JME Online First, published on July 24, 2017 as 10.1136/medethics-2016-103630

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Advances in neuroscience imply that harmful experiments in dogs are unethical

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Received 18 April 2016
Revised 18 May 2017
Accepted 9 June 2017

ABSTRACT

Functional MRI (fMRI) of fully awake and unrestrained dog 'volunteers' has been proven an effective tool to understand the neural circuitry and functioning of the canine brain. Although every dog owner would vouch that dogs are perceptive, cognitive, intuitive and capable of positive emotions/empathy, as indeed substantiated by ethological studies for some time, neurological investigations now corroborate this. These studies show that there exists a striking similarity between dogs and humans in the functioning of the caudate nucleus (associated with pleasure and emotion), and dogs experience positive emotions, empathic-like responses and demonstrate human bonding which, some scientists claim, may be at least comparable with human children. There exists an area analogous to the 'voice area' in the canine brain, enabling dogs to comprehend and respond to emotional cues/valence in human voices, and evidence of a region in the temporal cortex of dogs involved in the processing of faces, as also observed in humans and monkeys. We therefore contend that using dogs in invasive and/or harmful research, and toxicity testing, cannot be ethically justifiable.

INTRODUCTION

More than 200 000 dogs are used worldwide in 'harmful' research and toxicity testing (experiments likely to cause pain, suffering and distress, not conducted for veterinary purposes, and often terminal) every year, with much of these used as the non-rodent species in the evaluation of the safety of new drugs and chemicals. This continues in spite of opposition by the majority of the public, and also formidable scientific and ethical arguments against it. For example, recent analyses have shown that the testing of new human drugs in dogs has little or no scientific basis or justification, because canine data are not significantly predictive of the efficacy and safety of new drugs in humans.[1] This is due, in part, to major differences in the cytochrome P450 'CYP' enzymes that metabolise drugs.[2] These differences, in level, activity and amino acid sequence, occur even between breeds and strains of the same species, meaning extrapolation of data between species, such as between dogs and humans, is unreliable (see ref [3]). Ethical concerns are based on the stressful nature of the laboratory environment, and experimental manipulations and procedures that often may also be painful and terminal (see, eg, ref [4]). Dogs are known to react to unfamiliar objects, sounds, people, situations and manipulations, as well as restraint and association with prior unpleasant experiences, with reactions known to reliably indicate conflict and stress, as well as anxious postures (see ref [5]). Barren, restricted environments (common features of most laboratory kennels), kennel noise and restricted sight lines are acknowledged stressors, and together these factors lead to well-characterised stereotypies—repetitive, invariant behaviour patterns with no obvious goal or function, which include circling, pacing, whirling, jumping, wall bouncing, and repetitive grooming or self-biting—as well as other abnormal behaviours such as polydipsia or polyphagia (eating and drinking to a great degree), compulsive staring and excessive barking, for example (see ref [5]).

Such welfare concerns constitute a large part of the ethical objection to dog experimentation. A variety of ethical approaches exist (recently and elegantly summarised in a report by the Oxford Centre for Animal Ethics,[6] and, eg, the works of Peter Singer,[7] Tom Regan[8] and others). One is instrumentalism, in which dogs are viewed as scientific instruments, a means to an end to be used in experiments for the benefit of humans, or even to increase knowledge, usually providing there is no unnecessary cruelty. Although it may be argued that no dog experiments are absolutely instrumentalist, as the welfare of the dogs is considered alongside human benefits (see below), it may be argued that some dog experiments are—or almost are—practically instrumentalist because they are approved and conducted even in the face of low likelihood of success, and/or low benefit and/or high severity (based on animal welfare scientist Patrick Bateson's 3D Cube[9]). Another is an approach based on dogs' rights to life and to not be harmed, precluding their use in scientific experiments at all, or at the very least in invasive research that is likely to infringe these rights and to cause them pain and suffering. This approach is based on societal morals, increasingly underpinned by scientific knowledge, that, it is argued, afford rights to and acknowledge attributes in non-humans such as dogs, which include intrinsic worth as individuals, with lives deserving of respect, and therefore a right not to be harmed (unless it is for their own good, such as in remedial surgery). Such attributes include the capacity for various emotions, feelings and cognitive abilities, including pain, shock, fear, foreboding, trauma, anxiety, stress, distress, anticipation and terror, as well as positive attributes such as pleasure, joy, anticipation, rewards and so on. These elevate the ethical status of dogs and challenge moral anthropocentrism (that humans should always have absolute priority in our moral thinking), instrumentalism (that animals exist for human beings, to serve their interests) and dualism (that humans should be distinguished and separated from other animals).[6] There are also utilitarian or 'greater good' approaches of variable 'stringency', in which

