: 1998, 1999, 2016, 2018, and 2019.
(StatsNZ)

Predator-free 2050

A grand imagined future

- Predator free 2050 is an outstanding goal
- But can it be done with current tools?
- Do we have the funding, political will and appetite to ramp up our use of toxins?

- Is it time to implement new tools?
- What tools do we have?

Tools are a problem

- Broad range pesticides (serious environment and health issues)
- Targeted toxins (small market, hard to make, off target effects)
- Gene editing (Genetic modification)
- Gene Drives (Very genetic modification)
- Pest trapping/shooting (expensive, ethical implications)
- Biocontrol (bringing in new species, off target effects, failure, hitchhikers)

AN EXAMPLE: EVERYONE HATES WASPS…

- Highest recorded Vepsula densities are in New Zealand, with up to 40 nests per hectare (Lester, Haywood et al. 2017).
- The biomass of Vespula in honeydew beech forests is similar to or greater than the combined biomasses of birds, rodents and stoats (Thomas, Moller et al. 1990).
- Annually cost approximately $133 million to the New Zealand economy (MacIntyre and Hellstrom 2015)
- One of the top 100 of the World's Worst Invasive Alien Species" (Lowe, Browne et al. 2000)

So what solutions do we have for insects?

- Insecticides
- Biocontrol
- RNAi interference (doesn't work well in wasps)
- Trojan female systems (modelling suggests wont work in wasps)
- Gene Drives

INSECTICIDES

Insecticides are a tried and true approach to insect control.

Vespex for wasp control is a good solution, but seems unlikely it could be rolled out across all problem areas

Insecticides are coming under scrutiny for effects on beneficial insects (especially bees)

New insecticides aren't in the pipeline

Sphecophaga v. vesparum

'Experiments to measure the impact of wasps on native invertebrates suggest that wasp abundance needs to be reduced by 80-90% of current levels (Toft & Rees 1998; Beggs & Rees 1999).
Even if the parasitoid achieved a 25% suppression,
further control tools are required to achieve conservation gains.'

Beggs JR; Harris RJ. 2000.
Can the wasp parasitoid *Sphecophaga vesparum* significantly reduce the density of *Vespula* wasps?
New Zealand Journal of Zoology 27: 73-74

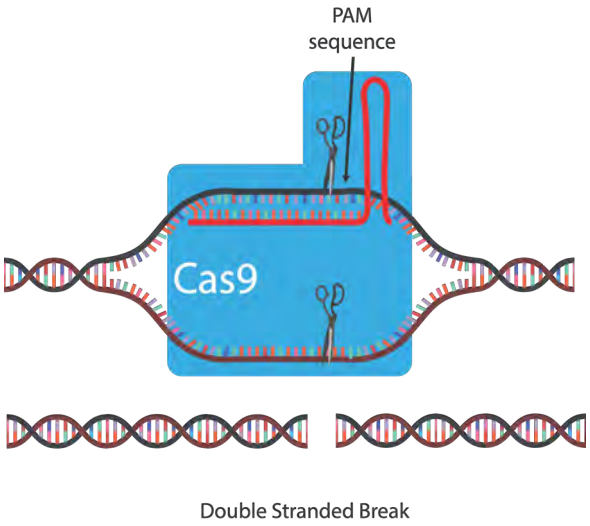
THE GENE DRIVE PROPOSAL PROVIDES THE GREATEST HOPE FOR TURNING BACK THE RELENTLESS AND DEBILITATING TIDE OF INVASIVE MAMMALIAN PESTS IN NEW ZEALAND.

Emeritus Prof Sir Alan Mark

Gene Drives are based on gene editing technology

The **Nobel Prize** in Chemistry 2020 was awarded jointly to Emmanuelle **Charpentier** and Jennifer A. **Doudna** "for the development of a method for genome editing.

What is Gene Editing?



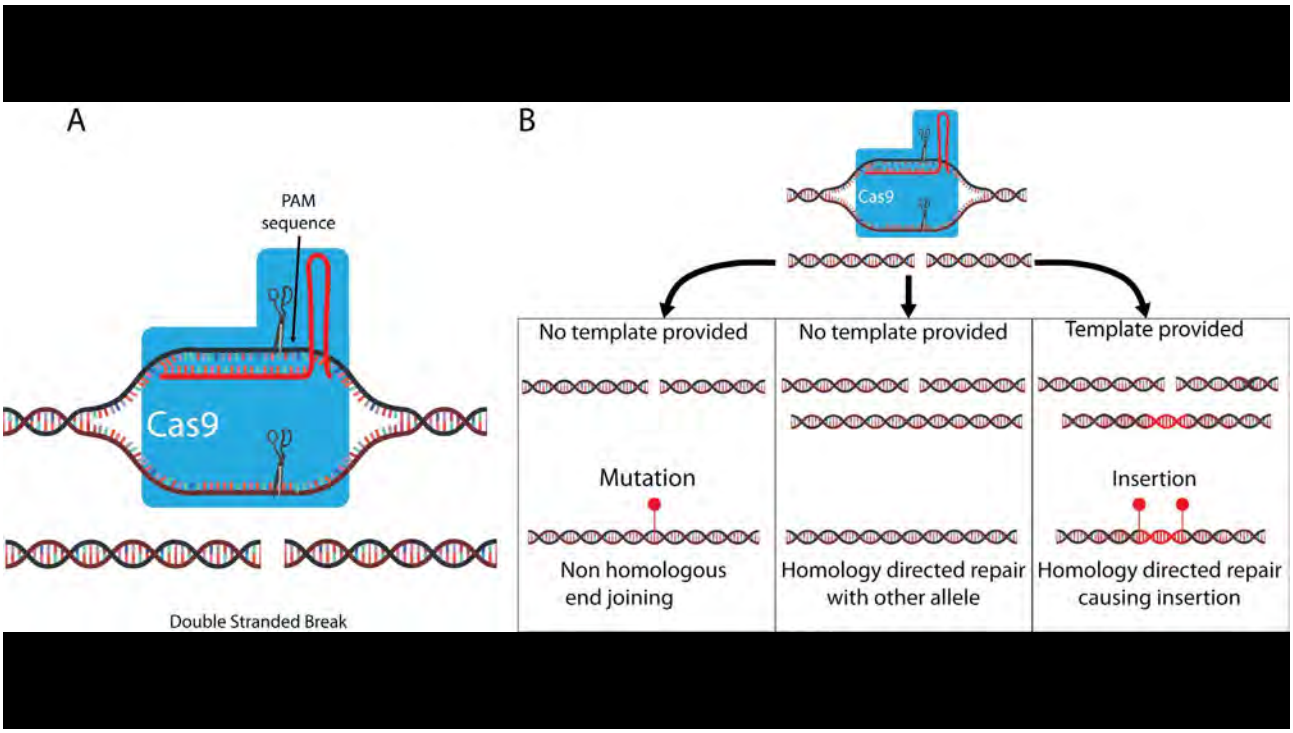
All you need is

1) **a Cas9 protein**

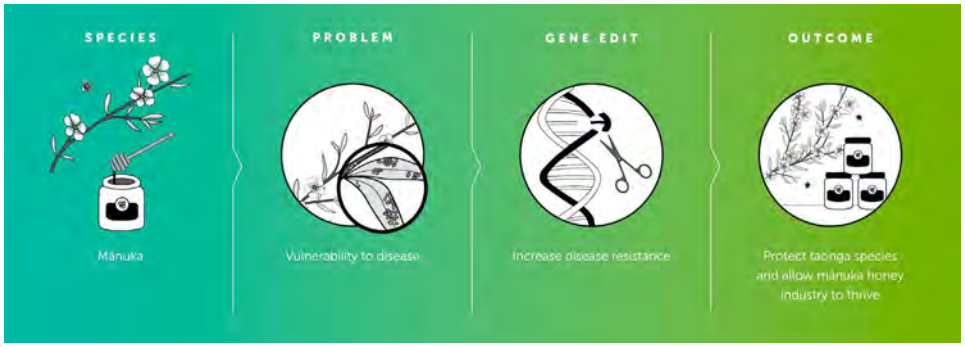
protein found in bacteria

2) a guide RNA

RNA that is homologous to the region that you want Cas9 to cut the genome



Scenario 4 –Protecting taonga species used in the primary industries



Royal Society Te Apārangi Gene Editing panel report

Scenario 4 –Protecting taonga species used in the primary industries

AGRICULTURAL/ENVIRONMENTAL CONSIDERATIONS

Disease resistance would need to be introduced into a range of mānuka varieties, while ensuring growth is not affected.

ETHICAL/SOCIAL CONSIDERATIONS

Active engagement with Māori collectives would be needed on whether this approach is appropriate and useful.

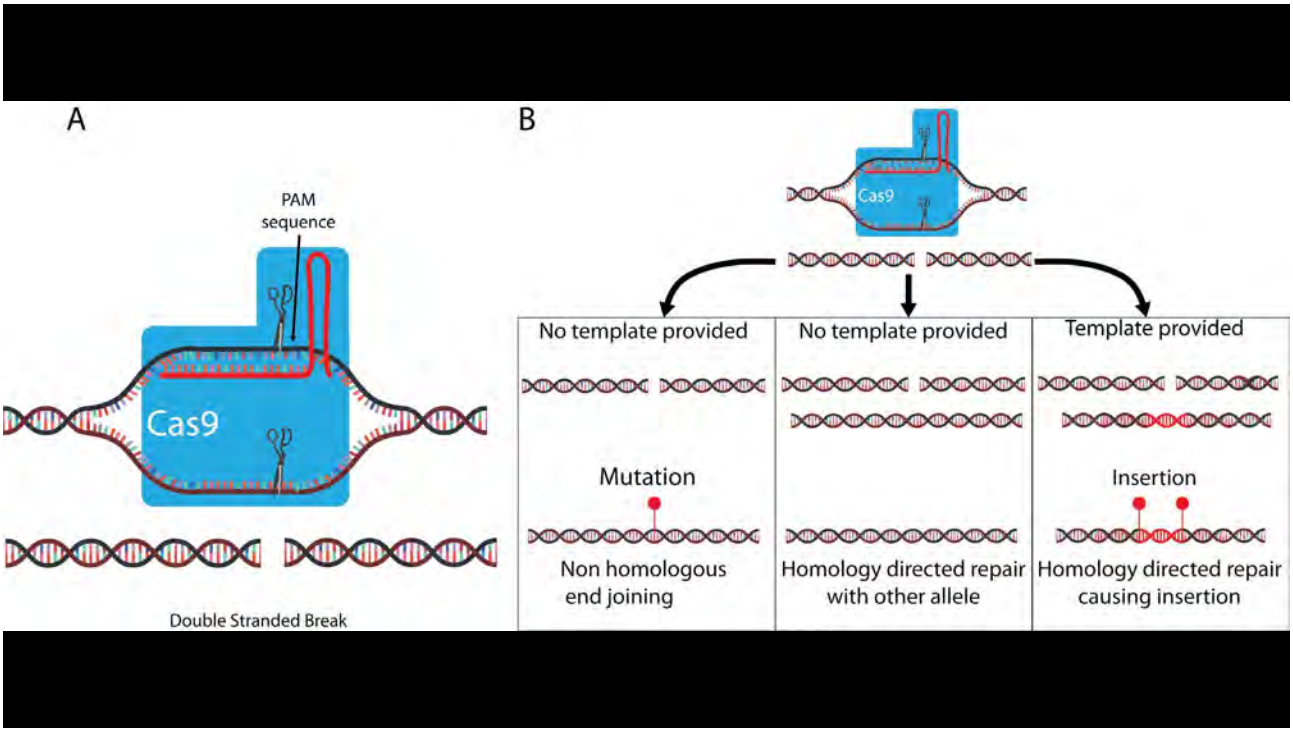
LEGAL CONSIDERATIONS

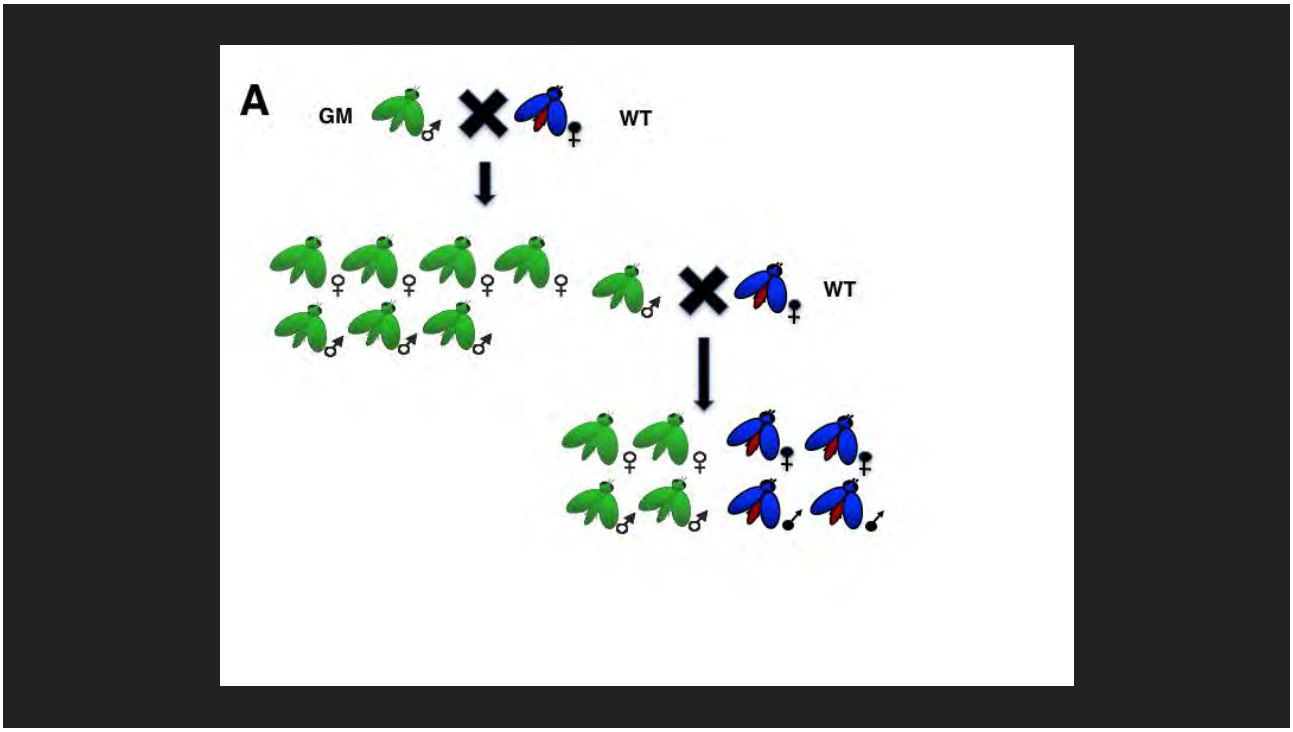
As taonga, mānuka need to be preserved and sustainably managed under the Resource Management Act, the National Parks Act and the Biosecurity Act.

RISKS AND POTENTIAL BENEFITS

Mānuka would be protected from disease, but honey from gene-edited mānuka could be considered unnantural.

