Exercise Prescription for Health: The Role of Genetics and Epigenetics

Prescripción de ejercicio para la salud: el papel de la genética y de la epigenética

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Preamble

It was Prof. Per Olaf Astrand in the Sixties of the last Century, who stated: "There are many results of scientific studies concerning the effects of physical training and an active lifestyle in the field of primary and secondary prevention of specific diseases, the so-called "Current Exercise Prescriptions".

Based on that, Prof. Astrand raised the following question: "But do we have the right to manipulate the lifestyle of 100 persons in a program if we save only 3/10/50/70/90 lives, where the remaining 97/90/50/30/10 did not like the program or did not respond but were forced to participate".

This was a very wise future direction verbalised at that time. A plethora of genetic and epidemiological studies were born of this insight. These helped to differentiate females and males with high genetic risk and those with low genetic risk for different non-communicable diseases. Within these studies coronary artery diseases are the best ones evaluated. Hand in hand with these findings, a lot of scientific studies, from which the "Heritage-study" by Claude Bouchard was one of the first. This revealed, that prescribed and strictly controlled training regulations my show different effects concerning high responders and low responders (Bouchard C. *et al.,* 1995).

Introduction

When prescribing exercise and physical activity, universally valid and applicable regulations are necessary, to make it useable and practicable for all health professionals. Therefore a lot of national and world-wide functioning federations as European Federation of Sport Medicine (EFSMA), WHO, International Federation of Sport Medicine (FIMS), American College of Sport Medicine (ACSM) and many others have developed training regimens for all humans of both sexes, over the whole age range and under different environmental conditions.

Consequently, a lot of world-wide epidemiological studies showed a risk reduction between 20 and 50% for morbidity and mortality of different chronic non-communicable diseases. These included, among others, cardiovascular diseases, type II diabetes, hyperlipidemia, breast- and colon cancer, Alzheimer's disease, dementia, respiratory diseases, when people are active, (desirable) over their whole lifespan.

Combining results from genetic research, both on risk factors and on the effects of endurance and strength training, it would be the optimal solution to finish up with a "Personalized Exercise Prescription" in the future. Although a lot of traits and genetic polymorphisms are well known in both areas, research is just at the starting line to guarantee validity and objectivity in this just mentioned personalization. The same is true for the prediction of talented young athletes and/or the maximum performance as it is clearly stated in a paper from Webborn N. *et al.*, 2015. As a consequence of this a lot of research has and must continue to be done like the Athlome Project (Pitsiladis Y. *et al*., 2016).

To increase the health in different populations, especially in older aged individuals and to maintain mobility and high quality of life, it is essential to combine the state of the art knowledge of the genetic and the epigenetic influence on different diseases using general recommendations and to break them down to personalized advice. A very impressive example was recently published by AV. Khera, *et al.,* 2016: "Genetic Risk, Adherence to a Healthy Lifestyle and Coronary Disease".

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Introducing the topic, the authors stated, "that both genetic and lifestyle factors are key drivers to develop coronary disease, that is a leading cause of death worldwide". This a state of affairs, which is known as "Sedentary Death Syndrome" (Lees SJ et Booth FW, 2004), the Exercise Deficiency Syndrome (Cummiskey *et al*, 2018) and Exercise deficiency disorder (EDD) (Faigenbaum *et al,* 2011).

Exercise Deficiency Syndrome

We are suggesting that a diagnosis of Exercise Deficiency Syndrome (EDS) should be the first step in a one on one exercise program prescription. Medicine to-day is practiced by first making a diagnosis. This diagnosis usually has a ICD code or a WHO number. This diagnosis has a differential diagnosis. Based on all the information available to the physician at that time, including from office tests, wet laboratory and exercise physiology laboratory a decision is made on a management plan. There is then a follow up with objective testing and a prognosis for that diagnosis. We see a diagnosis of EDS as the first move to act on these non-communicable diseases.

The editors of the journal where EDD was coined said it was a medicalizing of behavioral disorders (Faigenbaum *et al* 2011. Editor's comment). This is not correct and needs to be fought vigorously by the medical exercise community. What we have found is that many gyms, internet companies, and some of our own medical organizations have already commercialized exercise prescription for health. Some have done this without any reference to the science and proof of the use of exercise in the prevention and management of disease. They have dumbed down exercise as a scientific modality of management as they pursue a low grade approach to exercise as a modality of prevention and management in healthy people and to a lesser extent in patients with chronic disease (Faigenbaum AD *et al*., 2011).

Genome-wide associations

In the Khera paper the authors state, that since 2007 analyses of genome-wide associations have identified more than 50 independent loci associated with the risk of coronary artery disease. On the other hand, there is – as mentioned before – strong evidence, that the promotion of healthy lifestyle behaviours, mainly non-smoking, avoiding obesity, regular physical activity and healthy diet patterns improve the cardiovascular health in the general population. To calculate the risk of coronary events, they summarized the adjusted hazard ratios for coronary events of three prospective cohort studies, according to genetic and lifestyle risks.

Epidemiology

The Arteriosclerosis Risk in Communities (ARIC-Study), the Women's Genome Health Study (WGHS) and the Malmoe Diet and Cancer Study (MDCS), was all together a cohort of nearly 50.000 persons. Participants at *low genetic risk with a favorable lifestyle* (non-smokers, without obesity (BMI <30), physical activity at least once weekly and healthy diet pattern) served as the reference group and *1,00 as a reference favourable lifestyle.*

Table 1. Adjusted hazard ratio for coronary events depending upon genetic risk and lifestyle.

