
Effects of 32-Year Leisure Time Physical Activity Discordance in Twin Pairs on Health (TWINACTIVE Study): Aims, Design and Results for Physical Fitness

Tuija Leskinen,¹ Katja Waller,¹ Sara Mutikainen,¹ Sari Aaltonen,¹ Paula H. A. Ronkainen,¹ Markku Alén,^{1,2} Sarianna Sipilä,¹ Vuokko Kovanen,¹ Merja Perhonen,³ Kirsi H Pietiläinen,^{4,5} Sulin Cheng,¹ Harri Suominen,¹ Heikki Kainulainen,⁶ Jaakko Kaprio,^{4,7} and Urho M Kujala¹

¹ Department of Health Sciences, University of Jyväskylä, Finland

² Department of Medical Rehabilitation, Oulu University Hospital and Institute of Health Sciences, University of Oulu, Finland

³ CorusFit Oy, Jyväskylä, Finland

⁴ Department of Public Health, University of Helsinki, Finland

⁵ Obesity Research Unit, Helsinki University Central Hospital, Finland

⁶ Department of Biology of Physical Activity, University of Jyväskylä, Finland

⁷ Department of Mental Health and Alcohol Research, National Public Health Institute, Helsinki, Finland

The physically active lifestyle is associated with low future morbidity and mortality, but the causality between physical activity and health is not always clear. As some inherited biological characteristics and childhood experiences may cause selection bias in observational studies, we sought to take them into account by identifying 16 twin pairs (7 MZ, 9 DZ, mean age 60 years) discordant for leisure time physical activity habits for thirty years. We conducted detailed health-related examinations among these twin pairs. Our main aims were to study the effects of physical activity and genes on fitness and body composition, with special reference to body fat compartments, metabolic syndrome components and related diseases and risk factor levels, status of arteries, structure and function of the heart, bone properties, and muscle and fat tissue-related mechanisms linked to physical activity and chronic disease development. Our physical activity assessments showed that inactive co-twins were on average 8.8 MET hours/day less active than their active co-twins through out their midlife (2.2 ± 2.3 vs. 11.0 ± 4.1 MET h/day, $p < .001$). Follow-up fitness tests showed that physically inactive co-twins were less fit than their active co-twins (estimated VO_{2peak} 26.4 ± 4.9 vs. 32.5 ± 5.5 ml/kg/min, $p < .001$). Similar differences were found in both MZ and DZ pairs. On the basis of earlier epidemiological observations on nonrelated individuals, these physical activity and fitness differences are large enough to cause differences in many mechanisms and risk factors related to the development of chronic diseases and to permit future analyses.

Keywords: physical activity, fitness, twin study

Various studies have shown that physical fitness and participation in physical activity have a genetic component (Beunen & Thomis, 1999; Bouchard et al., 1986; Stubbe et al., 2006). The genetic component of physical activity may be shared with that of chronic diseases. Some inherited biological characteristics may both make it easier for some individuals to achieve high levels of physical activity or fitness and favor them with low morbidity or with longevity (Kujala et al., 2002; Kujala et al., 2003; Morris et al., 1956). Consequently, it is difficult to estimate the true extent of the effect of physical activity on delaying morbidity or mortality from observational follow-up studies of nonrelated individuals. Randomized controlled trials (RCTs) indicate that exercise is a powerful means of enhancing fitness and reducing disability among elderly subjects with or without chronic diseases; however less is known about the actual progression of diseases (Kujala, 2004).

When studying the associations between physical inactivity/activity and health outcomes we are faced with two specific issues: (1) genetic selection may explain some of the associations between baseline physical activity and morbidity/mortality in observational follow-up studies, and (2) RCTs that investigate the effects of exercise on health outcomes are usually of a too-short duration to document the long-term effects on health. The latter often use proxy measures and biomarkers as risk indicators. To tackle these limitations in

Received 2 June, 2008; accepted 21 November, 2008.

Address for correspondence: Urho M. Kujala, Department of Health Sciences, University of Jyväskylä, PO Box 35 (LL), FIN-40014, Finland. E-mail: urho.m.kujala@jyu.fi

our study design, we investigated monozygotic (MZ) and dizygotic (DZ) twin pairs, discordant for leisure time physical activity (LTPA) habits, to document the specific effects/associations of long-term physical activity on different health outcomes while controlling for genes and childhood family environment.

This study protocol article reports the aims and design of the TWINACTIVE study and results for physical fitness.

Background and Main Aims of the TWINACTIVE Study

We have previously used the Finnish Twin Cohort (Kaprio et al., 2002) to investigate whether genes or other familial factors cause selection bias in epidemiological studies of the associations between physical activity and future morbidity and mortality. In this cohort results from both individual-based analyses and pairwise analyses of DZ twin pairs discordant for physical activity show that baseline physical activity is associated with reduced future premature mortality (Kujala et al., 1998; Kujala et al., 2002). However, the fact that we were not able to confirm this by studying MZ twin pairs persistently discordant for physical activity (Kujala et al., 2002) suggests that genetic selection may play a role. In relation to specific diseases, we have found that among MZ twin pairs discordant for physical activity type 2 diabetes mellitus develops earlier among physically inactive twins

when compared to their physically active co-twins (Kujala et al., 2000). In addition, among male MZ pairs, physically active twins tend to have less coronary heart disease compared to their inactive co-twins (Kaprio et al., 2000).

To obtain a more detailed picture of the effects of physical activity and genetic factors on health, we identified middle-aged MZ and DZ twin pairs discordant for LTPA habits for 30 years and conducted detailed health-related examinations among these twin pairs. We were interested in the effects of physical activity and genes on fitness, body composition, with special reference to body fat compartments, metabolic syndrome components and related diseases and risk factor levels, status of arteries, structure and function of the heart, bone properties, and muscle and fat tissue-related mechanisms linked to physical activity and the development of chronic disease (see Table 1 for measures and outcomes).