Royal Society Te Apārangi Gene Editing panel report


A
PAM
sequence
Cas9
Double Stranded Break
B
Cas9
No template provided
No template provided
Template provided
Mutation
Insertion
Non homologous
end joining
Homology directed repair
with other allele
Homology directed repair
causing insertion


A
GM
WT
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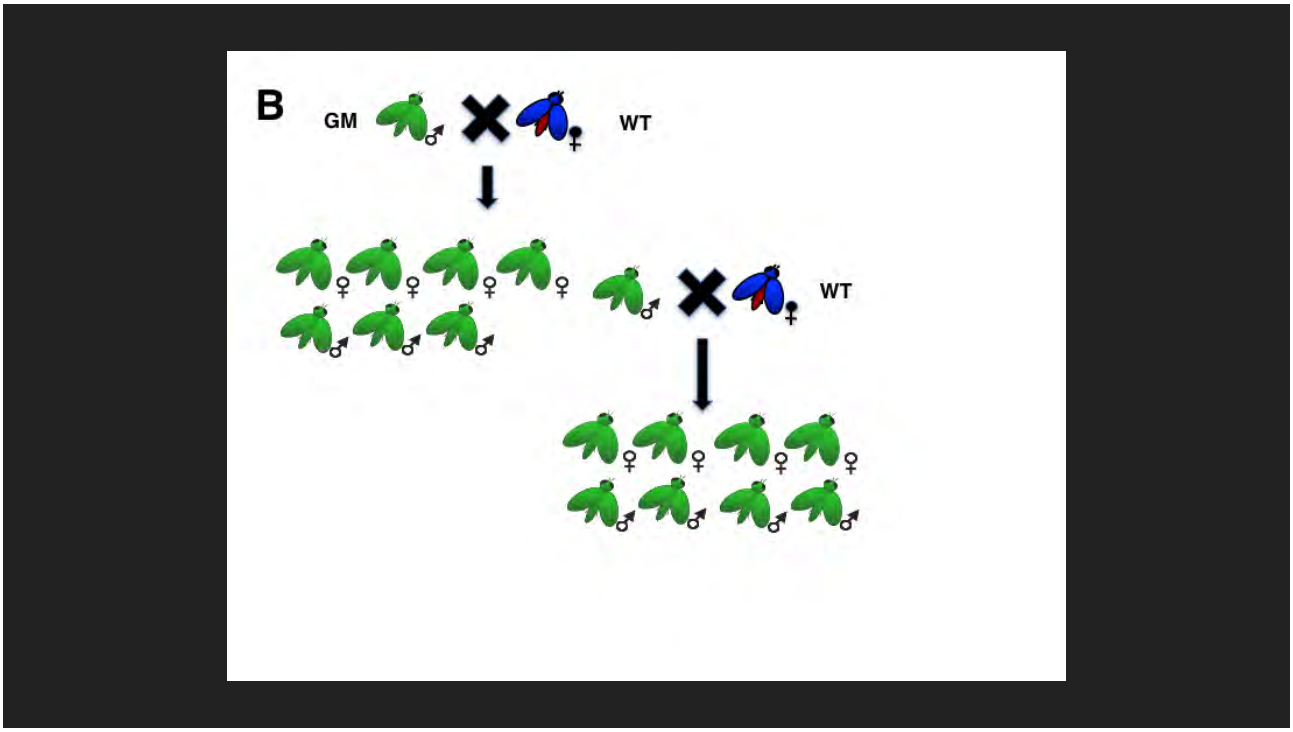
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GM
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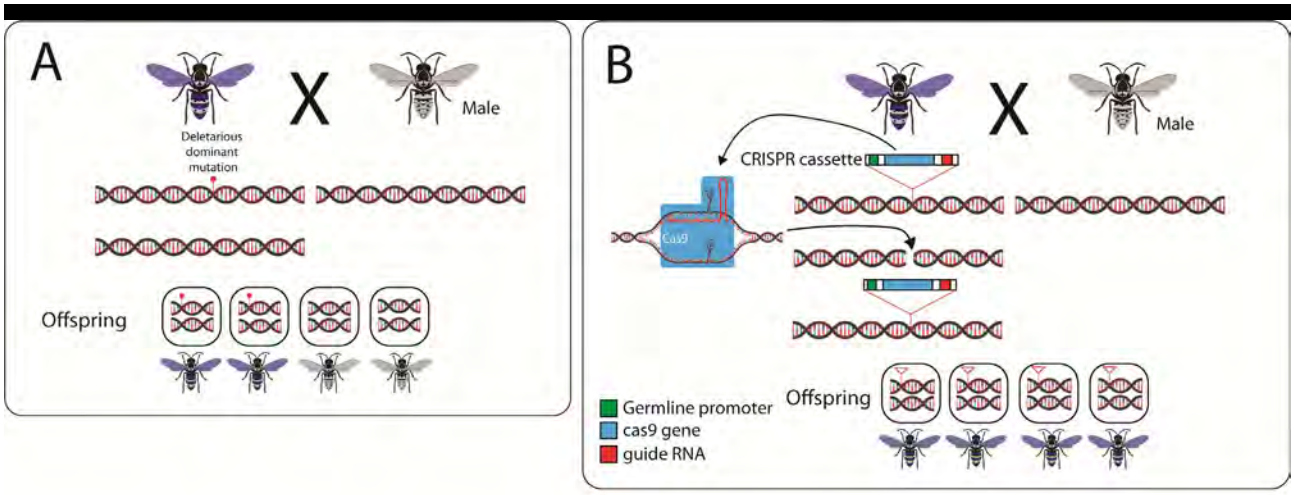
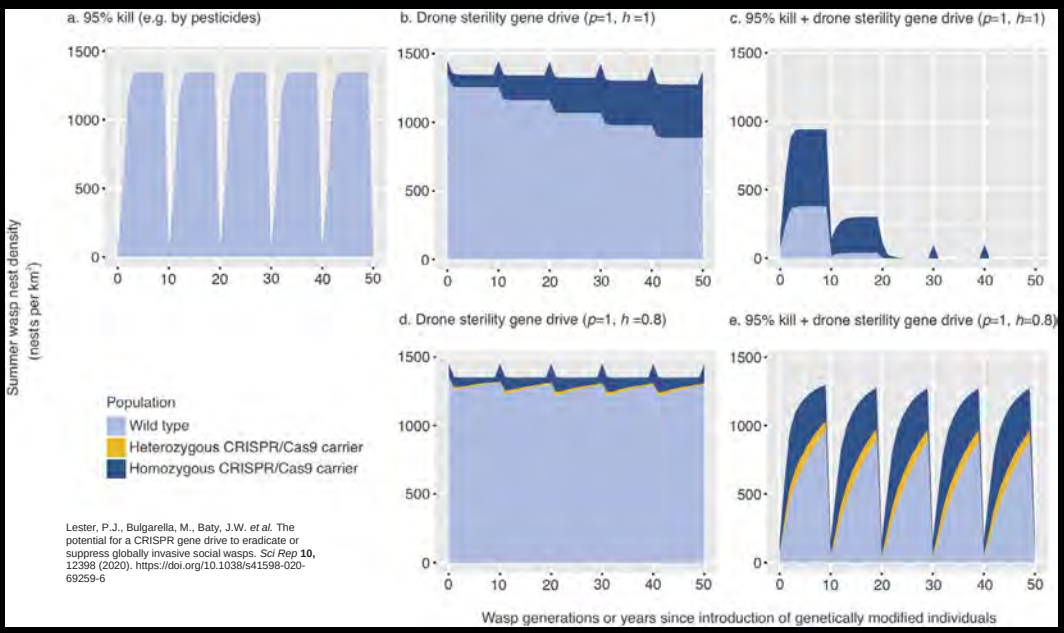
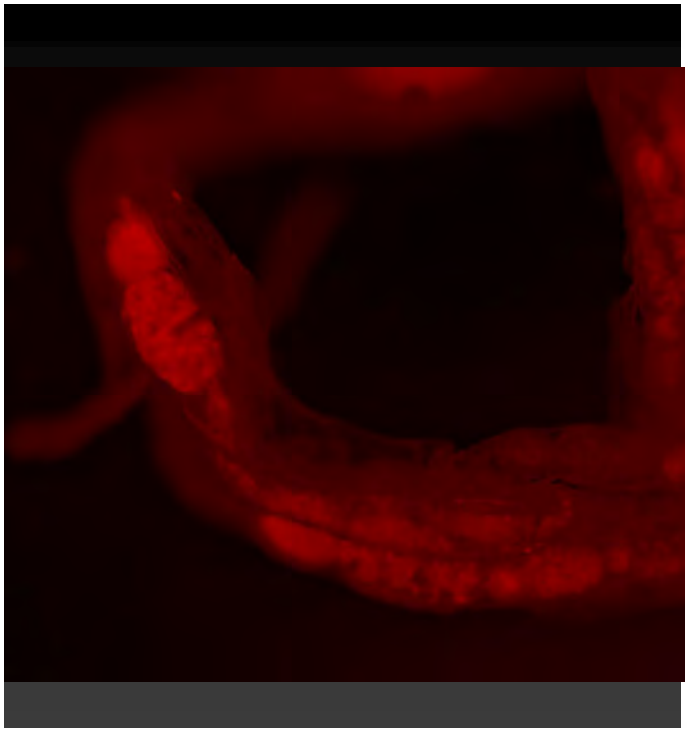

A
Deletarious dominant mutation
X
Male
Offspring
B
X
Male
CRISPR cassette
Germline promoter
cas9 gene
guide RNA
Offspring

Gene Drives



Lester, P.J., Bulgarella, M., Baty, J.W. *et al.* The potential for a CRISPR gene drive to eradicate or suppress globally invasive social wasps. *Sci Rep* **10,** 12398 (2020). https://doi.org/10.1038/s41598-020-69259-6



New Genetics and Society, 2020
https://doi.org/10.1080/14636778.2020.1799344

Biotechnologies in pest wasp control: taking the sting out of pest management for Māori businesses?

Symon Palmer* and Ocean Ripeka Mercier

Te Kawa a Māui (School of Māori Studies), Victoria University of Wellington, Wellington, New Zealand

In Aotearoa New Zealand, the government's ambitious target of becoming "predator-free" by 2050 has reignited public discussion on biotechnologies. The disproportionate abundance of German and common wasps in New Zealand disrupts native biodiversity and costs $133 million annually to the economy, making exotic wasps an expedient trial pest species for novel biotechnological controls. Māori businesses occupy primary industries said to benefit from wasp control. A Māori-centered mixed-method study gauged the perceptions of eight Māori businesses about the potential use of five specific new biotechnological controls in pest management. Participants raised concerns about risk and side effects; called for further information and a reconfiguring of how information is presented, reflected on previous pest challenges; and took positions in reference to Māori customary concepts. While all agree that doing nothing is not an option, careful, informed deliberation is required on whether and how best to move forward with these new biotechnological controls.

Keywords: Māori business; biotechnology; pest control; wasps; New Zealand; biodiversity and conservation

Introduction

In Aotearoa New Zealand (hereinafter Aotearoa) the government's ambitious Predator Free 2050 campaign (PF2050) aims to eliminate three mammalian predators (rats, stoats, and possums) by 2050, with an interim goal to "achieve a breakthrough science solution capable of eradicating at least one small mammal predator" by 2025 (Predator Free 2050 2018, 29). Meanwhile the exotic invertebrates German *Vespula germanica* and Common wasp *Vespula vulgaris* prevail in beech forests in the north of the South Island, where the natural beauty of the surrounding lakes and tramping tracks through the bush draw national and international tourists. Behind this seemingly idyllic scene, these introduced wasps

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Painful problems

- Once you release a gene drive- how do you stop it?
- Can you stop a gene drive spreading to some place the thing you target is valued?
- Might it spread to non-target species
- Will releasing a gene drive affect our clear green image?
- Will it work?
- Risks and Benefits.

So what about the PF2050 three?

NZ Genome sequenced (GA)
NZ population genomics done (GA)
Gene editing/transgenics done
Nascent gene drive systems in mice

NZ Genome sequenced (BHNSC)
No population genomics
No Gene editing/transgenics done
Tools to do so being developed

NZ Genome sequenced (MWLCR)
No population genomics
No Gene editing/transgenics done
No tools

The most important issue

- Gene drives are not possible without genetic modification.
- Public opinion is thus a key factor in deploying a gene drive
- without data on effectiveness it is hard to see how public consultation could be undertaken
- In terms of science and public support we are a long way from deploying a gene drive

So what about ethics?

(otherwise called speculating outside my area of expertise)

- How do we balance our responsibilities to predators and prey?
- Is a gene drive system more ethical than spreading toxins?
- Is there a limit to what we should do in defence of our natural ecosystems?
- Is the imperative to do something, justification for the use of any technology?

Please discuss

So what can we do? (in my opinion)

Research

- We need to develop new tools and ways of thinking to help us manage environments. This take deep knowledge of our problems.
- We need to generate the biological data that supports public debate, and ethics thinking, on the deployment of new tools.
- We need to do our work openly, and share data and results with the public to ensure transparency
- We need to provide the people of Aotearoa with the tools, technologies and knowledge that empowers them to build/support resilient ecosystems

Acknowledgments

Prof Phil Lester, Josh Gilligan, Gemma McLaughlin, Royal Society Te Apārangi Gene Editing panel, Prof Max Scott, Prof Luke Alphey, Prof Ocean Mercier, Prof Alexei Drummond, Prof Peter Gluckman

Hector's and Maui dolphin research 1984–2024

Liz Slooten
Department of Zoology, University of Otago

Introduction

This article provides an overview of research on Hector's and Māui dolphins. Having started their research programme on the behaviour, ecology and conservation biology of these endemic dolphins in 1984, Liz Slooten and Steve Dawson intend to continue this research until at least 2024. Simple solutions to help save these dolphins are outlined below.

New Zealand dolphin behaviour and ecology

Once called Hector's dolphin (*Cephalorhynchus hectori*) with a North Island sub-species Māui dolphin (*Cephalorhynchus hectori maui*), these dolphins are now more commonly known as New Zealand dolphin. Just as the name of our other endemic marine mammal (*Phocarctos hookeri*) changed from Hooker's sealion to New Zealand sealion about a decade ago. The New Zealand (NZ) dolphin is one of four species in the genus Cephalorhynchus (Figure 1). All four have a very restricted range and a small population size numbering in thousands, rather than tens of thousands of individuals. *Cephalorhynchus eutropia* is only found in Chilean waters, *Cephalorhynchus heavisidii* only off the coastline of South Africa and Namibia, and *Cephalorhynchus commersonii* only off Argentina and the Kerguelen Islands (Figure 2).

Most other dolphin species have much wider distributions and populations numbering in the hundreds of thousands or millions of individuals. For example, bottlenose dolphins and common dolphins are found in all the world's oceans. We are incredibly lucky to have our very own endemic dolphin, found only in New Zealand waters.

I started research on NZ dolphins in 1984, together with Steve Dawson. We both retired from classroom teaching in May 2021 and are continuing our research and our connection with the University of Otago as Professors Emeritus. We started out with the idea that I would study the behaviour of NZ dolphin and Steve would study their sounds. I had just completed a study on the behaviour of the endemic mosquito *Opifex fuscus* (Slooten & Lambert, 1983, 1984), and Steve had just completed a study of chaffinch song (Dawson & Jenkins, 1983). Dolphins use sound for communication, finding their way around, finding food, etc. So, it seemed natural to study their sound and behaviour, in order to make sense of their ecology and social organisation.

Figure 1. All four species in the dolphin genus that NZ dolphin belongs to. Top left: NZ dolphin (Hector's and Māui dolphin). Top right: Chilean dolphin. Bottom left: Commersons dolphin. Bottom right: Heaviside's dolphin.

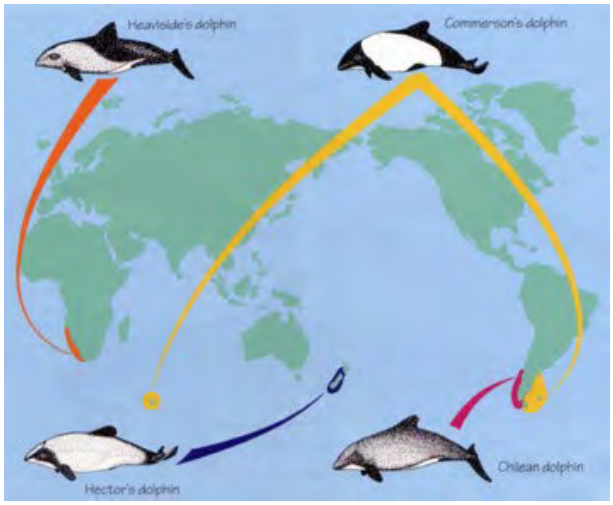

Figure 2. Distribution of the dolphins shown in Figure 1.

