

Free [ADP] is considered to be an important regulator of cellular energy processes. It is common to calculate free [ADP] in muscles from the creatine kinase (CK) reaction by the equation: $[ADP] = ([ATP][CR]) / ([PCr]KH+)$. The equilibrium constant (K) is derived from in vitro measurements while all the concentration on the r.h.s. of the equations can be determined with MR spectroscopy or other assessments. Results of our study on the conversion between ADP and ATP in wild type (WT) mice and mice deficient in CK and adenylate kinase (AK) (MAK=/=) cast doubt on the validity of calculating the free ADP concentration in this way. To explain the results we propose a model in which the CK reaction proceeds via transiently free ADP, which is drawn from a pool of bound ADP.

Saturation transfer is a technique that can be used to assess reaction rates; a spin system is magnetically saturated, the transfer of this saturation to other spin systems is monitored and provides information on reaction rates. To evaluate the ADP↔ATP conversions we performed saturation transfer experiments on WT and MAK=/= mice. The saturation of β-ADP will lead to a transfer of saturation to β-ATP because of the CK and AK reactions.

On saturation of β-ADP we expected to observe at least 60% saturation transfer to β-ATP in the WT mice and no saturation transfer to β-ATP in the MAK=/= mice. Contrary to this expectation we found β-ATP to be saturated about 25% in both mice. This is possibly due to so-called transferred nuclear overhauser effects (NOE's) within ATP. Absence of the expected saturation transfer can only be explained if the β-ADP system is present in a state in which it cannot be saturated while still being involved in the CK reaction. To explain these results we propose a model in which free ADP, participating in the CK reaction, is drawn from a pool ADP that cannot be saturated, because of binding to large molecular structures.

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OUTCOME MEASURES; POSTER PRESENTATIONS

P4.33

The Motor Function Measure (MFM), an outcome measure for neuromuscular disorders: Preliminary results in congenital muscular dystrophy (CMD)

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The Motor Function Measure (MFM; www.mfm-nmd.org) is a scale designed for the assessment of motor function and progression of weakness in neuromuscular disorders. It is applicable to both ambulant and non-ambulant patients with a wide range of severity. The scale exists in two versions, one with 32 items for patients over 6 years of age (MFM-32), the other with 20 items for children aged from 2 to 6 years (MFM-20). Concerning the development of the scale, factor analysis identified three functional dimensions: D1 = standing position and transfers (13 items; 8 items in the short version), D2 = axial and proximal motor function (12 items; 8 in the short version), and D3 = distal motor function (7 items; 4 in the short version). We evaluated the applicability of the MFM to CMDs with a view to its use as an outcome measure in future clinical trials.

From the MFM databank, results in CMD were available for 66 patients (51 adults aged 6–72 years evaluated with the MFM-32 and 15 infants aged 3–6 years evaluated with the MFM-20). Diagnosis was confirmed genetically in 50% of cases, with a majority having the UCMD subtype (COL6 genes), but also a few cases with merosin

deficient CMD (LAMA2 gene), rigid spine syndrome (LMNA and SEPN1 genes) and alphadystroglycanopathy (FKRP and POMT2). Ambulation had been achieved by 75% of patients. Results confirm the ability of the scale to describe the motor capacities of patients. The total MFM score correlates with the functional severity of the disease where severe = never walked, moderate = lost ability to walk, and mild = still able to walk. Discrimination between ambulant and non-ambulant patients was observed in all sub-scores. For patients evaluated serially with the MFM, individual curves show either a stable course or more often slowly declining scores, depending on the stage of the disease.

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Progress using the Motor Function Measure for NMDs

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The Motor Function Measure (MFM; www.mfm-nmd.org) is a tool to measure the progress and severity of patients with neuromuscular diseases. It consists of a number of short tests of muscle function (32 in the adult scale, 20 in the pediatric scale), covering balance, strength and coordination, each of which take about a minute to perform, so the whole examination takes about half an hour. Only standard equipment (adjustable examination table, stopwatch, etc.) is required. Each test is scored from 0 to 3 and summed to give a percentage score, with three sub-scores (for standing and posture; axial and proximal, and distal motor function) which can be used independently.

The MFM was launched in 1998 in a widely consultative design process by a network of French doctors and physiotherapists in response to a perceived need for a functional evaluation suitable for all neuromuscular patients, wheelchair-using or not and tracheotomized or not. Initial testing and validation of the scale covered a range of muscle dystrophies and other myopathies (Bérard Neuromusc. Dis., 2005) and showed good reliability, construct validity and responsiveness. Other publications have since reported its use in other neuromuscular conditions, and its use both in clinical management and as a trial outcome measure (see the bibliography at the website).

Exact criteria for the scoring of the tests are given in the user's manual, which is available free from the website, in English, French, Portuguese and Spanish so far. Training and certification is available for physiotherapists and others wishing to perform the tests. There is ongoing research on the scale using a distributed database.

