

**PW 11:  
DM1 and DM2 –  
Clinical findings**

PW11-128	<p><b>SEVERE CARDIAC INVOLVEMENT IN YOUNG DM1 PATIENTS</b>  WAHBI K<sup>1</sup>, MEUNE C<sup>2</sup>, BECANE HM<sup>1</sup>, LAFORËT P<sup>1</sup>, BASSEZ G<sup>1</sup>, EYMARD B<sup>1</sup>, DUBOC D<sup>2</sup>  (1) Myology Institute - Pitié Salpêtrière - APHP, Paris, FRANCE. (2) Cochin Hospital - APHP, Paris, FRANCE.</p>
To contact the author:: karim.wahbi@psl.aphp.fr	<p>Cardiac involvement is frequent in DM1 and represents the primary cause of death in 20 to 29% of patients. However, few data concerning cardiac complications in young DM1 patients are available. We report a series of 27 DM1 patients aged 10 to 20 year old (16.3+/-2.6 years; male=20) with cardiac complications requiring a specific pharmacological treatment or the implantation of a device (pacemaker or cardioverter defibrillator). DM1 clinical phenotype was congenital (n=3), infantile (n=10), mild (n=12) or exclusively cardiac (n=2). Symptoms were present in 20 patients (palpitations=14, syncope or near syncope=7, sudden death=2) and occurred during exercise in 11 patients. Cardiac complications were supraventricular arrhythmias (n=9), atrio-ventricular block (n=3), ventricular arrhythmias (n=2), left ventricular dysfunction (n=1). Combined complications, i.e. arrhythmias and/or conductive disease and/or ventricular dysfunction were present in 10 patients.</p> <p>This study confirms the existence of severe cardiac involvement in young DM1 patients. Supraventricular and ventricular arrhythmias induced by exercise are the most frequent complications. Therefore, cardiac investigations are necessary in patients &gt; 10 year old. An exercise testing should be performed, principally in patients who practice sport. As cardiac complications are frequently combined, cardiac follow up should be particularly close in patients who have even only mild abnormalities.</p>

PW11-129	<p><b>SELECTIVE COGNITIVE DYSFUNCTION IN THE CHILDHOOD FORM OF DM1</b>  ANGEARD N<sup>1</sup>, GARGIULO M<sup>1</sup>, JACQUETTE A<sup>2</sup>, RADVANYI H<sup>3</sup>, EYMARD B<sup>1</sup>,  HÉRON D<sup>2</sup>  (1) Institut de Myologie - Groupe Hospitalier Pitié-Salpêtrière, Paris, FRANCE. (2)  Département de Génétique - Groupe hospitalier Pitié-Salpêtrière, Paris, FRANCE. (3)  Département de Biochimie génétique - Hôpital Ambroise Paré, Boulogne, FRANCE.</p>
<p>To contact the author::  nathalie.angeard@paris5  .sorbonne.fr.</p>	<p><b>Background</b>  Previous studies have shown variable degree of cognitive impairment in the childhood form of DM1 (Steayert et al., 1997; Gossens et al., 2000). It ranges from mental retardation to subnormal intelligence but dysfunction in verbal working memory and visuospatial abilities. Negative correlation with the CTG expansion size has also been reported (Angeard et al., 2007).</p> <p><b>Method</b>  We present here the results of a neuropsychological study on 20 subjects aged from 7 to 17 years with the childhood phenotype and no mental retardation (inclusion criteria).</p> <p><b>Results</b>  Concerning global cognitive abilities, the mean FSIQ was in the subnormal range with a significant dissociation between verbal (VIQ = 91) and non-verbal scores (PIQ = 78). In neuropsychological measures focusing on mental flexibility, cognitive inhibition and planning, the sample study scored significantly lower than the normative reference population. Concerning memory, we observed a dissociation depending on the nature of the information to be treated: in the memorization of a list of words or a story, subject obtain normal scores in immediate and delayed recall but impaired performances for the geometrical figure.</p> <p><b>Conclusion</b>  The pattern of dysfunction in speed of processing and planning observed in the children and adolescents could be related to those observed in the adult classical form of DM1 (Meola et al., 2007). Short-term and long-term verbal memory preservation could be used to elaborate well-adapted rehabilitation.</p>

