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Assessment of Neurodevelopmental Needs in Duchenne Muscular Dystrophy

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Abstract : Duchenne muscular dystrophy (DMD) is a severe form of X-linked muscular dystrophy caused by mutations in the dystrophin gene resulting in progressive skeletal muscle weakness. Boys with DMD also have significant cognitive disabilities. The intelligence quotient of boys with DMD, compared to peers, is approximately one standard deviation below average. Detailed neuropsychological testing has demonstrated that boys with DMD have a global developmental impairment, with verbal memory and visuospatial skills most significantly affected. Furthermore, the total brain volume and gray matter volume are lower in children with DMD compared to age-matched controls. These results are suggestive of a significant structural and functional compromise to the developing brain as a result of absent dystrophin protein expression. There is also some genetic evidence to suggest that mutations in the 3' end of the DMD gene are associated with more severe neurocognitive problems. Our working hypothesis is that (i) boys with DMD do not make gains in neurodevelopmental skills compared to typically developing children and (ii) women carriers of DMD mutations may have subclinical cognitive deficits. We also hypothesize that there may be an intergenerational vulnerability of cognition, with boys of DMD-carrier mothers being more affected cognitively than boys of non-DMD-carrier mothers. The objectives of this study are: 1. Assess the neurodevelopment in boys with DMD at 4-time points and perform baseline neuroradiological assessment, 2. Assess cognition in biological mothers of DMD participants at baseline, 3. Assess possible correlation between DMD mutation and cognitive measures. This study also explores functional brain abnormalities in people with DMD by exploring how regional and global connectivity of the brain underlies executive function deficits in DMD. Such research can contribute to a better holistic understanding of the cognition alterations due to DMD and could potentially allow clinicians to create better-tailored treatment plans for the DMD population. There are four study visits for each participant (baseline, 2-4 weeks, 1 year, 18 months). At each visit, the participant completes the NIH Toolbox Cognition Battery, a validated psychometric measure that is recommended by NIH Common Data Elements for use in DMD. Visits 1, 3, and 4 also involve the administration of the BRIEF-2, ABAS-3, PROMIS/NeuroQoL, PedsQL Neuromuscular module 3.0, Draw a Clock Test, and an optional fMRI scan with the N-back matching task. We expect to enroll 52 children with DMD, 52 mothers of children with DMD, and 30 healthy control boys. This study began in 2020 during the height of the COVID-19 pandemic. Due to this, there were subsequent delays in recruitment because of travel restrictions. However, we have persevered and continued to recruit new participants for the study. We partnered with the Muscular Dystrophy Association (MDA) and helped advertise the study to interested families. Since then, we have had families from across the country contact us about their interest in the study. We plan to continue to enroll a diverse population of DMD participants to contribute toward a better understanding of Duchenne Muscular Dystrophy.

Keywords : neurology, Duchenne muscular dystrophy, muscular dystrophy, cognition, neurodevelopment, x-linked disorder, DMD, DMD gene
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