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Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

Effects of high-intensity training on muscle fibre characteristics of the multifidus muscle in persons with non-specific chronic low back pain

Ron Van Reet
Steffen Vangansewinkel

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie, afstudeerrichting revalidatiewetenschappen en kinesitherapie bij musculoskeletale aandoeningen

PROMOTOR :
dr. Anouk AGTEN

COPROMOTOR :
Prof. dr. Frank VANDENABEELE

BEGELEIDER :
De heer Sjoerd STEVENS

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www.uhasselt.be
Universiteit Hasselt
Campus Hasselt:
Martelarenlaan 42 | 3500 Hasselt
Campus Diepenbeek:
Agoralaan Gebouw D | 3590 Diepenbeek

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Lorzestraat 40/002, 2480, Dessel, Belgium, 02/06/2019 V.R.R.

Kaulillerweg 30, 3910, Pelt, Belgium, 02/06/2019 V.S.

Content

Research context

In the daily practice, non-specific chronic low back pain (NSCLBP) is a common pathology. Because of the high incidence of NSCLBP, it is clinically and socially relevant to offer an effective and efficient treatment. To this day, no perfect treatment protocol exists. Most of these protocols use low to moderate intensity exercises. At this moment, the way of thinking about the treatment of low back pain seems to be changing. Is the 'careful' approach the best approach? Or is there no need to be that careful? So the aim of this study was to determine the effects of a more aggressive training protocol, i. e. high-intensity training (HIT), on muscle fibre structure and other health related outcome measures. To this day, the amount of studies regarding the effects of HIT on patients with NSCLBP is scarce.

The present study is part of a master thesis and an ongoing randomized controlled trail (RCT). The intervention of the RCT took place at the REVAL building at the University of Hasselt between October 2016 and December 2018. People with NSCLBP were recruited and randomly divided into one of five groups, four intervention groups and one control group. All intervention groups performed a HIT protocol and the control group performed a moderate intensity training (MIT) protocol.

The two students, who performed this master thesis, weren't involved in the development of the research protocol, the recruitment of participants, and the development of the training program. But the HIT programs were provided with help of the students. So occasionally the students were able to observe and guide the participants through the exercise program.

As mentioned before, five exercise programs were provided. Because of lack in time and other influencing factors, it wasn't possible to include all participants and all five exercise programs in this master thesis. The students were able to choose one intervention group to include in the master thesis. Eventually, the high-intensity core strengthening program was chosen.

Muscle biopsies of the multifidus muscle were taken by the researchers of the ongoing RCT. Post measurements and analysis of the samples of the core strengthening group were performed by the master thesis students by using the AxioVision program. Interpretation of the data and complete writing of this master thesis study was also performed by the students.

Effects of high-intensity training on muscle fibre characteristics of the multifidus muscle in persons with non-specific chronic low back pain

Effects of high intensity training in persons with non-specific chronic low back pain

Abstract

Background: Non-specific chronic low back pain (NSCLBP) is one of the most common pathologies worldwide. In this condition, no specific cause of the pain is known, which makes it difficult to treat and prevent. In healthy people, high-intensity training (HIT) has shown to improve several health related and physiological parameters. But less is known about the effects in patients with NSCLBP.

Objectives: The aim of this study was to determine if HIT is able to change muscle fibre type characteristics in patients with NSCLBP and if this is accompanied by changes in pain, disability, physical activity, force or fear avoidance.

Participants: Five patients (2 men and 3 women) between 25 and 60 years old with NSCLBP were recruited. This experimental group performed a 12 week high-intensity core strengthening program, in which 2 sessions per week were conducted.

Measurements: Muscles biopsies of the multifidus muscle were taken before and after the HIT program. A micro biopsy and immunofluorescence technique were used to visualize muscle fibres. A maximal exercise and strength test were used to determine exercise capacity and strength. Questionnaires were used to determine pain, disability, physical activity level and fear avoidance beliefs.

Results: After the intervention, no significant changes in the percentage, mean cross-sectional area (CSA) and relative CSA (rCSA) of all muscle fibre types were observed. For the secondary outcome measures, only significant differences were observed in NPRS ($p = 0.0109$ & 0.0313), relative VO2max ($p = 0.0416$ & 0.1250) and absolute VO2max ($p= 0.0393$ & 0.0625).

Conclusion: HIT induced a change in NPRS and VO2max, but didn't alter muscle fibre type characteristics. More research of high quality regarding this topic is necessary.

Key words: High intensity training, non-specific chronic low back pain, muscle fibre type characteristics, muscle biopsy, multifidus muscle

Introduction

High-intensity training (HIT) describes physical exercise that is characterized by brief, intermittent bursts of vigorous activity, interspersed by periods of rest or low-intensity exercise (Gibala, Little, Macdonald, & Hawley, 2012). Two of the most well-known types of HIT are high-intensity cardiorespiratory training, i.e. high-intensity interval training (HIIT) at 80-100% peak heart rate (HRmax) or aerobic capacity (Keating, Johnson, Mielke, & Coombes, 2017), and high-intensity resistance training (HIRT) with resistances ranging from 60-100% one repetition maximum (1 RM).