One of the chapters in my PhD thesis was on NZ dolphin behaviour, using behaviour sequence analysis, which was relatively new at the time (Slooten, 1994). I followed methods used by two psychologists who were studying the interactions between children and their parents (Bakeman & Gottman, 1986). Steve worked with staff and students in the electrical engineering department at Canterbury University on analysing NZ dolphin sounds (Dawson & Thorpe, 1988). Between us, we

found that the dolphins make different sounds depending on whether they are feeding, socialising, playing or doing something else (Dawson, 1991a).

We noticed early on that when two groups of dolphins meet, the amount of social and sexual behaviour increases much more than you would expect from the increase in the number of dolphins. For example, a doubling of the number of dolphins tends to cause a trebling or quadrupling of the amount of social and sexual behaviour (Slooten, 1994). Many years later, research by Trudi Webster for her MSc thesis explained why they do this. She found that small groups of up to six or seven NZ dolphins tend to consist of only males or only females (Webster et al., 2009). Therefore, it's not surprising that there is a great deal of social activity when these small groups get together.

NZ dolphin calves are very large compared to the size of their mother. This means a relatively long gestation, of about 10–11 months and very obvious 'foetal fold marks' when they are born. All dolphins have these fold marks, which are caused by the calf having to bend to one side, then the other, in the last month or two before it is born. In NZ dolphins these foetal fold marks are especially obvious, resulting in colouration markings that last more than six months but fade well within a year. This makes it really easy for us to tell which calves are 'young of the year'.

They have very small home ranges of about 50 km of coastline, resulting in a very patchy distribution (Rayment et al., 2009). Dolphin 'hotspots' are consistent over many decades and have high densities of red cod, ahuru, yellow-eyed mullet and other fish species favoured by NZ dolphins (Brough et al., 2019; Miller et al., 2013). These small home ranges have led to several, heavily impacted areas losing their local dolphin population altogether. For example, NZ dolphins were commonly seen south of Dunedin in the 1800s and are now very rarely seen there (Diver, 1866; McGrath, 2020). A keen surfer (who also happens to be a scientist) from Raglan used to see Māui dolphins almost every time he went surfing, sometimes in large groups. These days he only rarely sees Māui dolphins, and only ever in very small groups, mostly single individuals or two–three dolphins. NZ dolphins are occasionally seen at Coromandel Peninsula (e.g. DOC, 2019), but were more common there in the past (McGrath, 2020).

Like other dolphin species, NZ dolphins use sound for finding their food (Dawson, 1991b). Their brains clearly show that they use sound for echolocation and communication, with the parts of the brain used to process sound highly developed. The complexity and density of dolphin brains is similar to humans, with human brains more specialised for vision and dolphin brains more specialised for sound. NZ dolphins are themselves food for other species, in particular orca and sharks. The orca, or killer whale, is itself a 'dolphin', the largest species in the delphinidae. I guess it's a 'dolphin eat dolphin' world out there!

Conservation problems and solutions

The most serious conservation problem, for NZ dolphin and most other dolphin species in the world, is fishing (e.g. Read et al., 2006). The problem is very simple: dolphins are killed in fishing nets. The solution is even simpler: we need to make the transition from fishing nets to selective, sustainable fishing methods like fish traps, or pots, hook-and-line methods and jigging instead of trawling for squid.

The good news is that the solution to the dolphin 'bycatch' problem is well known and it works. It's simply a matter of using dolphin-safe fishing methods in dolphin habitat. The first protected area for NZ dolphin was created in 1984 around Banks Peninsula. The survival rate of the dolphin population in this area has increased by 5.4% (Gormley et al., 2012). This has increased the probability of population growth or recovery from 7% before protection to 41% after gillnetting at Banks Peninsula was banned from the shoreline to 4 nautical miles offshore (Gormley et al., 2012). A worse than 50% chance of population growth is still not a sustainable solution, but the Banks Peninsula protected area shows that reducing the overlap between dolphins and gillnets dramatically improves the viability of the local dolphin population.

What we need to do now is to protect these dolphins throughout their habitat, as recommended by the IUCN (Figure 3). Nobody is asking people to stop fishing, or to fish somewhere else. We just need to use fishing methods that don't kill dolphins. Right now, we are stuck in a feedback loop (Figure 4). A small increase in protection, followed by research showing the number of dolphins killed is still unsustainable, followed by another small increase in protection,

and 'round it goes again. We may have time to get around that feedback loop one more time and still have some NZ dolphins left, in some areas. But time has run out for the North Island and several small South Island dolphin populations. The latest population estimate for the west coast of the North Island is 54 dolphins alive during 2020 and 2021 (Constantine et al., 2021). Dolphin mortality is about 12% per year, so right now there are fewer than 50 Māui dolphins left alive in the world. Several South Island populations also number 40–50 individuals, including the dolphin populations off Otago and in Porpoise Bay in the Catlins (Harvey, 2021; Turek et al., 2013).

Two recent examples provide a glimpse of a sobering future if we continue to delay effective protection. The Baiji or Yangtze River dolphin reached about 50 individuals in 1998, and by 2006 was extinct (Turvey et al., 2007). The Vaquita, a small porpoise found in the upper gulf of California numbered about 50 individuals in 2015. Recent surveys suggest that Vaquita may now number fewer than 10 individuals (Rojas-Bracho et al., 2021). It may go extinct this year. Bycatch in fishing nets has been a driving factor in the decline of both these species, as it is also for NZ dolphin and all but one of the Critically Endangered dolphins and porpoises in the world (Brownell et al., 2020). NZ dolphins are found nowhere else in the world, so we are the only country that can save them.

The IUCN (2012) recommended full protection for NZ dolphins, banning gillnets and trawling throughout their habitat (Figure 3). This means all NZ waters less than 100 metres deep, except for the area between Cape Reinga and Coromandel Peninsula. Our research shows that this would result in population recovery at about 2% per year (de Jager et al., 2019; Martien et al., 1999; Slooten, 1991, 2007, 2020; Slooten & Davies, 2011; Slooten & Dawson, 2010, 2016, 2017; Slooten & Lad, 1991). NZ dolphin populations would slowly recover to their numbers before 1970. This would take many decades, because dolphins are slow breeders and NZ dolphins are no exception. At the IUCN World Conservation Congress in 2021, the Director General explained that the vast majority of IUCN Resolutions have been acted on. Only 8% of the Resolutions are being ignored by the relevant countries. Unfortunately, NZ is part of this group of 8%.

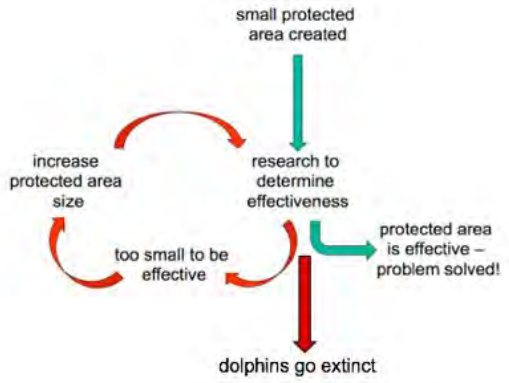

Figure 4. Dolphin conservation feedback loop. In response to a conservation threat, in this case dolphin deaths in fishing nets, a small protected area is created. Research finds that the area is too small. After a small increase in the protected area, research finds that the population is still not sustainable, and so on. Eventually, either the problem is solved or the dolphins go extinct. Since 2000, one dolphin species has gone extinct, the Baiji or Yangtze River dolphin. The Vaquita or Mexican harbour porpoise appears to be in the process of going extinct. We will need to act quickly and decisively to avoid the same fate for NZ dolphins, in particular the North Island sub-species (Māui dolphin) and the smallest of the South Island populations.

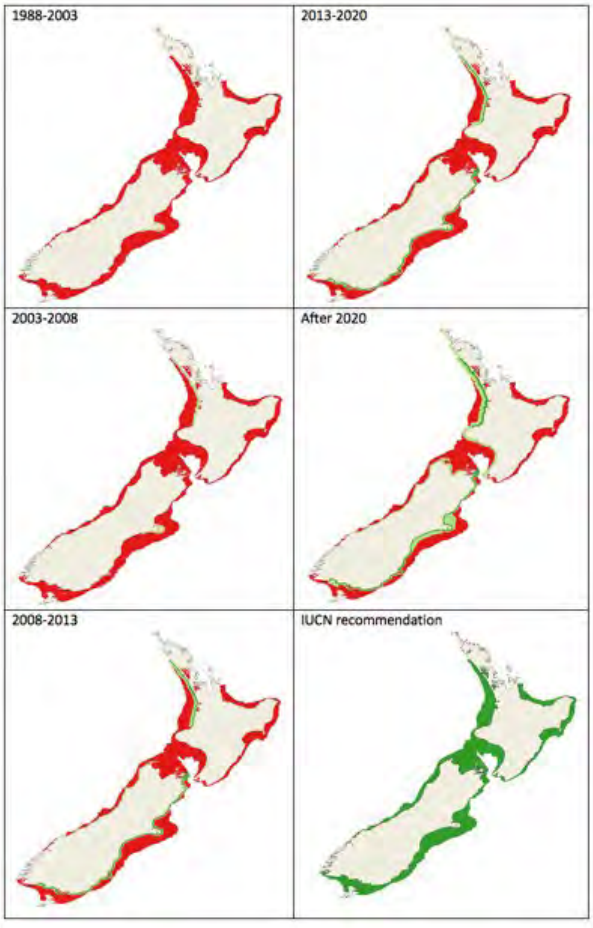

Figure 3. History of dolphin protection: The distribution of Hector's and Māui dolphin is indicated in red, areas where gillnets are banned in light green and areas where both gillnets and trawling are banned in dark green.

Instead of acting on the advice from the IUCN, the Scientific Committee of the International Whaling Commission and other national and international experts, we have allowed literally thousands of dolphins to be killed in fishing nets in the last few decades (Davies et al., 2008; de Jager et al., 2019; Slooten, 2020; Slooten & Davies, 2011; Slooten & Dawson, 2010, 2016). New Zealand's progress reports to these organisations typically talk about doing 'more research' and make it clear that NZ will continue to drag its feet in providing effective protection to save NZ dolphins (e.g. Vance, 2021). This is starting to become an international embarrassment. The US Court of International Trade is considering a ban on fish exports from NZ to the USA, potentially causing a loss of 200 million dollars in revenue to NZ. This is likely to be followed by similar action from EU countries and others.

For more information on the biology and conservation of NZ dolphins, see the references below and the NZ Whale and Dolphin Trust website: http://whaledolphintrust.org.nz/

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Inviting a journalist into your animal house: A case study in responding to negative press

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Abstract

In 2015, a researcher at the institution for which I worked made headlines across the United States for violating the federal Animal Welfare Act. The institution's response included issuing a statement detailing our handling of the incident and hosting the journalist who broke the story on a tour of the animal facility. Our risk management framework allowed us to be transparent about what had happened because it incorporated the following elements:

1. Culture. The institution is committed to safety, and this extends to the safety of animals. It also recognises that animal welfare is foundational to high quality animal-based science.
2. Post-approval monitoring. The institution has a robust post-approval monitoring program to assess whether projects are conducted in accordance with approval and identify areas for improvement.
3. Governance. Policies and procedures describe roles and responsibilities and ensure appropriate management and reporting of incidents involving animals.
4. Communication. All safety incidents are reported daily, and senior leaders are immediately informed of concerns.
5. Trust. Senior leaders trust the team's expertise and follow their recommendations.
6. Teamwork. My team received media training and we collaborated with senior leaders, Public Relations and Legal in responding to the media coverage.
7. Continuous improvement. The institution used the incident as an opportunity to improve.
8. Openness. The institution adopts an open approach to reporting and were open with our staff, the media and our stakeholders about what had happened and why and our corrective actions to prevent reoccurrence.

Introduction

In 2015, the institution for which I worked made headlines across the US for violating the federal law that governs the care and use of animals for scientific purposes. At the time, I was the animal care and use program manager.

In response, we issued a statement to the press that described our handling of the incident that resulted in the violation and our reporting to the regulatory body. We then invited the journalist who broke the story on a tour of our animal facility, and when she accepted, we gave her unrestricted access on a normal working day and answered her questions in detail.

And nothing bad happened. There was no follow-up article. There was no story to tell, no controversy, no public outcry. Even though we'd clearly had a serious incident, overall, we had a high performing program that we could be proud of and open about.

Risk management

Most organisations are unwilling to be open with the media or public about using animals for scientific purposes because they fear the risk of doing so. However, since many organisations lack a formal risk management framework for animal care and use, they often don't understand the *actual* risks of openness, and so instead rely on judgments about *perceived* risks. Commonly considered risks are prosecutorial, financial and reputational in nature.

Openness is unlikely to increase prosecutorial risk, as the industry is already heavily regulated. Financial risks are also small, as funders and donors generally understand the activities they support. Financial risk is usually only realised in relation to reputational damage; donors may withdraw in the face of scandal. There has, at times, been a justifiable safety risk to staff working with animals for scientific purposes, but this appears to be a small risk in Australia and New Zealand.

Generally, the main risk of openness is reputational in nature. However, not openly discussing animal care and use for scientific purposes and letting others (media and animal rights activists) own the narrative may be an even bigger *actual* risk than the *perceived* risk of freely choosing openness.

Figure 1. The foundations of a high performing animal care and use program. These individual elements are risk treatments that eliminate or mitigate inherent risks related to animal care and use for scientific purposes as part of a risk management framework.

Figure 2. Post-approval monitoring (PAM) activities include daily checks and facility inspections, incident reports, annual and final reports (progress reports), conditions of approval on AEC-approved projects, internal audit and veterinary consultations.

The foundations of a high performing animal care and use program

Our risk management framework allowed us to be transparent about what had happened because it incorporated the following elements (Figure 1). These elements, or practices, are effectively risk treatments; they eliminate or mitigate inherent risks related to animal care and use for scientific purposes.

Although listed separately for the purposes of discussion, these risk treatment practices are inter-related and serve to reinforce and complement one another. For our institution, having a good understanding of the *actual* (vs perceived) program risks and how those risks were controlled allowed us to make an informed risk-based decision about how to respond to the negative press. Ultimately, we determined that there was very little risk in being open with the media and inviting further scrutiny.

The risk treatment practices are discussed individually below.

Culture

Figure 1 illustrates that culture encompasses the other practices; it is the single most important element of an animal and use program and underpins the risk management framework.

Culture is a set of shared beliefs that guide behaviour. The shared beliefs at this institution are that the safety of animals is paramount, and that animal welfare is foundational to high-quality animal-based science. The entire staff are proud of their work; they believe it is important, justified and conducted with integrity. Senior leadership has a low-risk appetite which they believe best serves the institution and its stakeholders. These shared beliefs drive the practices (i.e., the behaviours) described in Figure 1, and those practices result in a low-risk, high-performance program that we could be proud of and open about.

Post-approval monitoring

Post-approval monitoring, or PAM, is a multi-modal quality assurance program that generates quantifiable data about the current level of performance and risk in the animal care and use program (Figure 2). These data inform senior leadership about the 'health' of a program over time.

A well-managed, multi-modal PAM program promotes best practice, empowers investigators for being responsible for their own compliance, assesses AEC performance and identifies project-specific problems that require correction. When data is collated, PAM identifies broader trends of risk and opportunity across the institution that can easily be communicated to those responsible for managing it. This directs efforts to where the biggest gains or risks are while ensuring that individual problems are also managed effectively. Importantly, PAM measures improvement over time, and ensures accountability for performance.

Without a well-managed, multi-modal PAM program providing performance data, institutions tend to manage *perceived* risk, without understanding the *actual* risk. This often leads to internal over-regulation and unnecessary administrative burden.