To cite: Bailey J, Pereira S. *J Med Ethics* Published Online First: [please include Day Month Year]. doi:10.1136/medethics-2016-103630

the harms caused to the dogs in experiments are weighed against the benefits they provide to humans (involving a 'harm:benefit analysis' (HBA)). While a rights-based approach, rather than a utilitarian perspective, is the standpoint taken by the authors, the latter is the dominant form of reasoning within science,[10] and therefore is the rationale we use to argue against dog experimentation in this review.

In assessing harms to dogs from experimentation—central to the HBA—it is clearly of paramount importance to attempt to correctly establish and appreciate the genuine level of suffering the dogs experience. This is heavily dependent on an accurate comprehension of their sentience—something we argue is not done currently, and which therefore, along with general exaggeration of human benefits, leads to the HBA being greatly skewed and biased (see Discussion and Conclusion). Efforts to better understand canine sentience, however, continue and are more powerful than ever. Alongside this growing concern about the use of dogs in harmful experiments, there have been increasing efforts to understand the canine mind. For many years, this has been elucidated via ethological research, which, while elegant and greatly informative, may suffer from inherent vagaries and inconclusive inferences, and can only go so far.[11] Such limits and caveats, however, are inherent in any approach, and these should not negate or detract from the weight of evidence. Simply applying Occam's razor, it is abundantly obvious that animals behave as though they feel pleasure. For instance, they play—something not restricted to primates and, for example, dogs, but which extends to many species, including many birds, reptiles, fishes and cephalopods (see refs [12 13]). They also appear to take great pleasure in food and sex, act as though they enjoy touch and physical sensations such as sunbathing, seem to experience various emotions and many more (see refs [13–15]). In spite of these, there has always existed a poor attitude in part of the scientific community, and at large—rightly criticised by many—that insists on ever more 'proof' of these qualities in non-humans, or denying non-humans these experiences and abilities while simply accepting them in humans (human sentience is no more 'provable', scientifically); a quasi-embargo of properly addressing these concepts or at least on avoiding their discussion in any great detail.[13] All these things are scientifically and ethically inconsistent, and therefore they result in poorer and less ethical science.[12 13]

It is of course difficult, if not impossible, to *prove* sentience in other beings; that is accepted. However, we readily accept the existence of sentience in other humans based on weight of evidence, and consistency—and science—demand we ought to do likewise with non-humans.[13] Further, the quest to understand canine cognition and sentience has taken great strides in recent years, with non-invasive functional MRI (fMRI) scanning of fully awake, unrestrained, trained volunteer dogs, which was first reported in 2012 by Gregory Berns' group (Emory University, Atlanta, Georgia, USA).[16] Unlike many experiments involving dogs, these imaging investigations may be regarded as not ethically troublesome, in that they involve neither dedicated breeding and housing of dogs specifically for experimentation, nor techniques that are invasive and/or harmful to those dogs, and they would not, therefore, be considered as 'animal experiments' in most countries' legislation. Those who may have moral objections to harmful dog experiments generally, including the authors, therefore have no objections to this type of research in principle. Indeed, it is helping the ethical case against using dogs in invasive/harmful research, as it has helped to 'fill the gap' left by traditional methods of study, allowing investigation of *how* dogs' brains function with regard to what they perceive, the similarity of their emotional responses to those of humans, their cognitive abilities and their social intelligence.[17] Together with a surge in canine cognition research generally, both neuroscientific and behavioural, there is now substantial evidence to support the contention that dogs are able to perceive, feel and understand much more deeply than previously thought. Examples include the activity of the brain's caudate nucleus, which is associated with pleasure and emotion; the comprehension of language and emotion in human voices; and the processing of faces and facial expressions (see ref [17]).

In this brief review, we discuss recent evidence in this field, including claims by some researchers that canine cognition and sentience are much more advanced than previously accepted. We argue that scientific evidence demands we reassess and redefine the way we treat dogs, and give dogs the protection they consequently deserve from any act or procedure that would cause pain, distress or harm.