PW11-130	<p><b><u>ELECTROPHYSIOLOGICAL ASSESSMENT OF CENTRAL AND PERIPHERAL EXERCISE-RELATED FATIGABILITY IN MYOTONIC DYSTROPHY TYPE 1.</u></b>  BOËRIO D<sup>1</sup>, LEFAUCHEUR JP<sup>2</sup>, BASSEZ G<sup>3</sup>, HOGREL JY<sup>1</sup>  (1) Institut de Myologie, GH Pitié-Salpêtrière, Paris, FRANCE. (2) Service de Physiologie – Explorations Fonctionnelles, CHU Henri Mondor, Créteil, FRANCE. (3) Service d’Histologie, Centre de Référence Maladies Neuromusculaires, Créteil, FRANCE.</p>
<p>To contact the author::  d.boerio@institut-myologie.org.</p>	<p>Fatigue frequently occurs in various neuromuscular disorders specially in myotonic dystrophy type 1 (DM1). However its pathophysiology remains unclear. This study aimed to investigate the effects of exercise-related fatigability on central and peripheral properties in DM1.</p> <p>Ten DM1 patients and 10 healthy subjects were enrolled. Muscle, peripheral nerve and cortical excitability were studied using high spatial resolution surface EMG, stimulations of the ulnar nerve, and transcranial magnetic stimulation to obtain motor evoked potentials (MEP). Tests were performed before and after an isometric contraction of adductor digiti minimi sustained 45s at 60% of maximal voluntary contraction (MVC). Force and myoelectric characteristics [root mean square (RMS), mean power frequency (MPF) and muscle fibre conduction velocity (MFCV)] were analysed.</p> <p>At baseline DM1 patients displayed less intracortical facilitation of MEP (234.8±130.2% vs. 100.3±94.7%, p=0.0164), reduced supernormality and rheobase (107.7±22.3% vs. 124.4±7.5%, p=0.0065; 4.1±0.7mA vs. 5.6±1.8mA, p=0.0545 respectively). Mwave amplitude to ulnar stimulation and MFCV were smaller. Furthermore force, RMS, MPF and MFCV values were lower at MVC.</p> <p>During the exercise the force remained unchanged, MPF and MFCV decreased in both groups. Only controls presented RMS decline.</p> <p>After the task, the percentage of refractoriness decreased in DM1 patients (-14.66±12.29%, p=0.0078). Conversely MEP amplitude and intracortical inhibition were reduced, threshold and Mwave duration increased and RMS at MVC decreased in controls.</p> <p>Besides muscular impairments, DM1 patients displayed at baseline subtle impairments of motor cortex suggesting an alteration of pyramidal cells excitability and a deregulation of glutamaergic circuitry. Likewise changes in supernormality and rheobase may support an alteration of membrane potential. The exercise induced barely slight modifications of neuromuscular properties. Unlike DM1, the task implied important modifications of pyramidal cell excitability associated with functional</p>