We hypothesized that long-term physical activity would be found to have beneficial effects on many of the studied variables and outcomes among the MZ pairs discordant for physical activity. The existence of some intra-pair differences among the discordant DZ pairs, but not among the MZ pairs, would indicate the presence of a genetic component. We also hypothesized that skeletal muscle properties, known to be influenced by genes, would be associated with different metabolic syndrome features and these

Table 1

Timetable of Data Collection During Laboratory Visits in 2007

VISIT 1	
Before	Structured instructions for the measurements. Assessments of 5-d diet and 7-d activity using diaries.
Day 1	
11 am	Blood sample.
12 pm	Standardized interview to assess smoking habits, use of alcohol, dietary habits and exercise attitudes.
1 pm	Echocardiography of cardiac cavity, wall dimensions, systolic and diastolic function of left ventricle.
1.45 pm	Standardized clinical examination. Assessment of medication and health status.
2.15 pm	Resting electrocardiography.
2.30 pm	Symptom-limited maximal clinical exercise test.
3.15 pm	Maximal isometric left knee extensor strength, and left and right hand grip strength measurement.
4 pm	Measure of properties of bone by peripheral quantitative computed tomography.
10 pm	Fast begins.
Day 2	
7.30 am	Anthropometric measurement and assessment of body composition using bioelectrical impedance.
8 am	Fasting blood and DNA sample in order to study atherogenic and metabolic abnormalities.
8.15 am	Oral glucose tolerance test.
8–10 am	Standardized LTPA interview to assess leisure time MET index.
12 pm	MR imaging from abdomen and thigh. MR angiography of macroscopic arteries.
VISIT 2	
Before	Structured instruction of exercise before/after biopsy. Overnight fast.
Day 3	
8–10 am	Muscle and subcutaneous adipose tissue biopsies for histological, biochemical and gene expressional studies.

associations may partly explain why DZ twins are more discordant for physical activity than MZ twin pairs. In agreement with earlier cross-sectional data, we have already documented in longitudinal studies on unrelated individuals that skeletal muscle properties (in particular proportion of type I muscle fibers) predict different components of metabolic syndrome in men (Hernelahti et al., 2005; Karjalainen et al., 2006).

Subjects and Methods

Baseline LTPA Questionnaires

The Finnish Twin Cohort includes same-sex twin pairs born in Finland before 1958 and with both co-twins alive in 1975 (Kaprio et al., 2002). In the cohort, there were 1772 MZ, 3551 DZ and 340 twin pairs with unknown zygosity composing the cohort who were 24 to 60 years old, employed and healthy in 1981 (Kujala

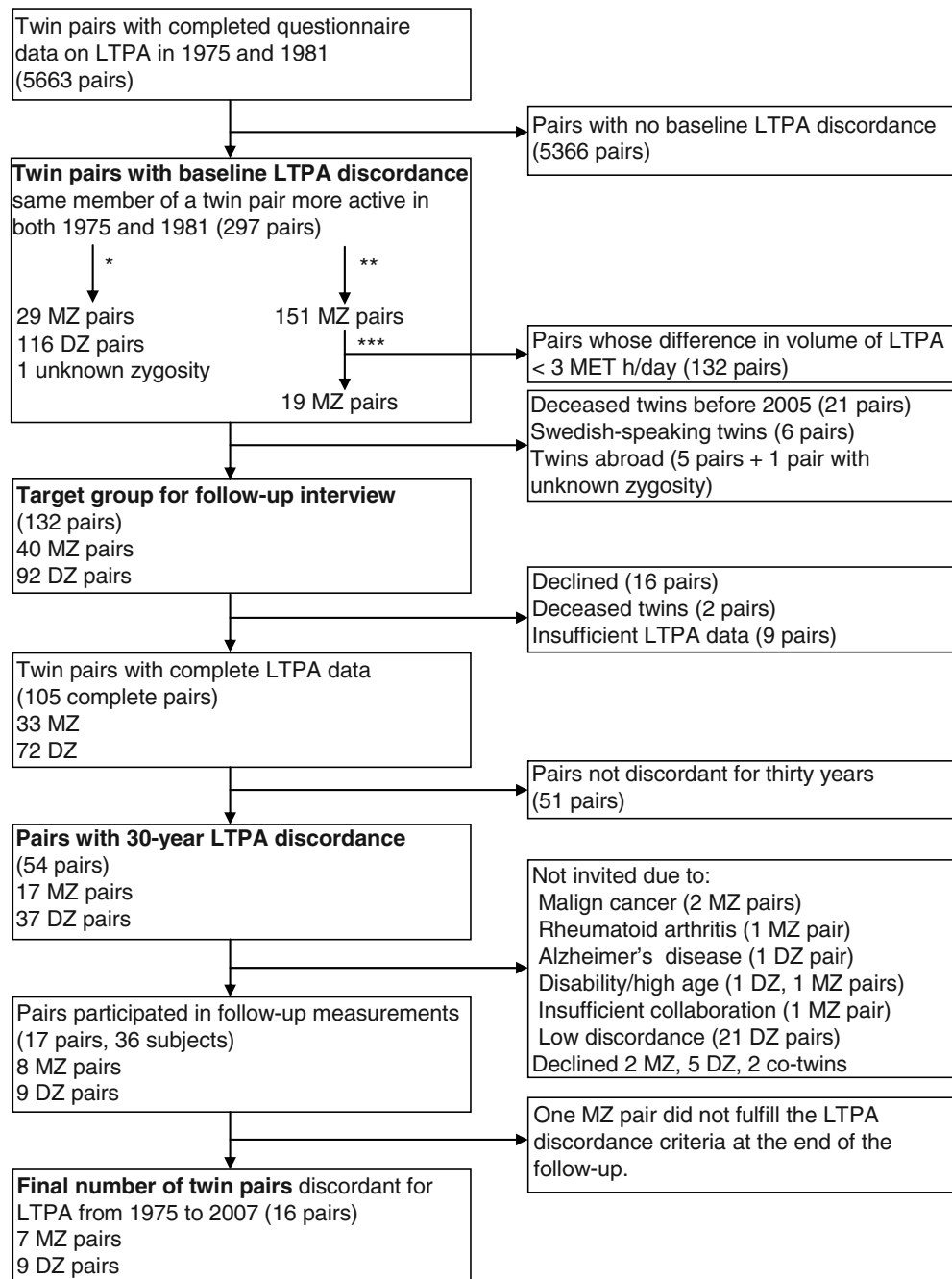


Figure 1

Flow chart of the comprehensive selection of twin pairs discordant for leisure time physical activity (LTPA).

