

## **Scientific report review: Liraglutide, 7,8-DHF and their co-treatment prevents loss of vision and cognitive decline in a Wolfram syndrome rat model.**

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### **What we already know:**

Prof Mario Plaas and his group have developed a rat model of Wolfram syndrome, that seems to have most of the features of Wolfram syndrome in humans. They are not exactly the same: these 'Wolfram' rats tend to have cataracts, which are less common in humans; and these cataracts contribute to vision loss.

Previously, Prof Plaas' group has shown that the anti-diabetic medicine Liraglutide, given by injection, can improve the diabetes in these rats, and seems to reduce inflammation in the rat brains. However, it was not clear if liraglutide on its own could stop progression of the neurodegeneration.

Recently, a group of compounds, 'neurotrophic factors', have been shown to promote brain health and are good candidates to treat neurodegeneration. The natural compounds are difficult to use as treatments, so scientists are developing new versions that might be used in the clinic one day

### **What they did:**

They treated Wolfram rats with a combination of liraglutide, and a neurotrophic factor called 7,8-DHF.

### **What they found:**

They found that in combination, these drugs improved diabetes better than either drug on its own; stabilised vision; and even showed an improvement in vision over time. The vision did not get back to normal, but the improvement seems genuine. They then sacrificed the rats and looked down the microscope at the optic nerve cells. These cells showed evidence of recovery from the neurodegeneration.

### **What does the research mean?**

So several medicines, including drugs such as sodium valproate being tested in the TREATWOLFRAM clinical trial, have been shown to be protective for brain cells. Liraglutide showed some signs that it might protect brain cells from damage caused by Wolfram syndrome. This new paper shows that if you combine liraglutide with 7,8-DHF, to treat Wolfram rats, the brain cells show some recovery, and even improvement in function. This is the first clear evidence in rats that drug treatments may prevent, and even improve, the neurodegeneration in Wolfram syndrome. This is really exciting and high quality research. It is reassuring to see that drug treatments can work, and that gene therapy is not the only route to a treatment.

7,8-DHF is not licensed for use in the clinic, and lots of safety studies will need to be done before it can be used in humans. However, this combination treatment shows a way forward, and it may be that one day soon, people with Wolfram will be treated with a 'cocktail' of treatments, each working in different ways, to stop the progression, and even improve some aspects of the condition.