



Effect of exercise training on neuromuscular function of elbow flexors and knee extensors of type 2 diabetic patients



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ABSTRACT

Purpose: The effects of exercise training on neuromuscular function of arm and leg muscles in type 2 diabetic patients (T2D) was investigated. **Methods:** Eight T2D sedentary male patients (61.0 ± 2.3 years) and eight sedentary healthy age matched control subjects (H, 63.9 ± 3.8 years) underwent a 16-week supervised combined endurance and resistance exercise program. Before and after training, maximal isometric (MVIC), isokinetic (15, 30, 60, 120, 180, 240° s⁻¹) torque and muscle endurance of the elbow flexors (EF) and knee extensors (KE) were assessed. Simultaneously, surface electromyographic signals from biceps brachii (BB) and vastus lateralis (VL) muscles were recorded and muscle fiber conduction velocity (MFCV) estimated. **Results:** Following training, maximal torque of the KE increased during MVIC and isokinetic contractions at 15 and 30° s⁻¹ in the T2D ($+19.1 \pm 2.7\%$ on average; $p < 0.05$) but not in the H group ($+7 \pm 0.9\%$; $p > 0.05$). MFCV recorded from the VL during MVIC and during isokinetic contractions at 15 and 30° s⁻¹ increased ($+11.2 \pm 1.6\%$ on average; $p < 0.01$), but in the diabetic group only. Muscular endurance was lower in T2D (20.1 ± 0.7 s) compared to H (26.9 ± 1.3 s), with an associated increase in the MFCV slope after training in the KE muscles only. **Conclusion:** The effect of a combined exercise training on muscle torque appears to be angular velocity-specific in diabetic individuals, with a more pronounced effect on KE muscles and at slow contraction velocities, along with an associated increase in the MFCV. MFCV appears to be a more sensitive marker than torque in detecting the early signs of neuromuscular function reconditioning.

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1. Introduction

Deleterious changes in muscle contractile properties (Oberbach et al., 2006) as well as degeneration of the motor nerves (Ijzerman et al., 2011) in type 2 diabetes increase the risk of physical disability (Andersen, 2012; Drouin et al., 2009), with a reduction in muscle strength, power and muscle mass being well documented in this patient population (Leenders et al., 2013; Park et al., 2006, 2009; Shah et al., 2011; Volpato et al., 2012). Recent findings suggest that these muscular deficiencies are greater in the lower than in the upper limbs. Further, the extent of diabetes-related muscle weakness is seen to be dependent on both the muscle contraction type and velocity with the greater deficits seen at the higher contraction velocities (Sacchetti et al., 2013). This trend is similar to what is observed for the decay of muscle function that occurs with

aging (Bazzucchi et al., 2004). The combination of diabetes and aging may accelerate the strength decline especially in the lower limbs and compromise the quality of life of these individuals. Indeed, older men with type 2 diabetes have been found to have a two- to threefold increased risk of developing physical disability, in which the decline in the functional capacity of the neuromuscular system is a contributor (Park et al., 2006).

The benefits of exercise training for counteracting the detrimental effect of diabetes on both glyco-metabolic control and neuromuscular function have been well reported. Resistance training in particular has been seen to improve both muscle strength and mass as well as insulin sensitivity (Brooks et al., 2007; Cauza et al., 2005; Dunstan et al., 2002; Holten et al., 2004; LeBrasseur et al., 2011; Mann et al., 2014). For these reasons, it may be desirable that type 2 diabetes patients would begin an appropriate exercise training program as soon as possible after diagnosis to prevent, or at least limit, the decline in neuromuscular function. More information, however, is needed on the effects of

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exercise training on the torque–angular velocity relationship, which reflects the fundamental mechanisms of force generation during different contractile tasks (Larsson et al., 1979). Similarly, muscle endurance, another important determinant of performance during functional task/activities of daily living, has been poorly explored in relation with diabetes, with the few investigations performed leading to conflicting results (Almeida et al., 2008; Andersen et al., 2005; Andersen, 1998; Fritschi and Quinn, 2010). The use of surface electromyography (EMG), a non-invasive measure of myoelectric activity, allows a greater understanding of the activation patterns of the muscle of interest. In particular, the propagation velocity of the action potential along the muscle fiber (muscle fiber conduction velocity, MFCV) is one of the physiological characteristics correlated to the derangement of neuromuscular function since it is directly related to sarcolemmal excitability/function (Merletti et al., 2003) with Sacchetti et al. (2013) reporting a decrease in the MFCV of the vastus lateralis muscle in diabetic patients during isometric contractions in comparison to healthy matched individuals.

The present study, thus, has been designed to understand to what extent qualities such as muscle strength and endurance are compromised in diabetic patients in the early phases of the disease, and whether an active lifestyle, combined with a limited number of training sessions (i.e. sustainable by all patients), is effective in preserving their neuromuscular function. Specifically, in this study a particular emphasis was paid to the characterization of the torque–velocity relationship, muscle fatigability and the myoelectric activity of diabetic individuals both pre and post training when compared to their age matched healthy counterpart.

2. Methods

2.1. Subjects

Eight type 2 diabetic patients (T2D) and eight healthy control subjects (H) gave their informed consent to participate in the study, which was approved by the local ethics committee. All diabetic patients were treated with diet and oral hypoglycemic agents (metformin) but not insulin or other drugs, were free from clinical signs of diabetic peripheral neuropathy and had relatively short history of the diseases (mean diabetes duration of 5.2 ± 1.3 years). They were accepted for the study only if they had total HbA_{1c} levels <9% on therapy. Subjects' main characteristics are shown in Table 1. None of the subjects was involved in a regular exercise program for at least 6 months before entering the study. All the

age-matched healthy subjects had normal glucose tolerance (assessed by a 75-g oral glucose tolerance test), and none was taking any medication.

