

Research involving animals

Information Sheet L

Motor neurone disease is a devastating, rapidly progressing condition. Currently, there is no treatment that will halt the progress of the disease, although one drug, riluzole, has shown a modest benefit for some people. The MND Association funds and promotes research that leads to new understanding and treatments and brings us closer to a cure for MND. This information sheet will explain why are animals used in research and what is being done to ensure their welfare.

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Disclaimer: *Please note that information provided in this information sheet is based on a review of the currently available literature. This information sheet was written by the MND Association staff who are not clinicians and so any information provided in this sheet should not be considered as clinical advice. You should always discuss potential treatments with your clinician.*



This symbol is used to highlight **our other publications**. To find out how to access these, see *Further information* at the end of this sheet.

1: Introduction

MND is a complex disease, affecting motor neurones that connect all the muscles in the body, and one where the symptoms, rate of progression and survival varies hugely between people affected.

The complexity of MND means that much research is required to develop an effective treatment, to be sure that it is safe and has a beneficial effect on the underlying cause of the disease. The search for effective treatments is ongoing in MND laboratories around the world.

Wherever possible, this research is conducted without animals being involved. In some cases, however, where no alternatives are available, this research will use animals. In these cases, the research is conducted in line with the law, using the guiding principles of, replacing, refining and reducing the use of animals.

The types of animals used in MND Association funded research includes rats, mice, zebrafish, fruit flies, worms and chick embryos. Here is the MND Association's position statement:

MND Association position statement on research involving animals

There is an urgent need for ongoing research if we are to stop motor neurone disease killing six people every day. We believe the use of animals in research is essential to understanding, preventing and ultimately finding a cure for MND. We only fund and support research involving animals when no alternatives are available, and where institutions can clearly demonstrate they comply with the rigorous laws that safeguard the welfare of animals used in research in the UK and across the EU. As with all research we fund, there must be a clear potential benefit to people with MND.

2: Why is research involving animals conducted?

There are two, connected reasons why scientists use animals in research studies. The first is to ensure that new drugs will be safe when they are first tested in people. (They are also used to find out whether drugs are likely to work in people, but safety is the primary concern). The second is to understand more about the disease or condition - what's going wrong in the body that's causing the symptoms. If a precise chemical or protein that's not working as it should can be found, then we can develop drugs to correct it. The chemical or protein to change is sometimes referred to as a drug 'target'.

Here is more information on each of these areas of research.

Ensuring drugs are safe

All drugs that people take have been developed to ensure the best balance between

the benefit that the drug may bring, against the risk that it may do harm.

New drugs that have never been given to humans before are constantly being developed, while at the same time existing drugs are being reconsidered for new uses. Whichever is the case, before these drugs can be made available to buy or be prescribed, the law requires they reach standards showing that they are safe and beneficial. There are safeguards in place to ensure no one is going to become seriously ill, or – if they have a condition already – made significantly worse or develop new symptoms.

Evidence that drugs are safe and beneficial is usually gathered from tests involving large groups of people, known as clinical trials. However, before regulators allow drugs to be given to humans, their safety and beneficial effect must be established by laboratory studies involving animals.

Understanding disease

As MND is such a complex condition, most of the research that the MND Association funds is to understand what's going wrong in motor neurones and the surrounding cells, so we can find new drug targets.

Some of these studies may involve growing animal cells from a specific tissue like nerve cells. As researchers only need a few cells from animals each time, fewer animals overall are used in these studies. At other times, it is important to study the effects of motor neurone damage on the rest of the body.

3: Animal welfare

Research involving animals is not undertaken lightly by the researchers themselves, their research institutes or by the Government. If animal research is conducted at all, the animals' welfare is a primary concern.

Care is taken to ensure that animals are as comfortable as they can be and that any suffering (as a result of them being used in research) is minimised. The animals live in a facility often known as the 'animal house', where their bedding, food and water are checked regularly, and they are given things to play with and kept stimulated, in much the same way as would happen with animals kept at home. The people who look after them are recruited for their interest in animal welfare.

When studies are being conducted by researchers, it's good practice to work in collaboration with those looking after the animals in the animal house. This way the animal house staff know what's happened to the animals and adjust their care and welfare appropriately.