Note: *Baseline discordance in volume (2 MET criteria) and intensity of LTPA (see text)

**Baseline discordance only in volume of LTPA (2 MET criteria) (see text)

***Baseline discordance in volume of LTPA (3 MET criteria) (see text)

et al., 2002). They all had completed the LTPA questionnaire administered in 1975 and in 1981 (Figure 1).

Assessment of LTPA volume (leisure time MET index) was based on a series of structured questions on leisure activity and physical activity during journeys to and from work (Kujala et al., 1998). The leisure time MET index was then calculated by assigning a multiple of the resting metabolic rate to each form of physical activity (intensity of activity \times duration of one session \times monthly frequency), which was then expressed as a sum score of leisure time MET hours/day. Assessment of the intensity of activity was based on the following question: Is your physical activity during leisure time about as strenuous on average as: (1) walking, (2) alternately walking and jogging, (3) jogging, (4) running? Those who chose 2, 3 or 4 were classified as engaging in vigorous activity (Kujala et al., 1998).

After calculating the leisure time MET indices, we found that 146 pairs (29 MZ, 116 DZ, and 1 unknown zygosity pair) were discordant for LTPA both in participation in vigorous activity and in volume of activity both in 1975 and 1981 (Figure 1). The criterion for the baseline discordance was that one co-twin was physically active (calculated leisure time MET index was > 2 MET h/day corresponding to about 30 min walking per day) while his/her co-twin was less active (leisure time MET index < 2 MET h/day) in both assessments (Kujala et al., 2002; Waller et al., 2008).

To increase the number of LTPA discordant MZ twin pairs, we set up another selection criterion and found that 151 MZ pairs were discordant in volume of activity (2 MET criteria as described above, vigorous activity discordance ignored). Among these MZ pairs, we selected only those 19 MZ pairs whose difference in volume of activity was > 3 MET h/day between the inactive and active co-twin in both 1975 and 1981, while the average intensity of a physical activity session was the same or greater in the active vs. inactive co-twin (Figure 1). This resulted in 165 comprehensively selected twin pairs (48 MZ, 116 DZ, 1 unknown zygosity pair) with baseline discordance for LTPA. These twin pairs constituted a target group for our follow-up interview on midlife LTPA habits. As our aim was to investigate the health effects of

physical activity in twin pairs with long-term persistent discordance for LTPA, pairs not persistently discordant for LTPA were excluded during later stages of the study (described later).

Follow-Up LTPA 1980–2005 Interview

Follow-up interviews were carried out during the years 2005–2007 with 132 twin pairs (40 MZ, 92 DZ pairs) as only those pairs were included in which both co-twins were still alive, lived in Finland, and spoke Finnish as their mother tongue. In total, 105 twin pairs (33 MZ, 72 DZ pairs), that is, 80% of available targeted pairs, completed the physical activity assessment section in the follow-up interviews (Figure 1).

The telephone interview included questions on current and past physical activity (for more details see Waller et al., 2008). In brief, physical activity was assessed by two sets of questions. The first shorter retrospective timeline assessment of LTPA volume and intensity (with 5-year intervals) was carried out using the same physical activity questions as in 1975 and 1981 (Figure 2). The mean MET index for all six time points from 1980 to 2005 was then calculated for both the inactive and active co-twins. To aid recall, twins were asked to describe their marital and work status for each year before the retrospective LTPA questions. The second set of questions was a detailed assessment of the volume of leisure time, daily (nonexercise activities such as gardening) and commuting activity over the previous 12 months (12-month MET index) using a modified version of the Kuopio Ischemic Heart Disease Risk Factor Study Questionnaire (Lakka & Salonen, 1997). As a result of these physical activity assessments, we found 17 MZ and 37 DZ twin pairs who, in addition to baseline discordance, were discordant for LTPA habits throughout the follow-up (i.e., 30 years).

Follow-Up Interview and Measurements in 2007

Before issuing an invitation to participate in the laboratory study measurements, we excluded pairs whose health status/medication would severely violate our study aims. Pairs were excluded for the following reasons: one co-twin had malign cancer (2 MZ pairs), oral corticosteroid treatment for rheumatoid arthritis (1 MZ pair), Alzheimer's disease (1 DZ pair), severe

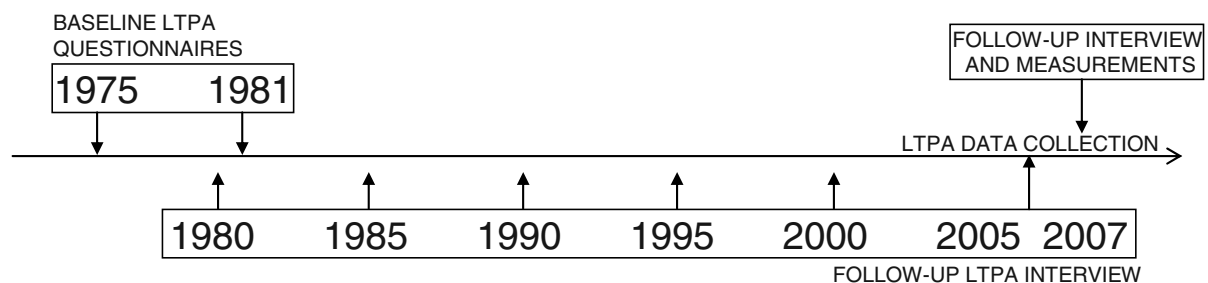


Figure 2

Timetable of physical activity and risk factor data collection.

disability/high age (1 DZ and 1 MZ pair) and insufficient collaboration (1 MZ pair). We also excluded 21 DZ pairs whose LTPA discordance was at the lowest level or not persistent. This procedure left us with 12 MZ and 14 DZ twin pairs. Of these 26 pairs who were invited to the laboratory, 8 MZ and 9 DZ twin pairs (overall 36 twin individuals) underwent our detailed health-related examinations.

