Lay Summary

BRAIN UK Ref: 22/006

TDP-43 pathology and loss of function in the skeletal muscle

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Amyotrophic lateral sclerosis is an incurable brain disorder characterized by the death of motor neurons. The death of these motor neurons is due to the accumulation of the protein, TDP-43. The protein accumulates in the cytoplasm of the cell and its connection with the nucleus is lost. This then prevents the function of TDP-43. When TDP-43 is not working, mRNAs are built incorrectly, and this leads to disease manifestations. The same pathological signature is found in the skeletal muscle of patients affected by several other muscular disorders.

So far, researchers have mostly tried to study these pathways in brain tissue, but these can only be assessed after the patient has died. On the other hand, muscle tissue is sampled shortly after the disease onset, therefore by assessing muscle tissue, we can understand the impact of TDP-43 dysfunction in early disease stages.

We aim to collect muscle biopsies and characterise TDP-43 mislocalization through imaging. We will then analyse its impact on mRNA metabolism through molecular biology assays.

Eventually, our findings will help scientists and clinicians to discover novel biomarkers and treatments for patients affected by these incurable diseases.