PW11-131	<p><b><u>EXCESSIVE DAYTIME SLEEPINESS IN MYOTONIC DYSTROPHY TYPE 1: CORRELATION WITH HYPOTHALAMIC-PITUITARY-ADRENAL AXIS DYSREGULATION</u></b></p> <p>FALORNI M<sup>1</sup>, VOLPI L<sup>1</sup>, CALSOLARO V<sup>1</sup>, BONANNI E<sup>1</sup>, MONZANI F<sup>2</sup>, EMDIN M<sup>3</sup>, SICILIANO G<sup>1</sup></p> <p>(1) Department of Neurosciences, University of Pisa, Pisa, ITALY. (2) Department of Internal Medicine, University of Pisa, Pisa, ITALY. (3) Department of Cardiovascular Medicine, CNR-Institute of Clinical Physiology, Pisa, ITALY.</p>
	<p>Excessive daytime sleepiness (EDS) is common in patients with Myotonic Dystrophy type 1(DM 1) and is a major factor that interferes with the social life of the disease.</p> <p>There are contrasting opinions in literature about the mechanism of EDS in DM1; according to some Authors, EDS could be caused by sleep-disordered breathing, hypercapnia or disturbance of sleep architecture, according to other Authors, it could be due to a central sleep regulation dysfunction, probably modulated from neuroendocrinal factors that govern sleep and awake.</p> <p>The aim of the present study was to assess the presence of sleep/wake cycle disturbance in a group of MD 1 patients and their possible correlations with hypothalamic-pituitary-adrenal axis dysregulation. The influences of baroreceptor and chemoceptor reflexes dysfunctions on EDS were also evaluated.</p> <p>Eight MD 1 patients and ten healthy age-matched controls were studied by means of an all-night polysomnographic recording, the multiple sleep latency test (MSLT), the evaluation of hypothalamic-pituitary-adrenocortical activity and baroreceptor and chemoceptor reflex study.</p> <p>The mean MSLT value was significantly lower in patients than in controls. Six of the eight patients were found to have pathological EDS, but only one presented nocturnal apnoeas and only one periodic leg movements .</p> <p>There weren't significantly differences in baroreceptor and chemoceptor reflexes, between patients and controls.</p> <p>Overall, we didn't find an hypothalamic-pituitary-adrenal axis dysregulation in DM1 patients;, even though an inverse correlation was found between aldosterone dosage in clino and orthostatism and MSLT, this indicating that an increase in aldosterone values is correlated with an enhancement of EDS.</p> <p>Our data suggest that EDS is common in MD 1 patients and that it is probably caused by a primary dysfunction of central sleep regulation, with aldosterone maybe playing an important role in sleep/wake cycle disturbance pathogenesis.</p>

PW11-132	<p><b><u>MYOTONIC DYSTROPHY OF STEINERT ABOUT TWO FAMILIES OF THE WEST ALGERIAN.</u></b>  BADSI D<sup>1</sup>, OUDRER N<sup>2</sup>, ZENTOUT H<sup>3</sup>, LITIM K<sup>4</sup>, OUBAICHE M<sup>5</sup>  (1) CHU, Oran, ALGERIA. (2) CHU, Oran, ALGERIA. (3) CHU, Oran, ALGERIA. (4) CHU, Oran, ALGERIA. (5) CHU, Oran, ALGERIA.</p>
To contact the author:: dounia_bads_i@yahoo.fr.	<p><b><u>Introduction</u></b>  Myotonic dystrophy (MD1) is the most common form of adult muscular dystrophy with autosomal dominant transmission.  It is an inherited disease in which there is an abnormal expansion of CTG trinucleotide repeat at 19q13.3  It is manifested as a chronic progressive multisystem disorder  In the present study, we report the clinical and molecular analysis of 14 Algerian patients MD1</p> <p><b><u>Methods</u></b>  Our transverse descriptive study was realized in the service of neurology of the CHU of Oran from January 2005 to January 2007  the patients were selected according to : Beginning and prevalence of the muscular attack at the distal level with facial participation, myotonia shown by the EMG, attack of other organs (eye, heart...), with an abnormal amplification of tri nucleotide CTG, repeated more than 50 times in gene MDPK.  For each patient, were taken: the distribution of the weakness and muscular atrophy. the complementary investigations comprised: a biological systematic assessment of CPK, LDH, T3, T4, TSH, FSH, LH, Testosterone, Phosphocalcic assessment and glycaemia, the electromyogram was carried out at all the case index as well as the cardiac assessment. The ophthalmologic examination was carried out among 14 patients. The genetic study carried out among 05 patients</p> <p><b><u>RESULTS:</u></b>  14 MD1 patients from 02 unrelated west Algerian families, mean age 25,7 years (with extremes ones going from 12– 65 years ), with 08 males and 06females. Autosomal dominant transmission was established at the 02 families.  - All the patients presented myotonia. the distal muscular weakness was observed among 11 patients , the cataract was observed among 02 patients and the cardiac attac among 04 patients,a sterility was observed among 04 patients associated.Only,02 patients had an isolated sterility. .</p> <p><b><u>CONCLUSION:</u></b><u>the phenotypical and genotypic analysis of our patients MD1 aoroach similar studies observed in other countries in the world</u></p>

