P.2.2

North Star ambulatory assessment in young DMD boys

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Very few studies have investigated early neurodevelopmental and motor aspects in preschool boys affected by Duchenne muscular dystrophy. This is mainly due to the age at diagnosis which is still on average above the age of four years. Although the first signs of concern can often be backdated to the second year of age, when DMD children show some signs of developmental delay and inability to develop new motor abilities the diagnosis is on average performed much later. The recent development of therapeutic approaches for DMD has highlighted the need to identify clinical outcome measures for planned therapeutic clinical trials that could be used as early as possible, ideally soon after diagnosis when the disease is still in the early phases.

There have been suggestions that the North Star Ambulatory Assessment, a functional scale already used in DMD children older than 4 or 5 years may be used in younger children.

The aim of this study was to assess the suitability of this scale in young children by performing the scale in a cohort of typically developing and DMD children all assessed before the age of 5 years. More specifically we aimed to identify if all the items were appropriate for children from the age of 3 years onwards.

Results: in the typically developing children the scale was easily administered in all. All the children above the age of 5 were able to pass all the items with a full score while children below the age 5 often failed some items, such as hopping on one leg. Children between the age of 3 and 4 also failed additional items such as standing on one leg, getting up from the floor without upper limb aid, lifting head from supine and standing on heels. DMD boys had similar findings but in a proportion of them other items were also failed.

Our results suggest that the NSAA can be easily administered in typically developing children and DMD young patients but the results should be interpreted taking into account age related difficulties due to the age appropriate development of motor coordination skills.

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P.2.3

Assessment of Upper Limb function in DMD patients: Comparison with normative data

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While there have been considerable advances for ambulant children with Duchenne Muscular Dystrophy (DMD), no prospective study has so far been devoted to outcome measures in non ambulant patients, with increasing complaints from families and patients. This information appears to be relevant not only for a better understanding of the disease progression but also for possible enrolment of patients in future trials.

As a result of an international effort, a new tool, the Performance of Upper Limb (PUL) was specifically designed to assess upper limb function in DMD boys. The purpose of the PUL is to assess changes that occurs in motor performance of the upper limb over time from when a boy is still ambulant to the time he loses all arm function when non-ambulant.

The aim of the present study was to use the PUL in:

(1) a cohort of typically developing children from the age of 3 years onwards in order to identify the age when the activities assessed in the individual items are consistently achieved.

(2) a cohort of DMD children and young adults to assess the range of findings at different ages.

We collected normative data for the scale validation on 258 typically developing children from 3 to 14 years old. A full score was consistently achieved (>85%) by the age of 3.5 years. Below the age of 3.5 years there was a significant number (>15%) who had difficulties in the items involving stacking cans, opening a Ziploc container, tearing a piece of paper and in lifting the heavier weights. After the age of 3.5 years difficulties were only occasionally found in tearing a sheet of paper.

When the PUL was performed in the 211 DMD patients (age range 2.8–23 years), we observed a progressive deterioration of scores with age, with early involvement of the proximal muscles that was more obvious after the age of 10 years. Even the oldest and weakest DMD patients were still able to perform some of the distal items, suggesting that the scale is capable of measuring small.

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P.2.4

Upper extremity reachable workspace evaluation in DMD using Kinect

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There is a lack of outcome measures evaluating upper extremity function in Duchenne Muscular Dystrophy (DMD) and a need to develop a quantitative low-cost method to evaluate upper extremity function in clinical trials.

We developed a 3D reachable workspace tool to quantify joint mobility within the patient’s functional space. Reachable workspace is defined as all points relative to the torso an individual can reach by moving their hands, and its envelope is defined by the encompassing surface area. Reachable workspace is associated with functional upper limb status and is applicable in evaluating patients with DMD, where weakness and dysfunction stems from early involvement of shoulder girdle muscles.

We developed a system based on the Microsoft Kinect to capture upper-limb movement during a specially devised workspace protocol. We are able to fit spherical surface data to the hand trajectory. The resulting envelope is quantified as a surface area using 3D surface plots projected to anatomical body planes. Surface area is normalized to the unit of the hemisphere of hand movement to facilitate comparison between individuals.

We collected data in 8 pediatric subjects with DMD aged 6–13 years (mean: 9.4 ± 2.5 years). All subjects were able to follow the movement protocol for assessment of the reachable workspace. Average normalized surface area for the dominant side was 0.749 (SD: 0.063) with a minimal surface area for the non-dominant side of 0.679 (SD: 0.090).
will examine reliability, accuracy and correlation with traditional functional outcome measures.