In healthy populations, little high quality evidence is available about the effects of HIIT and HIRT on muscle fibre characteristics. An important mechanism for skeletal muscle to adapt to training is exercised induced fibre type transition, which is accompanied by the alteration of myosin heavy chain (MHC) isoform composition (Pette & Staron, 1997). HIIT seems to have no effect on fibre type distribution and transition (Jakobsen et al., 2012; Jensen, Bangsbo, & Hellsten, 2004), but HIRT has shown to increase the percentage area of type IIa fibres and decrease the percentage area of type IIx fibres (Andersen, Andersen, Zebis, & Aagaard, 2010; Fry, Allemeier, & Staron, 1994; Jakobsen et al., 2012). Another important mechanism for skeletal muscle to adapt to training is an increase in the cross sectional area (CSA). HIIT seems to have no effect on mean muscle fibre CSA (Cocks et al., 2013) and fibre type specific CSA (Jakobsen et al., 2012; Jensen et al., 2004), but HIRT has shown to induce an increase in muscle fibre CSA of type II fibres (Andersen et al., 2010).

The effects of HIIT and HIRT on muscle fibre characteristics outside the healthy populations, remain to be investigated. Globally, low back pain (LBP) is one of the most common musculoskeletal pathologies. Worldwide, up to 84% of the population will experience LBP once in their life (Airaksinen et al., 2006). LBP can be divided into two main categories, specific and non-specific. Specific LBP is characterized by a specific cause or pathology. But in 23% of all persons with LBP, no specific cause or pathology is present and the diagnosis non-specific chronic low back pain (NSCLBP) is indicated (Airaksinen et al., 2006).

One of the contributing factors to LBP is lumbar muscle dysfunction, especially lumbar multifidus muscle dysfunction (Freeman, Woodham, & Woodham, 2010). At the lumbar spine the main mass of the paravertebral muscles is formed by the erector spinae and multifidus muscles. The multifidus muscle is a spinotransverse muscle (Macintosh, Valencia, Bogduk, & Munro, 1986) which runs craniocaudally deep and medially to the erector spinae muscle, lying

directly against the vertebral laminae. Both paravertebral muscles are responsible for holding a particular posture and stabilising the trunk (Kalimo, Rantanen, Viljanen, & Einola, 1989). A possible underlying mechanism for muscle dysfunction and LBP is an alteration in fibre type characteristics. Some studies have shown that the paraspinal muscles of patients with specific LBP contain significantly less type I fibres than healthy subjects (Mannion, Weber, Dvorak, Grob, & Muntener, 1997; Mazis et al., 2009). Furthermore, the paraspinal muscles of these patients have shown to contain significantly more type IIx fibres than healthy control subjects (Mannion, Weber, et al., 1997). In contrary, the baseline assessments of this study show a larger amount of type I fibres at the expense of type IIx fibres in people with NSCLBP (unpublished results). However, not all studies have been able to reveal differences in fibre type characteristics of NSCLBP patients (Crossman, Mahon, Watson, Oldham, & Cooper, 2004). Besides alterations in fibre type characteristics, another possible underlying mechanism for muscle dysfunction and LBP is lumbar muscle degeneration. This muscle degeneration, also called muscle atrophy, is characterized by a decrease in CSA of the lumbar paraspinal muscles (Barker, Shamley, & Jackson, 2004; Danneels, Vanderstraeten, Cambier, Witvrouw, & De Cuyper, 2000; Fortin & Macedo, 2013; J. Hides, Gilmore, Stanton, & Bohlscheid, 2008; J. A. Hides, Stokes, Saide, Jull, & Cooper, 1994; Ploumis et al., 2011). In NSCLBP patients moderate evidence is available for atrophy of the multifidus muscle (Goubert, Oosterwijck, Meeus, & Danneels, 2016).

In patients with NSCLBP, one study has shown that stabilisation and resistance exercise programs are effective in reducing LBP, and that cardiorespiratory and combined exercise programs showed no effect (Searle, Spink, Ho, & Chuter, 2015). Another study has shown core stabilization exercise is more effective than general exercise for decreasing pain and increasing physical function in patients with NSCLBP in the short term (Wang et al., 2012). But in general there seems to be no clear evidence that one particular type of exercise therapy is more effective than others in this population (Saragiotto et al., 2016; Smith, Littlewood, & May, 2014; van Middelkoop et al., 2010). The effects of HIT in patients with NSCLBP remain to be investigated.

This study investigated the effects of a HIT program on muscle fibre type characteristics, i.e. fibre type distribution and size, in patients with NSCLBP. The muscle fibre characteristics of the multifidus muscle were examined before and after a 12 week high-intensity core strengthening program.

Methods

Preface

This study is part of an ongoing randomized controlled trial (RCT) which takes place at the REVAL building at the university of Hasselt. The original study uses five intervention groups. Because of unforeseen circumstances, data of only one intervention group (i.e. lumbar HIT) was available on time. So only the lumbar HIT group was incorporated in this study. Five participants of this group were used in this study, and evaluated at baseline and after a 12 week training period.

Participants

Participants were recruited through distribution of flyers (e.g. local pharmacies, libraries, university facilities) and adverts on social media. The people who were interested received a letter with further information and an invitation for an intake session by one of the researchers. In- and exclusion criteria were evaluated and red flags for low back pain rehabilitation were questioned during this session. Later a doctor was consulted to confirm the diagnoses of NSCLBP and an informed consent was signed.

