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Whole-body vibration alters blood flow velocity and neuromuscular activity in Friedreich's ataxia

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Summary

The purpose of this study was to investigate the effects of whole-body vibration (WBV) on blood flow velocity and muscular activity after different vibration protocols in Friedreich's ataxia (FA) patients. After two familiarization sessions ten patients received six 3 min WBV treatments depending on a combination of frequency (10, 20 or 30 Hz) and protocol (constant or fragmented). Femoral artery blood flow velocity, vastus lateralis (VL) and vastus medialis (VM) electromyography (EMG), and rate of perceived exertion were registered. Peak blood velocity was increased with respect to basal values after 1, 2 and 3 min of WBV (14·8%, 18·8% and 19·7%, respectively, $P < 0·001$). Likewise, mean blood velocity was increased with respect to basal values after 1, 2 and 3 min of WBV (17·3%, 19·4% and 16·6%, respectively, $P < 0·001$). EMG amplitude of VL and VM was increased (39% and 23%, respectively, $P < 0·05$) and EMG frequencies decreased during the application of WBV. The results of this study suggest that higher frequencies (30 Hz) produce a greater increase in blood flow velocity and rate of perceived exertion. WBV is an effective method to increase blood flow and to activate muscle mass in patients with Friedreich's ataxia, and could therefore be considered to be incorporated in rehabilitation programs of this collective.

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Key words

Doppler ultrasound; electromyography; oscillating platform; rate of perceived exertion; rehabilitation; vibration frequency

Introduction

Friedreich's ataxia (FA) is the most common form of hereditary ataxia (Schols *et al.*, 1997). FA is a neurodegenerative disease due to a pathological expansion of a GAA triplet repeat in the first intron of the FXN gene encoding for the mitochondrial protein frataxin (Marmolino & Acquaviva, 2009). According to Delatycki *et al.* (2000) impairments in the neuromuscular system are essential clinical features of FA. The principal nervous system change includes the loss of cells in the dorsal root ganglia followed by degeneration in the posterior columns and spinocerebellar tracts. FA is characterized by ataxia, dysarthria, sensory loss, diabetes and cardiomyopathy (Lynch *et al.*, 2002b). Gait ataxia is usually the first sign to appear (Lynch *et al.*, 2002a), due to a lack of coordination and tremors developed in all extremities, with a progressive and symmetrical loss of strength (force-generating capacity) (Beauchamp *et al.*, 1995). The upper-extremity and trunk musculature is relatively spared until late in the disease process. As Beauchamp *et al.* (1995) stated in FA patients, the overall strength of the upper extremities was typically 80% of that of healthy subjects, and lower-limb strength averaged 70% of that of healthy subjects at the time when patients began to use a wheelchair for mobility (at a mean age of 18·2 years) (Beauchamp *et al.*, 1995). Maintenance of muscular function is critical for sustaining normal daily activity and functional independence (Reid *et al.*, 2008).

The application of whole-body vibration (WBV) with platforms has been shown to improve muscular activation (Hazell *et al.*, 2007), strength (Marin & Rhea, 2010b) and power (Marin & Rhea, 2010a), as well as peripheral circulation (Kerschan-Schindl *et al.*, 2001; Lohman *et al.*, 2007; Hazell *et al.*, 2008; Maloney-Hinds *et al.*, 2008; Lythgo *et al.*, 2009). However, the effects of WBV on the neuromuscular and circulatory systems are strongly dependent on the type of platform, protocols and vibration parameters (i.e. frequency) (Maloney-Hinds *et al.*, 2008; Marin & Rhea, 2010a; b). Thus, greater vibration frequencies induce a higher muscle activity than lower frequencies (Hazell *et al.*, 2007). Moreover, the most common protocol used to apply WBV consists of short bouts (30–90 s) with ∼60 s rest between sets. The effects induced by the application of longer bouts (3 min) on peripheral circulation has been poorly investigated.