PW11-133	<p><b><u>USING FORCE CURVE MODELLING FOR THE EVALUATION OF MYOTONIA</u></b>  HOGREL JY<sup>1</sup>  (1) Institut de Myologie, Paris, FRANCE.</p>
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<p>To contact the author::  jy.hogrel@institut-myologie.org.</p>	<p>Myotonic disorders are characterized by slowed muscle relaxation capacity in relation to the presence of myotonic potentials in the electromyogram. Several syndromes have been depicted presenting inability to relax the muscles after a brief intense contraction. The early clinical sign of myotonic syndromes is generally estimated by the clinician by asking the patient to strongly grip his hand and by evaluating an inefficiency to relax. Besides this subjective approach, quantitative assessment of myotonia has been sometimes considered by analyzing the rate of force relaxation after a strong contraction. The aim of this study was to provide a regression model in order to automatically fit the force relaxation curve and to propose a robust index to quantitatively assess myotonia in clinical settings for a reliable follow-up of patients. Grip strength was recorded using an analog handgrip dynamometer linked to a computer with devoted software. The subjects were asked to produce a steady effort at 70% MVC during a 10-s duration and then to relax. When a subject is asked to relax its contraction, the force globally decreases according to an asymmetric sigmoid function. All force curve analyses were then performed using a regression model according to a Richards equation. The inverse function leads to the direct computation of various relaxation times corresponding to given percentages of the strength maintained just before the relaxation.</p> <p>Eight control subjects and eight patients suffering from a myotonic dystrophy type 1 (DM1) participated to this pilot study to validate its principle. Absolute and relative relaxation times were automatically computed on force curve.</p> <p>Preliminary results show that the asymmetric sigmoid model is adapted to fit force relaxation curves with a high level of confidence. The difference between controls and DM1 was significant for all absolute and relative force relaxation times. Automatic myotonia assessment is a useful objective method for the follow-up of myotonic disorders.</p>
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<p>PW11-134</p>	<p><b><u>OBJECTIVE QUANTIFICATION OF MUSCLE DEGENERATION IN DM1 PATIENTS USING MRI</u></b>  HIBA B<sup>1</sup>, RICHARD N<sup>1</sup>, HÉBERT L<sup>2</sup>, VIAL C<sup>3</sup>, SAULNIER J<sup>2</sup>, NEJJARI M<sup>1</sup>, REMEC JF<sup>3</sup>, COTÉ C<sup>3</sup>, BOUHOUR F<sup>3</sup>, PUYMIRAT J<sup>3</sup>, JANIER M<sup>1</sup>  (1) Université Lyon1, ANIMAGE, Lyon, FRANCE. (2) Human Genetics Unit, Laval CHU, Québec, CANADA. (3) Department of Electroneurophysiology and Muscular Pathology, Wertheimer Hospital, Lyon, FRANCE.</p>
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<p>To contact the author::  bassem.hiba@cermep.fr.</p>	<p>An objective assessment of disease progression and muscle damage is required to prove therapies for muscle degeneration. In this context, we propose an objective MRI-based method for the assessment of the Tibias Anterior (TA) muscle degeneration in DM1 patients.</p> <p>20 patients were included in the study. Lower leg MRI examination was performed subsequent to genetic testing. TA muscular relative isometric strength (i.e. torque muscle) was also assessed for left and right legs using a hand-held dynamometer.</p> <p>3D high spatial anatomical images were acquired in the transversal orientation, covering the legs from knee to ankle. The same geometric parameters were used to acquire MR images using the following pulse sequences: T1; DP/T2 and 3-point Dixon.