Only Dutch speaking males and females between 25 and 60 years old with NSCLBP were included. Patients who went through a lumbar back surgery, exhibited co-morbidities (like neurological symptoms, diabetes and rheumatoid arthritis), experienced a pain increase of three points with a result of $\geq$8/10 (measured by the Numeric Pain Rating Scale (NPRS)) in the last 48h, were pregnant, had ongoing work disability for more than six months, followed another exercise program for LBP within the previous three months, or weren't able to attend regular therapy sessions, were excluded.

The following data about the participants was collected: gender, age (years), weight (kg), length (m), BMI (kg/m^2), average workhours a week and time onset of low back pain. The data is presented in table 1.

Procedure

Testing protocol

The assessments were executed at the exercise lab of REVAL. Testing took place on two consecutive days. During the first testing session, sociodemographic data was collected, a maximal exercise capacity and maximal isometric strength test was performed, and questionnaires concerning pain, disability, physical activity and movement related fear were completed. During the second testing session, a trained medical doctor with experience

performed a muscle microbiopsy. The maximal exercise capacity test, maximal isometric strength test, questionnaires and muscle microbiopsy procedure were repeated after the training period.

Primary outcome measures

Muscle biopsy collection and immunofluorescent staining

A muscle biopsy was performed before and after the training period to determine potential changes in muscle fibre type characteristics due to training. To obtain muscle samples of the multifidus muscle a microbiopsy procedure was used. The study of Agten et al. (2018) has shown that a percutaneous microbiopsy appears to be feasible and accurate, and safe to use to obtain muscle tissue from the paraspinal muscles. This technique uses a Magnum Biopsy System (MG1522; Bard) with 16-gauge core disposable biopsy needles (Magnum Needle, MN1610; Bard; length 100mm, length of the sample notch 22mm) and a 15-gauge coaxial needle (Magnum Needle, C1610B, Bard; length 7cm). Before obtaining the biopsy, the participants underwent an ultrasound examination (Philips iU22 Ultrasound machine with Philips C5-3 MHz Curved Array Transducer) to determine the correct puncture site. The use of ultrasonography to determine the puncture site is necessary to ensure biopsy of the correct muscles and to ensure the safety of the procedure (Agten et al., 2018). The biopsies were obtained at the right side of the vertebral column. Participants were placed in a prone position on a treatment table. The skin and the region was subcutaneously anaesthetized with 5 mL of xylocaine 1% after skin application of povidone-iodine. A small incision of approximately 2 mm was made through the skin at the entry site of the coaxial biopsy needle. This coaxial needle was used to provide a clear path through which the biopsy needle can be inserted to obtain muscle biopsies from the muscle without the need for repeated skin punctures. The samples were covered with optimum-cutting temperature compound (Tissue-Tek) and immediately frozen in isopentane, precooled in liquid nitrogen. Frozen samples were stored at −80 °C until further analysis. Muscle samples were divided into cryovials, per subject and per measurement. Immunofluorescent staining was performed to analyse major histocompatibility complex (MHC) expression. Primary antibodies, specific to laminin (ab11575, Abcam), MHC I (BA-F8), MHC IIa (SC-71) and MHC IIx (6H1) (Development Studies Hybridoma Bank, Iowa City, IA, USA) were used (Agten et al., 2018). The sections were counterstained with the appropriately conjugated secondary antibodies (Alexa Fluor 532,

Alexa Fluor 350, Alexa Fluor 488, Alexa Fluor 555; Life Technologies) to visualize the different muscle fibres and their endomysium (Bloemberg & Quadrilatero, 2012).

Muscle biopsy analyses

Muscle fibres are classified into at least three groups based on their contractile speed, myosin heavy chain (MHC) expression and metabolic capacity: type I (slow twitch, oxidative), type IIa (fast twitch, oxidative/glycolytic) and type IIx (fast twitch, glycolytic) fibres (Caiozzo, 2002; Schiaffino & Reggiani, 1996; Zierath & Hawley, 2004). These fibre types contain a single MHC isoform ("pure fibre types"). But some fibre types, like type IIax muscle fibres, contain more than one MHC isoform ("hybrid fibre types") (Pette & Staron, 2000). The latter muscle fibre type can be situated in between type IIa and type IIx fibres, because it contains MHC isoforms of both fibre types. The mean CSA and the percentage of type I, type IIa, type IIax and type IIx muscles fibres were examined in this study. Also, the relative area of the muscle occupied by a given fibre type (I, IIa, IIax and IIx) was determined. This measure is expressed as relative CSA (rCSA), and combines data on the distribution of fibre type (fibre type percentage) and the mean fibre type size (mean fibre type CSA).

For analyses, stained samples were cut into sections. The sections were viewed with a fluorescent microscope (Leica EL6000; Leica)(Agten et al., 2018). Images of the sections were captured with use of a camera attached to the microscope and analysed with specific computer running image analysis software (AxioVision Rel. 4.8.2 & ZEN 2.1, Carl Zeiss). Generally, 200-300 fibres were analysed per muscle sample. This amount seemed to be adequate, because at least 150 muscle fibres should be accessible to achieve a representative sample of the entire muscle (Ceglia et al., 2013). The software was used to determine the mean CSA and the percentage of each fibre type. The rCSA was calculated using the formula described in the study of Mannion et al. (1997a). The image analyses were performed by two students separately, and the results of both students were compared.