Final Number of Twin Pairs

After careful intrapair examination of the leisure time MET indices from 1975 to 2007, we found that 7 MZ (5 male and 2 female pairs) and 9 DZ pairs (6 male and 3 female pairs) fulfilled our discordance criterion. In one MZ pair the leisure activity MET indices were higher among the previously inactive co-twin and lower among his previously active co-twin at the last follow-up assessment. This pair was excluded from the data analysis. The zygosity of the twins was verified at the Paternity Testing laboratory (National Public Health Institute, Helsinki, Finland) using DNA extracted from venous blood sample with a battery of ten highly polymorphic gene markers.

Physical Activity and Fitness Assessments

In the follow-up measurements, LTPA volume (leisure time MET index 2007) and participation in vigorous physical activity were assessed by the same questions as used at the baseline and in the retrospective assessment. Detailed assessment of the volume of leisure time and of daily and commuting activity over the previous 12 months (total 12-month MET index 2007) was also carried out (Lakka & Salonen, 1997). Smoking habits and use of alcohol were collected with diary, questionnaire and interview methods, as used earlier in the cohort (Kujala et al., 1998; Waller et al., 2008).

The symptom-limited maximal clinical exercise test with a cycle ergometer was performed for the assessment of cardiorespiratory fitness using a slightly modified WHO protocol (Lange-Andersen et al., 1971). The testing protocol comprised of 2-minute stages, beginning with a learning stage at 20 W and a warm-up stage at 25 W. Thereafter the increase in workload was 25 W/stage. The recovery stage was performed at 25 W and lasted at least 5 minutes. At the end of each stage, heart rate was recorded from the electrocardiogram, blood pressure was measured and testee was asked to rate their perceived exertion (Borg's scale 6–20). During the recovery stage, these measurements were performed at the end of 1, 3 and 5 minutes. Total exercise time, peak load, and estimated oxygen uptake (for calculation see Table 5) were used as indices of cardiorespiratory fitness.

Ethical Approval

This study was conducted according to good clinical and scientific practice/guidelines and the Declaration of Helsinki. The ethics committee of the Central Hospital of Central Finland approved our study plan on August 15, 2006.

Statistics

We used pairwise analyses to study differences between co-twins of the twin pairs. First we analyzed the results for all the twin pairs and then for MZ and DZ twin pairs separately to find out whether the trends were similar for MZ and DZ pairs. The normality of variables was assessed by the Shapiro-Wilk test. Student's paired *t* test was used for normally distributed variables. For non-normally distributed variables the Wilcoxon signed rank test was used. The symmetry test (Stata) was used for categorical variables. 95% confidence intervals (CI) were calculated for the absolute mean differences between inactive and active co-twins. The level of significance was set at $p < .05$. Data were analyzed using SPSS 14.0 and Intercooled Stata 8 software.

Results

Subject Characteristics

There were no baseline differences in 1975 for anthropometrics, marital status, alcohol use, smoking habits or work-related physical activity between inactive and active co-twins. Inactive co-twins were less active in their leisure time than their active co-twins (−3.1 MET h/day, 95% CI −4.2 to −1.9 MET h/day, $p < .001$; see Table 2).

There were no statistical differences in alcohol use, smoking habits, or in work-related physical activity between the inactive and active co-twins in 2007. Inactive co-twins weighed 6.5 kg more (95% CI −2.2 to 15.3, $p = .12$) on average and had a 1.9 kg/m² higher mean body mass index (95% CI −0.4 to 4.1, $p = .09$) than their active co-twins (Table 3).

Physical Activity Discordance

Physical activity discordance, which showed a decreasing trend with time during the retrospective follow-up (1980–2005), is illustrated in Figure 3. In 2007, the leisure time MET index was on average 6.9 MET h/day lower ($p < .001$) among inactive co-twins compared to their active co-twins, also in both MZ (−7.0 MET h/day, 95% CI −11.4 to −2.6, $p = .018$), and DZ pairs (−6.7 MET h/day, 95% CI −9.9 to −3.6, $p = .008$). During the LTPA follow-up period, from 1980 to 2007, the inactive co-twins were on average 8.8 MET h/day less active than their active co-twins ($p < .001$; see Table 4). The mean differences were similar for both MZ and DZ pairs (Table 4) and for female (−9.0 MET h/day, 95% CI −13.1 to −4.8, $p = .043$) and male (−8.8 MET h/day 95% CI −1.9 to −5.6, $p = .003$) pairs. Eight of the active co-twins, but none of the inactive co-twins, reported having participated in competitive sports during adulthood ($p = .005$).