The previously mentioned benefits of WBV have been observed in healthy subjects; however, it has been reported that vibratory stimulation can be safely and easily employed in

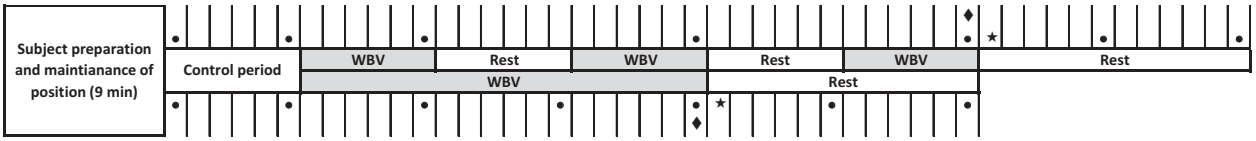

Figure 1 Sketch of the experimental phase in 10 s intervals showing the fragmented (top) and constant (bottom) protocols. Electromyography (diamonds), rate of perceived exertion (stars) and blood parameters (circles) were registered.

subjects with movement disorders as Parkinsonian patients (De Nunzio *et al.*, 2008). Then, it could be hypothesized that WBV would result in greater blood flow velocity and muscle activation in FA patients. Both aspects would be interesting for the maintenance of muscular function in this population; however, no study has focused on the application of WBV in FA patients. Thus, the purpose of this study was to investigate the effects of WBV on blood flow velocity and muscular activity after different vibration protocols in FA patients.

Methods

Subjects

Ten patients (seven male and three female) volunteered to participate in the study (age 38·1 ± 10·5 years; height 1·69 ± 0·09 m; mass 63·6 ± 12·9 kg). All the patients had FA, which was diagnosed to them 23·8 ± 11·6 years before the experimental phase, at the age of 14·3 ± 6·4 years. Five of the subjects were able to walk, although nine of them normally used wheelchair to move. Prior to data collection, subjects were informed of the requirements associated with participation and provided written informed consent. Moreover, subjects did not allow their sleeping, eating and drinking habits to change throughout study participation. The research project was conducted according to the Declaration of Helsinki and it was approved by the University Review Board for research involving human subjects.

Experimental design

Each subject was assessed in eight different sessions. In the first two sessions subjects were familiarized with the testing protocols as well as with vibration stimulus. Both sessions were carried out within the same week separated with at least 48 h. The other six sessions were carried out on Monday, Wednesday and Friday during the following 2 weeks. In each session a random WBV protocol was applied. The six WBV protocols arise from the combination of the dependent variables *frequency* (10, 20 or 30 Hz) and *protocol* (constant or fragmented). Three consecutive minutes of WBV were applied during the constant protocol while three cycles of 1 min of WBV and 1 min of resting period were applied during the fragmented protocol (Fig. 1). Dependent variables were blood parameters, muscle activity and rate of perceived exertion (RPE).

Treatment protocol

Once a subject came to the laboratory he/she was laid down and fixed to a tilt table with straps (Fig. 2). In the distal part of the tilt table, just beneath the feet, a vibration platform was placed (Galileo Home; Galileo®, Novotec, Germany). Knee angle was of 60° flexion (considering 0° the full knee extension). Subsequently, the tilt table was placed at 45° and the subject was kept in that position for a period of 10 min before the application of WBV. In that position the subject was prepared to register electromyographic (EMG) activity and ultrasound variables. The frequency of vibration was set at 10, 20 or 30 Hz. The amplitude of the vibration was set by the position of the feet on the WBV plate at 5 mm (peak to peak). Feet were placed parallel to each other 38 cm apart (measured from the midlines of the feet). The patients were exposed to the vibration each day for a total of 3 min continuous (constant) or fragmented (three bouts 60 s exposures, separated by 60 s rests).