Secondary outcome measures

Maximal exercise test

A maximal exercise test on an electronically braked cycle ergometer (eBike Basic, General Electric GmbH, Bitz, Germany) was performed to evaluate maximal workload (Wmax), because exercise intensity was defined as a percentage of the Wmax. Participants started at a low workload, and after each minute the workload was gradually increased (♂:

30W+15W/min, ♀: 20W+10W/min). Also, breath-by-breath gas exchange analysis (Cortex MetaMax 3B) was used to determine maximal oxygen uptake (VO2max).

Maximal strength testing

An isokinetic dynamometer (System 3 with dual position extension/flexion back attachment, Biodex, Enraf-Nonius, New York) was used to receive an indication of the maximal voluntary isometric muscle strength of the back extensors. The muscle strength was measured in a 90° hip angle, with the participants fixated in a seat at thighs and shoulders. Seat height was adjusted to bring the axis of the dynamometer in line with the anterior iliac spine of the pelvis of the participant. The peak extension torque of three maximal force measurements was recorded, with 30 seconds rest in between force measurements. Peak torque was expressed in Newton meter (Nm) and represents absolute force. Peak torque was also normalized for bodyweight (Nm/kg) and represents relative force.

NPRS

The Numeric Pain Rating Score (NPRS) was used to evaluate pain intensity. It is a reliable and valid scale to evaluate pain intensity (Hawker, Mian, Kendzerska, & French, 2011). It consists of a line indicating eleven consecutive scores (0-10) with zero representing one pain extreme (e.g., “no pain”) and ten representing the other pain extreme (e.g., “pain as bad as you can imagine” and “worst pain imaginable”). A reduction of two levels or more is demonstrated to be clinically relevant (Childs, Piva, & Fritz, 2005).

MODI

The Modified Oswestry Disability Index (MODI) was used to evaluate disability. It is a reliable and valid questionnaire to evaluate constraints experienced by people in their daily activities due to chronic low back pain (Fairbank et al., 2011). It consists of ten items addressing different aspects of function. Each item is scored from zero to five, with higher values representing greater disability (Fritz & Irrgang, 2001). The total score gives a percentage, which represents the degree of functional limitation.

PASIPD

The Physical Activities Scale For Individuals with Physical Disabilities (PASIPD) was used to measure physical activity. The PASIPD is a questionnaire consisting of 13 items, related to leisure, household and work-related physical activity in the last seven days. It has shown to be a reliable and valid measure to evaluate the physical activity of people with disabilities (van der Ploeg et al., 2007).

TSK

The Tampa Scale for Kinesiophobia (TSK) was used to evaluate movement related fear. It has shown to be a valid and reliable questionnaire for evaluating pain-related fear of movement in persons with low back pain (Swinkels-Meewisse, Swinkels, Verbeek, Vlaeyen, & Oostendorp, 2003). The questionnaire consists of 17 items. A higher score indicates more pain-related fear of movement.

Intervention

The program consisted of 24 therapy sessions (2x 1.5 hour/week), under the supervision of a trained physiotherapist. Participants performed a cardiovascular and core strength training program at high intensity. Participants had to finalize the training program within 16 weeks after the first training session. Participants who did not accomplish this were seen as a missing value. A protocol manual was used to assure accurate guidance through the program. Sessions missed by the participants because of low back pain were inventoried. Sessions missed by participants for a reason other than low back pain were postponed.

Lumbar HIT

Each session started with a five minute warm up on a cycle ergometer. After the warm up high-intensity interval cycling was performed comprising of five one minute bouts (110 RPM at 100% VO2max workload), separated by one minute of active rest (75 RPM at 50% VO2max workload). During the first six weeks of training, cycling bouts gradually increased by 10'' from 1' of maximal exercise to 1'50''. Recovery time (1') between bouts remained stable. The participants were instructed to stabilize the lower part of the back (stable core posture) and to hold the correct position during training. Thereafter, the participants performed a core strength training program, which consisted of a circuit of the following six static core exercises: glute bridge, glute clam, superman back extension, adapted plank, adapted side plank and shoulder retraction with hip hinge. On the first two sessions, participants were educated on activation of the (deep) core muscle system (m. transversus abdominus, m. multifidus, m. gluteii) and executing the exercises correctly. On the third session the training program was initiated, and participants performed one set of ten repetitions of a 10 sec. static hold. After these three habituation sessions, the repetitions for each exercise progressed to two sets of ten repetitions of 10 sec. static holds. The participants were encouraged to hold the last repetition until muscle failure. As soon as the exercises were executed correctly (on two consecutive days) they were made more difficult, to reach more demanding postures.

Data analysis

The JMP Pro 14 software was used to analyse data. Because the same sample of participants was tested before and after the intervention period, pre and post data was dependent. Thereby the difference between pre and post data was calculated and used for statistical analysis. First, normal distribution of the data was explored. Thereafter, a paired t-test (parametric) and a Wilcoxon signed-rank test (non-parametric) was used to explore if data was statistically significant. Because of the small sample size ($n < 20$) both, parametric and non-parametric, tests were used for data analysis. All data is expressed as means ± standard deviation (SD), and documented in table 2, 3 and 4 (appendices). An alpha-level of 5% (0.05) was considered statistically significant.

