Lay Summary

BRAIN UK Ref: 21/016

Brain involvement in dystrophinopathies

Dr Rahul Phadke, UCL Queen Square Institute of Neurology

Duchenne (DMD) and Becker (BMD) muscular dystrophy are inherited diseases that primarily affect boys. They occur due to errors (or mutations) in the DMD gene which is located on the X-chromosome. This gene carries the code to make an essential muscle protein called dystrophin. In DMD, dystrophin is absent, while in BMD a reduced amount of partially functional dystrophin is produced, leading to milder disease. Dystrophin is expressed in muscles, heart and in the brain. As a result, DMD mutations lead to progressive muscle weakness and wasting, heart disease and respiratory problems. Additionally, we know from several clinical studies that intellectual and behavioural problems affect nearly 50% of individuals with DMD. In the last few decades, better standards of care, and new treatments aimed at preserving muscle mass and function have contributed to an increase in individuals with DMD who are therefore living longer. Current knowledge of the expression and function of dystrophin in the human brain is incomplete. Our project seeks to better understand how the human brain is affected in DMD and BMD. We aim to study the expression of dystrophin in critical brain regions through different stages of human brain development. Using pre-clinical tools, we shall determine whether restoring dystrophin in the brain after birth rescues the neurological deficits. We also aim to define the spectrum of neurological deficits seen in affected individuals, and to create clinical tools to assess these complications. Ultimately, the goal of this project is to improve our understanding of dystrophin's function in the brain, thus working towards better treatments, and outcomes for individuals with DMD and BMD.