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Electromechanical delay components during skeletal muscle contraction and relaxation in patients with myotonic dystrophy type 1

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Abstract

The electromechanical delay during muscle contraction and relaxation can be partitioned into mainly electrochemical and mainly mechanical components by an EMG, mechanomyographic, and force combined approach. Component duration and measurement reliability were investigated during contraction and relaxation in a group of patients with myotonic dystrophy type 1 (DM1, n = 13) and in healthy controls (n = 13). EMG, mechanomyogram, and force were recorded in DM1 and in age- and body-matched controls from *tibialis anterior* (distal muscle) and *vastus lateralis* (proximal muscle) muscles during maximum voluntary and electrically-evoked isometric contractions. The electrochemical and mechanical components of the electromechanical delay during muscle contraction and relaxation were calculated off-line. Maximum strength was significantly lower in DM1 than in controls under both experimental conditions. All electrochemical and mechanical components were significantly longer in DM1 in both muscles. Measurement reliability was very high in both DM1 and controls. The high reliability of the measurements and the differences between DM1 patients and controls suggest that the EMG, mechanomyographic, and force combined approach could be utilized as a valid tool to assess the level of neuromuscular dysfunction in this pathology, and to follow the efficacy of pharmacological or non-pharmacological interventions.

Keywords: Electromyogram; Latency; Mechanomyogram; MMG; Muscle weakness; Myotonia

1. Introduction

Myotonic dystrophy type 1 (DM1, OMIM 160900) is the most frequent form of inherited muscular dystrophy in adulthood, with a prevalence of about 1:8000 [1]. The adult-onset form is the most prevalent, with common clinical exacerbation in the second or third decade of life. Clinical manifestations of adult-onset DM1 involve a broad spectrum of systemic complications, such as cardiac conduction abnormalities and cardiomyopathy, cataract, central nervous system dysfunction, gastrointestinal symptoms, and endocrine abnormalities [1–4]. The main features at the skeletal muscle level are muscle weakness and grip and percussion myotonia [1]. Distal muscles are generally more compromised than the proximal ones [1,5].

The mechanisms for muscle weakness, which involves difficulties to perform fine tasks with the hands, foot drop, and facial muscles ptosis, are not fully elucidated. Experimental evidence demonstrates that an alteration in the splicing of several proteins involved in Ca^{2+} homeostasis and in excitation–contraction coupling mechanisms may play a pivotal role [6–10]. Myotonia is characterized by a state of pathologically enhanced muscle excitability, in which involuntary trains of action potentials cause a delay in muscle relaxation after contraction [11]. This phenomenon has been associated with the alternative splicing of chloride channels at the muscle fibre level, which determines an alteration of membrane excitability [11]. Altogether, these skeletal muscle alterations in DM1 cause impairments in the cascade of the events involved in muscle contraction and relaxation.

Recently, a surface electromyographic (EMG), mechanomyographic (MMG) and force (F) combined approach has been proposed to get more insights on neuromuscular activation [12–16] and relaxation [15,17,18]. While surface EMG has been already widely used to monitor skeletal muscle

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electrical activity, MMG records and quantifies the low-frequency transverse oscillations propagating from the active muscle fibres to the skin surface during contraction [12,21], thus representing the mechanical counterpart of EMG. During muscle contraction, three main mechanisms contribute to MMG generation, as shown in Fig. 1: (i) the gross lateral movement of the contracting fibres at the beginning of contraction (MMG complex), generated by the shortening of contractile elements before the slack of the elastic-connective tissue has been fully taken up, and F has been transmitted to the tendon insertion point [15]; (ii) the subsequent vibrations at the resonance frequency of the muscle (MMG ripple), reflecting the dimensional changes of the active fibres propagating towards the muscle surface [19–22]; and (iii) the gross lateral movement of the muscle at the end of contraction (R-MMG complex), due to the maximum acceleration of muscle surface caused by cross-bridge detachment and series elastic component (SEC) detensioning [23,24].