Post measurements of fibre type CSA, fibre type percentage and relative fibre type CSA were performed by two assessors separately. The IBM SPSS Statistics 25 software was used to estimate inter-rater reliability by calculating intraclass correlation coefficients (ICC). ICC values were calculated for each fibre type separately, and only for two out of three primary outcome measures (fibre type CSA and fibre type percentage). Thereafter, standard error of measurement (SEM) and minimal detectable change (MDC) were calculated via the following formulas: SEM = SD x $\sqrt{(1 - ICC)}$ & MDC = SEM x 1.96 x $\sqrt{(2)}$ (Abilitylab, 2016). Also, the SEM values were expressed as a proportion of the corresponding mean values (%SEM).

Ethics and trial registration

The overarching RCT has been approved by the medical ethical committee of Hasselt University and of Jessa Hospital (Hasselt, Belgium).

Results

Primary outcome

Fibre type CSA, fibre type percentage and relative fibre type CSA

For CSA of type I, type IIa, type IIax and type IIx fibres no significant differences were found between pre and post measurements (type I: Δ pre = 8712.68, Δ post = 8322.82, p = 0.7144 & 0.8125; type IIa: Δ pre = 5709.66, Δ post = 5626.36, p = 0.9583 & 1.0000; type IIax: Δ pre = 3796.03, Δ post = 4262.58, p = 0.6057 & 0.8750; type IIx: Δ pre = 3367.74, Δ post = 3778.61, p = 0.7200 & 0.6250).

For percentage type I, type IIa, type IIax and type IIx no significant differences were found between pre and post measurements (type I: Δ pre = 62.98, Δ post = 65.91, p = 0.6527 & 0.6250; type IIa: Δ pre = 22.00, Δ post = 20.73, p = 0.7523 & 0.8125; type IIax: Δ pre = 11.78, Δ post = 10.95, p = 0.9582 & 0.8750; type IIx: Δ pre = 6.99, Δ post = 2.71, p = 0.1964 & 0.1250).

And also for rCSA of type I, type IIa, type IIax and type IIx no significant differences were found between pre and post measurements (type I: Δ pre = 73.50, Δ post = 74.80, p = 0.8553 & 1.0000; type IIa: Δ pre = 17.40, Δ post = 17.13, p = 0.9563 & 1.0000; type IIax: Δ pre = 7.58, Δ post = 6.50, p = 0.8577 & 0.8750; type IIx: Δ pre = 3.78, Δ post = 1.56, p = 0.1933 & 0.2500).

The data of the primary outcome measures is documented in table 2.

ICC, SEM and MDC

The ICC for post measurements of fibre type CSA and percentage was calculated to estimate the inter-rater reliability. There was a wide variation and inconsistency between ICC values. But most values ranged between 0.50 and 1.00, which means moderate to excellent reliability. The ICC value of CSA type IIax was above 0.90, which corresponds with excellent reliability. The ICC value of CSA type I was between 0.75 and 0.90, which corresponds with good reliability. The ICC values of CSA type IIx, percentage type I, percentage type IIa and percentage IIx were between 0.50 and 0.75, which corresponds with moderate reliability. And at least the ICC values of CSA type IIa and percentage type IIax were below 0.50, which corresponds with poor reliability. For interpretation of ICC values the study by Koo and Li (2016) was used. Besides the ICC of these measurements, SEM and MDC values were also calculated and documented in table 3.

Secondary outcome

The absolute and relative VO2max were significantly higher after the intervention than before the intervention (VO2max(abs): Δ pre = 2.64, Δ post = 3.04, p = 0.0393 & 0.0625; VO2max(rel):

Δ pre = 37.49, Δ post = 39.45, p = 0.0416 & 0.1250). The results of the post exercise capacity test of participant 076 weren't used for data analysis, because the participant didn't perform a maximal test.

The NPRS score was significantly lower after the intervention than before the intervention (Δ pre = 5.80, Δ post = 3.80, p = 0.0109 & 0.0313).

The absolute and relative force seemed to be increased after the intervention (Force(abs): from Δ pre = 224.00 to Δ post = 237.80; Force(rel): from Δ pre = 3.14 to Δ post = 3.30), but the difference between pre and post measurements wasn't statistically significant (Force(abs): p = 0.2133 & 0.3125; Force(rel): p = 0.2358 & 0.2500).

The functional limitations (MODI) of the participants seemed to be decreased after the intervention (MODI: from Δ pre = 9.40 to Δ post = 6.00; MODI (%): from Δ pre = 18.80 to Δ post = 12.00), but the difference between pre and post measurements wasn't statistically significant (MODI: p = 0.3883 & 0.5000; MODI (%): p = 0.3883 & 0.5000).

For the other secondary outcome parameters also no significant difference were found between pre and post measurements. The mean (± SD) and p values of all secondary outcome are presented in table 4.

Discussion

Primary outcome

Fibre type CSA, fibre type percentage and relative fibre type CSA

The intervention has shown to have no effect on the mean CSA, percentage and rCSA of type I, type IIa, type IIax and type IIx fibres. A possible reason for finding no significant results could be the small sample size. This study was part of a broader research project, and because of a mismatch in timing of both studies only five muscle biopsy samples were available, causing a low power. Another reason for finding no significant results could be the duration of the intervention. A fibre type transformation of pre-existing type II fibres to type I fibres, without the formation of new fibres, may take longer than 12 weeks to expose (i.e. 60 to 124 days) (Windisch, Gundersen, Szabolcs, Gruber, & Lomo, 1998). Some studies have shown an intervention of 12 weeks or less is able to induce a fast to slow (Howald, Hoppeler, Claassen, Mathieu, & Straub, 1985) and slow to fast (Liu, Schlumberger, Wirth, Schmidtbleicher, & Steinacker, 2003; Paddon-Jones, Leveritt, Lonergan, & Abernethy, 2001) fibre type shift. But it is important to know whether the transformation of fibre types occurred in original fibres that maintained their integrity (throughout the period of transformation) or was the result of the generation of new fibres (Windisch et al., 1998). This was unclear in the studies of Howald et al. (1985), Liu et al. (2003) and Paddon-Jones et al. (2001). Nevertheless these studies (Howald et al., 1985; Liu et al., 2003; Paddon-Jones et al., 2001) used interventions with a training frequency of three times a week or more. In the present study participants trained only one to two times a week. So taking all these finding into account, both the training duration and frequency may have been too low to induce a fibre type shift with and without the formation of new fibres.

