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A 9-year follow-up study of the natural progression of upper limb performance in myotonic dystrophy type 1: A similar decline for phenotypes but not for gender

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Abstract

This study aimed to document and compare the decline of upper limb performance among adults with myotonic dystrophy type 1 according to phenotype and gender. A longitudinal descriptive design compared upper limb performance at baseline and follow-up of 70 women and 38 men with the late-onset or adult phenotypes. Grip strength and pinch strength as well as gross dexterity and fine dexterity were assessed. All four performance measures decreased significantly ($p < 0.001$). The decline over time was similar for individuals with the late-onset and adult-onset phenotypes, but differed according to gender. For late-onset and adult-onset phenotypes respectively, women lost less grip strength than men: 0.4 and minus 0.8 kg (2.0% and −9.4%) in women vs. minus 7.4 and minus 3.1 kg (−19.2% and −30.7%) in men. A similar situation was found for gross dexterity: minus 3.0 and minus 3.2 blocks (−4.6% and −5.9%) in women vs. minus 12.4 and minus 8.7 blocks (−19.4% and −16.6%) in men. Pinch gauge had the smallest standard deviations and was one of the only measurement tools with significant detectable changes in relation to the standard error of measurement. Given these results, health professionals and researchers should consider phenotype and gender differently when planning health services or future studies. Indeed, as their upper limb strength and dexterity differed, even if their decline was similar, the phenotypes should not be pooled. Finally, the use of the pinch gauge to assess long-term change in upper limb ability seems preferable to the three other measurements.

Keywords: Myotonic dystrophy; Disease progression; Muscle strength; Upper limbs; Longitudinal study; Rehabilitation

1. Introduction

Myotonic dystrophy type 1 (DM1), an autosomal dominant disease, results from the expansion of an unstable trinucleotide cytosine-thymine-guanine (CTG) repeat mutation located in the 3′ untranslated region of a gene (19q13.3), encoding the myotonin protein kinase (*DMPK*) [1]. DM1 is often compared to premature aging [2,3]. Several systems are affected, especially the muscular, cardiac, respiratory, ocular, gastrointestinal, reproductive, and central nervous systems [4]. Of these, the muscular system plays a key role in the accomplishment of daily activities and social roles [5]. In DM1, symmetric muscle wasting is generally observed in the neck and distal upper/lower limbs, which slowly progresses to the trunk [6,7]. A delay in muscle relaxation (myotonia) is also observed [8].

Although a common general pattern of muscle wasting progression is observed, the severity of the disease varies widely among individuals and across affected systems. In addition, from a clinical standpoint, impairments and disabilities are also highly heterogeneous, making planning of health services challenging. This phenomenon, although only partly understood, has given rise to a plethora of clinical

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pictures. These pictures exist on a continuum of severity that is classified into the following four phenotypes: late onset, adult (classic), childhood onset and congenital [9]. Although no international consensus is yet available, a juvenile phenotype was recently considered in the continuum [10]. Compared with the late onset and adult phenotypes, the childhood onset and congenital phenotypes are generally associated with more severe symptoms and younger age at onset [9].

These impairments and disabilities have important personal and financial consequences for people with DM1, since they lead to restriction in social participation [11], reduction of quality of life [12,13], and medical and indirect costs amounting to $US32,236 per year [14]. Among potential explanatory factors, muscle weakness of the upper limbs and difficulty performing tasks that require fine manual dexterity were respectively demonstrated to be associated with social participation restrictions [5] and activity limitations [15]. Indeed, individuals with DM1 reported difficulties handling, lifting and grasping objects, opening doors or jars, and reaching objects over their head, all of which are associated with moderate to severe restrictions in the accomplishment of daily activities [16]. Moreover, upper limb disabilities have been shown to be associated with household-related needs and, specifically, hand weakness was reported to be a criterion for referral to rehabilitation services [17]. However, to adopt a prognostic approach, i.e., offer rehabilitation interventions and services in a timely manner, it is important to have a better understanding of the progression of disabilities over time. In addition, according to the Food and Drug Administration (FDA), studies of the natural history of disease are a key aspect of upcoming clinical trials [18]. Describing the decline of upper limb performance over a long time period will lead to a better understanding of the natural progression of DM1. In addition, the characterization of muscle strength impairment over time according to adult vs. late-onset phenotype has been reported as essential to facilitate monitoring in clinical settings [19].

