Physical activity, heritability and health in Finnish twins and male former elite athletes

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**Background and aims:** This long-term research project is based on the studies that have used the former Finnish elite athlete cohort (see Kujala et al. JAMA 1996;276:216-220 and Sports Med 2003;33:553-561) and the Finnish Twin Cohort as subjects (see Kujala et al. JAMA 1998;279:440-44). These longitudinal studies have shown that continuous physical activity is associated with reduced future morbidity and mortality, as well as a reduced need for hospital care and medication. However, these studies have also shown that selection issues including genetic pleiotropy explains some of the associations between baseline physical activity and future morbidity/mortality seen in follow-up observational studies. Some individuals have inherited high aerobic fitness and these subjects find it easy to exercise and have low metabolic syndrome risk factor levels. We use differing study designs and methods to investigate which detailed mechanisms of disease and health outcomes can really be influenced by exercise. In particular, it will be possible to investigate monozygotic twin pairs, who have had discordant physical activity habits for a long period during their adult life. This is done so that the overall effects of a long-term physically active lifestyle on different health outcomes, including obesity, disability, and mortality can be documented. This co-twin-control study design controls for genes and childhood family environment. We also study the effects of specific genes. We carry out these studies in collaboration with the University of Helsinki. Subgroups of the twins (such as physical activity discordant twin pairs) and former athletes have participated in clinical investigations in Jyväskylä.

**Cohorts and selected findings:** We use different target groups (healthy vs. chronically ill; physically active vs. inactive). The main target group, the older Finnish Twin Cohort, includes all same-sex twin pairs born in Finland before 1958 and with both co-twins having been alive in 1967. Of the cohort members, 15 904 subjects (7811 men and 8093 women) were at work and apparently healthy in 1981, supplied complete questionnaire data on the intensity of their physical leisure activity in 1975 and 1981, and were aged 24 to 60 years (see Kujala et al. Am J Epidemiol 2002;156:985-993). Regarding this cohort, we are investigating how persistent (1975, 1981 and 1990) work-related loading and physical leisure activity are related to the need for medicating metabolic syndrome diseases, using the Finnish reimbursable medication register. We also use other Finnish registers to determine the disease-free life expectancy by physical activity history among the cohort. Pairwise analyses of the discordant physical activity twin-pair members make it possible to adjust for genes. The apparently healthy baseline study cohort includes 3551 (1756 male and 1815 female) dizygotic pairs and 1772 (823 male and 949 female) monozygotic pairs. In a clinical sub-study of those 146 same-sex twin pairs who had discordant levels of physical leisure activity (both in terms of participation in vigorous activity and volume of activity in 1975 and 1981), we in Jyväskylä first carried out a detailed telephone interview about the continuation of physical activity, occurrence of diseases and disability (see Waller et al. Int J Obesity 2008;32:353-361 and Med Sci Sports Exerc 2010;42:658-664) and continued with a series of detailed clinical examinations (TWINACTIVE study; see Leskinen et al. Int J Obesity 2009;33:1211-1218 and Ma et al. J Bone Mineral Res 2009;24:1427-1433). These studies have in particular shown the beneficial effects of long-term physical activity on body composition, including reduction of ‘high risk’ ectopic fat and improved adipocyte function. Further, we have extended this research by using metabolomics platform to show the multi-dimensional metabolic effects of exercise (Kujala et al. Circulation 2013;127:340-348). Recently, we have also carried out studies with younger twin cohorts using rather similar research designs and focusing on
disease prevention (FITFATTWIN study). These studies have shown that reducing physical activity is a strong risk factor for obesity (Rottensteiner et al. Obesity 2014;22:20161-2070) and that physical activity has an effect on brain morphology already at young adulthood (Rottensteiner et al. Med Sci Sports Exerc 2015;47:509-518). The latest MOBILETWIN study data collection included objective monitoring of physical activity in 800 73-year-old twins investigating predictors of later life mobility (see: bioRxiv 205856; doi: https://doi.org/10.1101/205856).

Among male former elite athletes, their brothers and baseline healthy controls we have studied selection issues and the associations between different types of physical activity and fitness characteristics on later health issues.

**Methods:** Our measurements include: objective physical activity monitoring, neuropsychological functioning, cardiovascular/aerobic fitness and muscle strength, body composition, including visceral fat measured by MRI, systolic and diastolic function of the left ventricle measured by echocardiography; the status of macroscopic arteries measured by contrast-enhanced MR-angiography; brain morphology measured by MRI; a very detailed series of metabolic-syndrome related parameters from blood samples, metabolomics, histological and gene expression studies of skeletal muscle and adipose tissue; and properties of bone measured by peripheral quantitative computed tomography. Muscle biopsy samples are used for muscle fibre typing, microscopical ectopic fat storage documentation, gene expression analyses, and immunological protein level analyses. All these deepen our understanding of the associations between genetic selection, physical activity, and the development of chronic disease.

**Collaborators:** For the names of the collaborators, see the list of selected publications. The main national collaborators are the University of Helsinki, Finnish Twin Cohort study (PI Jaakko Kaprio), and the National Public Health Institute.

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**Selected publications from the project:**

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2016


2015


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