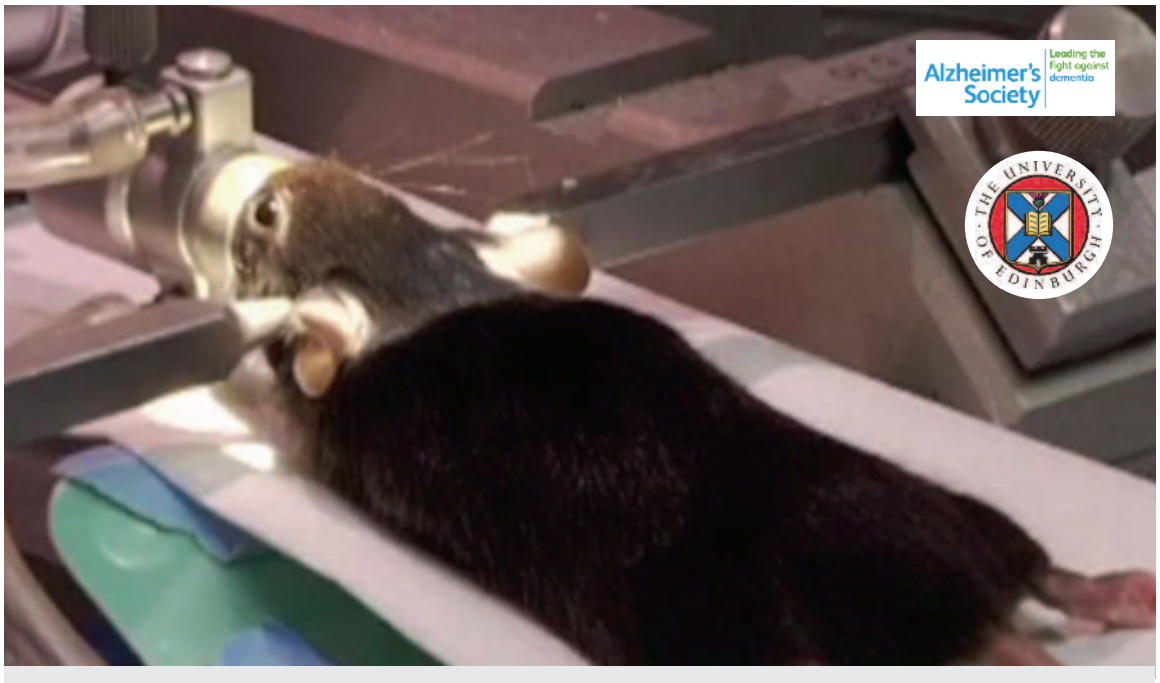
Alzheimer's Society-funded mouse experiments at Edinburgh University – cruel and without medical benefit



Introduction

Animal Aid, during the course of researching its *Victims of Charity* report, has discovered an ongoing series of animal experiments conducted at Edinburgh University that has been funded, in large part, by the Alzheimer's Society. These experiments involve inflicting strokes and traumatic brain damage on mice, studying how the animals respond to memory testing and then analysing the chemicals in their brains. Animal Aid has rigorously examined the justifications given for such work, and the details of exactly what the mice endured. This Briefing shows how the series of experiments is both extremely cruel and without scientific merit.

The first of the research papers we cite was published in 2006, and the most recent in 2011. The Alzheimer's Society, in the autumn of 2011, granted more than £335,000 to an Edinburgh researcher to continue the experiments for a further three years. This is despite the experiments already being highly repetitive.

Animal Aid has produced a robust, detailed critique of the experiments. In early May 2012, we sent our dossier to the two principal Edinburgh researchers and to the Chief Executive of the Alzheimer's Society, asking for their comments. No replies have been received to date.

Mice are complex, sensitive animals

Mice used in experiments are no less complex or vulnerable than their wild counterparts. The laboratory environment is completely alien to them, and already fraught with potential stressors even before they are subjected to the procedures described in this report.