Recent research on canine cognition

The caudate nucleus shows important similarities in humans and dogs

The caudate nucleus is a structure deep in the brain (part of the basal ganglia), which, among other things, is associated with positive emotions and expectations, enjoyment, social rewards, learning and memory (see ref [17]). For the first time, in 2012, Berns *et al* reported on fMRI studies of fully awake and unrestrained dogs showing similarities in caudate activity in dogs and humans. Dogs presented with human hand signals that were associated with a food reward showed a response in the caudate nucleus that was not present with hand signals associated with no food reward, in a manner similar to experiments on both humans and non-human primates.[16] A subsequent investigation validated these findings in a greater number of dogs, showing that this caudate response was similar to a comparable human study, and that caudate activation was actually more consistent in dogs than in humans.[18] To further understand the significance of human interaction in the lives of dogs, the same researchers (Berns *et al*) investigated canine brain responses to familiar and unfamiliar human and dog odours.[17] On average, only the 'familiar human scent' activated the caudate nucleus in dogs, suggesting that reward response is reserved for familiar humans rather than conspecifics, and that not only did dogs discriminate that scent from the others, but that they had a positive association with it. They concluded that, beyond illustrating the power of the dogs' sense of smell, this underlines the importance of human bonding and attachment in the lives of dogs.

Dogs are highly sensitive to verbal/visual communication and to human emotions

Dogs are exquisitely sensitive to verbal communication. Experiments have shown that they understand elements of speech, and, similarly to humans, use different parts of the brain to process its verbal components and its emotion and intonation. In other words, they pay attention to what we say and also to how we say it.[19] Recent fMRI experiments have suggested a dedicated 'voice area' in the canine brain, similar to those located in the human and macaque brain.[20 21] This first evidence of a 'voice area' in a non-primate was suggested by way of fMRI scanning of awake, unrestrained dogs, in which it was noted that human and dog brains show great similarities in the processing of emotionally loaded sounds (not sentences or words) in an area near the primary auditory cortex, allowing the perception of a speaker's identity and emotional state, for example.[22]

As well as being sensitive to verbal communication, dogs are also extremely sensitive to cues that signal communicative intent, in a manner previously attributed only to human infants.[23] For

example, they seem able to take into account humans' visual attention (ie, where they are looking) when making decisions and deliberating actions. Studies have shown that dogs have empathic responses to humans in distress, not limited to those whom they know/with whom they have a connection; they may be able to morally evaluate—in essence, to try to determine the difference between what is right and what is wrong in a personal situation by using logic—are in tune with human emotions, and to some degree may be able to understand how we are feeling and want to 'help' with behaviours that are '… consistent with empathic concern and comfort-offering', though which could be interpreted as emotional contagion.[24 25] For example, moral behaviours such as altruism, tolerance, forgiveness, reciprocity and fairness are evident in the play of canids: they have rules to ensure that play is not misinterpreted as spoiling for a fight, which include clear communication (like the 'play bow'), assessing partners' abilities to help establish an even footing (involving self-handicapping and submission), apologetic behaviour including understanding and forgiveness if things go too far, and sincerity and fairness (see ref [26]). In experiments similar to those performed in human investigations, dogs oriented towards humans—whether familiar or strange—when they were crying, rather than talking or humming, consistent with behaviour regarded as expressing empathic concern. They also appear to discriminate human emotions from human facial expressions, not limited to the mouth.[27] Indeed, there is evidence that—in common with primates for whom facial recognition and processing is very important—dogs also process facial information,[28] discriminating faces based on species and novelty.[29] Further, fMRI experiments suggest that this is effected by dedicated neural 'face processing' circuitry in visual cortical areas, rather than due to purely associative mechanisms (eg, associating a face with a meaningful outcome, such as food) in reward areas of the brain[30]; and, crucially, recent (2016) experiments have shown that dogs are able to *integrate* emotional information from visual (facial) and auditory (vocal) cues and inputs—the first time that integration of heterospecific emotional expressions in a species other than humans, as well as cross-modal integration of conspecific emotional expressions beyond primates, has been demonstrated.[31] The ethical significance of all of this lies in the importance to dogs of recognising others (canine and human) and their mental/emotional states and intentions, in facilitating social interactions and functional relationships (both short and long term), in communication, and in the ability to anticipate the behaviour of others and adapt and respond to situations quickly and appropriately in order to increase chances of survival.[27–29 31]

In summary, recent research may suggest that dogs are highly sensitive to cues that signal intent; can show empathic concern; have 'voice areas' in their brains similar to those of primates, enabling them to perceive emotions associated with vocal communications; can process and recognise faces, as well as perceive emotion from facial expressions; and can understand complexities of verbal content.