The MFM is useful as a key functional evaluation in the followup of patients with nearly all neuromuscular diseases, where necessary in conjunction with specific tests of muscular strength, pulmonary testing, echocardiography and imaging, and as an outcome measure in clinical trials.

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P4.35

Outcome measures validation study for mesoangioblasts transplantation in children affected by Duchenne muscular dystrophy

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The aim of this study is to establish a reliable tool of reproducible assessment of muscle strength in children affected by Duchenne Muscular Dystrophy (DMD) which will be selected for mesoangioblasts transplantation. We have developed a potential treatment for DMD based on infusion of cells (mesoangioblasts) from a healthy donor capable. The results of the current functional study will hopefully establish reliable qualitative and quantitative tool to assess results of a future cell therapy clinical trial with mesoangioblasts. This is a single centre, prospective, non-randomised, study of validation of outcome measures on 30 ambulant patients aged 5–12 years old affected by DMD including a cohort of 15 healthy aged matched males. We perform 2 days evaluation each 3 month for 1 year. During each assessment the following outcome measures are applied to DMD subjects: North Star Scale and 6 min walking test during the first day; quantitative assessment using the Kin Com 125 machine during the second day. The controls subjects will perform quantitative assessment twice in a year. Twice during this evaluation year patients perform spirometry, cardiac assessment and lower limb MRI. We divided the patients into three subgroups of age (5–7 years, 8–9 years, 10–12 years). The results of this preliminary part of the study show specific correlation between functional and quantitative tests in stronger children. Kin Com measurements correlate appropriately with functional tests for 10- to 12-years-old DMD boys, while show a major variability in muscle strength for 8- to 9-years-old DMD boys. The comparison with healthy subjects showed a difference of muscle strength that increases with age. This preliminary study demonstrates that our assessment may represent a useful tool to monitor the progress of DMD in ambulant children to determine the pre-transplantation story of the children who will be later treated with mesoangioblasts.

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P4.36

Upper limb evaluation in non-ambulatory patients with neuromuscular disorders

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Disease progression in children with neuromuscular disorder is frequently assessed by the 6-min walk test, that classically constitutes the clinical primary outcome of therapeutic trials. There is currently no validated and standardized method to assess upper limb function in non-ambulatory patients, which constitutes a major challenge for therapeutic trials.

Upper limb evaluation may be assessed either by direct muscular strength measurement, or by clinical scale, by questionnaire, or by clinical test that still have to be standardized and validated.

The aim of ULENAP (Upper Limb Evaluation in Non-Ambulatory Patients) is to study these different approaches on a group of 100 non-ambulatory patients with neuromuscular disorders. In each patient, strength of pinch, grip, hand flexion and extension is per-

formed on both limbs. In addition, limb function is evaluated through a hand function questionnaire, motor function measurement (MFM), taping, and a recently developed device to measure the ability of patients to hit two targets with fingers, the moviplate. Patients from the five participating sites will be followed up during 1 year in order to define the test which is the most sensitive to change.

Here, we present the feasibility and reproducibility of these different approaches, and the correlations that may be observed between strength and functional outcome measures.

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P4.37

Characterization of pulmonary function in patients with Duchenne muscular dystrophy

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Decline in skeletal muscle function in Duchenne Muscular Dystrophy (DMD) contributes to restrictive lung disease, chronic respiratory failure, poor cough and increased risk of pneumonia. These pulmonary complications cause the early morbidity and mortality in patients with DMD. Consequently, pulmonary function data in DMD patients provides important information and may provide clinically relevant measures for intervention studies testing the efficacy of emerging therapies for DMD. A decline in forced vital capacity (FVC) is observed in the second decade in DMD often leading the decline in pulmonary status and the initiation of non-invasive ventilation and assisted airway clearance devices. However, there is still a shortage of natural history data that describe and correlate the evolution of pulmonary function parameters beyond FVC, such as peak expiratory flow (PEF). *Methods:* Pulmonary function test (PFT) data was obtained prospectively from 62 DMD patients (age range 5–24 years) enrolled in an IRB-approved natural history study at the Children's Hospital of Philadelphia from 2005 to 2009. Data was collected by trained physical therapists. Spirometry flow-loops from all subjects was reviewed by a pediatric pulmonologist (OHM) and only data that met American Thoracic Society guidelines was included in the analysis. Both cross-sectional and longitudinal data were analyzed. Statistical analysis will be performed to describe and correlate the evolution of PEF and FVC as absolute values and as a percent of predicted. Use of steroid medication was also analyzed. *Results:* A predictable decline in both FVC and PEF % predicted was demonstrated from age 13 years onward. PEF % predicted was generally lower than the FVC % predicted up to age 13 years. *Conclusion:* Data from this study will assist in the selection of pulmonary function parameters that may capture an early decline in DMD and may serve as efficacy endpoints in clinical studies.

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P4.38

Swallowing disorders in pediatric neuromuscular diseases: A pilot study

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