When the press coverage broke, we were confident that we understood the current level of performance of the program.

Governance

Governance is the framework of rules, relationships, systems and processes within and by which authority is exercised and controlled in an organisation. Ethics, risk management, compliance and administration are all elements of governance. It is important both to have governance in place, and to commit to following it. This requires that stakeholders understand how to interpret and apply regulatory and policy instruments.

Our institution had robust unexpected adverse event and non-compliance governance, defined internal and external reporting processes, defined Freedom of Information Act request processes and robust AEC member training that stated roles, responsibilities and authorities – and, equally important, what members are not responsible for or authorised to do.

This meant that when the incident happened, everyone understood their role and what was required of them. Effective governance removes the emotion and conflict out of the situation and provides a clear framework for moving forward.

Communication

At this institution, the day starts with a 'safety huddle' where any safety incidents and near misses, including those that affected animals, are reported to all leaders. This complements PAM activities and provides another forum for leaders to identify trends. Senior leaders are also immediately informed of program concerns. This ensures that all stakeholders are on the same page about what had happened, and what is about to happen, and was important in managing our response to the incident, the press coverage and our subsequent actions.

Trust

When I briefed senior leaders about program concerns, they generally followed my recommendations. My expertise was recognised and respected, and I was trusted to do the job I was hired for. This trust reduced internal over-regulation and unnecessary administrative burden and ensured that roles, responsibilities and accountabilities were clear to all. That made it easy to determine who should be involved in decision-making at each step in this process.

Teamwork

All staff were trusted to do their jobs, so when we came together in cross-functional teams we were empowered to support each other effectively. In responding to the negative press, folks came together from all over the institution to ensure the best outcome for the institution and the investigator (note, any potential issues affecting animal welfare were long-since resolved). The negative press wasn't considered to be an animal ethics problem; it was an institutional problem, so it required an institutional response. This response reflects the cultural values of the institution. The animal ethics team briefed those responsible for community relations, the attending vet and I received media training from the media team, we worked closely with the legal team, and facility management facilitated the journalist's tour. This supported us in providing an informative and open tour for the journalist.

Continuous improvement

The institution uses lean methodology across every aspect of their operations and when things go wrong the focus is always on what processes failed, or what processes don't exist, that allowed the situation to occur. At each step of this journey from initial incident to press tour, we asked ourselves: How could we have done that better? What have we learned? Is this an isolated incident? Do we have data from our PAM program to suggest that this is a bigger issue? How do we prevent this from happening again? Bringing curiosity to problems, rather than blame, ensures the best outcome for all parties – including the animals themselves.

Openness

To support a culture of continuous improvement, safety and pride, and to service a low-risk appetite, an organisation must be committed to bringing problems to the surface so that folks can come together in cross-functional teams and solve them.

In this case, we extended that openness to the journalist who broke the story. We recognised that inviting the journalist into our animal house could result in more press and attention from animal rights activists, but we did it because it aligned with our shared beliefs.

Conclusion

Having an intentional culture supported by performance data and a robust risk management framework means there is very little *actual* risk in being open about how you care for and use animals for scientific purposes in your institution. We used the practices described here to create a program that could face public scrutiny. So, when our perceived reputational risk was realised as an actual risk, we faced it head on.

We were disappointed that the journalist didn't write a follow-up story about what she'd learned during her tour of our animal facility. But opening the door to her set us on the path to openness.

As people involved in animal care and use for scientist purposes, we have a responsibility to the public to inform them about our work. We also have a responsibility to those performing the work to create a safe space for them to talk openly and proudly about how they contribute to the world we live in. Our work is our story; we should own it.

If you already have a high performing program, then consider your next step towards openness. If you don't, adopt the practices above and you soon will.

Freedom of information legislation and animal research: Perspectives from anti-vivisection organisations in Australia, the United Kingdom and the United States

Rachel Smith
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Introduction

Freedom of Information (FOI) is particularly crucial when applied to more contentious societal issues. FOI is commonly used in the animal protection sector as many of the practices upon which animal protection campaigners focus take place behind closed doors. The use of non-human animals (hereafter 'animals') in research is one such issue.

To anti-vivisection organisations, transparency is essential to ensure the proper regulation of animal research and to bring to attention the unlawful suffering of animals by highlighting breaches of regulations. It is, therefore, essential to explore all means by which intelligence might be gathered to expose what is taking place. Campaigns may then be devised that eliminate, or to the extent that is possible, reduce objectionable practices.

However, FOI access is restricted by many exemptions, largely related to the personal safety of researchers (due to the perception that an individual researcher, their family or property may be at risk due to extremist actions), the protection of national interest and assurance of commercial confidentiality. These limitations will be explored with application to animal research.

Theoretical model

Openness is not without resistance or limitations.

A discourse analysis of publicly available documents (McLeod & West, 2016) captures three key discourses on transparency from groups most closely associated with animal research (animal protection groups, the research community and government/funders). In short, each party believes that transparency is necessary to the advancement of their own agenda.

1. Animal protection group: transparency is needed to counter secrecy.
2. Researchers: transparency is needed to counter misinformation and misunderstanding.
3. Government/funders: transparency is needed to counter public mistrust in science and politics.

These positions support the 'information deficit/ enlightenment model' – the belief that more information will lead to more knowledge and therefore less/more support for animal research, once the unknowing become 'enlightened' via the provision of information (McLeod & West, 2016). Thus, anti-vivisectionists claim increased knowledge will increase opposition to animal research, as it is the absence of information that is preventing public opposition, while animal researchers claim that increased knowledge will result in increased support for animal research, as that information will support the benefits of animal research.

Research design

Primary data was collected from semi-structured interviews with six senior representatives from organisations opposed to the use of animals in research. The scope is confined to Australia, the United Kingdom (UK), and the United States (US), all democratic countries with FOI legislation. For comparative purposes, national legislation regulating animals in research follows a similar framework in all three countries. Legislation from these three nations is often cited as a model framework for legislative provisions in other countries globally, as well as featuring prominently in terms of investment and leadership roles in medical research globally.

Additionally, a further area of commonality is the high number of animals used in research in the selected countries, which consistently rank in the top 10 users of animals in research.

Interview Summary

When asked what changes they would favour being introduced to the FOI system, the below were proposed:

1. More meaningful repercussions for agencies that don't abide by FOI legislation
2. Waiving the fees for public interest groups
3. A faster process
4. A more forthcoming approach
5. Removal of Section 24 of the ASPA

In short, a reversal in FOI response is sought by advocacy organisations from one of 'can't do' to 'can do'. "The automatic response is, we don't want to give this information, how can we find ways to not give the information. It would be really great if that was just flipped on its head and there was a real respect for the fact that people have a right to this information" (Cruelty Free International).

Conclusion

There are calls for greater transparency in animal research by researchers, regulators and anti-vivisection organisations, each believing that the more information is made available, the more likely the public will adopt their position on animal research. In practice, the flow of information is largely dependent on the scientific community and regulators. There may be resistance to the disclosure of information that could threaten safety, confidentiality or propriety information, or be perceived to be 'not in the public interest'.

Anti-vivisection organisations contend that the information released provides an insufficient level of detail to enable informed debate on the subject, and unnecessarily so, since exemptions should only be used where absolutely necessary rather than to counter legitimate opposition. In effect, this enables a 'selective openness', which simply serves to maintain the status quo.

Ultimately, while information on animal research remains controlled, anti-vivisection organisations must rely upon the gathering of intelligence to develop sound campaigns. As an advocacy tool, FOI is used to make animal research related requests in order to both gather data for campaigns and bring infringements to the attention of regulators. Such requests may be obstructed by the allegedly incorrect application of FOI exemptions, the existence of legislation that overrides FOI principles in the sensitive area of animal research, procedural issues such as over-charging of fees, non-responses or delays, or additional measures to prevent transparency imposed by government administrations, as evident from recent removal of public databases in the US.

Despite these barriers, anti-vivisection organisations assert that FOI has advanced their objective towards ending the use of animals in research and many feel successful FOI cases have set precedents that information should no longer be classified. As a result, advocacy organisations have been able to communicate verifiable information, at times discrediting the claims of animal researchers, and more accurately presenting the realities of the industry.

Recommendations to anti-vivisection organisations using FOI

1. Keep informed of local, national and international developments, such as changes to legislation, or key case or appeal outcomes
3. Follow the FOI guidance provided and keep requests clear and succinct, with requests for documentation relating to a particular scope within a defined timeframe, rather than framed as a question
4. Consider whether the information can be obtained outside of the FOI process
5. Challenge any unjust, excessive fees
6. Support initiatives such as declarations of openness in animal research and press for them to be implemented in practice
7. Try and form a respectful relationship with FOI administrators
8. Raise transparency as an issue of importance with the media
9. If possible, seek legal expertise if needed for complex or prolonged cases
10. Unite with other anti-vivisection organisations to combat unwarranted obstruction of their investigative efforts
11. Establish partnerships with organisations in other sectors also impacted by the limitations of FOI in order to unite in achieving respective goals.

Full paper available at: https://www.researchgate.net/publication/339295827_The_Effectiveness_of_Freedom_of_Information_in_Anti-Vivisection_Advocacy_in_Australia_the_United_Kingdom_and_the_United_States

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One Step at a Time – A technician's approach to openness

Carlee Mottley
University of Wollongong, Australia

As an Animal Technician I am mostly responsible for the daily care of laboratory animals (rats, mice and xenopus frogs). I monitor animal welfare and compliance to our governing code and legislations, coordinate daily operations of the animal facility, and my favourite part of the job involves training researchers in animal techniques such as injections and blood collection, or performing these myself. I get to enhance the lives of, and advocate for, animals who don't have a voice. I get to mentor budding researchers and foster a culture of empathy within my workplace, and play my small part in biomedical research and contribute to its benefit to society.

The ability for Animal Technicians to talk freely about their roles and to celebrate their achievements contributes significantly to enhancing their morale, and has undeniable flow-on effects for animal welfare. Ignoring or being denied the ability to talk freely about a job that we are normally passionate about due to fear of judgment or repercussion can potentially contribute to the development of compassion fatigue, a secondary traumatic stress disorder. Involving Animal Technicians in openness and outreach programs provides them with a sense of pride and has the potential to foster new skills. Implementing openness and outreach programs can be intimidating, but they don't always require expensive resources or commitment. Often these things are best approached like a marathon, one step at a time.

We started our openness journey at the University of Wollongong (UOW) in 2018 by participating in workplace seminars aimed at showcasing different technical skills within the faculty. This was the first time the animal facility had participated. Our talks focused on providing a background of our roles and some positive innovations such as our rodent rehoming program, improvements to researcher training and ways we address the 3Rs. The seminar increased our visibility in the workplace and provided animal facility staff with the opportunity to talk about something they loved while practising their public speaking skills.

In 2019 we organised a dedicated "Behind the Scenes in the Animal Facility" seminar in celebration of Animal Technician Week, and the university funded a catered afternoon tea for attendees. This seminar was open to all staff in the faculty. The seminar was also recorded and made available online for those who couldn't attend in person. Each animal facility staff member spoke about a relevant topic: why we conduct animal research, how many animals are used and the role of the Animal Ethics Committee, legislation we must abide by, refinements we have made to animal research at UOW, how we monitor and assess animal wellbeing, and how our animals contribute to science and society.

An anonymous feedback survey for attendees revealed the following information:

- Most attendees indicated that their understanding of animal research had improved after the seminar.
- Most attendees indicated that they feel more confident talking about animal research after attending the seminar.
- All attendees were satisfied with the level of care that research animals receive at UOW.
- Most attendees indicated that their views on animal research had changed for the better after attending the seminar.

The benefits of openness initiatives extend beyond those captured within survey results. Involving Animal Technicians in openness initiatives provides them with some creativity and ownership over their role in animal research. Enhanced workplace morale leads to secondary benefits to animal welfare and research outcomes. It's a win-win situation for everyone, so just keep putting one foot in front of the other.

ComPass – Competency Passport: Online training to enhance the knowledge base and skills for research and teaching animal users and AEC members.

Gail I Anderson
ANZCCART, Adelaide

ComPass is a suite of training materials designed for animal users in teaching and research that is free online and hosted on the ANZCCART web site. It has been put together by veterinarians and welfarists from numerous institutions across Australia and New Zealand. It will have five parts when completed.

First, there are seven online modules that make up the core material highlighting the content of the Australian Code and the NZ Guide for animal users and Animal Ethics Committee (AEC) members. The first two modules explain the considerations and definitions of what an animal is, how to apply to an AEC and what applicants need to include in their ethics applications. There is a module on animal wellbeing and how to assess this, another on adverse events and how to manage them, one of the 3Rs, and one on research design and the ARRIVE and PREPARE guidelines. The final content module is about euthanasia methods in various species. Module eight contains the quiz on the previous seven modules' content, that, when successfully passed, allows generation of a certificate of completion to provide to the users' AEC. Each module has links to resources to help the user understand the material more deeply as well as mini quizzes to help the reader assess their ongoing understanding of the material in preparation for the final quiz.

The second phase of the ComPass training consists of eight stand-alone modules that provide the technical background information and video links for skill acquisition for various procedures on animals. These include:

- Module 1) Minimally Invasive Procedures without anaesthesia that illustrates handling and injection methods, orally administered treatments, and a section on trapping of wildlife.
- Module 2) Anaesthesia Methods for Minor Procedures (with gaseous induction and duration less than 10 minutes).
- Module 3) Anaesthesia for Major Procedures including the management of comorbidities and the things that may go wrong and how to prevent them.
- Module 4) Aseptic Technique including preparation of the animal, the surgery team, the surgery room and the equipment for sterile technique.
- Module 5) Surgery Principles, Instruments and Suture Materials.
- Module 6) Performing a Post Mortem Examination using the rat as an exemplar.
- Module 7) discusses the Management of a Rodent Breeding Colony.
- Module 8) Includes content relating to understanding animal behaviour and how we might minimise stress in captive animals, drone use for observation of wild animals and describes some of the tests used in neuroscience research to assess various aspects of rodent behaviour.

Each of these modules has some formative quiz material as well as a summative final quiz that, when successfully passed, will generate a certificate of completion as proof for the trainee to their AEC. (Wildlife modules for both Australian and New Zealand species are in the design phase for the training ComPass suite.)

Phase 3 modules provide training guides for the trainers, some example standard operating procedures (SOPs) as well as templates for trainee skills assessment. These can be used to facilitate DOPS – i.e. the direct observation of practical skills both for training and competency sign off.

The first module includes training materials covering methods used in minimally invasive rodent handling, procedures and injection methods. The second module in Phase 3 includes training materials for use in teaching aseptic method, surgery skills and finally euthanasia methods for rodents. It also includes an SOP for writing SOPs!

These Phase 3 modules include the materials that you might find helpful to establish a technical skills training lab to assist in training novice animal users in these methods and to minimise animal use. These modules are resource rich for those wanting to use inanimate models for skills training to better comply with the 3Rs. There is also a narrated power point video presentation outlining the numerous stations that make up the technical skills training lab at the University of Adelaide provided as a stimulus for the development of training labs in other animal research facilities.

Phase 4 is still in development. It will provide resources for university veterinarians /animal welfare officers and senior technical staff. These resources will be aimed at those who may be in preparation for writing their membership examinations in either the Animal Welfare or Laboratory Animal Medicine Chapters through the ANZ College of Veterinary Scientists. This material will also be helpful for those making the change from general veterinary practice to animal welfare-based practice or laboratory animal medicine.

