**November 2021 - MND Research Article summary – Amy Keerie, PhD student, University of Sheffield**

**Novel drug shows a reduction in central nervous system (CNS) inflammation and improvement of disease symptoms in a mouse model of ALS**


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Neurodegenerative diseases, such as Alzheimer’s disease (AD), Parkinson’s disease (PD) and amyotrophic lateral sclerosis (ALS) are thought to be driven in part by inflammation of the central nervous system (CNS), known as neuroinflammation. Neuroinflammation in these diseases causes damage to the CNS leading to loss of neurons and the symptoms of these diseases.

A drug called RD2 has previously been shown to improve disease symptoms in a mouse model of AD and is now in human clinical trials for treating AD. RD2RD2 is another drug created by sticking two RD2 molecules together and is able to reduce neuroinflammation in a mouse model of AD. RD2 and RD2RD2 are part of a new group of drugs that have the benefit of being stable in the body and not causing an immune response. The authors of this paper wanted to extend this research to see if RD2RD2 could reduce neuroinflammation in ALS, and if so, whether this would lead to slowing of disease progression.

The mouse model of ALS that was used in this study was the SOD1G93A mouse model which is the most commonly used ALS mouse model. These mice have the mutated version of the SOD1 gene which is found in some ALS patients and become paralysed in a manner similar to ALS patients. In this study, SOD1G93A mice were dosed with RD2RD2 using a mini pump, which is a device surgically attached to the mice that administers the drug at a set speed over a 4-week period.

They compared a group of animals treated with placebo (10 mice) with animals administered with RD2RD2 (12 mice) and assessed the animals using a range of tests that look at behaviour and ability to move. The mice dosed with RD2RD2 had a significant improvement in movement compared to the placebo-treated mice suggesting the disease progression was slowed due to drug administration. They collected brain and spinal cord at the end of dosing and showed that the levels of activated immune cells (namely astrocytes and microglia) were lower and motor neuron numbers were higher in the drug treated compared to the placebo-treated mice. Together these data suggest that treatment of RD2RD2 in a mouse model of ALS reduces the amount of inflammation in the brain and spinal cord, leading to increased survival of motor neurons and therefore an improvement in disease progression.
symptoms. Although the detailed mechanism of action of RD2RD2 is unknown, it looks like an excellent candidate to explore in human ALS patients and potentially other neurodegenerative diseases that are driven by neuroinflammation.