When we assessed the volume of leisure time, daily and commuting activity over the previous 12 months (Lakka & Salonen, 1997), significant differences between inactive and active co-twins were found in total and leisure time physical activities but not in daily and commuting activities (Table 4). The trends were similar for MZ and DZ pairs. The two question-

Table 2

Baseline Characteristics in 1975

Characteristics	Inactive <i>N</i> = 16	Active <i>N</i> = 16	<i>p</i> value
Age (year; mean, range)	28 (18–42)		
Height (cm) (<i>N</i> = 15)	173.7 ± 9.8	172.9 ± 10.1	.57
Weight (kg)	69.3 ± 16.4	66.0 ± 9.4	.57
BMI (kg/m ²) (<i>N</i> = 15)	23.0 ± 4.2	22.3 ± 2.0	.88
Ever smoked regularly by 1975 (<i>N</i>)	6	9	.25
Leisure time MET index 1975 (h/day)	0.2 ± 0.3	3.3 ± 2.4	<.001
Alcohol (g/day)	6.0 ± 8.3	9.6 ± 12.8	.65
Marital status (<i>N</i>)			.37
Single	5	7	
Married	11	8	
Divorced	0	1	
Work related physical activity (<i>N</i>)			.23
Sedentary	3	7	
Standing or walking at work	3	4	
Light manual work	10	5	
Heavy manual work	0	0	
Occupational group (<i>N</i>)			.43
Upper white-collar	1	3	
Clerical work	5	5	
Skilled workers	4	6	
Unskilled workers	1	0	
Farmers	3	0	
Other	2	2	

Note: Data are mean ± *SD***Table 3**

Follow-up Characteristics Among Twin Pairs Discordant for LTPA in 2007

Characteristics	Inactive <i>N</i> = 16	Active <i>N</i> = 16	<i>p</i> value
Age (year; mean, range)	60 (50–74)		
Height (cm)	171.8 ± 10.4	171.1 ± 9.9	.63
Weight (kg)	79.5 ± 18.4	72.9 ± 11.9	.12
BMI (kg/m ²)	26.7 ± 3.5	24.8 ± 2.6	.09
Alcohol (g/day)	6.5 ± 4.7	10.3 ± 10.1	.16
Smoking (<i>N</i>)			.26
Current smokers	3	0	
Quitters	7	8	
Never smoked	6	8	
Work status (<i>N</i>)			.36
Employed	9	9	
Retired	5	5	
Unemployed	0	1	
Other	2	1	
Work-related physical activity (<i>N</i>)			.17
Sedentary	3	5	
Standing or walking at work	1	3	
Light manual work	5	0	
Heavy manual work	0	1	

Note: Data are mean ± *SD*

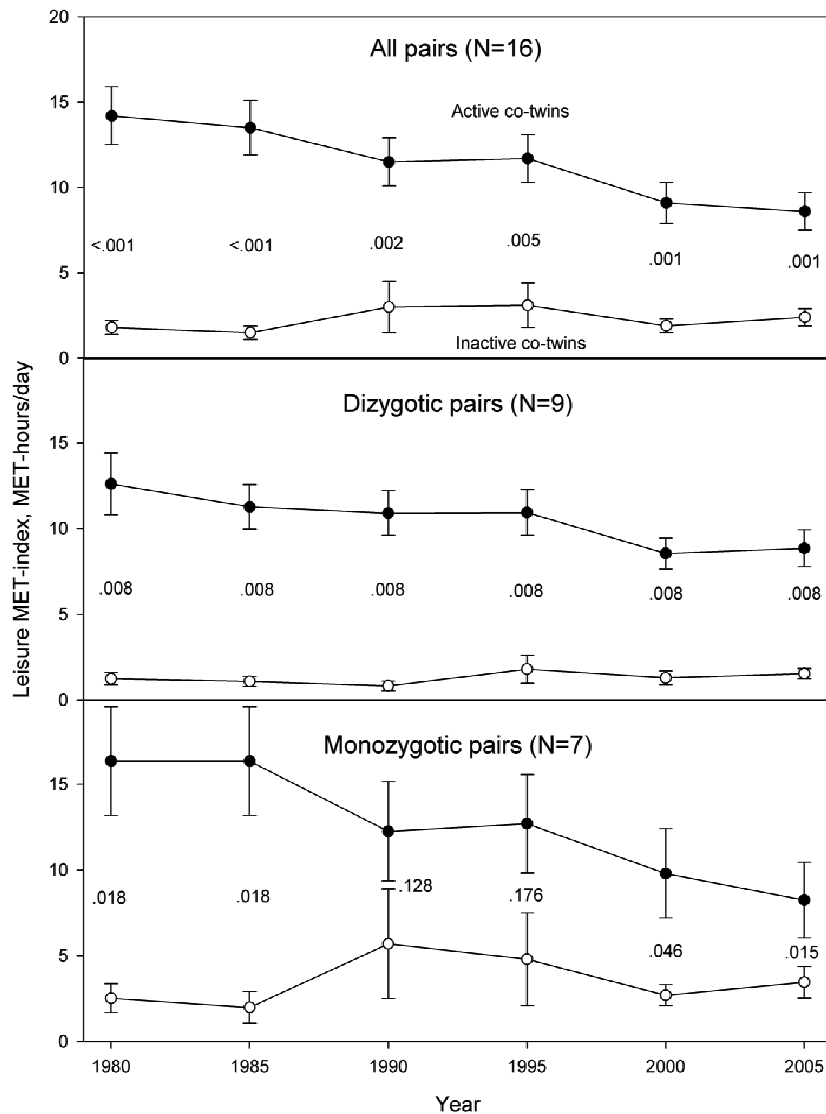


Figure 3

LTPA discordance in 1980–2005 on the basis of the retrospective telephone interview. Upper panel for all 16 pairs, middle panel for 9 DZ pairs, and lower panel for 7 MZ pairs. Results are shown as mean \pm SEM. Paired p values for statistical difference between inactive and active co-twins by Wilcoxon signed rank test.

naires on the volume of LTPA (the retrospective timeline vs. previous 12-month assessment) showed a good correlation ($r = 0.73$, $p < .001$, $N = 36$).