“We have found that the best way to continually improve standards is for my research team to work closely with animal-house staff to explain the experiments being carried out and why they are being done. In this way, those who look after the animals every day understand what effects the animals might be experiencing, and can therefore tailor their care.”

Professor Dame Kay Davies, University of Oxford, in journal Nature, May 2015



The maintenance of good welfare is written into the law. These strict rules are incorporated into research involving animals across the European Union. In the UK this is enforced by the Home Office.

The Home Office issue licences to conduct research using animals. These are only issued where there are clear reasons to use animals in research, and where no alternatives are available. It is necessary to attend training courses before a licence is granted. Once granted, Home Office inspectors ensure that the law is being stuck to and upheld. Researchers also have to provide regular updates to the Home Office on research underway.

4: Principles of the ‘3Rs’

One of the key principles of the legislation is the replacement, refinement and reduction of using animals in research, sometimes referred to as the ‘3Rs’.

- **Replace** the use of animals in research with alternatives where possible. For example, this might be the use of human tissue for research studies.
- **Refine** research studies to ensure the highest possible standards of animal welfare. For example, examining whether the same results can be obtained using a method that causes the animals less stress.
- **Reduce** the numbers of animals in experiments. For example, thinking carefully about the study design to ensure that no more than a statistically valid number of animals are used.

The National Council for the Replacement, Refinement and Reduction of Animals in Research (known as the NC3Rs) is a UK-based scientific organisation dedicated to replacing, refining and reducing the use of animals in research and testing (the 3Rs). They collaborate with scientists, organisations, research funders and regulatory authorities to support their ongoing commitment to replacing, refining and reducing the use of animals in research. You can read a more detailed description of the 3Rs on their website.

5: ARRIVE guidelines

As part of the NC3Rs commitment to encourage researchers to replace, refine and reduce the number of animals used in research they have published a set of guidelines, known as the 'ARRIVE' guidelines.

These guidelines set out what should be included in reports where the research has involved animals. The guidelines recommend being clear and comprehensive in describing the experiments and results. A poorly reported study will mean that the results may be incorrectly interpreted, and ultimately lead to a higher number of animals being used as experiments are unnecessarily repeated.

These guidelines have been adopted by the scientific journals that publish research reports, by research funders, including the MND Association, and by universities and research institutes.

6: Guidelines on MND research involving animals

The above guidelines and conditions apply to all studies that the MND Association funds, where research is conducted involving animals. Review of the appropriate use, number and species of animals proposed in studies forms an important part of how we assess applications for funding – part of what is known as peer review.

Where the research using animals is not justified, the MND Association will not fund it.

The international MND research community, to which the MND Association belongs, have also produced a set of guidelines for research using animals in the development of drugs for MND (ENMC Guidelines on pre-clinical drug studies). These are designed to provide results that are as reproducible as possible, and to optimise the successful 'translation' of drugs studies in animals to successful clinical trials, and ultimately to a licenced drug to treat MND.

7: Research the MND Association funds

The vision of the MND Association is a world free from MND. To achieve this we fund and promote research that leads to new understanding and treatments and brings us closer to a cure for MND.

Our research strategy outlines in detail how we plan to achieve our mission. It includes funding a broad portfolio of research projects. Reaching a new understanding of MND means funding research to understand the causes of MND and explore these causes in models of the disease. We are funding the development of effective treatments by searching for effective drug targets (see earlier for an explanation of drug targets) and performing drug screens. So-called 'biomarker' research allows us to optimise drug

treatments for people with MND – by speeding up the diagnosis of MND and informing us of how individuals, or groups of individuals, are responding to treatments. We also fund research to improve the management of symptoms of MND, known as healthcare research.

For more information on the types of research we fund, please see our 'research we fund' information sheet or look at our website.

Over half of the research projects we fund do not involve the use of animals. With those that do, we and the researchers we fund are committed to ensuring that the welfare of the animals is considered at all times and the projects are designed and conducted in accordance with the 3Rs and the ARRIVE principles.