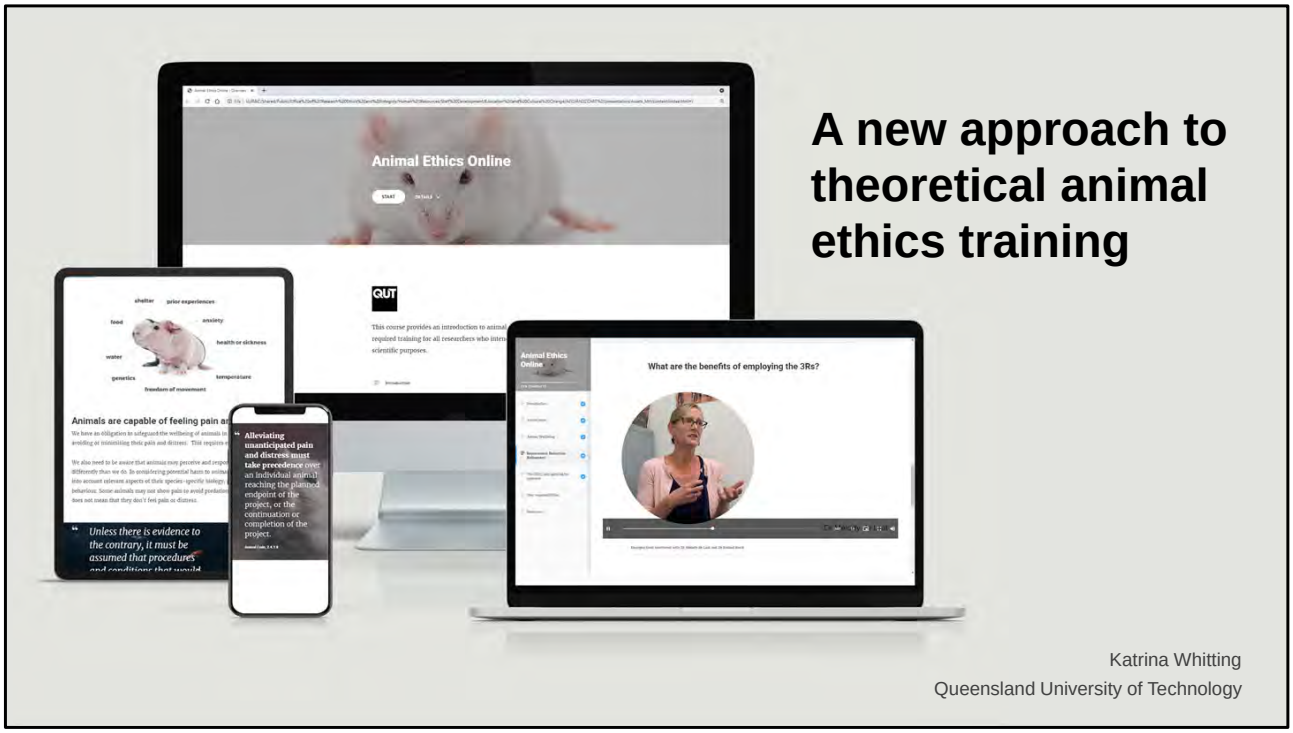
All of the ComPass material is presented using Rise 360, a programme that allows access from any internet-enabled device, so users can access it by digital phone, laptop or tablet device anywhere they have connectivity. So far, University of Adelaide, University of Western Australia and Macquarie University are using ComPass as their primary training and as well as many research institutes and private companies in Australasia.

Go to ANZCCART (Australia) and the ComPass page, as below, to enrol for free. https://anzccart.adelaide.edu.au/compass

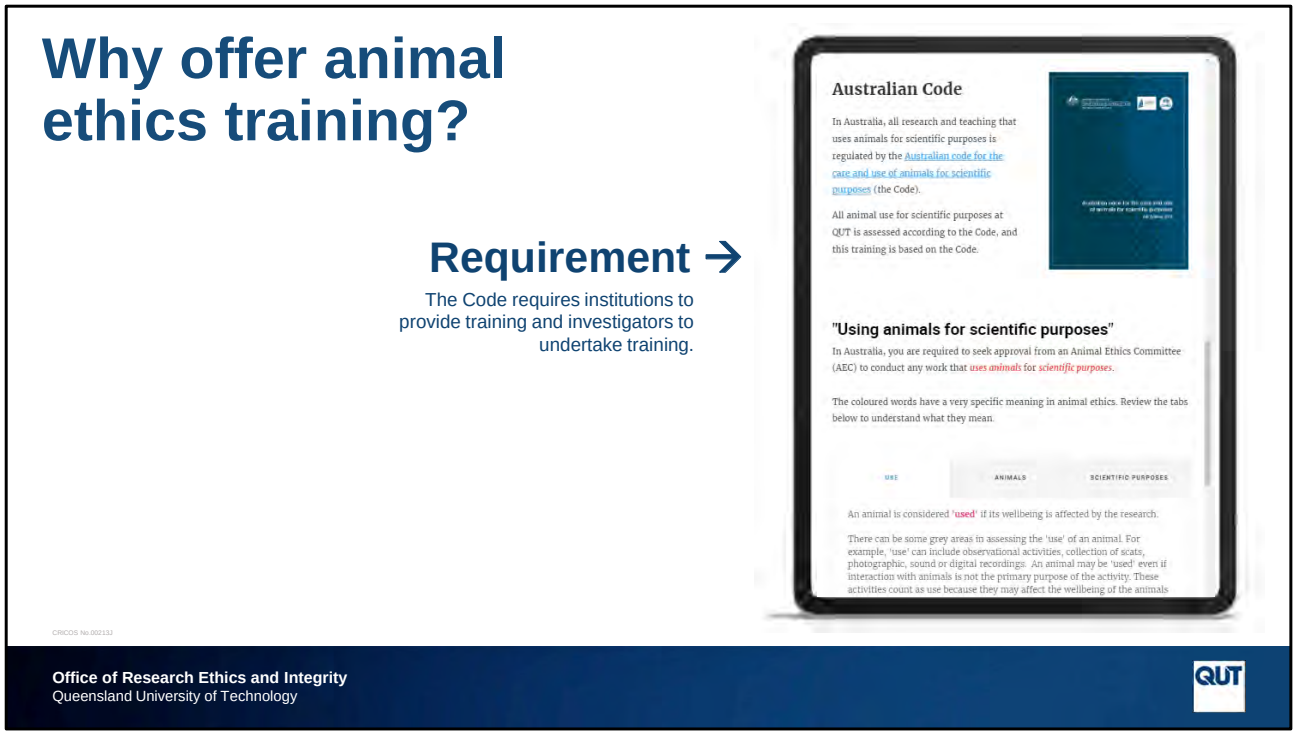
Gail Anderson and the ComPass team

A new approach to theoretical animal ethics training

Melissa Tate, Mark Hooper, Susan Johnson, Katrina Whitting
Office of Research Ethics and Integrity, Queensland University of Technology



Last year we revised our Animal ethics course which previously was a static powerpoint style with large sections taken directly from the Code. We decided to take a different approach so the new course would be more engaging and interactive.



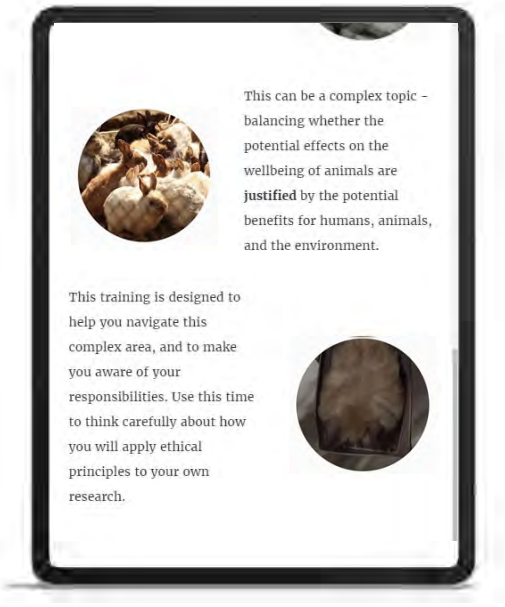
- We started by thinking about why we offer the training…
- As you know it's a requirement for "Institutions to ensure all people involved in the care and use of animals understand their responsibilities and the requirements of the Code".

Why offer animal ethics training?

Requirement →

Provoke thought →

Ethics is hard and complex! Requires critical thought. Researchers are good at thinking deeply. They just need the opportunity and the resources.



CRICOS No.00213J

Office of Research Ethics and Integrity
Queensland University of Technology

- Ethics can be a difficult and complex subject to understand. We wanted our new course to provoke critical thought. Rather than recite the Code and regurgitate facts, we wanted people to think philosophically about the deeper ethical principles behind it.
- However, we still had to provide links to access all the relevant Codes, Acts, Regulations, Guidelines and resources they'd need.

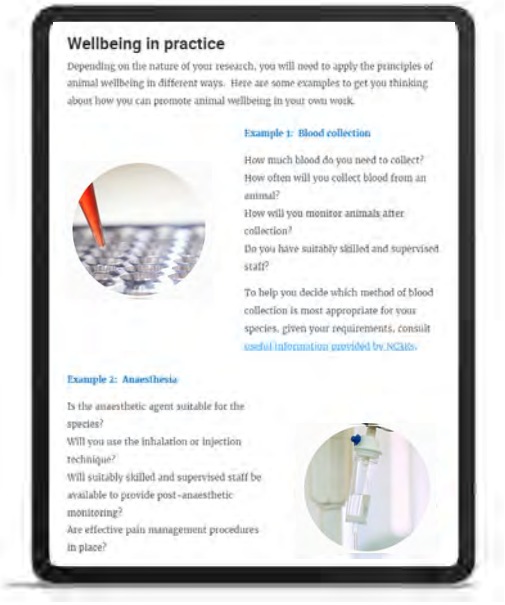
Why offer animal ethics training?

Requirement →

Provoke thought →

Put principles to practice →

The Code is full of principles and responsibilities. Researchers may need help applying the Code to their own work. The outcome should ultimately be improved animal welfare, best practice in animal care, better animal studies, etc.



CRICOS No.00213J

Office of Research Ethics and Integrity
Queensland University of Technology

- We wanted to encourage researchers to think about how to apply the governing principles of the Code to their own projects.
- Remember no two projects are the same, and we wanted to give them the tools to think ethically, put principles into practice and ultimately improve animal welfare and the quality of the science.

What did we require?

Introductory course

- We needed an introduction for all investigators working with animals.
- Further technical and practical training are provided via other avenues.
- Our aim was to keep this course under an hour, and for participants to feel it was time well spent.

Learning goals

- Clearly understand responsibilities
- Feel the *importance* of animal ethics
- Reflect on animal ethics in their own context
- Leave equipped with useful resources
- Know who to ask when they need help

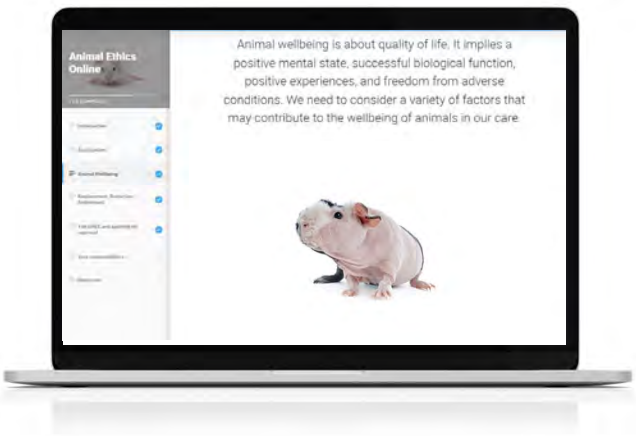
CRICOS No.00213J

Office of Research Ethics and Integrity
Queensland University of Technology

QUT

- So what did we require?
- The course needed to be a similar style to the suite of training offered by QUT that includes modules on Research Integrity, Human ethics, Biosafety etc.
- It also had to be easy to update to keep content relevant to current best practice as needed.
- The animal work at QUT is very diverse so we had to have a broad approach that covered all species and disciplines (rodent lab work, medical training workshops, invasive large animal procedures and wildlife studies).
- The course acts as an introduction to ethics and is compulsory for anyone working with animals. We then have more project specific technical and practical training to assess competency.
- We wanted the time spent completing the course to be proportionate to the amount of animal work (e.g. we have many experienced surgeons only using one animal per year, and also a lot of observational studies).
- We set the following learning goals...

What did we do?



← Focused on wellbeing

Ultimately, animal ethics training is not about codes and compliance. It's about animals.

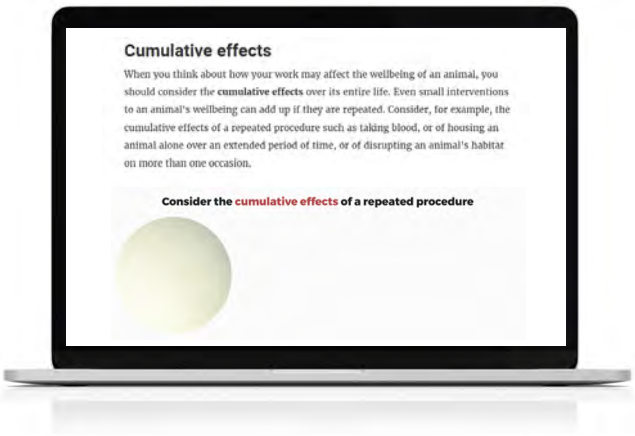
Animals are not just objects for achieving scientific goals.

Office of Research Ethics and Integrity
Queensland University of Technology

QUT

- So what did we do?
- We used the Articulate Rise program and designed the course so most people will complete it in under 1 hour. It is full of movement to keep users constantly stimulated and grab their attention.
- The course ultimately is about animal welfare or wellbeing in practice. It not only covers the Code but also the 5 freedoms and domains of animal welfare, and Best Practice methodology. We also explain how the perception and expression of animals is different to humans (e.g. how animals may not display pain because in the wild that could lead to predation).
- We aimed to connect people to the animals, so animals become more than just an object used to achieve their scientific goals. We use a lot of active images and we wanted them to understand how the animals 'feel' by using humanising examples, such as how rats enjoying tickling, how animals grieve when their mate dies, and how sheep can recognise each other.

What did we do?



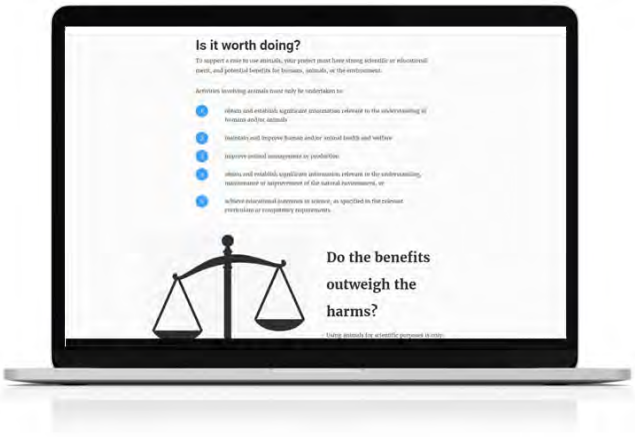
← Focused on wellbeing

← Encouraged reflection

We tried to encourage participants to "consider" or "reflect". For example, in this section participants consider the cumulative effects of a repeated procedure over the lifetime of an animal.

- We decided to use a 'spoken conversational style' with lay language, rather than a legalese or scientific style like the Code.
- We hoped to encourage reflection by using realistic images like this one, so people would consider and reflect on topics like the effects of cumulative suffering.
- We also wanted people to understand how animal wellbeing can affect the quality of their research. You of course can't rote learn ethics!

What did we do?



← Focused on wellbeing

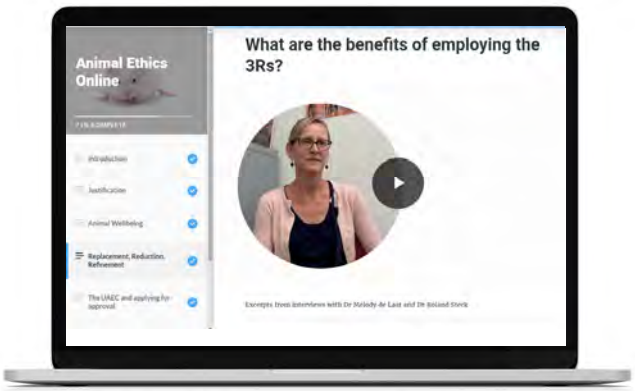
← Encouraged reflection

← Asked a lot of questions

The training is full of open-ended questions.