Physical Fitness

Statistically significant differences in fitness characteristics as measured by the symptom-limited maximal clinical exercise test were found between inactive and active co-twins (Table 5). Total exercise time was 144 seconds (2 min 24 s) shorter ($p = .002$) and achieved peak load 29.3 watts lower ($p = .003$) in inactive co-twins. Estimated peak oxygen uptake was also 6.1 ml/kg/min lower ($p < .001$) in inactive compared to active co-twins. The trends were similar for MZ and DZ pairs (Table 5) and for female (-6.4 ml/kg/min, 95% CI -11.6 to -1.2 , $p = .027$) and male (-5.9 ml/kg/min, 95% CI -10.0 to -1.9 , $p = .008$) pairs.

Fourteen out of 16 active co-twins achieved higher peak oxygen uptake than their inactive co-twins.

Comment

The overall aim of the TWINACTIVE study is to investigate the consequences of LTPA in comprehensively selected MZ and DZ twin pairs who have been discordant for LTPA habits during their adult lives. The present study reports the general aims and design of the TWINACTIVE study together with the LTPA and fitness data. LTPA discordance in leisure time activities was determined with repeated standardized questions. The mean MET difference throughout the follow-up was 8.8 MET h/day between inactive and active co-twins. This amount of METs (h/day) is the equivalent of a difference of 612.7 kcal (2611 kJ) in

Table 4
MET Indices (MET hours/day) Among Twin Pairs Discordant for LTPA

Variable	Inactive	Active	Mean difference (95% CI)	<i>p</i> value
All 16 pairs				
Mean MET index 1980–2007	2.2 ± 2.3	11.0 ± 4.1	–8.8 (–11.0 to –6.6)	< .001
Leisure time MET index 2007	1.6 ± 1.4	8.4 ± 4.1	–6.9 (–9.1 to –4.6)	< .001
Total 12-month MET index 2007	5.2 ± 4.4	9.6 ± 5.3	–4.4 (–7.0 to –1.8)	.003
Leisure time 12-month MET index	2.3 ± 1.8	7.2 ± 3.8	–5.0 (–7.1 to –2.9)	.002
Daily activity 12-month MET index	2.7 ± 3.8	2.1 ± 3.3	0.6 (–1.7 to 2.8)	.84
Commuting 12-month MET index	0.2 ± 0.4	0.2 ± 0.3	0.03 (–0.3 to 0.3)	.89
7 MZ pairs				
Mean MET index 1980–2007	3.4 ± 3.0	12.2 ± 5.4	–8.8 (–14.1 to –3.5)	.018
Leisure time MET index 2007	2.4 ± 1.4	9.4 ± 3.8	–7.0 (–11.4 to –2.6)	.018
Total 12-month MET index 2007	6.3 ± 6.0	10.5 ± 4.9	–4.2 (–8.2 to –0.2)	.063
Leisure time 12-month MET index	3.0 ± 2.2	9.1 ± 3.9	–6.1 (–9.9 to –2.3)	.028
Daily activity 12-month MET index	3.1 ± 4.9	1.4 ± 1.9	1.7 (–2.6 to 6.0)	.74
Commuting 12-month MET index	0.3 ± 0.6	0.05 ± 0.1	0.24 (–0.2 to 0.7)	.29
9 DZ pairs				
Mean MET index 1980–2007	1.3 ± 0.9	10.1 ± 2.8	–8.9 (–11.0 to –6.7)	.008
Leisure time MET index 2007	1.0 ± 1.0	7.7 ± 4.3	–6.7 (–9.9 to –3.6)	.008
Total 12-month MET index 2007	4.3 ± 2.6	8.8 ± 5.7	–4.6 (–8.9 to –0.2)	.021
Leisure time 12-month MET index	1.7 ± 1.2	5.8 ± 3.1	–4.1 (–6.9 to 1.3)	.021
Daily activity 12-month MET index	2.4 ± 2.8	2.8 ± 4.1	–0.3 (–3.4 to 2.7)	.95
Commuting 12-month MET index	0.1 ± 0.3	0.3 ± 0.4	–0.1 (–0.5 to 0.3)	.50

Note: Data are mean ± *SD*

Mean MET index 1980–2007, mean MET value from follow-up; Leisure time MET index 2007, leisure time MET index in 2007 according to retrospective questionnaire including journeys to and from work; Total 12-month MET index 2007, leisure time + daily (such as gardening) + commuting activities according to 12-month detailed physical activity questionnaire.

leisure time energy expenditure between inactive and active co-twins (173.3 ± 192.5 vs. 794.9 ± 303.3 kcal, 95% CI -783.8 to -459.5 , $p < .001$, when 1 MET corresponds to energy expenditure of 1 kcal/kg/h for the average adult). The activity level of inactive members of twin pairs corresponded to that of the most physically inactive 20% of the whole cohort, and the level of active co-twins to that of the active 50% of the whole cohort (Kujala et al., 1998), which means that the activity levels selected for study represent clinically relevant population groups. The inactive twins, again in both MZ and DZ pairs, were also less fit than their active co-twins, a finding that strongly supports the validity of our activity assessments.

On the basis of earlier epidemiological observations on nonrelated individuals, the intrapair differences in the level of physical activity observed in this study are large enough to cause differences in many mechanisms and risk factors related to the development of chronic diseases (Kelley & Goodpaster, 2001; Kohl, 2001) and mortality (Lee & Skerrett, 2001; Kujala et al., 1998). Myers et al. (2004) found that an increase in physical activity of 1000 kcal/week equals to an increase in fitness of 1 MET, and that these both conferred a mortality benefit of 20%. As several earlier studies have indicated, fitness differences also contribute to mortality and morbidity risk (Blair et al., 1989; Ekelund et al.,

1988; Gulati et al., 2003; Kokkinos et al., 2008; Lakka et al., 1994; Peters et al., 1983; Wei et al., 1999).

Physical activity interacts with a plethora of metabolic and health-related functions, which, like exercise capacity itself (Bouchard et al., 1998; Bouchard & Rankinen, 2001), are partly genetically regulated. Therefore, some of the associations between physical activity and metabolic and cardiovascular health may be explained by shared genetic factors. Our carefully identified twin pairs discordant for LTPA over 30 years represent a model that can be used to explore the long-term effects and underlying mechanisms of physical activity on metabolic and cardiovascular health, independent by genetic factors. The magnitude of the physical activity discordances found in this study is large enough to lay a foundation for such future analyses.

