Are sugars the answer to multiple sclerosis?

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What is the problem?

Multiple sclerosis (MS) is a long term autoimmune disorder of the central nervous system (CNS) which affects around 100,000 people in the UK. In MS, rather than protecting us against diseases and infections, the attack mechanisms of our immune system turn against the body and the myelin sheaths, which wrap around and protect the axons (the long nerve fibres) of your nerve cells, are destroyed (see Figure 1). This not only impairs the nerve cells' capacity to efficiently transmit signals from and to the brain (which is occurring continuously down your optic nerve from your eye to enable you to read this exciting poster), but also leaves the demyelinated nerve susceptible to degeneration (like an exposed electrical cable wire that's lost its insulation). This leads to an enormous range of symptoms, both physical and mental, including problems with vision, balance, dizziness, memory, thinking and fatigue.

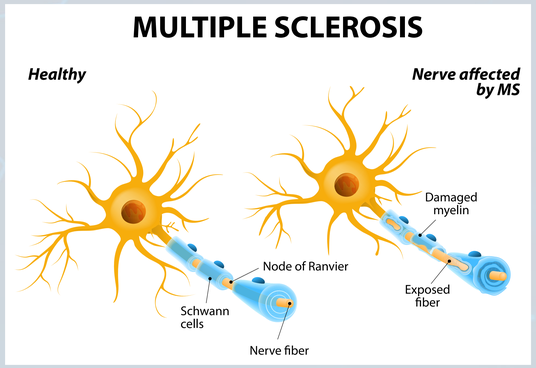

Figure 1 Depiction of a healthy nerve and one affected by multiple sclerosis. Image source: Shutterstock created by Designua (https://www.shutterstock.com/image-vector/multiple-sclerosis-ms-autoimmune-disease-nerves-239380201?src=8sahUOI9NCbJJ5RII_SRxA-1-20).

What are we interested in?

Gaffer taping the nerve: Remyelination is the process whereby new myelin sheaths form around demyelinated nerves (see Figure 2). This process is usually efficient and complete, however, in MS patients the mechanism is lost or transient, contributing to progression of the disease. We are trying to identify compounds which promote remyelination and, hence, could have potential as therapeutic agents for MS.

Specifically, we are interested in a group of molecules called heparan sulfates (HSs), which are long sulfated polysaccharide chains (sugar molecules which contain sulphur) that are attached to proteins on the cell membrane (the layer surrounding cells) (see Figure 3). HS orchestrates lots of cell signalling pathways by recruiting specific proteins to the cell surface and helping them bind to their partner receptor proteins on the cell surface (see Figure 3B and C). Once proteins bind to their receptor, signals are transmitted to the inside of the cell.

We wanted to determine whether modified versions of HS could affect the signalling environment around the demyelinated nerve to promote remyelination.

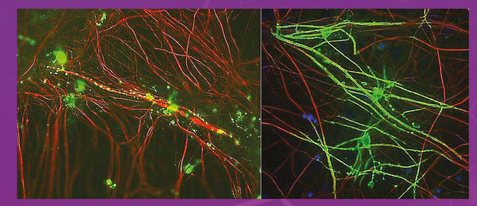

Figure 2 Nerve cells with little or no myelin are shown on the left. After remyelination, myelin (green) can be seen around the nerve cells.

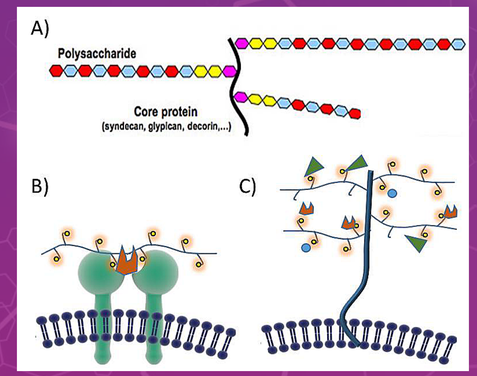

Figure 3 (A) Heparin sulfate (HS) is a long saccharide (sugar) chain attached to a core protein. **(B)** HS modulates cell signalling by helping specific proteins (red) bind to their binding site in their partner "receptors" (pale blue) at the cell surface. **(C)** HS also acts to recruit proteins (green, red and blue shapes) in the vicinity to the cell surface.