Mobilizing muscles like the biceps brachii, vastus lateralis and triceps brachii have been shown to contain 48% (Klitgaard, Zhou, & Richter, 1990), 52% and 50% (Schantz, Randall-Fox, Hutchison, Tyden, & Astrand, 1983) type I fibres. The study by Jorgenson, Nicholaisen and Kato (1993) showed that the multifidus muscle of healthy well-trained men consisted of 59% type I fibres. The study by Thorstensson and Carlson (1987) showed similar results with 62% type I fibres. So in healthy persons it seems that postural muscles, like the m. multifidus, contain more type I fibres than mobilizing muscles, like m. biceps brachii, m. vastus lateralis and m. triceps brachii. Before the present study, more type II fibres were expected to be present in the multifidus muscle of patients with NSCLBP in comparison to healthy subjects. A

dysfunction of the postural function was thought to be present and associated with a decrease in type I muscle fibres and an increase in type II muscle fibres. Because of the nature of the core strength training program, it could be able to increase the amount of type I fibres and consequently restore the postural function of the multifidus muscle. In the present study post measurements were complete for all fibre types in all five participants (in contrast to pre measurements), and were used for the description of this section. These measurements show the multifidus muscle of patients with NSCLBP contains 66% type I fibres, 21% type IIa fibres, 11% type IIax fibres and 3% type IIx fibres. Based on the findings of the present study and the findings by Jorgenson et al. (1993) and Thorstensson et al. (1987), the percentage type I fibres seems to remain consistent or even slightly increases in patients with NSCLBP. This finding is in contrast with the previous assumption about the association between a postural dysfunction and a decrease of type I fibres in the multifidus muscle of patients with NSCLBP.

In contrast to physiological factors, psychological factors may be responsible for the slight increase in type I fibres in patients with NSCLBP. In this population a correlation between pain catastrophizing and higher muscle activation during gait has been shown. Patients with high pain catastrophizing demonstrated a higher activation amplitude of certain trunk muscles (e.g. lumbar multifidus) (Pakzad, Fung, & Preuss, 2016). This seems to be a guarding strategy to limit spinal motion (Lamoth, Meijer, Daffertshofer, Wuisman, & Beek, 2006; van der Hulst, Vollenbroek-Hutten, Rietman, & Hermens, 2010), and to avoid further damage of tissue or pain. So pain catastrophizing seems to be responsible for altered muscle activation patterns in patients with NSCLBP. Altered muscle activation patterns, like muscle guarding, could lead to fibre type alterations, because a muscle guarding strategy involves muscles to sub maximally contract for a long period of time. During this type of muscle contractions type I fibres are stimulated the most. So if this strategy is present for a long period of time, it may cause a fibre type shift towards type I fibres.

ICC, SEM and MDC

Primary outcome measures were measured using the AxioVision program by ZENN. Measurements were performed by two investigators separately, and the average of both measurements was used for data collection. The inter-rater reliability of the measurements of both investigators was assessed by calculating the ICC. As mentioned before, the ICC values were widespread and inconsistent. But it was the first time both investigators used the AxioVision program, so both investigators were unexperienced in using the program. This may

explain the wide variation and inconsistency in ICC values. The ICC for rCSA wasn't calculated, because the rCSA values weren't measured using the AxioVision program. They were calculated using the formula described in the study of Mannion et al. (1997a). As mentioned before, the SEM and MDC values were also calculated using a formula. These values were high, which means it was difficult to find statistically and clinically relevant outcome.

Secondary outcome

In this study the physical activity level of the participants increased after the intervention, because of a significant increase in VO2max, and the LBP decreased after the intervention, because of a significant decrease in NPRS score. The coexistence of a higher physical activity level and less pain in patients with NSCLBP may suggest a link between those two findings.

It has been shown that patients with CLBP (specific and non-specific) have a lower level of aerobic fitness (i.e. VO2max) than healthy controls (Duque, Parra, & Duvallet, 2009). The study by Smeets, Wittink, Hidding en Knottnerus (2006) has also shown that the VO2max is significantly lower in men (10 mL/kg LBM x min(-1)) and women (5.6 mL/kg LBM x min(-1)) with NSCLBP compared to healthy controls. Another study demonstrated a moderate correlation between physical activity and disability for persons with NSCLBP, which indicates that persons with NSCLBP and high levels of disability are also likely to have low levels of physical activity (Lin et al., 2011). So it seems patients with NSCLBP and a lower VO2max, are less physically active and are likely to have a higher level of disability.