Ultrasound measurements

Blood parameters were registered through an ultrasound system (MyLab 25; Esaote, Genoa, Italy) using a pulsed color Doppler with a linear array transducer (LA 523, 7·5–12 MHz; length, 50 mm; Esaote, Genoa, Italy). The measures were performed on the right common femoral artery about 2 cm above the bifurcation into the superficial and deep femoral arteries. The transducer was positioned parallel to the vessel with an

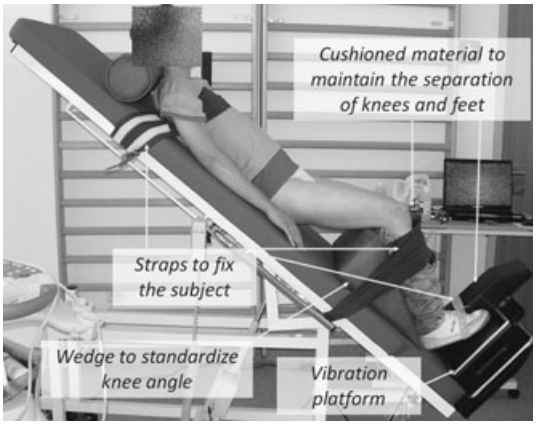

Figure 2 Placement of the subject on the tilt table during the application of the whole-body vibration.

insonation angle of 60°. At the beginning and at the end of the control period (Fig. 1) blood parameters were registered to analyse their reliability and to establish baseline values. Subsequently, blood parameters were analysed every 10 s during the application of each protocol. These measures were taken until 2 min after the end of the vibration stimulus. Due to the high number of recordings, only the following moments were used for the statistical analysis: baseline 1 and baseline 2 (to assess reliability and use the average of both as baseline), the end of minutes 1, 2 and 3 of WBV, and the end of minutes 1 and 2 of recovery after the last minute of WBV. Each image recorded by the ultrasound system corresponded to a period of 4 s. In that period there were between 3 and 5 beats, and the mean of these beats was analysed to obtain: mean, peak and minimum blood velocities (MBV, PBV and MiBV, respectively), and heart rate. During the recording of these variables the same investigator was holding the probe and used the screen of the ultrasound system as feedback to maintain the measure point in the middle of the vessel. Another investigator operated the ultrasound system to record the previously mentioned images. These roles were carried out by the same investigators throughout the experimental phase.

Surface electromyographic activity

Muscle activity of the vastus medialis (VM) and vastus lateralis (VL) was measured using EMG. One set (two measuring electrodes and a differential electrode) of surface electrodes (Ag/AgCl, Skintact, Austria) was placed longitudinally to the direction of the muscle fibres and approximately halfway from the motor point area to the distal part of the muscle. An inter-electrode distance of 2 cm was maintained. The reference electrode was placed in a neutral area away from the measuring electrodes. Before electrode placement, the area was cleaned with isopropyl alcohol, shaved and abraded to reduce skin impedance until it was lower than 5 kΩ (De Luca, 1997). The location of the electrodes on the skin was marked with permanent ink to ensure the same placement throughout the different sessions.

Myoelectric raw signals were detected with double differential technique. The surface electrodes were connected to a 14-bit AD converter (ME6000 Biomonitor, Mega Electronics, Kuopio, Finland) by pre-amplified cables (Mega Electronics, Kuopio, Finland). The total common mode rejection (CMRR) was of 110 dB, and data was low pass filtered (8–500 Hz) and sampled at 2000 Hz before being stored in a memory card (compact flash memory, 256 MB). On the basis of the frequency analysis, a band width of ±0·8 Hz around each harmonic was excluded from the root-mean-square calculation (Abercromby *et al.*, 2007; Mischi & Cardinale, 2009). EMG data analysis was performed across the use of specific software (MegaWin V 2·21; Mega Electronics, Kuopio, Finland). The last ten seconds corresponding to each rest minute and corresponding to each WBV application were chosen for data analysis across the use of the 'Marker Test' provided by the aforementioned software. EMG raw data was averaged by root mean square (EMG_{RMS}) to obtain the average amplitude of the EMG signal. The fast Fourier transform was used to obtain the frequency spectrum for each 1 s time interval, from which it was found the mean frequency (MF) and mean peak frequency (MPF). The EMG values during WBV were then normalized to a value corresponding to the previous rest minute (Fig. 1).