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P.2.5

**Performance of Upper Limb Scale for use in Duchenne muscular dystrophy – An iterative process to establish its suitability for clinical trials**


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In 2012 a group of international physiotherapists specializing in neuromuscular assessments devised a ClinRO to assess upper limb performance (PUL) for use in Duchenne muscular dystrophy (DMD). An exploratory Rasch analysis helped establish version one of the PUL although it was recognized at the time further analysis was required in a larger subset to confirm these preliminary findings and potentially remove redundant items. The aim of this study is to repeat the analysis in a larger cohort, again on an international level.

Over 300 assessments from both ambulant and non-ambulant individuals with DMD were analysed using RUMM2030 from Italy, UK, Belgium and USA. The age range was from 4 to 25 and data were examined for psychometric properties including clinical meaning, targeting, response categories, fit, reliability, dependency, stability and interval level measurement. Following analysis each item was reviewed both for scoring options and redundancy and a revised scale produced (Version two).

Psychometric analysis confirmed the preliminary findings and also highlighted areas where some items were potentially redundant. A shortened/revised scale was created by the expert group.

This iterative process of ClinRO development is essential to establish a robust measure. Further work needs to be conducted on reliability and responsiveness to confirm the PUL’s suitability for inclusion in clinical trials.

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P.2.6

**Comparison of 6MWD and person-reported functional measures in boys with Duchenne muscular dystrophy aged 4–12 years**

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30 m change in walking ability by 6MWT may not always be clinically meaningful from a quality of life perspective. Differing changes in ability may contribute to patient-reported function at differing levels of ability.

We describe correlation between measures, 1-year change in measures, and correlation of 1-year changes between measures for 6MWT, PedsQL and POSNA PODCI in 24 4–12 y.o. ambulatory DMD and 36 typical controls, and determine if minimal clinically-important differences (MCID) of HRQOL measures contribute to different estimates of walking distance change at differing levels of ability.

PedsQL total/physical function and PODCI global, transfer/mobility and sports/physical function demonstrated significant differences between DMD and controls (p < 0.00001). In DMD, 6MWT distance was correlated with PODCI, with the transfer/mobility scale showing the strongest relationship (r = 0.79). In DMD 6MWT distance weakly correlated with PedsQL. In DMD, 6MWT and PODCI global and transfer and mobility demonstrated significant one-year change and exceeded the amount of change representing MCID. In DMD, 6MWT change highly correlated with change in PODCI global and PODCI transfer/mobility scores (r = 0.76 and r = 0.93). PODCI global and PODCI transfer/mobility scales provided the best estimates of 6MWT performance. A “meaningful” 4.5 point change in a low PODCI transfer/mobility score of 30–34.5 was associated with a 5.6 m 6MWT change from 150.3 to 155.9 m. At PODCI levels closer to normative levels changes in 6MWT distance needed to affect a “meaningful” change in PODCI scores were associated with a 6MWT change of almost 46 m.

At lower levels of function, smaller increases 6-min walk distance result in meaningful change in quality of life. At higher levels of function, larger increases may be necessary to achieve the same QoL effect.

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P.2.7

**6 min walk test 12 month changes in DMD: Correlation with genotype**


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In the last few years a number of therapeutic approaches have become available for patients affected by Duchenne muscular dystrophy (DMD). The majority of the approaches proposed so far are specifically targeting distinct group of mutations, such as stop codon point mutations or groups of deletions as in exon skipping studies. Because of this, the number of patients eligible for these studies is limited to those having specific mutations or groups of mutations. This has raised the question of whether natural history data should be used as controls in studies with few eligible patients and, more specifically, whether individual groups of mutations follow the general natural history of boys of DMD or have distinct profiles of progression of functional impairment.

The aim of this study was to report 12 month longitudinal changes of the 6 min walk test (6MWT) in a large cohort of DMD ambulant patients subdivided according to type and site of mutations.

6MWT was performed in 198 DMD ambulant boys, older than 4 years at baseline and repeated after 12 months. 137 had deletions, 18 had duplications and 43 point mutations. Patients with deletions were further subdivided into subgroups according to whether they had mutations eligible for skipping in different exons, selecting those who were currently or likely to be part of clinical trials, eligible for skipping 44 (n = 18), eligible for skipping 45 (n = 16), eligible for skipping 44 (n = 18), eligible for skipping 51 (n = 27), eligible for skipping 53 (n = 28).