- The training is full of open-ended questions to make people think. We framed the principles of the code as questions rather than statements like "Is it good science?" "Is it worth doing?"
- For example, rather than explain the specific rules around blood collection from the Code we ask questions like "What volume of blood will you collect? Do you have appropriately skilled and supervised staff?" But then we direct them to the appropriate resources for more information.

What did we do?



← Focused on wellbeing

← Encouraged reflection

← Asked a lot of questions

← Asked experts too

We recorded interviews with some of our researchers and committee members, who provided their insights.

- We wanted to make the content relatable to people doing the course so we asked the experts! We included videos of our researchers, lecturers and committee members. Again with them responding to open-ended questions to provoke thought.
- This one explains some of the benefits of employing the 3Rs…

← Application tips

← Why ethics review is needed

← How ethics leads to better science

Dr Melody de Laat

- They provide tips on common mistakes in applications and how writing ethics applications is different to applying for grants.
- They explain why Committee review is necessary and how it is a helpful rather than an obstructive process.
- They also remind people that scientists aren't always experts in ethics, and how applying ethical principles ultimately leads to better science.

Professor Stuart Parsons

CRICOS No.002132

Office of Research Ethics and Integrity
Queensland University of Technology

QUT

How do we assess them?

Activities during the course

Interactive and test their knowledge of each section

Multi-choice quiz

29 question pool; users get 10 at random, need 80% to pass.

We want the quiz to be…

- **easy** for someone who is familiar with the Code and completed the training.
  (*No need to trick participants with technicalities*)
- **very hard** for someone who is not familiar with the Code and didn't pay attention to the training.
  (*Questions should be hard to guess. Not always: "all of the above".)*

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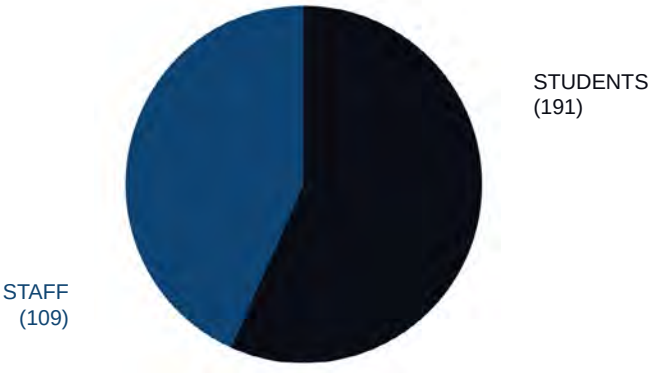
QUT

- So how do we assess them?
- Given the course includes the governing principles but doesn't 'recite' the Code as such, we needed to have a way of assessing they have adequate understanding of their responsibilities under the Code once they complete it.
- There are interactive activities scattered throughout the course that test their knowledge and must be completed to allow them to move on to the next section.
- At the end there is a multi-choice quiz; however, the quiz questions are different to what is asked in the activities to further test their understanding.
- There is a 29 question pool, and users get 10 questions at random, with 80% needed to pass.
- The quiz program allows us to monitor the difficulty of the questions and adjust them as necessary, depending on the results we see from the users.

What's happened so far?

300 participants

Staff: 109
Students: 191



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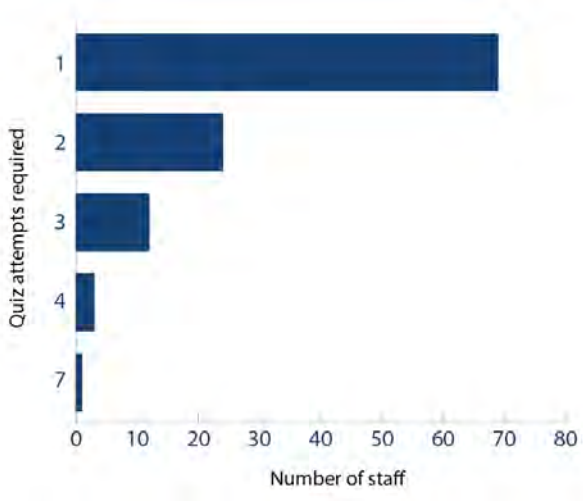
- So what's happened since we launched it last April?
- We require training to be recompleted every three years. We've had 300 completions to date with 'staff' also including committee members.
- We've recently had degrees like Biomedical science add it to their course content.

What's happened so far?

Most staff complete the quiz first try.
Some take two or three attempts.
One person took 7!



CRICOS No.002133

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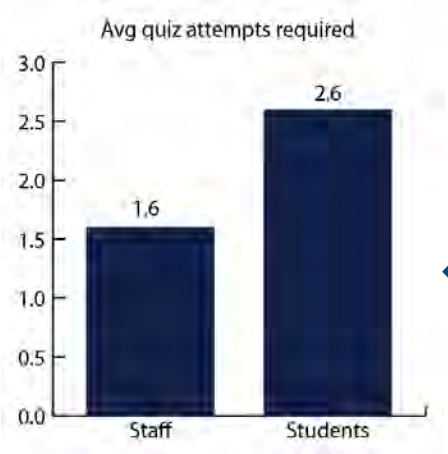
What's happened so far?



Students find the quiz harder, which is to be expected.

CRICOS No.002132

How have we done?

"Nice training set up and presentation. Very engaging. Quiz required some thought but happy to say I passed!"

"This training is comprehensive and fantastic. Well done! I actually enjoyed going through it!"

"I really enjoyed the new interface and the online questions. The system is much more usable than previous versions."

"…a well designed, thorough course."

CRICOS No.002132

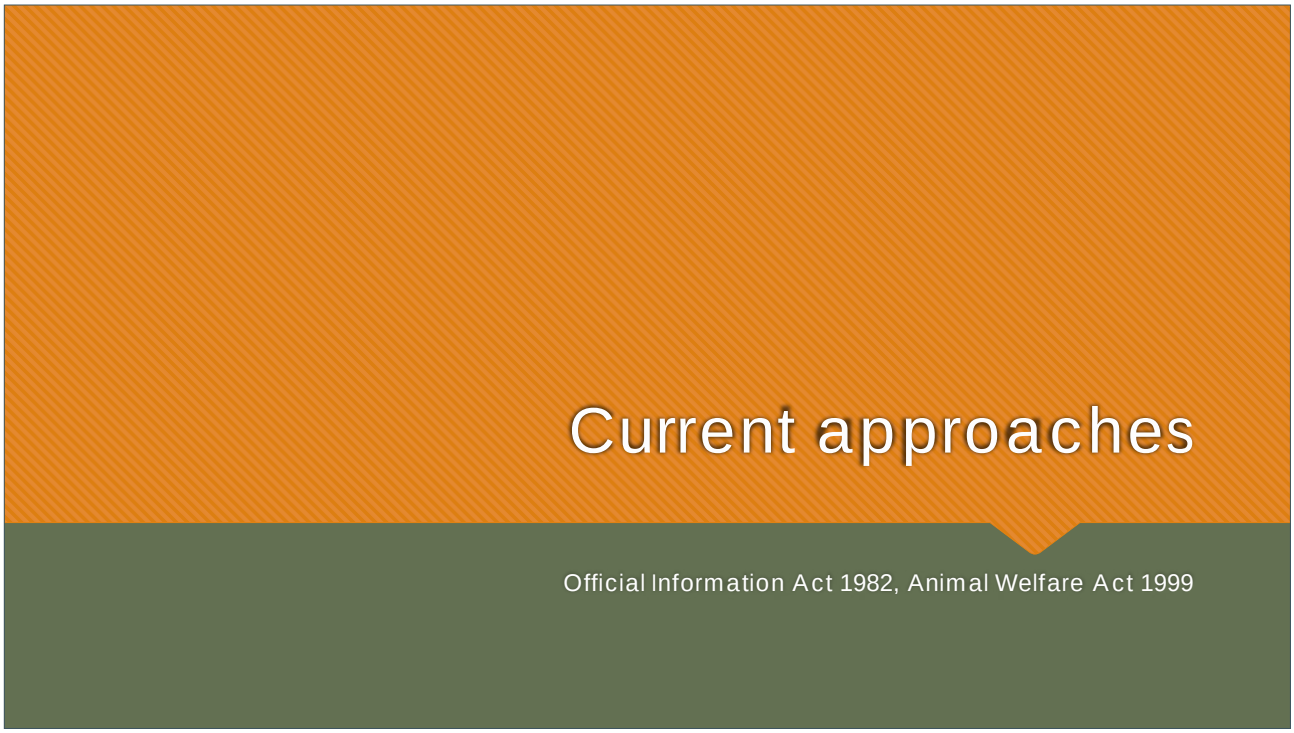
Office of Research Ethics and Integrity
Queensland University of Technology

So how has the course been received? Here's a few of the testimonials from our users…The overall response has been very positive, and people have found the course far more engaging than previously and have enjoyed the course.

I'd also like to acknowledge my co-workers who contributed to the course design and presentation.

Improvements to disclosure regime

Cassandra Kenworthy
Barrister



Official Information Act

Section 5 – Principle of Availability

"The question whether any official information is to be made available, where that question arises under this Act, shall be determined, except where this Act otherwise expressly requires, in accordance with the purposes of this Act and the principle that the information shall be made available unless there is good reason for withholding it."

"Good reason for withholding"

Section 5

- Section 6 – Conclusive reasons for withholding official information
- Section 9 – Other reasons for withholding official information

Section 6

6 Conclusive reasons for withholding official information

Good reason for withholding official information exists, for the purpose of section 5, if the making available of that information would be likely—

(a) to prejudice the security or defence of New Zealand or the international relations of the Government of New Zealand; or

(b) to prejudice the entrusting of information to the Government of New Zealand on a basis of confidence by—

(i) the Government of any other country or any agency of such a Government; or

(ii) any international organisation; or

(c) to prejudice the maintenance of the law, including the prevention, investigation, and detection of offences, and the right to a fair trial; or

(d) to endanger the safety of any person; or

(e) to damage seriously the economy of New Zealand by disclosing prematurely decisions to change or continue government economic or financial policies relating to—

(i) exchange rates or the control of overseas exchange transactions:

(ii) the regulation of banking or credit:

(iii) taxation:

(iv) the stability, control, and adjustment of prices of goods and services, rents, and other costs, and rates of wages, salaries, and other incomes:

(v) the borrowing of money by the Government of New Zealand:

(vi) the entering into of overseas trade agreements.

Section 6(d): replaced, on 1 April 1987, by section 3 of the Official Information Amendment Act 1987 (1987 No 8).

Section 6(e): inserted, on 1 April 1987, by section 3 of the Official Information Amendment Act 1987 (1987 No 8).

Section 9

9 Other reasons for withholding official information

(1) Where this section applies, good reason for withholding official information exists, for the purpose of section 5, unless, in the circumstances of the particular case, the withholding of that information is outweighed by other considerations which render it desirable, in the public interest, to make that information available.

(2) Subject to sections 6, 7, 10, and 18, this section applies if, and only if, the withholding of the information is necessary to—

(a) protect the privacy of natural persons, including that of deceased natural persons; or

(b) protect information where the making available of the information—

(i) would disclose a trade secret; or

(ii) would be likely unreasonably to prejudice the commercial position of the person who supplied or who is the subject of the information; or

(ba) protect information which is subject to an obligation of confidence or which any person has been or could be compelled to provide under the authority of any enactment, where the making available of the information—

(i) would be likely to prejudice the supply of similar information, or information from the same source, and it is in the public interest that such information should continue to be supplied; or

(ii) would be likely otherwise to damage the public interest;

(c) avoid prejudice to measures protecting the health or safety of members of the public; or

(d) avoid prejudice to the substantial economic interests of New Zealand; or

(e) avoid prejudice to measures that prevent or mitigate material loss to members of the public; or

(f) maintain the constitutional conventions for the time being which protect—

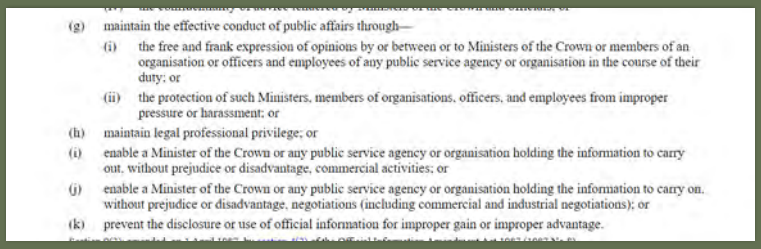
(i) the confidentiality of communications by or with the Sovereign or her representative:

(ii) collective and individual ministerial responsibility:

(iii) the political neutrality of officials:

(iv) the confidentiality of advice tendered by Ministers of the Crown and officials; or

Section 9 continued



(g) maintain the effective conduct of public affairs through—

(i) the free and frank expression of opinions by or between or to Ministers of the Crown or members of an organisation or officers and employees of any public service agency or organisation in the course of their duty; or

(ii) the protection of such Ministers, members of organisations, officers, and employees from improper pressure or harassment; or

(h) maintain legal professional privilege; or

(i) enable a Minister of the Crown or any public service agency or organisation holding the information to carry out, without prejudice or disadvantage, commercial activities; or

(j) enable a Minister of the Crown or any public service agency or organisation holding the information to carry on, without prejudice or disadvantage, negotiations (including commercial and industrial negotiations); or

(k) prevent the disclosure or use of official information for improper gain or improper advantage.

How to get the information

- Section 12 – Requests for information
- Section 15 – Decisions on requests (20 working days)
- Section 15A – Extension of time limits
- Section 16 - Documents

Issues for animal research and testing

- Researchers need confidentiality
- Privacy and health and safety of those involved
- Social license to continue research and testing
- Public want to know what's happening

Animal Welfare Act

Part 6 – Use of animals in research, testing and teaching

Animal Welfare (Records and Statistics) Regulations 1999

Section 183 Animal Welfare Act

- Code holders to keep records
- Code holders to provide annual returns to DG of MPI by end of January for proceeding year
- Offences for failing to comply
  - $5,000 for an individual
  - $25,000 for a body corporate

MPI annual report

Media

Quarter of a million animals used in research, testing and teaching in 2016

The majority of animals that fell into the high or very high impact category were rodents and rabbits. Photo / File

Key statistics in the report

- In 2016, 26 institutions carried out research under their own approved codes of ethical conduct, and 109 under another organisation's approved code.
- Livestock accounted for almost 65 per cent of the animals used.
- Cattle were the most commonly reported species making up 41 per cent of the total number, followed by sheep at 19 per cent, mice at 13 per cent and fish at 8 per cent.
- The majority of animals underwent procedures which had no impact or little impact on them, at nearly 84 per cent of the total number.
- The number of animals that experienced "high" or "very high" impact in 2016 changed with the number of animals in the "high" impact category increasing by 11.9 per cent and the number within the "very high" impact decreasing by 35.3 per cent.
- Of the animals categorised in the "high and "very high" impact categories, the large majority were rodents and rabbits (6897 out of 8596). These animals were classified in these impact grades largely due to use in vaccine testing, veterinary research, and production and evaluation of biological reagents and other medical research detailed in the report.
- There was a decrease in the number of animals that died or were euthanised, with the number of animals that were returned to owners or released to the wild up from the previous year.

MPI report for 2019

11.2 MANIPULATION GRADING OF ANIMALS REPORTED IN 2019

The table below gives details of the gradings for various groupings of animals.