DISCUSSION AND CONCLUSION

The ability to train volunteer dogs (who have the opportunity to opt out) to lie still while undergoing fMRI scans has recently opened up new avenues of research into canine cognition and greatly augmented what we can learn from ethological studies in this field. As reviewed here, fMRI studies of the canine brain have revealed positive and consistent responses in the caudate nucleus, specifically the nucleus accumbens, to objects and stimuli, including human individuals, that dogs liked. Positive emotions are invariably linked to caudate activations; specific parts of the caudate stand out for their consistent activation to many things that humans enjoy, and indeed caudate activation is so consistent that, under the right circumstances, it can predict our preferences for food, music and even beauty.[17] Canine responses were of a manner and magnitude similar to caudate responses in humans—a functional homology that may be indicative of dogs experiencing similar emotions to humans.[18] Further fMRI investigations, combined with behavioural studies, have demonstrated the sensitivity of dogs to human social interaction/bonding, and that dogs may prefer the company of familiar humans over the company of either familiar or unfamiliar dogs,[32 33] and that dogs may have evolved mechanisms especially tuned to social cues and therefore may have specialised neural machinery for face processing.[33–35] Dogs seem able to understand a significant amount of human language, including both verbal and emotional content.

In other words, there is formidable and mounting evidence illustrating and underlining the complex cognitive and emotional capacities of dogs. It is important to note that such evidence has, however, existed for some time from ethological studies, and indeed many would argue it has simply been obvious from the most cursory of observations to those who have interacted with dogs that they (and, in fact, many other non-human species) are intelligent, emotional and highly sentient beings. Such ethological investigations have demonstrated, and increasingly illustrate, the depth and breadth of their cognitive and emotional capacities. A recent review (2016) cites observational ethology and problem-solving experiments in the early 1970s and 1980s as being part of a 'rediscovery' of canine cognition investigations and comparative studies.[36] It cites numerous supporting studies that have increased our understanding of cognition in dogs, for example via tracking of eye movements (elucidating interest, preference, planning, intent, emotional perception and processing), touch-sensitive screens (recognition, categorisation, communication) and others, as well as non-invasive studies of canine neurobiology including electroencephalography (EEG) and fMRI. fMRI data have not, therefore, 'reinvented the wheel', but they have, importantly, expanded the methods by which scientists can access the minds of other animals, and this is an important move. Arguably, it should not really be necessary to prove to any greater degree what seems clear, when considering the suffering experienced by dogs undergoing invasive experiments, although the fact that this may be an inconvenient truth to a scientific establishment that uses many tens of thousands of dogs every year as research subjects may be a factor. Nevertheless, it seems—belatedly perhaps—that the deep, advanced, and in some ways 'human-like' nature of canine cognition and emotions are finally being recognised by the scientific community, given the degree and type of research being funded and conducted. fMRI data are cementing this, by showing us the mechanisms behind these qualities, which parts of the canine brain are working to achieve them and how. It means that dogs must, and do, suffer much more than is accepted currently within part of the scientific community, as evidenced by the type of dog research being conducted, the number of dogs used and the suffering associated with some procedures (see Introduction). This has profound and serious consequences for the use of dogs in harmful experiments and toxicity testing.

One omnipresent caveat of any discussion of fMRI data, despite more than quarter of a century of human fMRI studies and use, is their reliability, and the question of what fMRI images specifically represent in terms of neural activity (see ref [37] for a discussion). While the exact basis and mechanistic nature of fMRI