Mice are a prey species, which means that they are highly motivated to stay close to safe cover. They also find routine human contact very stressful unless they are properly habituated, and are especially upset by being caught or handled. They are, by nature, nest builders, and dislike barren open spaces. They are gregarious animals and form complex social networks, so any periods of isolation are highly damaging to their welfare. Mice have excellent and sensitive hearing, with a broad frequency range, including ultrasound. They use scent-marking to identify territories and as a means

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of communication. Wild mice are active from dusk to dawn. They live in often complex burrowed tunnel systems but also range widely over large territories.

Like other prey animals wholly unsuited to laboratory environments, mice have an inherent tendency to hide signs of pain or distress. They can become unwell and deteriorate quickly with often only subtle signs of suffering until illness is severe. They can die if they lose 20 per cent of their body weight – which is only six grams in a 30 gram mouse (source, RSPCA). Animals in laboratories are often selected on grounds of convenience and tradition, rather than their predictive value for human ailments. Mice, for example, breed prolifically and are relatively cheap to buy and maintain.

Dozens of mice given brain damage or strokes

During the course of the Alzheimer's Society-funded experiments, dozens of mice were grievously injured in high mortality procedures, subjected to repeated anaesthesia and neurosurgery, and forced to undergo sometimes weeks of crude cognitive testing before being killed. Brain damage was induced in the animals via high-pressure blasts delivered through holes in their skulls (termed 'injury hubs'). This 'fluid percussion injury' is so severe that it kills many animals outright. Strokes were induced in other mice by blocking one of the main arteries to their brains with a filament. Yet others had the blood flow to their brains reduced via the insertion of tiny coils into their carotid arteries. Finally, a minority had nerve poison injected directly into their brains. No mention is made of any painkilling medications being administered following these undoubtedly traumatic procedures.

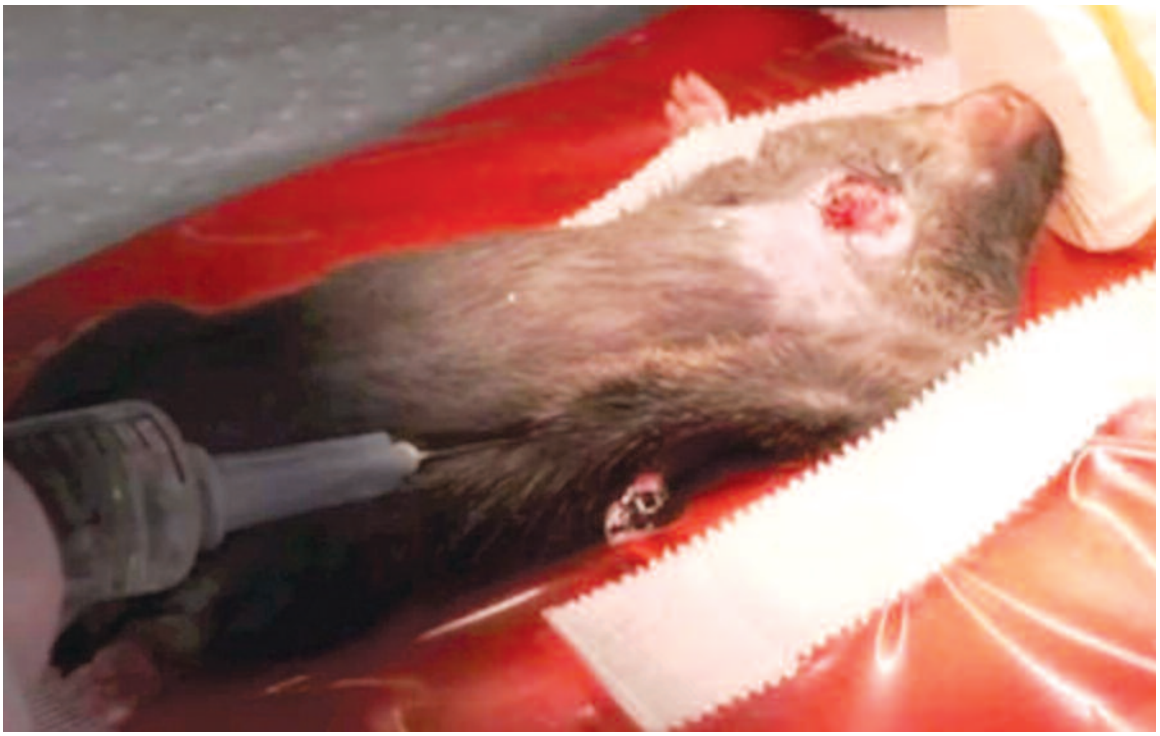
In one experiment, researchers gave a stroke to an unspecified number of mice. Six survived for a few hours before being killed. Their brains were then removed for examination. Before death, they had to endure three anaesthetics, firstly, to have their cerebral arteries blocked with a resinous filament. They were then allowed to recover in an incubator, with the filament still in place and an incision in their necks still open. They were anaesthetised for a second time to remove the filament and suture their wound. After nearly four hours, during which time the mice would have been suffering the effects of a severe stroke, they were anaesthetised for a third time and decapitated.