These findings can be interpreted according the fear avoidance model. Patients avoid activities causing pain, because it is interpreted as threatening by making the condition worse. As a consequence pain-related fear and avoidance behaviours evolve. This results in a decrease in the level of physical activity, disuse and an increase in the level of disability, which in turn will result in experiencing more pain during activities of daily living (Vlaeyen & Linton, 2000). But this process seems to be reversable. Through exercise patients reduce pain-related fear and avoidance behaviours. They develop a higher physical activity level and reduce the level of disability, which results in experiencing less pain during activities of daily living (Gordon & Bloxham, 2016).

These findings highlight that enhancing physical activity and reducing disability might be important treatment aims in this population (Lin et al., 2011). Based on these findings, the type of exercise seems to be less important. The patients have to be more active and increase

their physical activity level. Higher intensities may be more beneficial, because of the effect on the VO2max.

Besides the significant increase in VO2max and decrease in NPRS score, the present study showed no significant reduction in fear of movement and all other secondary outcome measures. But this might be because of the small sample size.

Recommendations for future research

As mentioned before, LBP is one of the most common musculoskeletal pathologies and in a lot of patients a specific cause or pathology remains unknown. So future research should use larger sample sizes to find clinically relevant outcome. Based on the findings of this study, it would be interesting to use a longer intervention period and a higher training frequency to potentially induce a fibre type shift. To receive more information about the differences in fibre type characteristics between healthy subjects and patients with NSCLBP a control group with healthy subjects should be incorporated. Also, a control group with NSCLBP patients who do not participate in the training program or a control group with healthy subjects who perform the same training program as the intervention group should be incorporated to enhance the quality of the study. It would also be interesting to compare HIT with MIT to confirm the effects of the intensity of training on the physical activity level and perception of pain. And at least long term follow-up would be interesting to evaluate the long term effects of such interventions.

Conclusion

After a 12 week high-intensity core strengthening program no significant differences were found in muscle fibre type characteristics measured by a biopsy of the multifidus muscle. For the secondary outcome measures, significant differences were found in VO2max and pain scores. So, in patients with NSCLBP, HIT seems to improve the general exercise capacity and reduce pain, although no alteration in muscle fibre type characteristics was found. More research of high quality with a longer intervention period and a higher training frequency is necessary to confirm these findings.

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Appendices

Table 1: Demographic characteristics of the participants

ID	Gender	Age	Working/wk	Onset	Weight pre	Weight post	Length	BMI pre	BMI post
34	♀	55	30	2013	58,2	59,6	1,664	21,02	21,52
44	♀	53	24	2014	70,2	69	1,746	23,03	22,63
53	♂	33	40	2016	78,7	77,2	1,859	22,77	22,34
76	♀	48	8	2010	68	70,2	1,778	21,51	22,21
78	♂	29	40	2016	89,4	93,6	1,831	26,67	27,92

Wk = week, BMI = body mass index, pre = before intervention, post = after intervention.

Table 2: Primary outcome – Fibre type CSA, fibre type percentage and relative fibre type CSA

	Mean pre	SD	Mean post	SD	Mean residuals	SD	P value T-test	P value Singed-Rank
CSA type I	8712,68	3170,59	8322,82	1049,36	-389,86	2218,15	0,7144	0,8125
CSA type IIa	5709,66	1808,14	5626,36	2389,94	-83,30	3349,10	0,9583	1,0000
CSA type IIax	3796,03	1679,61	4262,58	1957,3	544,26	1893,95	0,6057	0,8750
CSA type IIx	3367,74	1781,39	3778,61	1897,68	273,58	1389,11	0,7200	0,6250
Abs% type I	62,98	15,97	65,91	10,73	2,93	13,71	0,6527	0,6250
Abs% type IIa	22,00	4,12	20,73	6,86	-1,27	8,40	0,7523	0,8125
Abs% type IIax	11,78	11,08	10,95	4,82	-0,30	10,45	0,9582	0,8750
Abs% type IIx	6,99	4,02	2,71	2,99	-4,33	5,23	0,1964	0,1250
rCSA type I	73,50	14,81	74,79	13,13	1,29	14,86	0,8553	1,0000
rCSA type IIa	17,40	5,25	17,13	10,59	-0,27	10,47	0,9563	1,0000
rCSA type IIax	7,58	8,77	6,50	2,84	-0,86	8,76	0,8577	0,8750
rCSA type IIx	3,78	2,48	1,56	1,54	-2,37	2,84	0,1933	0,2500

SD = standard deviation, t-test = parametric statistical test, Singed-Rank test = non-parametric statistical test. No significant differences ($p > 0.05$).

Table 3: ICC, SEM, MDC and %SEM of the primary outcome measurements (fibre type CSA and fibre type percentage)

	Mean pre	SD	Mean post	SD	ICC	MDC	SEM	%SEM
CSA type I	8712,68	3170,59	8322,82	1049,36	0,839	1167,102	421,054	4,833
CSA type IIa	5709,66	1808,14	5626,36	2389,94	0,493	4716,960	1701,731	29,804
CSA type IIax	3796,03	1679,61	4262,58	1957,30	0,995	383,631	138,402	3,646
CSA type IIx	3367,74	1781,39	3778,61	1897,68	0,684	2956,907	1066,760	31,676
Abs% type I	62,98	15,97	65,91	10,73	0,674	16,982	6,126	9,728
Abs% type IIa	22,00	4,12	20,73	6,86	0,407	14,643	5,283	24,012
Abs% type IIax	11,78	11,08	10,95	4,82	0,547	8,992	3,244	27,539
Abs% type IIx	6,99	4,02	2,71	2,99	0,675	4,725	1,705	24,386

Pre = before intervention, post = after intervention, SD = standard deviation, ICC = intraclass correlation coefficient, MDC = minimal detectable change, SEM = Standard error of measurement, %SEM = SEM values as a proportion of the corresponding mean values. Excellent reliability = > 0.90, good reliability = 0.75-0.90, moderate reliability = 0.50-0.75, poor reliability = < 0.50.