N = ~50,000		
Participants at low genetic risk with a favorable lifestyle had 1,00 as a reference		
An adjusted hazard ratio (95% CI) for the with **low** genetic risk		
1.82	(1.51-2.19)	in the unfavourable lifestyle group
1.16	(0.98 to 1.38)	with the intermediate lifestyle,
1.00	as a reference	favourable lifestyle.
An adjusted hazard ratio (95% CI) for the group with **intermediate** genetic risk		
2.52	(2.18 to 2.92)	for the unfavourable lifestyle,
1.54	(1.34 – 1.77)	for the intermediate Lifestyle
1.33	(1.15 – 1.54)	for the favourable lifestyle.
An adjusted hazard ratio (95% CI) for the group with **high** genetic risk showed		
3.50	(2.97 – 4.12)	with unfavorable lifestyle,
2.24	(1.93 – 2.61)	with intermediate lifestyle and
1.90	(1.62 – 2.32)	for favorable lifestyle.

Results showed (Table 1) that an adjusted hazard ratio (95% CI) was always improved in groups with high, through intermediate to lower genetic risk for coronary events if the lifestyle improved from unfavourable, through intermediate to favourable lifestyle. This adjusted hazard ratio was also always better when the genetic risk was lower or intermediate compared to high. The authors concluded, that persons with a high polygenetic risk category, complying adherence to a healthy lifestyle were associated with a significant risk reduction of single coronary events and subclinical burden of "coronary artery disease". Although the absolute risk reduction was the highest in the group of high genetic risks, data strongly support, that exercise prescriptions, as an essential part of a healthy lifestyle are effective for everyone.

Conclusions

This and other studies show very clearly, that health politicians and all health professionals in the frame of Public Health, from WHO to regional authorities should promote a more active lifestyle in the population, because the costs of care of chronic non-communicable diseases in the community are increasing, are becoming unsustainable and need to be highlighted.

Under the viewpoint of this and other papers, every "Healthcare-Euro" must be considered for redirection into prevention because only lifestyle changes and healthcare are sustainable together. The exercise prescription for health, like the EPH-EFSMA Program (Cummiskey J *et al,* 2017), is a meaningful instrument (http://www.efsma-scientific.eu/exercise-prescription-for-health/) to help physicians and all other health professionals to advise patients with a very carefully designed exercise program, both for healthy and diseased persons and with the possibility to personalize it through individual advice with each patient (Löllgen H. *et al.,* 2004, 2017; Zupet P. *et al*., 2016; Cummiskey J, *et al*. 2017).

In addition, a close cooperation of all European federations active in the field of physical activity is strongly recommended as an European alliance against sedentary lifestyle and Exercise Deficiency Syndrome.

Dedicatory

† Devoted to the former EFSMA-Executive Member and President, an excellent scientist and sports physician and great friend.

Recommended bibliography

1. Bouchard C, Leon AS, Rao DC, Skinner JS, Wilmore JH, Gagnon J. The HERITAGE family study. Aims, design, and measurement protocol. *Med Sci Sports Exerc.* 1995;27(5):721–9.
2. Webborn N, Williams A, McNamee M, Bouchard C, Pitsiladis Y, Ahmetov I, *et al.* Direct-to-consumer genetic testing for predicting sports performance and talent identification: Consensus statement. *British Journal of Sports Medicine.* 2015;49(23):1486-91. doi:10.1136/bjsports-2015-095343.
3. Pitsiladis YP, Tanaka M, Eynon N, Bouchard C, North KN, Williams AG, *et al.* Athlome Project Consortium: a concerted effort to discover genomic and other "omic" markers of athletic performance. *Physiological Genomics.* 2016;48(3):183-90. doi:10.1152/physiolgenomics.00105.2015.
4. Khera AV, Emdin CA, Drake I, Natarajan P, Bick AG, Cook NR, *et al.* Genetic Risk, Adherence to a Healthy Lifestyle, and Coronary Disease. *N Engl J Med.* 2016;375(24):2349-58. Epub 2016 Nov 13.
5. Faigenbaum AD, Stracciolini A, Myer GD. Exercise deficit disorder in youth: a hidden truth; *Acta Pædiatrica.* 2011;100: p. 1425.
6. Cummiskey Joseph, Micallef-Stefface Kirill, Lollgren, Herbert, Borjesson, Mats Zupet, Petra, Bachl, Norbert, Pigozzi, Fabio, Cummiskey, Andrew, Natsis, Kostas, Debruyne,Andre: Diagnosis of Exercise Deficiency. (In preparation)
7. Cummiskey J, Lollgen H, Zupet P, Borjesson M, Natsis K, Cummiskey A, *et al.* The Four "E" Pillars of Exercise Prescription for Health: The EFSMA program. *EuJSM.* 2016;4(1):1-11
8. Lees SJ, Booth FW. Sedentary death syndrome. *Can J Appl Physiol.* 2004; 29(4):447-6.
9. Löllgen H, Löllgen D. Körperliche Aktivität und Primärprävention. *Dtsch Med Wochenschr.* 2004;129(19):1055–6. doi: 10.1055/s-2004-824858
10. Löllgen HH. Pre-participation cardiovascular evaluation for athletic participants to prevent sudden cardiac death. *Europace.* 2017;19(5):882-3. doi: 10.1093/europace/eux012.
11. Löllgen H, Bachl N. Cardiovascular prevention and regular physical exercise: Activity and training as the true "polypill". *Herz.* 2016;41(8):664-70.
12. Zupet P, Löllgen H. Exercise prescriptions for Health and Training Recommendations. www.efsma-scientific.eu.2016

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