Rating of perceived exertion

Each subject was given a set of scale-specific instructions for the use of the RPE scale. RPE was assessed at 0:10 of each stage, with the scale in sight (Suminski *et al.*, 2008; Gearhart *et al.*, 2009). Immediately after the WBV exposure the perceived exertion was verbally anchored (Fig. 1).

Statistical analysis

The normality of the dependent variables was checked and subsequently confirmed using the Kolmogorov–Smirnov test. A two-way ANOVA in frequency (10, 20 and 30 Hz) and protocol (constant and fragmented) was applied to analyse RPE after each treatment (minute 3). A three-way ANOVA in frequency, protocol, and time (baseline and minute 3) with repeated measures on time was applied to analyse EMG variables. Another three-way ANOVA in frequency, protocol and time (baseline, minutes 1, 2, 3 of WBV and minutes 1 and 2 of rest) with repeated measures on time was applied to analyse blood parameters. When a significant F-value was achieved in any ANOVA, pairwise comparisons were performed using the Bonferroni *post hoc* procedure. The reliability and variability of blood parameters were assessed with intraclass correlation coefficient (ICC) and coefficients of variation (i.e., CV = SD × 100/mean). Statistical significance was set at $P \leq 0{\cdot}05$. Effect size statistic, η^2, was analysed to determine the magnitude of the effect independent of sample size. Values are expressed as mean ± SD.

Results

Blood parameters

Table 1 shows the intra-session reliability and variability of the blood parameters. ICC and CV ranged from 0·730 to 0·928 and from 4·0% to 12·2%, respectively. No significant differences

Table 1 Intraclass correlation coefficient (ICC) and coefficient of variation (CV) to analyse the reliability and variability between the two baseline measures for blood parameters.

	ICC	CV (%)
Mean velocity	0·730	9·1
Peak velocity	0·914	5·3
Minimum velocity	0·928	12·2
Heart rate	0·901	4·0

were observed between both basal measures. Coefficients of correlation between MBV and PBV ranged from 0·001 to 0·289 ($P > 0·05$). No significant variation was observed throughout any protocol for MiBV or heart rate.

A time effect for PBV was observed ($P < 0·001$; $\eta^2 = 0·246$). PBV was increased with respect to basal values after 1, 2 and 3 min of WBV (14·8%, 18·8% and 19·7%, respectively, $P < 0·001$). Likewise, PBV remained increased with respect to basal values after the end of the WBV stimulus during 1 (12·8%, $P < 0·001$) and 2 min (11·6%, $P < 0·01$). There were no significant differences between PBV during minutes 1, 2 and 3 of WBV application. PBV during the rest period decreased with respect to minute 3 of the vibration stimulus ($P < 0·05$ in both measures).

A time effect for MBV was observed ($P < 0·001$; $\eta^2 = 0·211$). MBV was increased with respect to basal values after 1, 2 and 3 min of WBV (17·3%, 19·4% and 16·6%, respectively, $P < 0·001$). Likewise, MBV remained increased with respect to basal values after the end of the WBV stimulus during 1 (12·5%, $P < 0·01$) and 2 min (10·3%, $P < 0·05$). Accordingly, MBV remained increased with respect to minute 3 of vibration stimulus during in the first and second minutes of the resting period (12·5% and 10·3%, respectively, $P < 0·01$ and $P < 0·05$, respectively). There were no significant differences between MBV during minutes 1, 2 and 3 of WBV application.

A time*frequency effect was also observed for MBV ($P < 0·05$; $\eta^2 = 0·067$). *Post hoc* analyses revealed that at minutes 2 and 3 during the application of the vibration stimulus MBV was higher for 30 Hz with respect to 10 Hz (18·6% and 24·7%, respectively, $P < 0·05$). Furthermore, the 10 Hz frequency did not modify MBV with respect to basal values in any of the measures. The 20 Hz frequency increased MBV with respect to basal values only during minutes 1, 2 and 3 of treatment (20·2%, 18·4% and 17·8%, respectively, $P < 0·001$, $P < 0·01$ and $P < 0·05$, respectively). Finally, the 30 Hz frequency maintained the MBV increased during minutes 1, 2 and 3 of treatment (20·1%, 29·1% and 28·4%, respectively, $P < 0·001$), as well as during the first minute after the stop of the stimulus (17·5%, $P < 0·05$).