images are somewhat controversial and remain under scrutiny even now, it is generally accepted, based on much evidence, that the fMRI signal—based as it is on blood flow and oxygen levels ('blood oxygen-level dependent [BOLD] signals')—accurately represents neural activity. Another potential criticism is that the fMRI images central to the argument we present in this paper are simply evidencing neural activity associated with various stimuli and behaviours, as opposed to being correlates of conscious experiences. This type of argument is not novel, of course—even for humans—and it is accepted that the evidence herein and its like cannot *prove* conscious experiences. Nonetheless, there is increasing and convincing evidence from human studies (of course, humans can follow detailed and complex orders, and report verbally to researchers) that neuroimaging data strongly correlate to various mental states. An in-depth review published in 2015 describes how neuroimaging technologies such as fMRI and EEG can reveal detailed aspects of, for example, decisions, intentions, thoughts, imagining tasks, behavioural will and others in humans.[38] For example, in humans, fMRI signatures ('brain activation patterns') correctly identified intentions to perform specific tasks in 80% of instances,[39] revealed movement intentions before their initiation[40] and identified the type and duration of task being imagined with a mean accuracy of 95%.[41] Further support for the assertion of conscious experience versus stimuli/behaviour-associated neural activity has been provided by human research showing that *imagining* performing tasks generates highly similar patterns of brain activity to actually performing them, exemplified by imagining limb movement,[42] spatial navigation[43] and playing tennis.[44] In other words, fMRI patterns can be used as neural proxies for behaviour. Further, the evidence above is augmented and fortified by many studies that have been conducted over the past two decades,[45 46] comparing, for instance, imaging patterns in (1) healthy individuals and in patients assumed to be in a vegetative state or minimally conscious, and (2) in similar comparative experiments in humans who are awake and asleep. The former have demonstrated that many forms of awareness and cognition exist in some people in vegetative states, in whom specific neuroimaging patterns are *indistinguishable* from healthy individuals, and which are therefore indicative of *actual conscious experiences*, even to the degree that people assumed to be in a vegetative state can communicate, understand and respond to spoken commands and questions (eg, ref [47] and see ref [38]). For example, persons fulfilling all agreed criteria for being in a vegetative state or minimally conscious show the same fMRI patterns when instructed to perform mental imaging tasks, such as the tennis playing and spatial navigation just described.[48] The latter, comparing awake and asleep individuals, have shown that diverse mental states, including discrete emotional states and experiences, have associated 'brain states' in the form of 'coherent, emotion-specific patterns',[49–51] supporting the theory that '…posit emotions are represented categorically in the coordinated activity of separable neural substrates'.[52] A recent (2016) review[53] cites work demonstrating in humans that valenced brain states can be differentiated on the basis of neural activity (eg, refs [54 55]), including an experiment showing that nine different emotions could be predicted by fMRI activity, with an accuracy of 84% with the same subject and 70% with different subjects.[56] The same review reported the authors' own work, showing that fMRI could classify six different emotions with 37.3% accuracy, compared with chance levels of 14.3%.[53 57] Meta-analyses corroborate and strengthen this. Hamann[11] summarised a number of these in his review.[11] For example, the five basic emotions of happiness, sadness, anger, fear and disgust are 'characterised by consistent neural correlates' and can be reliably discriminated from each other,[58] and 'consistent regional brain activations' correspond to each basic emotion category.[59] More recently, Wager *et al*[60] analysed almost 150 studies involving well over 2000 participants, and concluded similarly that the five basic emotion categories are identifiable via patterns of brain activation, revealed by fMRI, across multiple brain systems such as 'the cortex, thalamus, amygdala, and other structures'.

The use of dogs in invasive and/or harmful experiments, as for other non-human species, currently rests on the aforementioned HBA (see Introduction)—that harms to the animals used must be minimised, and the benefits to others (often humans) from those experiments must be substantial. It can be argued that HBA analyses are not currently conducted appropriately. Inter alia, they are not conducted transparently; are often, if not always, rudimentary; are performed by individuals who have heavily invested in animal research; and the failure of animal experiments to translate to human benefits is not fully considered.[10] The harms—as mentioned in the Introduction—we argue are considerable, yet at the same time underappreciated and underacknowledged, especially so in light of the fMRI information reviewed herein.[4] These issues have been of sufficient importance to stimulate research into the living conditions and suffering of dogs in laboratories, as well as changes in these conditions to improve the welfare of these dogs. Significantly, however, attempts to ameliorate laboratory conditions for dogs (and also therefore to improve data from dog experiments) by providing social housing may still be inadequate: some dogs still become stressed, anguished, frustrated and bored, and it appears that at the very least more human social contact may be a sine qua non.[61] Evidence overall, therefore, reveals that harms from experimentation to the dogs involved may be much greater, widespread and intractable than previously accepted, skewing the HBA balance and demanding any benefits be much greater to redress it. Yet it increasingly appears that this HBA ratio is skewed even further by the actual value of dog experiments to humans (see, eg, refs [1–3]), which, as exemplified in the Introduction, we believe is much less than is claimed by advocates of dog research.