Cruel forced-swim test for weeks on end

In several experiments, the mice who survived their initial trauma (or who were not killed by the researchers) were forced to swim around in a pool of water (the Morris water maze) in order to find a submerged platform. Mice tend to panic when immersed in water, and the test is acknowledged by users as 'somewhat unpleasant'[1]. Some mice, with both their carotid arteries narrowed by the insertion of a microcoil, were subjected to the following regime of testing: a maximum of 32 tests per platform, on at least five platform locations, for ten days or more. Others were food-deprived prior to testing. The mice were then killed one or two months after the initial surgery, having spent the remainder of their lives being 'tested'.

Facile and predictable findings

Besides inflicting considerable suffering on animals, these experiments are clinically unwarranted. Their apparent purpose is to investigate how head injuries or a lack of oxygen to the brain are implicated in Alzheimer's Disease. In general, the researchers attempt to reproduce findings that have already been discovered from clinical, epidemiological or



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autopsy studies in humans (the conclusion drawn from some experiments was almost identical to the pre-existing knowledge set out in the researchers' introductory comments). The core 'finding' arising from much of the work is facile and predictable – brain damage impairs the ability of mice to learn. Clearly, it is well known that head trauma or cerebral hypoxia are undesirable in humans; it is hard to see how any clinical advance could come from demonstrating the same in mice. We already have public health programmes, trauma services and acute and community medical care, whose purpose is to prevent and treat these conditions. In addition, drugs like ibuprofen (already proven in clinical trials to have no benefit for Alzheimer's patients, and to cause them dangerous side effects) were tested on injured animal subjects.

Basic research on animals is a model of failure

The Edinburgh researchers themselves freely admit that their microcoil hypoperfusion model (the insertion of tiny coils into mouse carotid arteries) does not accurately parallel human disease. The damage induced in these healthy animals is fundamentally different from 'the heterogeneity of the human condition in which chronic hypoperfusion and cognitive decline can be influenced by several different factors, including ageing, neurodegenerative processes, episodic hypotension, mid-life histories of hypertension and high cholesterol, atrial fibrillation, aortic and carotid atherosclerosis and Type 2 diabetes'. Eliminating these so-called confounding factors does not lead to a better animal model of human disease. Instead, it ensures that these experiments are relevant only to certain kinds of mice injured in certain ways – not to a real-life human population.