Although previous studies have advanced knowledge of DM1, little is known about the decline of upper limb performance over time. To our knowledge, no study has investigated gross and fine manual dexterity decline. Moreover, studies investigating muscle strength decline showed conflicting results. On the one hand, a two-year longitudinal study showed a non-significant decrease in grip strength and a significant increase in lateral pinch strength, with no gender effect [20]. On the other hand, a cross-sectional study that took disease duration into account reported a significant rate of decline for grip strength and lateral pinch strength, with a gender effect [6]. For each year of disease, a rate of decline of 2% for women and 3% for men for grip strength, and a rate of decline of 1.6% for women and 2.5% for men for lateral pinch strength were found [6]. These discrepancies raise questions about the expected decline in grip and pinch strength over time as well as the gender effect on the rate of decline. Although recommended, none of these studies distinguished between DM1 phenotypes in their analyses [19]. This study aimed to document and compare the decline in upper limb performance among adults with DM1 according to phenotype and gender.

2. Materials and methods

2.1. Participants

This study used a longitudinal descriptive design comparing data from baseline (2002–2004) with data from follow-up (2011–2013). Participants were recruited through the Saguenay Neuromuscular Clinic registry (Québec, Canada). Individuals with DM1 (late-onset and adult phenotypes) confirmed by genetic analysis and 18 years of age or older were invited to participate (n = 416). Since they presented with more severe impairments and different prognoses, individuals with the childhood or congenital phenotype of DM1 were excluded as were those with another disease influencing upper limb performance (e.g., stroke). A sample of 200 subjects was then drawn randomly from this subset of the 416 individuals; the baseline sample selection criteria and process has been published previously [5,11,13,21–24]. The study was conducted at the Neuromuscular Clinic and at the participant's home by trained healthcare professionals. The Ethics Review Board of the *Centre intégré universitaire de santé et de services sociaux du Saguenay–Lac-St-Jean* approved the study protocol.

2.2. Measures

The equipment was the same and calibrated by the manufacturer before each data collection (baseline and follow-up). Although two different raters collected data at baseline and follow-up, the first rater trained the second rater and a standardized procedure and instruction to participant were used to minimize bias. The time of the year of the data collection was kept as constant as possible for most participants. Given the constraints of rater and participants, it was not possible to be consistent in time of the day for all participants.

2.2.1. Sociodemographic and clinical characteristics of participants

Sociodemographic characteristics of participants were assessed with a generic questionnaire for age, gender, employment status, and age at onset of symptoms. The number of CTG repeats was also reported for each participant. Overall progression of muscular impairment was measured using the DM1-specific Muscular Impairment Rating Scale (MIRS) with five stages based on manual muscle testing and the detection of myotonia [25]. Stage 1 indicates no muscular impairment while stage 5 indicates severe proximal weakness [25]. Information on phenotype was collected from the medical file. Patients are classified as late-onset phenotype if they met at least two of the following three criteria at the time of their diagnosis: (i) CTG <200; (ii) MIRS score of 1 (no muscular impairment) or 2 (minimal signs); (iii) age at onset of symptoms >40 years.

2.2.2. Strength

As they are both related to accomplishment of activities [17], grip and lateral pinch strength were measured. **Grip strength** was documented using the mean of three trials and following a standardized procedure with a Jamar dynamometer [26,27]. The Jamar dynamometer has very good to excellent intra-rater reliability in the DM1 population (intra-class