11.2.1 Summary of impact of manipulations in animals used for RTT in 2019

2019 summary	Total reported	Number in each manipulation grade				
		No/virtually no impact	Little impact	Moderate impact	High impact	Very high impact
Rodents and rabbits	80 143	2 620	34 480	36 258	891	5 894
Sheep and cattle	154 145	33 583	98 070	22 218	274	0
Aquatic species[1]	65 428	12 347	38 516	13 905	660	0
Other domestic species	5 269	838	3 980	451	0	0
Birds	8 115	389	3 102	4 624	0	0
Possums	1 389	146	124	583	536	0
Other[2]	1 105	147	485	470	3	0
Grade totals	**315 574**	**50 070**	**178 757**	**78 489**	**2 364**	**5 894**
Grade percentages		**15.9%**	**56.6%**	**24.9%**	**0.7%**	**1.9%**

[1] 'Aquatic species' includes amphibians, fish, marine mammals and cephalopods/crustaceans.
[2] 'Other' includes reptiles and "other species".

Animals featuring in the "very high" impact group were guinea pigs and mice. Animals were classified in this and the "high" impact grades for the following reasons.

Fish

- Fish were used in an environmental toxicity test for a regional council; a standard assessment. The fish that died under the toxicity test were graded as high impact.
- Fish were used in a trial looking at the effect of predator threat on small snapper. The fish graded as high impact died as a result of disease.
- One fish died due to a disease event.
- Migrating eels were captured to obtain fertilised eggs in a project aimed to help close the lifecycle of endangered New Zealand eel species.
- Fish trapping led to the death of 84 bignose galaxias (out of 2672 captured), probably due to low overnight dissolved oxygen levels in three spring heads. This occurred unexpectedly and affected around 3% of the fish captured and would have resulted in a higher level of impact on those fish.
- Fish were graded D due to the combination of various manipulations and sleep deprivation/varying photoperiods.
- Fish were left in containers on the seafloor for 2-3 hours, a process that is likely to be stressful.
- In a study involving the capture of fish using a spear gun, five fish that needed a secondary method of euthanasia (i.e. did not die immediately from being speared) were graded D.
- Fish were reported with an impact grading D as they were transported for 2-6 hours and underwent respirometry testing (for a period not exceeding 48 hours).

Possums

- Possums were used in a study to improve the efficiency of live trapping of this species.
- Possums were used in the testing of new traps, baits, deer repellents and baiting strategies. The research has produced several improved tools for controlling populations of possums.

Rodents and rabbits

- Rats were used in testing the efficacy of baits containing a kea repellent, providing for improved protection of kea during rat-baiting operations.
- Guinea pigs were used in veterinary research, and production & evaluation of biological reagents, as well as in batch release testing for animal vaccines. This is a regulatory requirement to demonstrate potency.
- Mice in the very high impact group were used in testing of antigens and animal vaccines mandated by regulation and in veterinary research, production and evaluation of biological reagents.
- Seven mice were given an incorrect dose of DMSO.
- Three mice were infected with S. aureus via intraperitoneal injection, intravenously or through a large intranasal inoculum to induce pneumonia.
- A mouse was found unexpectedly dead in the cage. A post-mortem examination showed no signs of suffering or abnormalities.
- A mouse was euthanased in a project assessing inflammatory markers associated with a murine model of colitis.
- Three captured wild rats became distressed and died in a trial investigating the potential for deterrents aimed at preventing them from crossing a border.
- Four rabbits should have been reported with an impact grading of C rather than grade D. The Committee approved a D grade in case the impact on the rabbits was more significant than anticipated as this was a new study, however the rabbits were only mildly affected, and a C grade would have been appropriate.

Other species

- Three weasels were part or a research trial testing the effectiveness of a long-life PAPP bait for weasel control.

Sheep

- Sheep were graded D in research into Facial Eczema.
- Sheep were dosed with facial eczema.

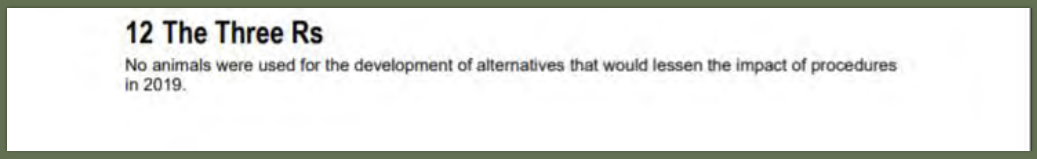
What's the problem?

- No information on stress or pain experienced
- No information on necessity of the experiment
- Notable lack of medical experimentation reported
- 1.5 pages detailing over 8,000 animals experiencing high or very high impact events
- No individual code holders identified

What's the problem?

Why is this information released if it's not transparent and is uninformative?

Final words of the report



12 The Three Rs

No animals were used for the development of alternatives that would lessen the impact of procedures in 2019.

Looking to the reporting of adverse patient events

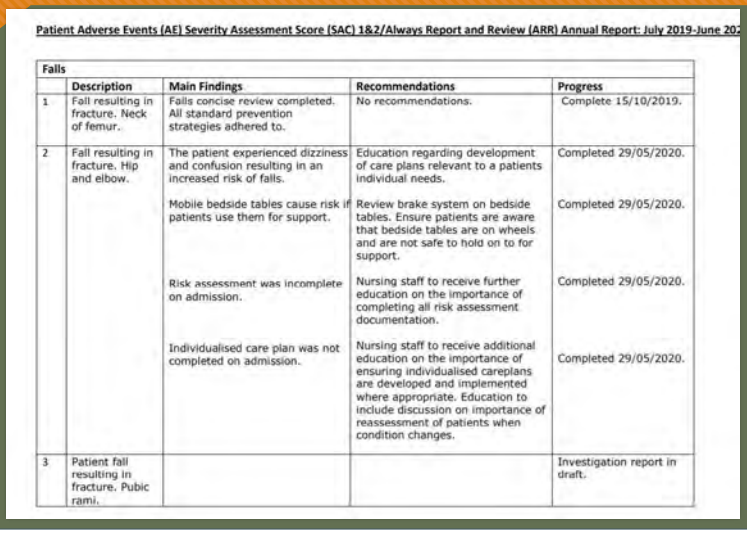
Monitored by HQSC

Each DHB classifies each error as SAC-1 to SAC-4

Each SAC-1 and SAC-2 event reported to HQSC

DHB and HQSC each produce annual reports on SAC-1 and SAC-2 events and proactively release them

Excerpts from SDHB 2019-2020 report

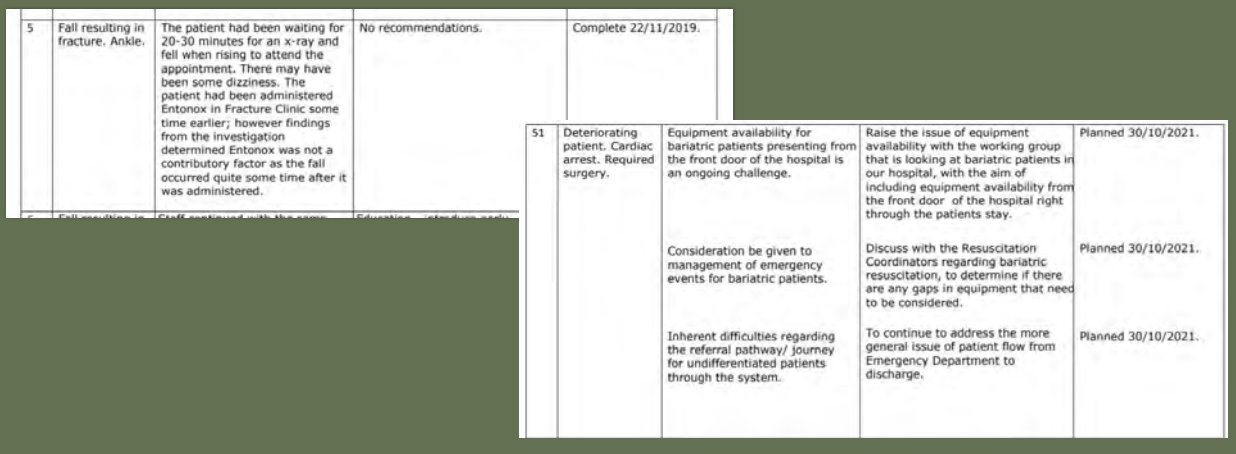


Patient Adverse Events (AE) Severity Assessment Score (SAC) 1&2/Always Report and Review (ARR) Annual Report: July 2019-June 202

Falls

	Description	Main Findings	Recommendations	Progress
1	Fall resulting in fracture. Neck of femur.	Falls concise review completed. All standard prevention strategies adhered to.	No recommendations.	Complete 15/10/2019.
2	Fall resulting in fracture. Hip and elbow.	The patient experienced dizziness and confusion resulting in an increased risk of falls.	Education regarding development of care plans relevant to a patients individual needs.	Completed 29/05/2020.
		Mobile bedside tables cause risk if patients use them for support.	Review brake system on bedside tables. Ensure patients are aware that bedside tables are on wheels and are not safe to hold on to for support.	Completed 29/05/2020.
		Risk assessment was incomplete on admission.	Nursing staff to receive further education on the importance of completing all risk assessment documentation.	Completed 29/05/2020.
		Individualised care plan was not completed on admission.	Nursing staff to receive additional education on the importance of ensuring individualised careplans are developed and implemented where appropriate. Education to include discussion on importance of reassessment of patients when condition changes.	Completed 29/05/2020.
3	Patient fall resulting in fracture. Pubic rami.			Investigation report in draft.

Excerpts from SDHB 2019-2020 report



5	Fall resulting in fracture. Ankle.	The patient had been waiting for 20-30 minutes for an x-ray and fell when rising to attend the appointment. There may have been some dizziness. The patient had been administered Entonox in Fracture Clinic some time earlier; however findings from the investigation determined Entonox was not a contributory factor as the fall occurred quite some time after it was administered.	No recommendations.	Complete 22/11/2019.
51	Deteriorating patient. Cardiac arrest. Required surgery.	Equipment availability for bariatric patients presenting from the front door of the hospital is an ongoing challenge.	Raise the issue of equipment availability with the working group that is looking at bariatric patients in our hospital, with the aim of including equipment availability from the front door of the hospital right through the patients stay.	Planned 30/10/2021.
		Consideration be given to management of emergency events for bariatric patients.	Discuss with the Resuscitation Coordinators regarding bariatric resuscitation, to determine if there are any gaps in equipment that need to be considered.	Planned 30/10/2021.
		Inherent difficulties regarding the referral pathway/ journey for undifferentiated patients through the system.	To continue to address the more general issue of patient flow from Emergency Department to discharge.	Planned 30/10/2021.

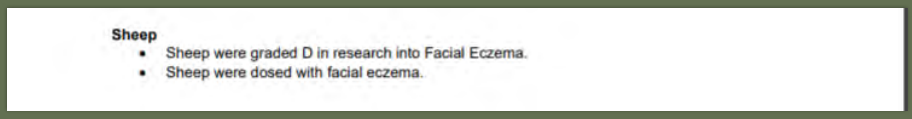
Strengths of the HQSC approach

- Proactive release of information
- Sufficient information to be useful
- Each person affected is represented
- Anonymised reporting

A model for RTT reporting?

- HQSC provides a template for better transparency
  - Which code holder performed the procedure?
  - How many animals were affected?
  - How much pain or distress was caused?
  - What was the purpose of the experiment?
  - Why was an animal used at all?
- Informs the public
  - Is this a test which has benefits that outweigh the pain or distress caused to the animal?
  - Informs where but not who performed the experiment

What it could look like

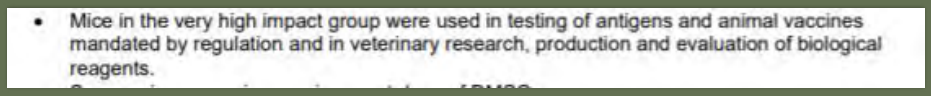


Sheep

- Sheep were graded D in research into Facial Eczema.
- Sheep were dosed with facial eczema.

12 sheep were dosed with facial eczema in order to test if a new antibiotic could effectively control the infection. Pain killers were provided and the sheep exhibited no signs of pain or distress, but the infection resulted in cosmetic disfiguration of their face. Researchers were unable to locate any local sheep with pre-existing infections.

What it could look like



- Mice in the very high impact group were used in testing of antigens and animal vaccines mandated by regulation and in veterinary research, production and evaluation of biological reagents.

40 mice were dosed with a new vaccine which reduces the incidence of *S. aureus*. The mice were then exposed to *S. aureus* to assess the vaccines efficacy. Mice showed mild discomfort upon dosing of the vaccine, and those infected with *S. aureus* experienced high temperatures, pneumonia and sepsis. Those mice were given analgesics and sedatives upon onset of symptoms, and were later euthanised. Rodent models were required by regulators in order to approve the vaccine.

Stories of openness: Conversations with animal rights and anti-vivisection groups, on the road towards an Openness Agreement for Australia and New Zealand

Malcolm France
Consultant in Laboratory Animal Care and Management, Sydney, Australia

About 15 years ago I came across a notice announcing that an animal rights reading group had been established at the university where I was working. I was in charge of the animal research facilities there and although the notice said that everyone was welcome to attend, I was worried. A perceived threat from animal rights activism had often been in the back of my mind and so it seemed rather unlikely that the welcome promised in the notice would extend to me.

I went home and told my wife this news but rather than humouring me as I had hoped, she suggested that I expand my horizons: why not go and hear what they have to say? I had to concede that she had a point.

Until then, I had been working from a poorly informed stereotype of what animal rights meant. I now know that it is a thought-provoking branch of philosophy that among other things encourages us to see the world through the eyes of animals.

Not really knowing what to expect, I went along to my first meeting and was immediately made to feel welcome. The participants were clearly committed to informed and respectful discussion and most impressively, they listened. The group's conveners, Siobhan O'Sullivan and John Hadley, at that time were both post-graduate students in political science and philosophy and since then have gone on to successful academic careers.

Attending those meetings opened my eyes to a perspective on animal ethics that was completely different but no less heart-felt than that which would be familiar to most of us from an animal research background. It was a light bulb moment in which I realised that having one's views tested in this way – by throwing them open to a radically different critique – is what universities should be all about.

I soon felt that being exposed to such different views was something that should be shared more widely so I began inviting Siobhan and John to speak at the animal ethics training sessions I ran for young scientists. It's worth pausing for a moment to think how they might have felt in that situation – they were advocating an animal rights position to an audience of around 200 scientists, many of whom quite likely held a negative, perhaps even hostile stereotype of animal rights. It could have been Daniel in the lions' den, but it wasn't. Invariably Siobhan's and John's contributions generated far more discussion than other parts of the program; it was always respectful and we never encountered the sort of polarisation that characterises so much of this debate in other forums.

Spurred on by such a positive engagement, I've since sought other opportunities to see how animal rights and animal research can come together in conversations to listen and to learn from each other.

A couple of times now I have met staunch opponents of animal research who told me that they had never been allowed to see inside an animal facility. This seemed crazy so I took them on a personal tour. Why not? I'm proud of the work we do, and they were respectful of that. The only part lacking in openness on those occasions was that I didn't tell my employer at the time!

One of my most interesting conversations in this space took place early last year. It arose through my role as Chair of the Animal Ethics Committee at the University of Wollongong.

Sometime previously, the committee had approved a project involving the controversial Forced Swim Test. The project had now come back to the committee because there had been an Unexpected Adverse Event.

During its review of the event, the committee was shown a video of the experiment and the incident in question. The committee decided to suspend the project so the incident could be reviewed in more depth. This proved to be among the most extensive reviews of a procedure by an AEC that I have seen. It spanned several meetings and out-of-session consultations, and I must acknowledge the full support and cooperation of the researchers at every stage.

As the review was approaching its conclusion, and quite by coincidence, the large US-based animal rights organisation, People for the Ethical Treatment of Animals (PETA), embarked on a major campaign to ban the Forced Swim Test. I had been aware of their campaign but initially avoided bringing it to the committee's attention because I didn't want it to influence their decision-making. I had also observed that PETA's focus was on institutions in the US and Europe so it seemed unlikely we would be approached.