What did we do?

Our lab has developed a model of the CNS in a dish which allows us to grow cells of the nervous system in the lab and study myelination. We damaged the myelin on our nerve cells to mimic a demyelination episode in MS (see Figures 4 and 5A-B) and then treated the cells with our modified HSs to look at their effect on the remyelination of the axons.

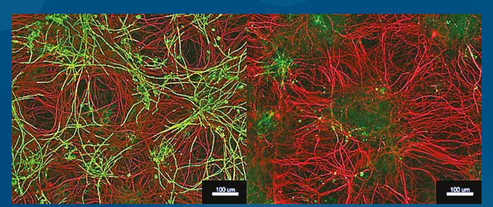

Figure 4A Nerve cells (red) grown in our lab in our standard culture are covered in myelin (green). We can treat these nerve cells to cause demyelination, as seen in **(B)** (1µm = a thousandth of a mm).

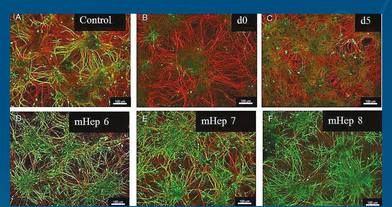

Figure 5 (A) shows nerve cells (red) grown in our lab which are covered in myelin (green). We can treat these nerve cells to cause demyelination as seen in **(B)**. The addition of our modified HSs (mHep6 **(D)**, mHep7 **(E)** and mHep8 **(F)**) to our demyelinated nerve cells resulted in increased myelination (green) after 5 days compared to **(C)**, our demyelinated cells grown in the absence of HS, which were used as a control (1µm = a thousandth of a mm).

What did we find?

We found that treatment with our modified HSs after our nerve cells had been demyelinated (see Figures 5A-B and 6) increased the level of remyelination (see Figures 5C-E and 6). When we added our modified HSs to our standard culture systems they developed normally and there was no effect on the normal myelination, which leads us to believe that the modified HSs are causing their effect by interacting with proteins unique to the injury environment. We do not know if the modified HSs may be recruiting factors which promote remyelination or if they may be binding to and preventing the action of factors normally present in MS that prevent remyelination in MS patients. We are currently trying to determine this by identifying what proteins the modified HSs interact with.

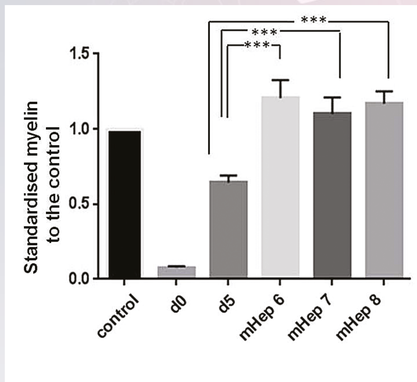

Figure 6 Quantification of the amount of myelin in nerve cells that had been treated with modified HSs after they had been demyelinated, as described in Figure 5.

What does this mean?

Treatment with modified HSs may have a beneficial effect in promoting remyelination in the CNS and we hope these HSs may be candidates to be developed into treatments for MS.

Who am I?

My undergraduate degree was in Biochemistry from the University of Liverpool and I am now in the 3rd year of my PhD at the University of Glasgow, trying to identify new therapeutic agents for the treatment of multiple sclerosis. I would like to thank Medical Research Scotland for funding my studentship and giving me the opportunity to pursue science as a career.

George started his PhD project entitled *"Development of glycomolecules as novel therapeutics for the treatment of multiple sclerosis"* in 2015 and while principally based at the University of Glasgow, supervised by Professor Hugh Willison, he is also working closely with Glycomar Ltd.