

# Novel aspects of exercise training to promote human metabolic health

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# CHAPTER 9

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**What is the contribution of the results from this thesis to the scientific community and societal challenges?**

To address the growing prevalence of obesity and obesity-related co-morbidities, effective strategies to treat obesity-related co-morbidities are urgently needed. In this regard, the results of **chapter 2, 3 and 6** illustrate the following:

- 1) Exercise training performed in the afternoon confers greater benefits than exercise training performed in the morning when it comes to improvements in skeletal muscle insulin sensitivity, body composition and exercise performance in obese, metabolically compromised individuals.
- 2) High intensity interval training (HIIT) is an effective and time-efficient exercise modality to improve metabolic health in obese adults.

Thus, these results contribute to the still unsolved questions about how to optimize the benefits of exercise training in human metabolic health. Also, these results indicate that HIIT is an alternative training regime to conventional combined aerobic/resistance exercise, which might circumvent the common report of lack of time by individuals to not adhere to exercise programs nowadays.

The results of **chapter 4** provide novel insights about potential targets of intervention to treat exercise intolerance in metabolically compromised and elderly individuals. These finding may inspire future research to explore specific nutritional supplements aiming to enhance exercise tolerance. The relevance of these results is that premature muscle fatigue prompts a poor exercise adherence and increases the risk of stumbling and falls and compromises subjects independence.

Since obesity and aging are major societal challenges in the last decade, associated with a variety of co-morbidities causing a substantial health care cost, the targeted treatment of exercise intolerance and premature muscle fatigue can enhance the quality of life of subjects and reduce the health care costs.

As last, the results of **chapter 4, 5 and 6** underscore the use the magnetic resonance spectroscopy (MRS) technique to investigate how muscle and liver adapt to exercise training. Interestingly, the MRS technique was applied to investigate dynamic responses of the muscle tissue to exercise *in vivo* with a high time resolution, which was (up to now) mostly investigated via taking multiple muscle biopsies in a short time window.

### **To whom are the research results interesting and relevant?**

The results of this thesis are interesting and of relevance for different entities such as researchers, metabolically compromised and elderly individuals, health care professionals and clinical practice, as well as nutritional and pharmaceutical companies.

#### Researchers

The results of **chapter 2 and 3** demonstrate that exercise timing impacts the benefits of exercise in human metabolic health. Thus, researchers might take advantage of such findings to investigate if the benefits of exercise on metabolic health can be optimized or possibly even amplified if timed to the central or peripheral muscle clock. In this regard, food ingestion before and after exercise is an important aspect to consider as nutrients are known to interact with the molecular clock machinery and to influence exercise responses.

In addition, researchers interested to investigate skeletal muscle mitochondrial function can benefit from the results in **chapter 5** of the present thesis as here we validated the use of surrogate markers from human biopsies relative to the gold standard measures (high resolution respirometry). Thus, researchers who do not possess such gold standard technique can analyze specific markers from muscle samples to conclude about mitochondrial function. Moreover, we also validate non-invasive markers for skeletal muscle and whole-body oxidative capacity and investigate to what extent they reflect skeletal muscle mitochondrial function, from which in turn researchers can benefit who cannot obtain muscle biopsies from human volunteers.

#### Metabolically compromised and elderly individuals

The results of **chapter 3, 4 and 6** are of interest for metabolically compromised and elderly individuals, especially to understand the potential of regular exercise training to promote metabolic health. These results can be helpful to stimulate a healthy lifestyle and to motivate individuals to engage in regular exercise programs. To attain those goals, it is crucial to disseminate the scientific results of the studies outlined in this thesis into layman's terms.

#### Health care professionals and clinical practice

The results of **chapter 6** of the present thesis can be helpful for health care professionals who support obese, metabolically compromised and elderly individuals while performing therapeutic physical activity. Nowadays, endurance-type combined with strength-type exercise are conventional exercise regimes recommended for obese and elderly individuals aiming to improve plasma glucose homeostasis. The results of **chapter 6** show that high intensity interval

training (HIIT) is an effective methodology to improve plasma glucose homeostasis, which in turn highlights HIIT as an alternative exercise strategy to be implemented into the clinical practice. In addition, the results of this thesis demonstrate that timing of an exercise training session is a crucial environmental cue when aiming to improve glucose homeostasis and elucidates that performing afternoon exercise training might be more optimal than exercising at morning hours.

#### Nutritional and pharmaceutical companies

The results of **chapter 4** of the present thesis reveal the slow responsiveness of skeletal muscle mitochondria at the onset of exercise as a potential underlying cause of premature muscle fatigue in metabolically compromised and elderly individuals, which can be used as target of interventions. These findings can be of interest to nutritional companies as the supplementation with products able to elevate the acetyl-coa content in muscle (e.g., carnitine and ketone bodies mono-esters beverages) might accelerate the mitochondrial responsiveness at the onset of exercise, and eventually improve physical function. For these compounds to be optimally effective, it is however essential that they reach the muscle in their active form and supplement the endogenous stores. Thus, smart delivery and targeted release approaches may need to come into play here. Also, for this, involvement of food tech industry would clearly be an asset.

In addition, the present findings can draw attention to pharmaceutical companies to elaborate specific acetyl-coA precursors in muscle tissue or to develop controlled substances that promote the enzymatic activation of CrAT protein.

#### **How can these target groups be involved in and informed about the research results, so that the acquired knowledge can be used in the future?**

The results of the present chapters are or will be published as original scientific articles in international, peer reviewed and open access journals. Hence, the findings of this thesis will become fully available online and will be of free access for the different entities interested worldwide. Importantly, some of the results of this thesis have been disseminated to the scientific community on national (Annual Dutch Diabetes Research Meeting) and international scientific conferences (Cell Symposia: Exercise Metabolism, Muscle Clocks and Diabetes Symposia, Metabolism in Action – Copenhagen and at the European Association for the Study of Diabetes) via poster and oral presentations. In such way, the acquired knowledge from the

present thesis was and will be spread within the scientific community to promote novel research ideas as well as to generate collaborative work with (inter)national peers.

Next to presenting the results of this thesis to the scientific community, all individuals who voluntarily participated in the studies received an information brochure summarizing the study results. One way to disseminate the research results to the no scientific community in layman terms is the use of social media. Also, meetings can be organized with individuals interested in research to inform them about the investigation results as well as the importance of a healthy lifestyle.