Acknowledgments

The authors wish to thank all the twins and Risto Puurtinen, Shumei Cheng, Aila Ollikainen, Erkki Helkala, Eeva-Maija Palonen, Kirsti Salo, Eija Pöllänen, and Mervi Matero for their skillful help in the study. TWINACTIVE study was supported by the Academy of Finland, Finnish Ministry of Education, Finnish Cultural Foundation (T.L.) and Juho Vainio Foundation.

Table 5
Physical Fitness Characteristics Among Twin Pairs Discordant for LTPA in 2007

Variable	Inactive	Active	Mean difference (95% CI)	p value
All 16 pairs				
Total exercise time (s)	663.1 ± 194.6	807.1 ± 201.7	-144.1 (-225.0 to -63.1)	.002
P _{peak} (W)	138.9 ± 39.9	168.1 ± 42.0	-29.3 (-46.5 to -12.0)	.003
P _{peak} /kg (W/kg)	1.8 ± 0.4	2.3 ± 0.5	-0.6 (-0.8 to -0.3)	< .001
P _{peak} /kg (W/FFM)	2.4 ± 0.5	3.0 ± 0.6	-0.6 (-0.9 to -0.2)	.002
VO _{2peak} ^a (ml/kg/min)	26.4 ± 4.9	32.5 ± 5.5	-6.1 (-9.0 to -3.2)	< .001
VO _{2peak} (ml/FFM/min)	33.6 ± 5.9	39.6 ± 6.3	-6.1 (-9.4 to -2.7)	.002
VO _{2peak} (ml/min)	2086.2 ± 520.0	2362.2 ± 510.4	-276.4 (-485.1 to -67.7)	.013
7 MZ pairs				
Total exercise time (s)	676.1 ± 175.1	830.9 ± 242.4	-154.7 (-303.5 to -5.9)	.044
P _{peak} (W)	140.9 ± 36.5	173.0 ± 50.4	-32.1 (-63.2 to -1.0)	.045
P _{peak} /kg (W/kg)	1.9 ± 0.5	2.3 ± 0.5	-0.4 (-1.0 to 0.1)	.083
P _{peak} /kg (W/FFM)	2.6 ± 0.6	3.0 ± 0.6	-0.4 (-0.9 to -1.9)	.099
VO _{2peak} ^a (ml/kg/min)	27.4 ± 5.3	32.2 ± 6.0	-4.8 (-10.5 to 0.9)	.083
VO _{2peak} (ml/FFM/min)	35.2 ± 6.6	39.7 ± 7.0	-4.5 (-10.0 to 1.1)	.099
VO _{2peak} (ml/min)	2090.5 ± 424.4	2433.9 ± 616.7	-343.4 (-665.4 to -21.4)	.040
9 DZ pairs				
Total exercise time (s)	652.9 ± 218.5	788.7 ± 177.1	-135.8 (-254.1 to -17.5)	.029
P _{peak} (W)	137.3 ± 44.5	164.3 ± 36.9	-27.0 (-52.5 to -1.5)	.041
P _{peak} /kg (W/kg)	1.7 ± 0.4	2.3 ± 0.5	-0.6 (-1.0 to -0.3)	.002
P _{peak} /kg (W/FFM)	2.3 ± 0.5	3.0 ± 0.6	-0.7 (-1.1 to -0.2)	.010
VO _{2peak} ^a (ml/kg/min)	25.7 ± 4.7	32.8 ± 5.4	-7.1 (-10.8 to -3.4)	.002
VO _{2peak} (ml/FFM/min)	32.3 ± 5.3	39.6 ± 6.2	-7.3 (-12.3 to -2.3)	.010
VO _{2peak} (ml/min)	2082.9 ± 609.8	2307.2 ± 442.0	-224.3 (-559.2 to 110.6)	.161

Note: Data are mean ± SD; P_{peak} load weighted for time exercised at highest load; FFM, fat free mass (kg); ^a(11.016 · P_{peak} / body mass) + 7 (ACSM, 2000).

References

- American College of Sports Medicine. (2000). *ACSM's guidelines for exercise testing and prescription* (6th ed.). Baltimore: Williams & Wilkins.
- Beunen, G., & Thomis, M. (1999). Genetic determinants of sports participation and daily physical activity. *International Journal of Obesity and Related Metabolic Disorders*, 23, S55-S63.
- Blair, S. N., Kohl, H. W. III, Paffenbarger, R. S. Jr, Clark, D. C., Cooper, K. H., & Gibbons, L. W. (1989). Physical fitness and all-cause mortality. A prospective study of healthy men and women. *The Journal of the American Medical Association*, 262, 2395-2401.
- Bouchard, C., Lesage, R., Lortie, G., Simoneau, J., Hamel, P., Boulay, M., Pérusse, L., Thériault, G., & Leblanc, C. (1986). Aerobic performance in brothers, dizygotic and monozygotic twins. *Medicine and Science in Sports and Exercise*, 18, 639-646.
- Bouchard, C., Daw, E., Rice, T., Pérusse, L., Gagnon, J., Province, M., Leon, A., Rao, D., Skinner, J., & Wilmore, J. (1998). Familial resemblance for VO_{2max} in the sedentary state: The HERITAGE family study. *Medicine and Science in Sports and Exercise*, 30, 252-258.
- Bouchard, C., & Rankinen, T. (2001). Individual differences in response to regular physical activity. *Medicine and Science in Sports and Exercise*, 33, S446-S451.
- Ekelund, L. G., Haskell, W. L., Johnson, J. L., Whaley, F. S., Criqui, M. H., & Sheps, D. S. (1988). Physical fitness as a predictor of cardiovascular mortality in asymptomatic North American men. The Lipid Research Clinics Mortality Follow-up Study. *New England Journal of Medicine*, 319, 1379-1384.
- Gulati, M., Pandey, D. K., Arnsdorf, M. F., Lauderdale, D. S., Thisted, R. A., Wicklund, R. H., Al-Hani, A. J., & Black, H. R. (2003). Exercise capacity and the risk of death in women: the St James Women Take Heart Project. *Circulation*, 108, 1554-1559.
- Hernelahti, M., Tikkanen, H.O., Karjalainen, J., & Kujala, U. M. (2005). Muscle fiber-type distribution as a predictor of blood pressure: A 19-year follow-up study. *Hypertension*, 45, 1019-1023.
- Kaprio, J., Kujala, U. M., Koskenvuo, M., & Sarna, S. (2000). Physical activity and other risk factors in male twin-pairs discordant for coronary heart disease. *Atherosclerosis*, 150, 193-200.