Table 4: Secondary outcome – Physical activity, pain, disability, movement related fear and strength

							P value	
	Mean pre	SD	Mean post	SD	Mean residuals	SD	T-test	Singed-Rank
VO2max(abs)	2,64	0,72	2,84	0,72	0,20	0,14	0,0393*	0.0625
VO2max(rel)	37,49	3,16	37,31	5,90	-0,18	3,81	0,0416*	0,1250
NPRS	5,80	0,84	3,80	1,79	-2,00	1,22	0,0109*	0,0313*
MODI	9,40	7,63	6,00	1,87	-3,40	7,86	0,3883	0,5000
MODI %	18,80	15,27	12,00	3,74	-6,80	15,72	0,3883	0,5000
PASIPD	16,88	8,68	15,48	6,04	-1,40	5,88	0,6229	0,4375
TSK	33,80	4,66	31,20	9,88	-2,60	8,41	0,5276	0,8750
Force (abs)	224,00	48,44	237,80	65,91	13,80	34,91	0,2133	0,3125
Force (rel)	3,14	0,81	3,30	1,11	0,16	0,45	0,2358	0,2500

Pre = before intervention, post = after intervention, SD = standard deviation, t-test = parametric statistical test, Signed-Rank test = non-parametric statistical test.
*Significant difference ($p < 0.05$).

www.uhasselt.be
Campus Hasselt | Martelarenlaan 42 | BE-3500 Hasselt
Campus Diepenbeek | Agoralaan gebouw D | BE-3590 Diepenbeek
T + 32(0)11 26 81 11 | E-mail: info@uhasselt.be

UHASSELT
KNOWLEDGE IN ACTION

INVENTARISATIEFORMULIER WETENSCHAPPELIJKE STAGE DEEL 2

DATUM	INHOUD OVERLEG	HANDTEKENINGEN
27/09/18	Algemene bespreking MPII	Promotor: Copromotor/Begeleider: Student(e): Student(e):
04/12/18	Bespreking inleiding en methode	Promotor: Copromotor/Begeleider: Student(e): Student(e):
19/03/19	Bespreking methode	Promotor: Copromotor/Begeleider: Student(e): Student(e):
22/03/19	Bespreking statistiek	Promotor: Copromotor/Begeleider: Student(e): Student(e):
23/04/19	Bespreking resultaten en discussie	Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):

In te vullen door de promotor(en) en eventuele copromotor aan het einde van MP2:

Naam Student(e): Van Reet Ron **Datum:** 27/05/2019

Titel Masterproef: Effects of high-intensity training on muscle fibre characteristics of the multifidus muscle in persons with non-specific chronic low back pain

1) Geef aan in hoeverre de student(e) onderstaande competenties zelfstandig uitvoerde:
   - NVT: De student(e) leverde hierin geen bijdrage, aangezien hij/zij in een reeds lopende studie meewerkte.
   - 1: De student(e) was niet zelfstandig en sterk afhankelijk van medestudent(e) of promotor en teamleden bij de uitwerking en uitvoering.
   - 2: De student(e) had veel hulp en ondersteuning nodig bij de uitwerking en uitvoering.
   - 3: De student(e) was redelijk zelfstandig bij de uitwerking en uitvoering
   - 4: De student(e) had weinig tot geringe hulp nodig bij de uitwerking en uitvoering.
   - 5: De student(e) werkte zeer zelfstandig en had slechts zeer sporadisch hulp en bijsturing nodig van de promotor of zijn team bij de uitwerking en uitvoering.

Competenties	NVT	1	2	3	4	5
Opstelling onderzoeksvraag	Ø	O	O	O	O	O
Methodologische uitwerking	O	O	O	Ø	O	O
Data acquisitie	Ø	O	O	O	O	O
Data management	O	O	O	O	Ø	O
Dataverwerking/Statistiek	O	O	O	O	Ø	O
Rapportage	O	O	O	O	Ø	O

2) Niet-bindend advies: Student(e) krijgt toelating/~~geen toelating~~ (schrappen wat niet past) om bovenvermelde ~~Wetenschappelijke stage~~/masterproef deel 2 te verdedigen in bovenvermelde periode. Deze eventuele toelating houdt geen garantie in dat de student geslaagd is voor dit opleidingsonderdeel.

3) Deze ~~wetenschappelijke stage~~/masterproef deel 2 mag wel/~~niet~~ (schrappen wat niet past) openbaar verdedigd worden.

4) Deze ~~wetenschappelijke stage~~/masterproef deel 2 mag wel/~~niet~~ (schrappen wat niet past) opgenomen worden in de bibliotheek en docserver van de UHasselt.

Datum en handtekening Student(e)	Datum en handtekening promotor(en)	Datum en handtekening Co-promotor(en)
27/5/19	27/5/19 A. Agten	27/5/19