During the on-phase of muscle contraction, the time lag between the onset of muscle electrical activation (EMG onset) and the beginning of F generation (F onset) has been traditionally defined as the electromechanical delay [25]. This time lag includes the electrochemical and mechanical events from motor unit action potential propagation at the sarcolemmal level to force transmission at the tendon insertion point. Similarly, a latency between the cessation of muscle electrical activation (end of EMG signal) and the beginning of F decay has been assessed during the relaxation phase [26], and defined as the relaxation electromechanical delay [27]. This latency spans from the cessation of sarcolemmal electrical activation to the cross-bridges and SEC return towards their pre-contraction status.

When also MMG is recorded, the three signals allow the partitioning of the total electromechanical delay ($Delay_{TOT}$) into (i) a mainly electrochemical component, which includes the events from the propagation of the motor unit action potential at the sarcolemmal level to myosin head rotation and pressure wave transmission to the skin surface [28,29], and (ii) a mainly mechanical component, which reasonably provides a potential index of the time required for taking up the muscle–tendon unit slack, before F transmission becomes efficient at the tendon insertion point [12–14,16]. When the muscle is electrically activated, the simultaneous recording also of the stimulation current (Stim) offers an additional $Delay_{TOT}$ component between Stim and EMG onset, related to the pre-synaptic and synaptic events [16].

At the end of a voluntary contraction, the total electromechanical delay during relaxation ($R\text{-}Delay_{TOT}$) can be partitioned with the addition of MMG in one mainly electrochemical and three consecutive mainly mechanical components. The first component includes the events from the cessation of the electrical activation of the sarcolemma and the beginning of Ca^{2+} reuptake in the sarcoplasmic reticulum to the transition of cross-bridges from force-generating to non-force-generating status, together with the pressure wave transmission to the skin surface. The second component comprises the beginning of the rapid change in sarcomere length and the increase in the detachment rate of cross-bridges. The third component incorporates the main phase of cross-bridge

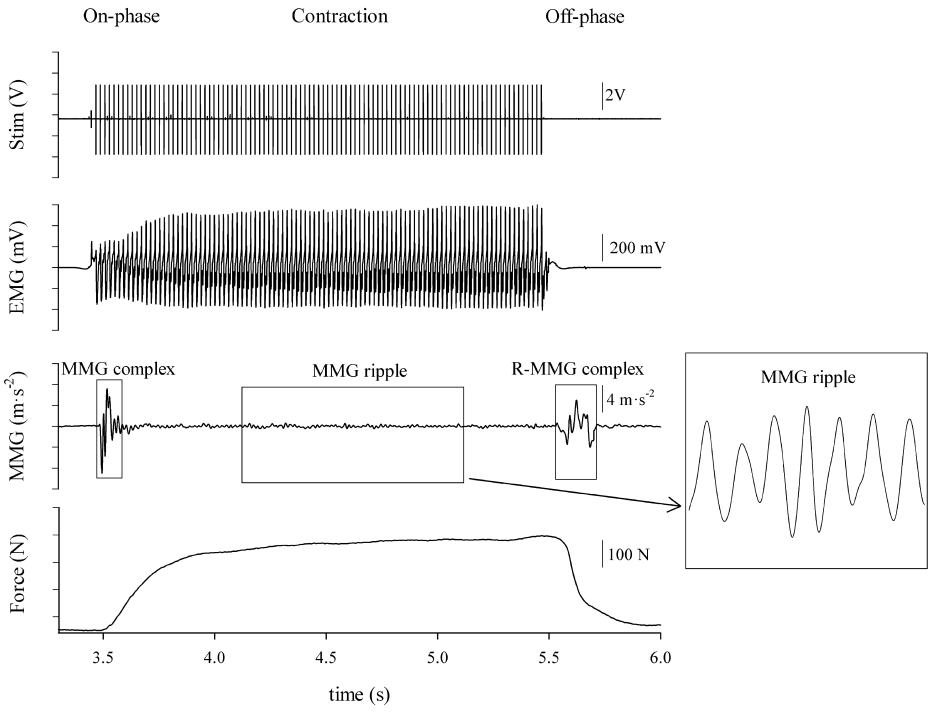

Fig. 1. Stim, EMG, MMG and F signals in a representative participant. Stimulation current (Stim), electromyographic (EMG), mechanomyographic (MMG), and force (F) signals during muscle contraction.