</p> <p>An automatic segmentation algorithm was developed in order to delineate between normal and diseased tissues on T1 images. Main T2 value of TA's normal tissue was assessed from DP/T2 weighted images. Finally, Grey-level average values measured from fat and water images of 3-point Dixon sequence, were used to define fat to water ratio in the TA muscle.</p> <p>Normal and degenerated tissue volumes, oedema severity, quantified as the main T2 value in normal tissue, and fat infiltration, quantified as fat to water ration, were assessed for TA muscles. An excellent correlation was found between normal tissue volume and muscle strength.</p> <p>In this in-progress work, we have validated the use of MRI for quantitative assessment of entire muscle (TA) degeneration in DM1 patients. The muscle composition parameters we proposed could be used as markers for the severity and progression of the disease and for therapy effect quantification.</p>
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<p>PW11-135</p>	<p><b><u>CORRELATION BETWEEN MEASURES OF MUSCLE STRENGTH, FUNCTION AND QUALITY OF LIFE IN PATIENTS WITH MYOTONIC DYSTROPHY TYPE-1 (DM-1):IMPLICATIONS FOR CLINICAL TRIALS</u></b>  PANDYA S<sup>1</sup>, DILEK N<sup>1</sup>, MARTENS B<sup>1</sup>, QUINN C<sup>1</sup>, MOXLEY R<sup>1</sup>  (1) University of Rochester, Rochester, USA.</p>
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<p>To contact the author:: shree_pandya@urmc.rochester.edu.</p>	<p><b>Objective:</b> To document the correlations between measures of muscle strength, function and QOL in DM-1.</p> <p><b>Background:</b> Research funding agencies and Regulatory agencies are increasingly requiring clinical outcome measures that are reliable, responsive and reflective of all domains of health and disease in therapeutic trials. For an optimum choice of outcome measures, it is essential that we understand the relationships - both cross sectional and longitudinal - between these measures from various domains.</p> <p><b>Methods:</b> Patients participating in various DM-1 trials at our center routinely undergo evaluations of muscle strength (Manual muscle tests and Quantitative muscle tests), function (Timed Function Tests) and Quality of Life (Sickness Impact Profile) at baseline and follow up evaluations.</p> <p><b>Results:</b> Data from 50 genetically confirmed DM-1 patients who had undergone all of the above evaluations at baseline were analyzed using Pearson correlation coefficients. Statistically significant (<math>p &lt; .0001</math>) relationships were documented for measures of leg muscle strength (MMT) and time to go 30' (<math>r = .74</math>), ascend and descend 4 steps (<math>r = .60</math>) and SIP – physical domain (<math>r = .64</math>). Longitudinal relationships are still being analyzed.</p> <p><b>Conclusions:</b> We have documented the relationships between various outcome measures in DM-1. This allows us to make appropriate informed decisions about the choice of outcome measures for various clinical trial phases.</p>
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<p>PW11-136</p>	<p><b><u>ISOKINETIC KNEE WEAKNESS IN MYOTONIC DYSTROPHY: ONE YEAR REPORT</u></b>  BAYLE n<sup>1</sup>, BOYER F<sup>2</sup>  (1) physical medicine and rehabilitation, reims University, reims, FRANCE. (2) physical medicine and rehabilitation, reims University, reims, FRANCE.</p>
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The role of strengthening exercise to improve functional abilities and weakness of persons with neuromuscular diseases is controversial. In literature, a previous study has shown that strength training in patients with myotonic dystrophy provide neither positive nor negatives effects (muscle damage).