Here are a few examples of the research we fund, showing the principles of the 3Rs in practice:

Replacement

Using patient blood samples to create induced pluripotent stem cell models of MND (grant reference: 982-797)

Induced pluripotent stem cell (iPSC) technology has enabled researchers to create and study living human motor neurones in the lab, derived from patient cells. In many studies the use of iPSCs has replaced the use of rat or mice motor neurones. Most researchers use patient skin biopsy samples as a starting point to create iPSCs. However, more iPSC lines are needed, so another way to create them is under investigation. In a research project funded by the MND Association, Professor Chris Shaw is using white blood cell samples, collected from people living with MND and already in storage, to create a large number of new iPSC models of MND.

Ultimately the motor neurones created from the iPSCs will be used to understand what goes wrong on a cellular level in MND and to look at ways to treat the condition.

Refinement

Use of mice running wheels to assess motor function (grant reference: 983-797)

Dr Richard Mead holds the Kenneth Snowman MND Association Lectureship in Translational Neuroscience for his work at the Sheffield Institute for Translational Neuroscience. One of the objectives of his five-year post is to establish better ways to assess potential new drugs for MND. He and colleagues have shown that measuring mice muscle strength on running wheels, rather than more physically demanding tests, can be a reproducible sign of early motor neurone dysfunction. These results mean fewer animals are required to get the same data and also that the way the motor function is measured is less stressful for them.

Reduction

The development of a mice cell culture drug screening tool (grant reference: 831-791)

One way of identifying potential drugs for MND is to test drugs that pharmaceutical companies have left 'on the shelf'. These drug collections, known as drug libraries, may have been left as a company's priorities changed or the drugs didn't show benefit for another disease or condition. Professor Kevin Talbot and his colleague Dr David Gordon have been awarded an MND Association project grant to develop an initial automated drug screen for some of these drugs. The screen will be conducted on isolated motor neurones taken from a mouse model of MND. Only the promising drugs will go on to be tested in mice themselves, and also in human cells. Using this automated screen in mouse motor neurones means that far fewer mice will be required for this first stage.



For further information about how clinical trials are conducted, see: Information sheet D – *Clinical trials*.



For further information about how clinical trials are conducted, see: Information sheet E – *Research we fund*.

8: How do I find out more?

Useful organisations

We do not necessarily endorse any of the following organisations, but have included them to help you begin your search for further information.

The contact details are correct at the time of publishing, but may change between revisions. If you need help to find an organisation, contact the Research Development Team (see *Further information* at the end of this sheet for details).

Understanding animal research

Organisation aiming to achieve understanding and acceptance of the need for humane animal research in the UK.

Website: www.understandinganimalresearch.org.uk

National Centre for Replacement, Refinement and Reduction

Organisation leading the discovery and application of new technologies and approaches to replace, reduce and refine the use of animals for scientific purposes.

Website: www.nc3rs.org.uk

Home Office information

Provides guidance on how to carry out scientific research and testing using animals.

Website : www.gov.uk/research-and-testing-using-animals

Useful links

University websites talking about animal research

www.cam.ac.uk/research/news/fighting-cancer-animal-research-at-cambridge

www.ucl.ac.uk/animal-research

Researcher speaks about animal research

World view column, Nature, 7 May 2015, volume 521, page 7

bit.ly/keep-the-directive-that-protects-research-animals

Further information

You may find these information sheets from the MND Association helpful:

D – *Clinical trials*

E – *Research we fund*

We also provide the following guides:

Living with motor neurone disease – our main guide to help you manage the impact of the disease

Caring and MND: support for you – comprehensive information for unpaid or family carers, who support someone living with MND

Caring and MND: quick guide – the summary version of our information for carers

You can download most of our publications from our website at www.mndassociation.org/publications or order in print from the MND Connect helpline, who can provide further information and support.

MND Connect can also help locate external services and providers, and introduce you to our available services, including your local branch, group, Association visitor or regional care development adviser.



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MND Association website and online forum

Website: www.mndassociation.org

Online forum: forum.mndassociation.org or through the website

We welcome your views

Your feedback is really important to us, as it helps improve our information for the benefit of people living with MND and those who care for them. If you would like to provide feedback on any of our information sheets, you can access an online form at: www.surveymonkey.co.uk/r/infosheets_research

You can request a paper version of the form or provide direct feedback by email: research@mndassociation.org.