2.2. Exercise training program

All subjects underwent a 16-week exercise training program, designed following the ACSMs guidelines for exercise participation in individuals with type 2 diabetes (ACSM, 2010). Exercise was performed 3 times weekly under the direct supervision of a sport scientist. Each session started with a warm-up consisting in 10-min low intensity endurance exercises on a cycle ergometer or a treadmill and 3 sets of 15 abdominal crunches separated by 2-min rest. The core of the training session incorporated aerobic training followed by the resistance training. Subjects rested for 4 min between the two modalities of training. At the end of the training, subjects performed also 10 min of cool down with stretching exercises. The aerobic training was performed on a treadmill or a bicycle ergometer. In order to equally distribute sessions between treadmill and bicycle ergometer, all subjects carried out 2 sessions on treadmill and 1 on bicycle ergometer in week 1 and *vice versa* 2 sessions on bicycle ergometer and 1 on treadmill in week 2. This alternation was repeated for the subsequent weeks. Participants progressed from 20 min per session at 40–60% of the heart rate reserve (HRR; weeks 1–8) to 40 min per session at 60–80% of the HRR (weeks 9–16). Heart rate monitors (Polar, Finland) were used to adjust the workload in order to achieve the target heart rate. For the resistance training, 1 repetition maximum (1-RM) was assessed twice on 5 different weight machines (leg press, leg extension, bench press, cable curl, cable pull down). The training loads were calculated with respect to the highest 1-RM value obtained at baseline and at week 9. Resistance training consisted of 3 sets of 10 repetitions at a load progressing from 60% to 80% of 1RM.

2.3. Overview of the experimental protocol

Each subject visited the laboratory on three occasions. In the first visit, subjects were familiarized with the experimental procedures. Participants then returned to the laboratory on two additional days, the first before the training period (PRE) and the second 5 days after the 16 weeks of training program (POST). The same experimental protocol was followed both PRE and POST. The elbow flexion (EF) and knee extension (KE) torques of the dominant limb were measured with a dynamometer (Kin-Com, Chattanooga, USA). Participants were seated comfortably on the dynamometer and stabilized by chest, waist and thigh straps. The elbow angle was fixed at 90° (180°, full extension) with the upper arm parallel to the trunk and the forearm in a neutral position (halfway between pronation and supination). The wrist was secured in a padded cuff attached to the load cell. The rotational center of the lever arm was aligned to the distal lateral epicondyle of the humerus. The knee joint was set at a 90° angle (180°, full extension) as well as the hip joint. The lower leg was attached to the lever arm of the dynamometer with the ankle secured in a resistance pad. The center of rotation of the lever arm was aligned to the lateral femoral epicondyle of the knee.

The surface electromyographic signals (EMG) were recorded with a linear array of four electrodes (silver bars 5 mm long, 1 mm thick, 10 mm apart; OTBioelettronica, Turin, Italy) from the biceps brachii (BB) and from the vastus lateralis (VL) muscles. These two muscles were considered as representative of upper and lower limbs muscle respectively as previously reported (Bazzucchi et al., 2004; Harwood et al., 2008; Theou et al., 2013). After gentle skin abrasion and cleaning with ethyl alcohol, electrodes were attached on the skin over the BB along the line

Table 1

Anthropometric and metabolic variables of diabetic and control subjects before (PRE) and after (POST) the 16-week training program. Values are reported as mean \pm SD *different from POST $p < 0.05$.

| | Diabetic subjects | | Control subjects | |
|----------------------------|-------------------|-------------------|------------------|------------------|
| | PRE | POST | PRE | POST |
| Age (years) | 61.0 \pm 2.3 | | 63.9 \pm 3.8 | |
| BMI (kg m ⁻²) | 36.0 \pm 2.9 | 29.8 \pm 3.7* | 27.4 \pm 2.6 | 26.3 \pm 3.1 |
| BB Skinfold thickness (mm) | 9.2 \pm 2.7 | 8.6 \pm 3.4 | 8.2 \pm 4.1 | 7.8 \pm 3.2 |
| VL Skinfold thickness (mm) | 28.6 \pm 10.5 | 26.5 \pm 9.8 | 25.7 \pm 9.3 | 25.1 \pm 8.7 |
| HbA1C (%) | 6.9 \pm 0.6 | 6.3 \pm 0.7 | 5.7 \pm 0.1 | 5.6 \pm 0.2 |
| Total cholesterol (mg dl) | 194.0 \pm 19.3 | 178.4 \pm 18.0* | 189.6 \pm 21.7 | 181.1 \pm 11.0 |
| HDL (mg dl) | 44.8 \pm 7.5 | 49.2 \pm 11.2 | 49.2 \pm 6.6 | 52.8 \pm 6.9 |
| LDL (mg dl) | 180.0 \pm 23.9 | 139.0 \pm 22.8* | 163.0 \pm 21.6 | 149.2 \pm 15.2 |
| Triglycerides (mg dl) | 153.8 \pm 29.0 | 118.6 \pm 32.9* | 113.0 \pm 10.1 | 104.3 \pm 11.0 |

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