This study reports on nineteen patients, aged 22 to 45 years old, with myotonic dystrophy followed in the physical medicine and rehabilitation departement of Reims University, whose strength is measured once a year by isokinetically knee torque. There was no strengthening exercise training for those patients during the year between the two measures. The rehabilitation program only consist on stretching, splinting and for some of them balneotherapy.

We calculated the variation rate of two years intensity peak (Newton x Meter) of right and left Knee extensors and flexors, at 60 degrees/seconds and 180 degrees/second, for 13 of those 19 patients.

The result was a loss of peak torque (from 1 to more than 50 NewtonMeter) on knee flexors and extensors for all the patients.

The main purpose of this preliminary report is to point out the natural evolution (loss of strength) in patients with myotonic dystrophy, without strength training, in order produce reference appraisal, which will evaluate the effect of strength reinforcement on this loss of muscle strength.

PW11-137

**PHENOTYPIC ANALYSIS OF ALGERIAN PATIENTS WITH MYOTONIC DYSTROPHY (MD1)**

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<p>To contact the author:: sifimina@yahoo.fr.</p>	<p><b>INTRODUCTION</b> Myotonic dystrophy (MD1).is the most common form of adult muscular dystrophy with autosomal dominant transmission. It is an inherited disease in which there is an abnormal expansion of CTG trinucleotide repeat at 19q13.3. It is manifested as a chronic progressive multisystem disorder. In the present study, we report the clinical and molecular analysis of 25 Algerians patients (MD1) from 11 unrelated Algerian families.</p> <p><b>PATIENTS AND METHODS:</b> Our patients were sélectioned according to the following criteria: - Beginning and prevalence of the muscular attack at the distal level with facial participation, myotonia, attack of other systems (eye, heart...), with an abnormal amplification of tri nucleotide CTG, repeated more than 50 times in gene MDPK. - Using a muscular disability rating scale (MDRS) we measured the severity of the weakness - The complementary investigations comprised: a biological systematic assessment of CPK, LDH, T3, T4, TSH, PTH, FSH, LH, testosterone, phosphocalcic assessment and glycaemia), the electromyogram (EMG) was carried out at all the cases index as well as the cardiac assessment, the ophthalmologic examination with a slit lamp was carried out among 15 patients. The diagnosis of DM1 was made on the basis of molecular genetic analysis at 20 patients in the laboratory of genetic diagnosis of the CHRU of Strasbourg</p> <p><b>RESULTS:</b> Mean age at assessment was : 38 years, with 14 males and 11 females, autosomal dominant transmission was established at 09 families. All the patients presented a myotonia, the distal muscular weakness was observed at 23 patients with facial participation at 16 patients, the cataract was observed among 11 patients, the cardiac attack at 07 patients and the baldness at 11 patients The genetic study confirmed the diagnosis of MD1 in all tcases</p> <p><b>CONCLUSION:</b> Phenotypic and genotypic analysis of Algerian patients with DM1 approaches those observed in the other countries.</p>
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<p>PW11-138</p>	<p><b><u>LOWER LEG MRI FINDINGS IN MYOTONIC DYSTROPHY</u></b> COTÉ C<sup>1</sup>, BASSEM H<sup>2</sup>, HEBERT L<sup>1</sup>, JANIER M<sup>2</sup>, PUYMIRAT J<sup>1</sup> (1) CHUQ Research Center, Quebec, CANADA. (2) Hopital Neuro-cardiologique, Lyon, FRANCE.</p>
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The aim of the study was to evaluate if a typical pattern of muscular involvement could be identified, and if correlation exists between severity of MRI anomalies and clinical findings. MRI findings were edema and fatty degeneration, ranging from mild to complete fatty replacement of the muscle. Each muscle of the legs was evaluated separately, using this chart: 0 = normal aspect; 1= edema; 2= mild atrophy; 3= moderate atrophy; 4= complete atrophy / fatty replacement. In most patients, the Medial Gastrocnemius and Soleus muscles were involved earliest and most severely, whereas Posterior Tibial and Popliteus muscles were generally spared. Comparison of DM1 patients with moderate (MDRS=3) and severe (MDRS=4) muscle disability rating scale revealed that the most frequently affected muscle in patients with moderate muscle disability were the Median Gastrocnemius, the Soleus and the Hallux Long Flexors whereas, the Popliteus and the Tibialis Posterior were spared. In more affected DM1 patients with a MDRS = 4, the most frequently affected muscles were the Tibialis Anterior, Hallux Long Extensor, the Median Gastrocnemius and the Soleus. There was a significant correlation between MRI score and the duration of the disease. In contrast, there was no correlation between the MRI score and the number of CTG repeats. For the Tibialis Anterior, we have compared the MRI scores with the QMT values obtained with a dynamometer type Chatillon. There was a significant correlation between the MRI scores and the QMT values. This correlation was observed for males ( $p= 0.05$ ,  $n=9$ ) and females ( $p < 0.05$ ,  $n= 7$ ). No correlation was found between the MRI scores and the QMT values for the eversors and muscles of the posterior compartment. MR imaging appears as a valuable tool to depict abnormalities of each specific muscle in DM.