A time*protocol effect was also detected for MBV ($P < 0·05$, $\eta^2 = 0·045$). During minutes 1, 2 and 3 of the vibration stimulus, MBV was increased during the application of the constant protocol (11·5%, 15·7% and 17·2%, respectively, $P < 0·01$), as well as during the application of the fragmented protocol (23·0%, 23·7% and 16·0%, respectively, $P < 0·001$). However, only after the application of the constant protocol the MBV remained increased with respect to basal values in the first minute after the stop of the stimulus (14·0%, $P < 0·05$).

Surface electromyographic activity

The three-way ANOVA (time*frequency*protocol) applied to EMG amplitude showed a time effect for VM ($P < 0·05$; $\eta^2 = 0·094$), thus values at minute 3 were higher with respect to baseline (23·0%, $P < 0·05$). Likewise, a time effect for the EMG amplitude of VL ($P < 0·01$; $\eta^2 = 0·187$) was observed, thus values at minute 3 were higher with respect to baseline (39·4%, $P < 0·05$). No other significant effect or interaction was found for EMG amplitude.

Regarding MF values for the VM, the three-way ANOVA showed a time effect ($P < 0·01$; $\eta^2 = 0·127$) and a time*frequency effect ($P < 0·05$; $\eta^2 = 0·138$). *Post hoc* analysis on time effect showed a decrease in the MF at minute 3 with respect to baseline values (from 67·4 ± 3·2 Hz to 58·4 ± 3·1 Hz, $P < 0·01$). *Post hoc* analysis on time*frequency effect showed a decrease in MF for the 10 Hz stimulus (from 74·7 ± 5·8 Hz to 58·2 ± 5·6 Hz, $P < 0·01$) and for the 20 Hz stimulus (from 71·5 ± 5·5 Hz to 56·5 ± 5·3 Hz, $P < 0·05$). Concerning MF values for VL, a time effect was observed ($P < 0·01$; $\eta^2 = 0·132$). As with VM, *post hoc* analysis showed a decrease in the MF at minute 3 with respect to baseline values (from 69·7 ± 3·6 Hz to 58·6 ± 2·8 Hz, $P < 0·01$). Regarding MPF, there was a time effect for the VL ($P < 0·05$; $\eta^2 = 0·120$) but not for the VM ($P = 0·089$; $\eta^2 = 0·059$). MPF for the VL decreased from 94·6 ± 4·1 Hz to 83·7 ± 3·5 Hz ($P < 0·05$).

Rating of perceived exertion

The two-way ANOVA showed a frequency effect ($P < 0·01$; $\eta^2 = 0·207$) while no protocol or protocol*frequency effects were observed. *Post hoc* test on frequency showed that RPE with 30 Hz was higher with respect to 10 Hz (4·9 ± 1·9 vs. 2·5 ± 1·6, respectively, $P < 0·001$). On the contrary, RPE with 20 Hz (3·9 ± 2·4) was similar with respect to 30 and 10 Hz.

In the fragmented protocol a repeated measures ANOVA showed a time effect ($P < 0·01$; $\eta^2 = 0·170$). *Post hoc* test showed that RPE after minutes 2 and 3 were higher compared to minute 1 (3·9 ± 2·0 and 3·4 ± 2·0, respectively, $P < 0·05$).

Discussion

To the best of our knowledge, this is the first study to apply WBV on a tilt-table on ataxia patients. The primary finding of this study was that WBV alone can significantly increase leg blood flow velocity and EMG activity in ataxia patients. Moreover, this study provides evidence that a high frequency of vibration (30 Hz) generated more neuromuscular activation than a low frequency (10 Hz). Increasing frequency produced systematic increases in leg blood flow velocity, EMG and RPE. These findings suggest that greater frequencies may be used during WBV treatment to elicit a greater neuromuscular stimulus. Furthermore, after the application of the constant protocol (3 min continuous) the MBV remained increased with respect to basal values, suggesting that this protocol could provide more interesting effects in a long-term application.