Then an email arrived marked urgent: the Vice-Chancellor had received a letter from PETA. And it wasn't just a standard form letter: it referenced papers published by University of Wollongong researchers and was copied to individual academic and non-academic staff. The team at PETA had done their homework.

The letter read in part: "We are writing on behalf of PETA … and our combined 6.5 million members and supporters. It has been brought to our attention that University of Wollongong employees have described forcing rats to undergo forced swim test experiments in published papers… Because the forced swim test lacks scientific value and causes immense suffering to animals, we have launched a global campaign aimed at ending its use entirely. We are confident that we will convince a growing number of key stakeholders that they should end the use of this test."

The University had become sensitive to this sort of correspondence because some years previously, opponents of a particular animal research project (which was still only at the pre-approval review stage) had organised a campaign that at its peak resulted in a storm of 2,000 emails sent in protest to the ethics office in the space of just one weekend.

While we wondering how to respond, I discovered a video that PETA had produced on animal research called 'Test Subjects'. It featured three PhD scientists sharing similar experiences of frustration when trying to raise ethical concerns about their animal studies, especially in relation to the utility of the animal models they were working with. After repeatedly having their concerns dismissed, they eventually felt compelled to abandon their research careers and use their scientific training to support PETA's campaigns against animal research. They hadn't been listened to. Pertinently, one of those three scientists was now spear-heading PETA's campaign against the Forced Swim Test.

After watching the video, I suggested that instead of just responding to PETA in writing, the University should take a more open approach and seek a conversation with PETA. I have been impressed with the University of Wollongong's willingness to engage thoughtfully in ethical matters such as this, so I wasn't surprised when they agreed to us setting up a Zoom meeting. PETA accepted our invitation and we met online with three of their representatives.

The tone of our conversation was respectful, and the scientific training of the PETA representatives added helpful insight. We talked comfortably for about an hour. They listened to us, and I hope they felt we listened to them too. We described our experience with the Forced Swim Test and explained that the University did not have a fixed institutional policy on it but would of course follow the AEC's position regarding it. I felt we achieved far better communication through that conversation than would ever have been possible had the parties tried to convey their views in writing.

The experience reminded me that having a conversation is different to just talking. Conversations also require listening, and sometimes this can be hard. I can understand why reaching out in the way we did with PETA is something that some institutions would be hesitant about, and that building trust takes time. But I have found conversations such as these to be deeply rewarding.

I enjoy reading about the history of the anti-vivisection debate and have often found it instructive. The thing that strikes me most is how little the arguments have changed over time: it has essentially been a century and a half of stalemate. I really feel that if the ethical debate over animal research remains stuck in this sort of trench warfare – a polarisation of animal research versus animal rights – it is never going to move forward.

Reaching out to those with a different – and perhaps radically different – ethical position I think is a way forward. Rather than being a threat, I see it as an opportunity that can help avoid the echo-chamber of confirmation bias. We might not fundamentally change our position nor might those we engage with fundamentally change theirs. But at the very least, we should be able to come away better-informed and acknowledging that the issues are far more complex than they might have seemed. And on this point, I must commend

ANZCCART New Zealand for the diversity of views they have brought together at this conference – it is wonderful to see presentations by Tara Jackson from the New Zealand Antivivisection Society and Rachel Smith from Humane Research Australia among many others.

I'll conclude with a short reflection on the meaning of the word 'ethics' because I think it ties in well with the idea of having challenging but respectful conversations. This idea is articulated clearly in a report by The Ethics Centre, which is a Sydney-based organisation established over 30 years ago with the purpose of supporting sound ethical decision-making in everyday life. The Ethics Centre's report notes that an open society is not marked by a uniformity of ethical perspectives. Rather, it says:

Ethics invites (perhaps requires) engagement with alternative points of view. At the very least…ethics encourages people to challenge their assumptions about what ought to be done, about how we ought to live. This is only possible if there is an arena in which people can explore these questions; in part, by encountering the views of others who might hold radically opposed positions.

This says to me that we need to be prepared to go out on a limb, and that we will make better ethical decisions if we dare to have conversations with those whose ethical position challenges our own.

Investigating the boundaries of openness: Conversations with animal rights and anti-vivisection organisations

Jodi Salinsky
Animal Welfare Officer, Office of Research Strategy and Integrity, University of Auckland, Te Whare Wananga o Tamaki Makaurau and ANZCCART New Zealand, Royal Society Te Aparangi

Outline

- How this started
- What happened next
- What has been achieved
- What could be achieved in NZ
- Why is this so important

How did this start?

- NZ Board of ANZCCART meeting
- Tara Jackson, NZAVS invited guest
- It was a little weird, but fine…
- We ate a plant based lunch together and chatted
- Seemed so far apart with things at the time…

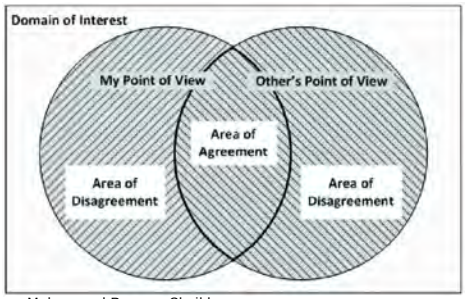
What happened next

- Positive email communication about an OIA or two
- Phone call about an NZAVS communication sent out
- Respectful communication both sides
- Made me think…could there be more…?
- Further conversations and emails

Te Tari Rautaki Rangahau, Matatika
Office of Research Strategy and Integrity

What has been achieved

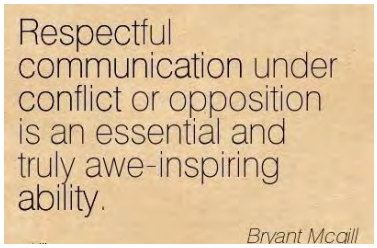
- Solid foundation of a relationship
- Areas of agreement known
- Openness Agreement feedback
- Rehoming of animals project



Muhammad Ramzan Sheikh
Bahauddin Zakariya University | BZU · School of Economics
PhD Economics, Post Doc (LSE) UK

What could be achieved in NZ

- Funding for replacement research
- Rehoming of animals (NZ network?)
- Registry of animal research
- Review of AEC structure/processes



Te Tari Rautaki Rangahau, Matatika
Office of Research Strategy and Integrity

Why is this so important

- Most people working in animal research want replacement of animals as the long-term goal
  - When scientifically validated and legal methods become available
- Fewer animals, Better science, Faster cures
  - GetReal! podcast tagline
- Animal and human welfare a priority

- This is the 3Rs (Replacement, Reduction, Refinement)
- We can possibly get some places faster together…


We all do better when we work together. Our differences do matter, but our common humanity matters more.
Bill Clinton

The Minimal Anaesthesia Model: Development and refinement of the concept and subsequent practical applications

Craig Johnson
Tāwharau Ora, Massey University

Introduction

I have been fortunate to have worked in animal welfare science during a very exciting time in the discipline. Over the course of my career, the concept of welfare has moved from a five freedoms approach emphasising the absence of harms to a five domains model that considers the importance of positive welfare and integrates the affective state of animals into its considerations. This change in emphasis has allowed the concept of a life worth living to become the benchmark for considerations of animal welfare and led to the increasing recognition of sentience in non-human animals.

My contribution has been primarily in the development of a new technique, the minimal anaesthesia model, that enables the quantitative measurement of a mammal's perception of pain when it is subjected to a noxious stimulus. This technique clearly links an animal's affective state with changes in physiological variables derived from the electroencephalogram (EEG) and as such has been a component of the literature that forms the basis for our present understanding of affective state in animals.

This paper will cover my work in the development of the minimal anaesthesia model and its applications in three areas where I have used it as an applied tool. Rather than focus on the research studies themselves, my aim is to explore the theoretical background of the model and its use. More details of the specific applications can be find in the studies themselves which are referenced here.

Development and validation of a minimal anaesthesia model of pain perception

In the 10 years following my PhD I worked on ways of using the electroencephalogram as an indicator of potential pain perception in anaesthetised animals. The model I developed has become known as the minimal anaesthesia model. It is entirely original and uses data recorded from the electroencephalogram of anaesthetised animals to measure responses to stimuli and indicate if these stimuli would be perceived as painful if the animal were conscious. This model enables pain research to be undertaken without inflicting pain on the experimental animals involved because they are anaesthetised for the duration of the experiment. All data are collected prior to the animal's recovery from anaesthesia and so pain relief can be provided using standard clinical techniques even when the animals concerned form part of a control group. In addition to the refinement represented by the ability to always provide pain relief, the inclusion of a control group that does not receive analgesia during data collection gives studies performed using this model enhanced statistical power and enables an overall reduction in the number of animals used in such studies. To date the minimal analgesia model has been adapted for use in 13 different species of mammal. The National Animal Ethics Advisory Committee's 3Rs award in 2006 was given in recognition of the development of this model.

During my anaesthesia residency at the Animal Health Trust (Newmarket, UK) I demonstrated a change in certain EEG-derived variables to changing partial pressures of halothane (Johnson et al., 1994). Subsequently, during my PhD at the University of Cambridge, I characterised the EEG response to other inhalation anaesthetics (Johnson & Taylor, 1998) and also a number of injectable anaesthetics (Johnson & Taylor, 1997, 1999; Johnson et al., 2000a; Johnson et al., 2000b; Johnson et al., 2003). One of the interesting findings was that the ratio between an agent's effect on the F50 (median frequency of the EEG) and F95 (95% spectral edge frequency of the EEG) appeared to be an indication of the potency of the agent as an analgesic. Potent analgesics such as alfentanil (Johnson & Taylor, 1997) appeared to reduce this ratio to a greater extent than narcotics such as thiopentone (Johnson et al., 2000a).

Subsequent work after my move to Bristol University (Murrell et al., 2003; Murrell et al., 2005) indicated that surgical stimulation presented under minimal general anaesthesia with halothane resulted in an EEG response that was opposite to that elicited by analgesic agents and that surgical stimulation in the presence of analgesic agents resulted in a response of reduced magnitude. The initial validation of this technique was undertaken in horses, but I have since carried out studies demonstrating the model in 12 other species of mammals and similar validations to that in the horse have been demonstrated in four of these: horse (Murrell et al., 2003; Murrell et al., 2005); cattle (Gibson et al., 2007); rat (Murrell et al., 2010); and red deer (Johnson et al., 2005). A more detailed discussion of the development of this model can be found in my review of the model as applied to slaughter (Johnson et al., 2012).

In order to be able to properly apply a research methodology it is important to understand its characteristics and limitations. Over the course of the minimal anaesthesia model's development, I have conducted a number of experiments (Johnson et al., 1995; Murrell et al., 2010; Murrell et al., 2007; Murrell et al., 2008) to investigate this aspect with the aim of better understanding the model itself and so being better able to interpret data obtained when using the model. The appropriate use of electrophysiological and other tools to assess pain perception in the research environment has become a particular interest of mine, which I have explored in two review articles (Johnson, 2016; Murrell & Johnson, 2006).

Use of opioids in equine anaesthesia

For many years, opioids have been known to cause increases in locomotor function in conscious horses (Mama et al., 1992; Pascoe et al., 1991). In contrast to other species, their effects on the minimum alveolar concentration (MAC) of inhalation agents have been shown to be equivocal, some studies reporting no change in MAC (Pascoe et al., 1993) and others an increase in some horses rather than reduction (Matthews & Lindsay, 1990). These studies have often been taken to indicate that opioids do not contribute to anaesthesia in horses in the same way as in other species. Other data indicate that the effects of opioids on the cerebral cortex are similar to those in other species, for example compare Johnson et al. (1997) with Scott et al. (1985).

The effects of opioids are more complex and potentially more confusing in horses than in other commonly anaesthetised species, but they have been shown to have similar effects on the sensory nervous system of horses as they do in other species. The increased motor function and equivocal effects on MAC seem to be direct effects on the motor systems rather than reflecting a change in anaesthesia per se. Since this has become clear, opioids have been more widely used in equine anaesthesia and shown to be beneficial in terms of quality of recovery and incidence of post-operative complications, particularly colic (Love et al., 2006).

Development of awareness and pain perception in neonates

Neonatal mammals develop the ability to perceive pain by means of complex interactions of structural and biochemical factors that govern the function of the central nervous system. The onset of neurological milestones such as vision, hearing and complex behaviour occur at different times (relative to birth) in altricial and precocial species and I have demonstrated that the onset of the ability to perceive pain also occurs at different times in these different groups (Diesch et al., 2009; Diesch et al., 2010; Johnson et al., 2005; Johnson et al., 2009; Lizarraga et al., 2007; Kells et al., 2017a; Kells et al., 2019). In addition to pain perception at the time of injury, it has been shown that when humans are subjected to painful procedures such as circumcision very early in life, they can develop a long-lasting increased susceptibility to pain (hyperalgesia) that can persist into their adult life (Buskila et al., 2003; Taddio et al., 1997). Using sheep as a model, I have demonstrated that this hyperalgesia is dependent on the timing of the stimulus (McCracken et al., 2010) and that a single noxious stimulus delivered prior to the onset of pain perception causes persistent changes in brain function (Impey et al., 2012) as well as altered responses to future painful stimuli when compared to the same stimulus delivered after the onset of pain perception (McCracken et al., 2010). I have demonstrated physical (Kells et al., 2017b), molecular (Lizarraga et al., 2008, 2006) and functional (Impey et al., 2012) changes in the nervous system that may be responsible for these findings. These results have important implications for the need to provide pain relief for noxious stimuli even before animals develop the ability to perceive pain. In New Zealand they have resulted

in changes to the Code of Welfare for Painful Husbandry Procedures, which now contains a gold standard that analgesia should be provided for animals at all ages.

Welfare issues associated with killing of animals (especially in slaughter, but also in other contexts)

One of the benefits of the minimal analgesia model compared to other research techniques used in pain research is that data are recorded with no time lag. In contrast, techniques that rely on changes in the endocrine system, for example, are associated with a delay that can be as long as 30 minutes between stimulus and response. The instant response seen with this model means that it can be used to record pain responses even in animals that are physiologically unstable. A major application of this feature of the model has been its use to evaluate the welfare impacts of techniques used to kill animals in different circumstances. My use of the minimal anaesthesia model to investigate slaughter in cattle without prior stunning (Gibson et al., 2009a; Gibson et al., 2009b) demonstrated clearly for the first time that the act of slaughter by ventral neck incision is associated with noxious stimulation that would be likely to be perceived as painful in the period between the incision and loss of consciousness (Mellor et al., 2009). Additional studies carried out in conjunction with this demonstrated that stunning with a captive bolt resulted in immediate cessation of EEG activity (Gibson et al., 2009c) and that such stunning was protective against the response to ventral neck incision (Gibson et al., 2009d). This research has resulted in legislative changes in New Zealand, the proclamation of a fatwa (Islamic religious teaching statement) in Jordan and a reconsideration of stunning prior to slaughter in several countries. Commercial slaughter in New Zealand now requires stunning prior to bleeding and in the UK, the proportion of cattle that are stunned prior to halal slaughter has risen from 0% in 2007 to 80% in 2014.

Concluding remarks

The use of the minimal anaesthesia model, especially when combined with other techniques such as behavioural analysis, has proven to be a very powerful way to investigate an animal's perception of noxious stimuli. In particular it enables clear links between physical responses and the underlying affective state of the animal to be made. These links have both expanded our understanding of the development and mechanisms of pain perception in the central nervous system of mammals and also enabled the extent to which animal husbandry procedures such as castration, tail docking and killing are painful to be measured. These latter applied studies have been used as the basis for significant changes to the ways in which painful procedures are carried out. They have contributed to new ways of providing pain relief in a variety of contexts and to changing legislation to ensure that means of mitigating are used in practice.

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