PW11-139

**TYPE 2 MYOTONIC DYSTROPHY CAN BE PREDICTED BY COMBINED TYPE 2 MUSCLE FIBRE CENTRONUCLEATION AND SCATTERED ATROPHY**

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In myotonic dystrophy type 2 (DM2), CCUG expansions form pathogenic ribonuclear accumulations that are detectable by in situ hybridization (ISH). Clinical DM2 diagnosis is often overlooked due to a poorly specific presentation and a muscle biopsy showing a "denervation-like" pattern of unknown specificity, combining: (1) increased fibre size variation, (2) centronucleation, (3) small angulated fibres, (4) type 2 fibre atrophy, and (5) nuclear clumps. Here, we checked the presence of these alterations in a series of 2100 consecutive muscle biopsies in patients selected for unidentified myopathy with no inflammation or neuropathy. Then, we used automated [CCUG]8 ISH as a reference standard to evaluate the value of each histological feature for DM2 detection. Among 104 included patients, ISH identified 8 DM2+ and 96 DM2- cases. Multivariate analyses identified the combination of "type 2 fibre atrophy" and "centronucleation" as the most relevant (Se=1.0, Sp=0.92), whereas these changes were mutually exclusive in non-DM2 patients ( $p < 0.0001$ ). Relevance of the combination was confirmed in an additional independent series (15 DM2+ vs 17 DM2-). Further investigation uncovered that centronucleation selectively affects type 2 fibres in DM2, and, conversely, type 1 fibres in DM1 ( $p < 0.0001$ ). These results will facilitate the routine detection of DM2 and further substantiate a distinctive muscle pathophysiology, designating DM2 as a type 2 fibre myopathy.

PW11-140

**MYOTONIC DYSTROPHY TYPE 2 (DM2/PROMM) MISDIAGNOSED AS FIBROMYALGIA: CLINICAL, ELECTROPHYSIOLOGICAL, HISTOPATHOLOGICAL AND GENETIC DATA.**