Leg blood flow velocity was increased during the application of WBV in FA patients. Blood flow is known to be increased within the initial 1–5 s, at the onset of dynamic exercise, reaching a steady state after 30–90 s of low to moderate exercise intensities in healthy individuals (Saltin *et al.*, 1998). Increases in

metabolic demand and muscle pumping effect may play an important role in this fact (Saltin *et al.*, 1998; Clifford & Tschakovsky, 2008). In this sense, there is evidence supporting that WBV leads to an increased metabolic demand measured by oxygen uptake in a linear relationship with vibration frequency (Rittweger *et al.*, 2002), which is in agreement with our results. However, the magnitude of blood flow response observed in our study is lower than in others carried out with healthy subjects (Kerschan-Schindl *et al.*, 2001; Lythgo *et al.*, 2009). Using an oscillating platform, Kerschan-Schindl (2001) found a two-fold increase in mean blood flow in the popliteal artery (9 min, 26 Hz, 3 mm), and Lythgo *et al.* (2009) found a fourfold increase in mean blood velocity in the femoral artery (1 min, 30 Hz, 4·5 mm). These greater responses in comparison to our results could be due to the fact that: (1) the tilt table provides weight unloading, and since blood flow highly correlates with work output (Saltin *et al.*, 1998), a reduction in work output due to unloaded weight may result in a smaller increase in blood flow (Hazell *et al.*, 2008); (2) as greater the active tissue, higher the metabolic demand; since muscle weakness is a feature of FA (Pandolfo, 2009), the O_2 demand should be reduced and subsequently would elicit a reduced response; (3) the degenerative process due to FA could induce a vascular disease that would limit the hemodynamic response to exercise.

EMG amplitude of VL and VM was increased and EMG frequencies decreased during the application of WBV in FA patients. These changes have been reported for WBV application in healthy subjects using frequencies between 15 and 30 Hz (Torvinen *et al.*, 2002). However, no significant difference was noted depending on the frequency. It could be expected that 30 Hz would increase EMG amplitude more than 10 Hz, since the acceleration of the platform is higher as frequency increases. Furthermore, greater EMG amplitudes with high frequency WBV training (40 and 45 Hz) have been reported when compared to lower frequencies (25 and 30 Hz) (Hazell *et al.*, 2007). In this study, the individual EMG response was variable and the sample size was small, therefore the lack of statistical significance could be due to a type II error.

Mechanical vibration of the muscle induces an involuntary contraction reflex named 'tonic vibration reflex' (Gillies *et al.*, 1971). The deformation of the soft tissues caused by vibration is capable of activating muscle spindles and leading to an enhancement of the stretch–reflex loop (Cardinale & Bosco, 2003). Thus, the excitatory inflow during vibration stimulation is mainly related to the reflex activation of the α-motor neuron (Cardinale & Bosco, 2003). This neurological activation could be of interest in the rehabilitation of FA patients, since the neuropathology of these patients induces a degeneration of posterior columns in the spinal cord and of the pyramidal tracts (Pandolfo, 2009). Since no proven treatment can stop the progression of FA (Pandolfo, 2009), rehabilitation should be focused on physical exercise programmes that contribute to the delay of neurological function loss (Pérez-Ávila *et al.*, 2004). On the other hand, vibration treatment has been successfully employed in patients with Parkinson (De Nunzio *et al.*, 2008) or spinal cord injury (Ness & Field-Fote, 2009) to improve walking function. In this sense, the convenience of including WBV in the rehabilitation routines of other physical disabilities should be studied. In conclusion, WBV is an effective method to increase leg blood flow and to activate muscle mass in patients with Friedreich's ataxia, and could therefore be considered to be incorporated in rehabilitation programmes of this collective.

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