Investigating the effect of Duchenne muscular dystrophy on the brain

In this study Professor Volker Straub and his team are aiming to understand how a lack of dystrophin protein affects brain structure and function in boys with Duchenne muscular dystrophy. This will allow scientists and clinicians to improve standards of care and to offer more targeted help for families. The results will also provide new readouts to measure the effectiveness of potential treatments at alleviating these symptoms, when tested in clinical trials. This could lead to improved treatments in the future with increased therapeutic benefits for boys and young men with Duchenne muscular dystrophy.

What are the researchers aiming to do?

Duchenne muscular dystrophy is caused by a mutation in the dystrophin gene. This results in dystrophin protein not being made in the body. Dystrophin protein works as a shock absorber in muscles to protect them from damage during contraction.

Dystrophin protein is also present in the brain. Its function there is less well understood, but is believed to be important; it is not uncommon for boys with Duchenne muscular dystrophy to have psychological problems, such as attention deficit and hyperactivity disorders and obsessive-compulsive disorders. They can also have difficulties with cognitive processes such as thinking, understanding and remembering; many boys (approximately 30 to 40 percent) have learning difficulties or dyslexia and in some cases even severe forms of autism spectrum disorders.

Professor Volker Straub and his team are aiming to better understand the effects of the lack of dystrophin protein in the brain of boys with Duchenne muscular dystrophy. A recent study carried out by researchers in the Netherlands showed changes in brain structure and function in boys with Duchenne muscular dystrophy compared to healthy individuals. Professor Straub and his team will be working with
these scientists to investigate their findings further using the same non-invasive tests in a different group of individuals.

Dystrophin is found in the body in many different forms; two of the smaller dystrophin proteins are found in the brain and are thought to be important there. The study carried out in the Netherlands showed that a lack of one of these shorter dystrophin proteins was associated with more structural changes in the brain and a higher incidence of cognitive dysfunction. In this study, Professor Straub and his team will investigate the effects of the other shorter dystrophin protein.

To do this, they will recruit four groups of 10 participants. The first group will consist of people with a mutation in the dystrophin gene that affects all forms of the protein. The second group will consist of people with a mutation in the gene that is most abundant in muscle but that leaves the smaller protein that is most abundant in the brain intact. The third group will consist of people affected by another muscle-wasting condition (limb girdle muscular dystrophy) that does not affect the brain and finally the fourth group will consist of healthy controls. The scientists will assess the changes that occur in the brain of people with Duchenne muscular dystrophy in comparison to the other groups. They will use magnetic resonance imaging (MRI) scans to assess brain structure and a questionnaire to measure psychological and cognitive changes. The boys will be assessed twice - two years apart - to see how these things change over time; this has not been previously investigated.

**How will the outcomes of the research benefit patients?**

This project will increase our understanding of the effects of the lack of dystrophin protein on brain structure and function in boys with Duchenne muscular dystrophy. The scientists will investigate different ways of imaging the brain in Duchenne muscular dystrophy. This will help other clinicians and scientists in the future to better assess brain function in boys with the condition. The tests will also be useful for measuring the ability of potential new treatments to improve brain dysfunction. These measurements, known as outcome measures, will be particularly useful in clinical trials and will allow scientists to develop treatments that address the dysfunction seen in the brain as well as that seen in muscles, which will be a huge advantage for boys with Duchenne muscular dystrophy.

The research will also aid clinicians in providing more targeted help for families, for example practical support for boys with learning difficulties or attention deficit and hyperactivity disorders.

**Grant information**
Project leader: Professor Volker Straub  
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For further information

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