In conclusion, in accordance with our intuitions, simple observation and experience, ethological/behavioural research and fMRI experiments, dogs are able to morally evaluate; don't just 'hear' and have a basic understanding of some words, but also 'listen' to human intonation to perceive emotional states and intent; understand to some degree human 'communicative intent' and perspective, involving to a large extent the eyes; possess neural machinery for face processing, enabling identification and perception of emotions; and so on. Perhaps most importantly and crucially, dogs are able to experience positive emotions, empathic-like responses and demonstrate human bonding at least comparable with human children, via similar neural mechanisms: '…there is a consensus that the mind of a dog is very similar in capacity and behaviors to the mind of a human 2 to 3 year-old',[62] and 'The ability to experience positive emotions, like love and attachment, would mean that dogs have a level of sentience comparable to that of a human child. And this ability suggests a rethinking of how we treat dogs'.[63]

It is this *degree* of (and type of) sentience that is at the crux of this review, and of its conclusions and demands for change. We argue that the evidence for the extent of canine sentience was already out there from ethological studies, but we also show the evidence collated herein comprising recent, ethical fMRI brain imaging of 'volunteer' dogs augments and fortifies it. Our inference of these canine fMRI experiments, and the weight of

evidence regarding what they indicate, is supported by fMRI experiments involving humans—comparative studies involving healthy, asleep, minimally conscious and vegetative state individuals—showing that imaging 'brain activation patterns' are reliable indicators of conscious thoughts, intentions and emotional states/feelings. Because all this evidence shows that dog cognition and sentience are advanced and complex, and that dogs must experience a variety of emotions, including positive emotions such as love/attachment, pleasure and empathy, we argue that this should prompt a more empathic view and response from us—particularly, perhaps, from ethicists and others involved in HBAs and approving, licensing and conducting invasive experiments involving dogs. Because HBAs, by their nature, assume some degree of uncertainty about feelings and emotions in dogs, our review challenges this assumption and demands a change in how HBAs are performed. My colleagues and I would argue, based on what we see as formidable evidence, that HBAs must as a matter of urgency factor in this evidence, and the associated and inescapable conclusion that canine feelings and emotions are real and genuine—and therefore dogs in laboratories and in invasive and harmful experiments suffer much more than we currently accept, resulting in greater harm. This is a position supported by philosophical and ethical deliberations: Peter Singer argues that sentience gives rise to interests, and these involve pursuing and experiencing pleasure, as well as avoiding pain and suffering[64]; Tom Regan, that lives involving pleasure have intrinsic value[65]; the ability to experience pleasure leads to a capacity for quality of life[66]; and others. Harm to animals in laboratories, therefore, results when pain or suffering results directly from experimental procedures, caging and so on, and from denying those animals much of their agency, control over their circumstances and the freedom to pursue their natural behaviours and associated pleasures (eg, exercising, foraging, exploring, choosing social partners and so on[13 67 68]). Further, there is a strong argument that animal welfare is compromised if an individual cannot flourish emotionally, and that happiness and pleasure (and so unhappiness and suffering) depend on emotions and moods, as well as pleasant and unpleasant experiences.[69]

We think it is fitting to conclude with neuroscientist Gregory Berns' statement following his work: 'The fMRI data makes it harder to deny that dogs have feelings very much like we do and that they deserve a consideration under the law that treats them as more than a piece of furniture. We have raised the bar for treating the dogs as sentient individuals with free will. There are still over 50 000 dogs used in research every year [in the U.S. alone], so it is an uphill battle. Most of these dogs are either bred as 'laboratory-dogs' – usually beagles – or are acquired from shelters. I hope that our research will show that dogs have many of the same emotions that we do, and that it will become harder to justify using them as research subjects'.[70]

The authors believe that regulatory authorities worldwide should recognise the urgency to review and re-evaluate the need, ethics and legalities of the use of dogs in invasive research and testing, given our current knowledge and increasing scientific evidence of dog sentience and cognition.

Acknowledgements The authors acknowledge the dedication of the scientists working in the field of canine cognition, without which this review would not have been possible.

Contributors Both authors contributed significantly to the concept, research, writing and editing of this manuscript.

Funding Cruelty Free International Trust.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

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Advances in neuroscience imply that harmful experiments in dogs are unethical

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J Med Ethics published online July 24, 2017