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<p>To contact the author:: 13216@imas.imim.es.</p>	<p>Background: A number of patients with molecularly confirmed DM2 diagnosis proved to have had fibromyalgia as their previous diagnosis. It seems possible that some families with DM2 phenotype have neither mutation.</p> <p>Objectives: To show how a myotonic dystrophy type 2 may have been missed in patient with fibromyalgia and how muscle biopsy may be useful to the diagnosis of DM2.</p> <p>Patient/Methods: A 63 year-old Spanish woman with healthy non-consanguineous parents had presented with widespread muscle-skeletal pain with onset at 45 years of age and with a mild and non-progressive proximal upper limbs weakness. The osteotendinous reflexes were present and she presented a slight atrophy of thigh muscles with rather bulky calves. Absence of clinical myotony. Repeated CK levels were elevated 1 to 8 folds. There was no facial muscles, cardiac, hepatic or CNS involvement. The diagnosis considered was Fibromyalgic Syndrome of unknown aetiology. The electrophysiological study showed myogenic patterns and abundant myotonic discharges. The electrophysiological study of the patient's daughter, who presented some muscle-skeletal pain and a minimal proximal upper limbs paresis without clinical myotony, showed abundant myotonic discharges.</p> <p>Results: Lower limb CT Scan showed a minimal atrophy in proximal muscles; the leg muscles were not atrophic but a slightly hypodense pattern was found in deep posterior compartments. Muscle biopsy (deltoid) showed various morphological alterations: Nuclear changes, pycnotic nuclear clumps, angular atrophic fiber, great predominance of type 1 fibers and selective and preferential type 2B fiber atrophy in contrast to type fiber 1 atrophy in DM1 patient. Search for the molecular defect on DM1 and DM2 genes resulted negative.</p> <p>Conclusions: The results of this study confirm that there are patients with DM2 disease phenotypes among fibromyalgic patients due to similar clinical symptoms. Muscle biopsy may be useful to the diagnosis of DM2.</p>
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<p>PW11-141</p>	<p><b><u>DM2 PHENOTYPE CAUSED BY UNINTERRUPTED SHORT (CCTG)55 REPEAT EXPANSION IN ZNF9 GENE</u></b>  SUOMINEN T<sup>1</sup>, BACHINSKI L<sup>2</sup>, RAHEEM O<sup>3</sup>, HAAPASALO H<sup>4</sup>, KRESS W<sup>5</sup>, KRAHE R<sup>2</sup>, UDD B<sup>6</sup>  (1) University of Tampere, Medical School, Neurogenetics, Tampere, FINLAND. (2) Department of Cancer Genetics, University of Texas M. D. Anderson Cancer Center, Houston, USA. (3) University of Tampere, Department of Pathology, Neuromuscular Pathology, Tampere, FINLAND. (4) Department of Pathology, Pirkanmaa Hospital District, Center for Laboratory Medicine, Tampere, FINLAND. (5) Institute of Human Genetics, University of Wuerzburg, Biozentrum, Am Hubland, Wuerzburg, GERMANY. (6) Department of Neurology and Medical School, Tampere University Hospital, Tampere, FINLAND.</p>
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Myotonic dystrophy type 2 (DM2) is caused by (CCTG)<sub>n</sub> repeat expansion in the first intron of *ZNF9* gene, with the smallest reported disease causing expansion of 75 repeats. Repeat region consists of a complex motif (TG)<sub>12-26</sub>(TCTG)<sub>7-12</sub>(CCTG)<sub>3-9</sub>(G/TCTG)<sub>0-4</sub>(CCTG)<sub>4-15</sub> of which only the uninterrupted (CCTG)<sub>n</sub> repeats have been suggested to cause DM2 phenotype.

Here we report that in one patient with mild clinical phenotype of DM2 disease only 55 CCTG repeats were seen in DNA samples isolated from both peripheral blood leukocytes and muscle tissue. This small repeat expansion was not detected by chromogenic in situ hybridization from muscle sections, but was seen with a modified Southern technique and a PCR based method which amplifies the repeat region (RP-PCR, repeat primed). The repeat region was further analyzed by cloning and small-pool PCR to define the instability and the number of CCTG repeats in the complex motif. We could identify an instable expansion allele consisting of 55 CCTG repeats with no G/TCTG interruptions compatible with a disease causing small DM2 mutation. The patient has muscle weakness since age 50 years and early cataracts. Myotonia is seen neither clinically nor on EMG. Muscle biopsy shows findings characteristic of DM2 with highly atrophic type 2 fibers, nuclear clump fibers and increased number of internal nuclei.

The finding of 55 CCTG repeats containing DM2 mutation suggests that even shorter than previously reported expansion of (CCTG)<sub>75</sub> can cause DM2 disease. Further studies include haplotype analysis to assess whether this small expansion is of same founder origin as the general European DM2 mutation.