The Edinburgh experiments are basic research, involving the laboratory destruction of animal physiology and anatomy in the hope of finding out something clinically relevant. One of the leading critics of animal experiments, Dr Ray Greek, quotes several sources to support his contention that basic researchers using animals contrive connections to human medicine in order to attract funding. This is despite the fact that basic research, according to one authority, has approximately a 0.004 per cent chance of leading to anything clinically useful[2]. Greek also highlights how researchers carrying out basic studies on animals justify such work on the grounds that it benefits patients – *yet admit that such benefits are unlikely to arise.*

An example of the systematic failure of basic research in the field of dementia is set out by Geerts, of ***In Silico Bioscience***, from 2009:

'The tremendous advances in transgene animal technology, especially in the area of Alzheimer's Disease, have not resulted in a significantly better success rate for drugs entering clinical development. Despite substantial increases in research and development budgets, the number of approved drugs in general has not increased, leading to the so-called innovation gap'[3].

'Cures that work in rodents have never worked in humans...'

It is clear from the above that experiments conducted using transgenic mouse models of Alzheimer's Disease (such as the mice used by the Edinburgh team) have been central to the failure of many Alzheimer's drugs. Candidate therapies tested in these models and judged as successful (either biochemically or in behavioural testing) have gone on to fail in human trials. Using mice to mock up neurodegenerative diseases has been characterised in a *Nature* article as 'nearly useless'[4].

Part of the problem is that the 'experimental Alzheimer's Disease' that researchers produce in animals is emphatically not the same as the human

variety. Professor Lawrence Hansen, a highly distinguished specialist in geriatric neuropathology, has recently spoken out on this issue:

'Setting aside the ethical dimensions (which we should never do) of inflicting pain and suffering on any animal, even mice and rats, the amoral scientific problem with using rodents as models for neurodegenerative diseases is that rodents do not naturally develop Alzheimer's Disease or Parkinson's Disease. The only way to get what looks even a little like AD or PD pathology in rats and mice is to make them transgenic – that is, to insert human disease-causing genes into the rodents. This does create a Frankenstein-like mutant model with some expression of AD or PD pathology, which can be manipulated to make it go away. But reversing artificially induced AD or PD changes in animals that never naturally develop them is a far cry from curing the human diseases. The "cures" that work in the rodents have never worked when applied to humans... The species differences that have evolved over millions of years make animal models largely useless, except for the purposes of enhancing scientific careers and attracting lots of grant money'[5].

Victims of Charity

Despite these failings, the Alzheimer's Society currently remains committed to animal-based research, with many of its current projects still ploughing the same infertile furrows. Animal Aid has produced a fully referenced scientific report, ***Victims of Charity***[6], which critically examines charity-funded animal research. Numerous researchers and commentators are quoted expressing serious misgivings about the value and relevance of this work to patients. The substantive criticisms in the report have yet to be credibly refuted by any of the charities scrutinised.

Humane research and proper provision for patients

Animal Aid is, of course, acutely aware of the devastating consequences of Alzheimer's Disease. We, like the general public, are keen to see research undertaken that is both humane and has a good prospect of leading to genuine medical advancement. To that end, we have produced a detailed briefing about effective non-animal research methodologies to accompany the main ***Victims of Charity*** report[7]. While the search for 'cures' is undoubtedly important, we believe that a huge burden of unmet need revolves around non-medical issues. We should be aiming to be a world leader in the care and compassion we afford to dementia sufferers, not just in the number of published papers, citations, or research posts.

Cruel and medically irrelevant animal experiments must end

We also believe that charity donors should be informed about the nature of the work they are asked to support. The current lack of transparency and balanced debate around this issue is a serious deficiency. The public has a right to know just what sort of research it is paying for, and how successful it is. The Alzheimer's Society has told us, via the Association of Medical Research Charities, that it is not willing to debate these matters in public. Animal Aid regards this position as completely untenable, one that suggests a lack of confidence in the strength of its pro-animal research argument. Given the above, we intend to press both the Society and Edinburgh University to give a clear commitment that they will end all involvement in irrelevant and cruel animal experiments.

The photographs in this Briefing show mice undergoing the same brain injury and stroke experiments as those conducted by Edinburgh University. They come from a short film, which can be viewed on our website. Please note that it contains graphic images: **www.animalaid.org.uk/go/edinburgh**

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