On your bike: how muscles respond to exercise

We all know that exercise makes us fitter and healthier – but what changes take place in our cells to make this happen?

By Maléne Lindholm and Susanna Wallman Appel

Next time you are working out in the gym, or pounding the streets running or jogging, ponder this: the idea of ‘muscle memory’ – that today’s exercise has effects on our muscles years from now – has never been demonstrated scientifically. Does it really exist, and if so, how does it work? These are some of the questions we hope to answer in our on-going research, which aims to pin down the changes that occur in muscles when we exercise, and how our muscles ‘know’ to respond differently to, say, endurance training as opposed to strength training.

Helping us to investigate these questions is a large team of volunteers. Not only must they cycle to exhaustion in our gym, but before and after a strenuous exercise regime lasting several weeks, we take a tiny sample of their leg muscle under local anaesthetic (figure 1). The aim of our research is to help people optimise their training programmes for maximal fitness, and potentially to help develop new treatments for people who cannot exercise because they are paralysed or have joint diseases.

We assess the fitness of our volunteers before and after participation in the studies by measuring their maximal oxygen uptake. They cycle on an exercise bike against increasing resistance until exhausted, while wearing a mask to collect their expired air (figure 2). We measure the amount of oxygen they take up, which gives us information about the fitness level of their heart and working muscles.

We then extract a tiny piece of muscle from each participant’s leg and take a small biopsy sample of muscle fibres (figure 1). We use a microscope to study the muscle fibres and compare our findings before and after exercise (figure 3). We use different staining techniques to reveal different structures within the cell. One specific histone modification is stained in red, with the nuclei in blue and the cell membrane in green. To find out if a change has occurred, we would compare it with an image taken before training.

Helping us to investigate these questions is a large team of volunteers. Not only must they cycle to exhaustion in our gym, but before and after a strenuous exercise regime lasting several weeks, we take a tiny sample of their leg muscle under local anaesthetic (figure 1). The aim of our research is to help people optimise their training programmes for maximal fitness, and potentially to help develop new treatments for people who cannot exercise because they are paralysed or have joint diseases.

We assess the fitness of our volunteers before and after participation in the studies by measuring their maximal oxygen uptake. They cycle on an exercise bike against increasing resistance until exhausted, while wearing a mask to collect their expired air (figure 2). We measure the amount of oxygen they take up, which gives us information about the fitness level of their heart and working muscles.

We then extract a tiny piece of muscle from each participant’s leg and take a small biopsy sample of muscle fibres (figure 1). We use a microscope to study the muscle fibres and compare our findings before and after exercise (figure 3). We use different staining techniques to reveal different structures within the cell. One specific histone modification is stained in red, with the nuclei in blue and the cell membrane in green. To find out if a change has occurred, we would compare it with an image taken before training.
The more mitochondria the muscles have, the more fat and sugar they can metabolise and the more energy they can release.

But what we don’t yet understand is exactly how exercise causes such changes. We are pursuing this question along two lines: first, how does exercise lead to more mitochondria in skeletal muscle cells? And second, how does exercise change the way in which the cell’s DNA is used?
**Building mitochondria**

Mitochondria are constructed from protein molecules, so factors that boost the production of mitochondrial proteins can increase the number of mitochondria in a cell. One factor that acts as a key regulator of the production of mitochondrial proteins is a molecule called PGC-1α (figure 4).

For a gene to be expressed – that is, used to make a protein – the DNA information held in the nucleus must first be copied, or transcribed, onto an mRNA molecule. The mRNA molecules then move out of the nucleus to sites in the cell where protein molecules are constructed.

The transcription process is controlled by DNA-binding molecules called transcription factors. These attach to the DNA strand at very specific points, either blocking or promoting the transcription process. PGC-1α acts in concert with transcription factors to promote the expression of many genes coding for mitochondrial proteins.

We have recently discovered that one variant of PGC-1α is not present at all before exercise, but high levels of it can be found after only one hour of cycling. This suggests that certain genes are turned on exclusively by exercise, and this may be a clue to the effects of exercise training on health. We are now investigating possible protein modulators of PGC-1α, which may attach to this protein to increase or decrease its activity in boosting mitochondrial protein production.

**Epigenetic factors**

We are also exploring the possible impact of exercise on epigenetics. Epigenetic changes affect how the DNA is used, without affecting the genetic information encoded within it. In our cells, DNA is wrapped around coin-shaped proteins called histones. Attaching small chemical molecules to the DNA strand or to histones affects the ability of transcription factors to reach their target genes. For example, adding a methyl (CH₃) molecule to DNA generally makes the adjacent genes less accessible and thus less active, whereas attaching an acetyl (COCH₃) group to histones usually relaxes that part of the DNA strand, making it more accessible for transcription (figure 5).

Using the biopsy material from our volunteers, we aim to see if such epigenetic effects remain after a prolonged period without physical training, and whether they influence how an individual responds to a later period of training. Based on the results of these experiments, we will be able to investigate whether ‘muscle memory’ truly exists and, if so, how it works.

**Resources**

To learn more about the role of exercise in the prevention and treatment of different diseases, see:


The publication is currently available in English, Chinese, French, Russian and Spanish.

For more information about the physiological effects of exercise, see:


Information aimed at 14- to 16-year-old school students, with an online activity. See the BBC’s GCSE Bitesize website (www.bbc.co.uk/schools/gcsebitesize; search for ‘effects of training and exercise’) or use the direct link: http://tinyurl.com/8xfks6

‘How the body responds to exercise’ video on the US Teachers’ Domain website (www.teachersdomain.org) or via the direct link: http://tinyurl.com/chvndus

‘Where do you get your energy’ video on the US Teachers’ Domain website (www.teachersdomain.org) or via the direct link: http://tinyurl.com/cfwct6g

The following research articles provide more information about the scientific details:


If you enjoyed this article, you may like to browse the other cutting-edge science articles in Science in School. See www.scienceinschool.org/cuttingedge

Acknowledgement

The authors would like to thank Associate Professor Carl Johan Sundberg for providing us with the opportunity to work in his lab and for valuable input on this article.

Maléne Lindholm and Susanna Wallman Appel are carrying out doctoral research on the effects of exercise on human skeletal muscle function and the concurrent health benefits. They both hold masters degrees in biomedicine from the Karolinska Institutet in Stockholm, Sweden, where they also teach physiology.

To learn how to use this code, see page 65.

Figure 5: Adding a methyl (CH3) molecule to DNA generally makes the adjacent genes less accessible and thus less active (A), whereas attaching an acetyl (COCH3) group to histones usually relaxes that part of the DNA strand, making it more accessible for transcription (B)