- Kaprio, J., Pulkkinen, L., & Rose, R. J. (2002). Genetic and environmental factors in health-related behaviors: studies on Finnish twins and twin families. *Twin Research*, 5, 366–371.
- Karjalainen, J., Tikkanen, H., Hernelahti, M., & Kujala, U. M. (2006). Muscle fiber-type distribution predicts weight gain and unfavorable left ventricular geometry: A 19-year follow-up study. *BMC Cardiovascular Disorders*, 6, 2.
- Kelley, D. E., & Goodpaster B. H. (2001). Effects of exercise On glucose homeostasis in Type 2 diabetes mellitus. *Medicine and Science in Sports and Exercise*, 33, S495–S501.
- Kohl, H. W. III (2001). Physical activity and cardiovascular disease: evidence for a dose response. *Medicine and Science in Sports and Exercise*, 33, S472–S483.
- Kokkinos, P., Myers, J., Kokkinos, J. P., Pittaras, A., Narayan, P., Manolis, A., Karasik, P., Greenberg, M., Papademetriou, V., & Singh, S. (2008). Exercise capacity and mortality in black and white men. *Circulation*, 117, 614–622.
- Kujala, U. M., Kaprio, J., Sarna, S., & Koskenvuo, M. (1998). Relationship of leisure-time physical activity and mortality: The Finnish twin cohort. *The Journal of the American Medical Association*, 279, 440–44.
- Kujala, U. M., Kaprio, J., & Koskenvuo, M. (2000). Diabetes in a population-based series of twin pairs discordant for leisure sedentariness. *Diabetologia*, 43, 259–263.
- Kujala, U. M., Kaprio, J., & Koskenvuo, M. (2002). Modifiable risk factors as a predictors of all-cause mortality: The roles of genetics and childhood environment. *American Journal of Epidemiology*, 156, 985–993.
- Kujala, U. M., Marti, P., Kaprio, J., Hernelahti, M., Tikkanen, H., & Sarna S. (2003). Occurrence of chronic disease in former top-level athletes. Predominance of benefits, risks or selection effects? *Sports Medicine*, 33, 553–561.
- Kujala, U. M. (2004). Evidence for exercise therapy in the treatment of chronic disease based on at least three randomized controlled trials: Summary of published systematic reviews. *Scandinavian Journal of Medicine & Science in Sports*, 14, 339–345.
- Lakka, T. A., Venäläinen, J. M., Rauramaa, R., Salonen, R., Tuomilehto, M., & Salonen, J. T. (1994). Relation of leisure-time physical activity and cardiorespiratory fitness to the risk of acute myocardial infarction. *New England Journal of Medicine*, 330, 1549–1554.
- Lakka, T. A., & Salonen, J. T. (1997). The physical activity questionnaires of the Kuopio Ischemic Heart Disease Study (KIHD). A collection of physical activity questionnaires for health-related research. *Medicine and Science in Sports and Exercise*, 29, S46–S58.
- Lange-Andersen, K., Shephard, R. J., Denolin, H., Varnauskas, E., & Masironi, R. (1971). *Fundamentals of exercise testing*. Geneva: WHO.
- Lee, I-M., & Skerrett, P. J. (2001). Physical activity and all-cause mortality: What is the dose-response relation? *Medicine and Science in Sports and Exercise*, 33, S459–S471.
- Morris, J. A., Morris, J. N., & Raffle, P. A. (1956). Physique of London busmen; Epidemiology of uniforms. *Lancet*, 271, 569–570.
- Myers, J., Kaykha, A., George, S., Abella, J., Zaheer, N., Lear, S., Yamazaki, T., & Froelicher, V. (2004). Fitness versus physical activity patterns in predicting mortality in men. *The American Journal of Medicine*, 117, 912–918.
- Peters, R. K., Cady, L. D., Bischoff, D. P., Bernstein, L., & Pike, M. C. (1983). Physical fitness and subsequent myocardial infarct in healthy workers. *The Journal of the American Medical Association*, 249, 3052–3056.
- Stubbe, J., Boomsma, D., Vink, J., Martin, N., Skytthe, A., Kyvik, K., Rose, R., Kujala, U. M., Kaprio, J., Harris, J., Pedersen, N., Hunkin, J., Spector, T., & de Geus, E. (2006). Genetic influences on exercise participation in 37,051 twin pairs from seven countries. *Plos One*, 1, e22.
- Waller, K., Kaprio, J., & Kujala, U. M. (2008). Associations between long-term physical activity, waist circumference and weight gain: A 30-year longitudinal twin study. *International Journal of Obesity*, 32, 353–361.
- Wei, M., Kampert, J. B., Barlow, C. E., Nichaman, M. Z., Gibbons, L. W., Paffenbarger, R. S. Jr, & Blair, S. N. (1999). Relationship between low cardiorespiratory fitness and mortality in normal-weight, overweight, and obese men. *The Journal of the American Medical Association*, 282, 1547–1553.