

Featured Article

Objectively measured physical activity profile and cognition in Finnish elderly twins

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Abstract

Introduction: We studied whether objectively measured physical activity (PA) and sedentary behavior (SB) are associated with cognition in Finnish elderly twins.

Methods: This cross-sectional study comprised twins born in Finland from 1940 to 1944 in the Older Finnish Twin Cohort (mean age, 72.9 years; 726 persons). From 2014 to 2016, cognition was assessed with a validated telephonic interview, whereas PA was measured with a waist-worn accelerometer.

Results: In between-family models, SB and light physical activity had significant linear associations with cognition after adjusting for age, sex, wearing time, education level, body mass index, and living condition (SB: β -estimate, -0.21 [95% confidence intervals, -0.42 to -0.003]; light physical activity: β -estimate, 0.30 [95% confidence intervals, 0.02 – 0.58]). In within-family models, there were no significant linear associations between objectively measured PA and cognition.

Discussion: Objectively measured light physical activity and SB are associated with cognition in Finnish twins in their seventies, but the associations were attributable to genetic and environmental selection.

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Keywords:

Cognition; Physical activity; Twins; Accelerometry; Dementia; Genetics; Exercise; Actigraphy; Sedentary behavior; Aged

1. Introduction

In recent years, studies of objectively measured physical activity (PA) using accelerometers have shown that not only low PA but also sedentary behavior (SB) predisposes to health hazards [1,2]. Most studies of PA and cognition are

based on self-reported PA. In such cross-sectional studies, PA has been associated with better cognition in the most robust studies ($n > 2000$ and a valid measure of PA and cognition) [3,4].

So far, only four studies appear to have assessed associations of objectively measured PA profiles with cognition in a cross-sectional study of an elderly population [5–8]. Kerr et al. [5] showed that moderate-to-vigorous physical activity (MVPA), measured using waist-worn accelerometers, was associated with a better processing speed and executive function performance ($n = 217$). Light physical

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activity (LPA), regardless of the amount, was not associated with cognition when models were adjusted for demographic variables. Barnes et al. [6] did not distinguish between the intensity of PA but found that elderly women in the lowest PA quartile performed worse on cognitive tests. In their study, PA was measured using a wrist-worn accelerometer in a large sample ($n = 2736$). The most extensive cross-sectional study of objectively measured PA and cognition is that of Zhu et al. ($n = 7098$) [7]. Using waist-worn accelerometers, they showed that higher levels of MVPA, but not LPA or sedentary time, were associated with better performance on cognitive tests in the elderly. These results were similar to the findings by Kerr et al. [5]. A smaller study (by Johnson et al. [8], $n = 188$, waist-worn accelerometer) contradicts the earlier findings. They found that LPA, but not sedentary time or MVPA, was associated with better executive functioning in community-dwelling older adults. Kerr et al. and Barnes et al. [5,6] did not analyze SB.

The majority of longitudinal studies on PA and cognition have relied on self-reported PA. A comprehensive meta-analysis of longitudinal studies provides support for the positive association of PA with a lower incidence of cognitive impairment [9]. Longitudinal studies of PA and cognition with objectively measured PA are scarce. Middleton et al. used doubly labeled water and calorimetry to measure energy expenditure during PA among 197 seniors with an average age of 75 years, with a follow-up of 5 to 8 years, and found a dose-response between higher baseline energy expenditure and a decreased incidence of cognitive impairment [10]. In one wrist-worn accelerometer study of 716 adults with an average age of 82 years at baseline, higher baseline levels of PA were associated with a reduced risk of Alzheimer's disease and mild cognitive impairment 4 years later [11]. In another study using waist-worn accelerometers, Zhu et al. found an association between baseline MVPA and later cognition, but no significant association of later cognition with baseline LPA or baseline sedentary time in their 3-year follow-up study that included 6452 older adults [12]. These short follow-up times imply that sub-clinical symptoms and signs of dementia may have affected the persons' motivation and ability to exercise, producing through reverse causality a spurious association or lack of it.

An association between PA and cognition may also be due to unmeasured confounders including genetic factors that are known to affect both cognition and PA [13]. One way of controlling for genetic confounding is to study relationships in twins, especially monozygotic twins who share the identical genomic sequences.

The aim of this study was to determine if subject's objectively measured PA and SB are associated with cognition in an elderly population of twins in Finland. Our twin study design enables us to assess the effect of genetics and child-

hood environment with separate between-family and within-family analyses.

2. Methods

2.1. Study population

Our study sample was selected from the Older Finnish Twin Cohort (FTC) study (Fig. 1). The FTC comprises all same-sex twins born before 1958, with both co-members alive in 1975 [14]. Comprehensive health questionnaires were sent to all cohort members in 1975 and in 1981. In 2014 to 2016, those born from 1940 to 1944 were interviewed using two cognition-screening telephonic interviews namely a telephonic assessment for dementia [15] and the Telephone Interview for Cognitive Status [16].

All those who participated in the telephonic cognition interview were offered the possibility of participating in an objective, 1-week PA and SB measurement with a waist-worn accelerometer (Hookie AM20; Traxmeet Ltd, Espoo). The accelerometer used a commonly used digital triaxial acceleration sensor (ADXL345; Analog Devices, Norwood, MA) and stored the raw acceleration signals with 100-Hz sampling frequency (± 16 g measurement range and 0.004 g measurement resolution). These measurements were performed in a mean of 3.4 weeks (standard deviation [SD], 5.5) after the cognition interviews. The participants' mean age at the time of the telephonic interview was 72.9 (range, 71.1–75.0) years. The number of twins with completed cognition interview, accelerometer monitoring, and full information on all covariates was 726 (including both twins from 250 twin pairs, of which 110 were monozygotic, 125 were dizygotic, and 15 of unconfirmed zygosity).

The questionnaire studies in 1975 and 1981 were approved by the National Board of Health of Finland. Answering and returning the questionnaire was considered as consent to participate in the study. During the course of the cohort study, the participants were repeatedly informed about the study and could withdraw from it at any time if they so wished. Written informed consent was obtained from all who participated in the telephonic interview. The cognition interview and the accelerometer part of the study were approved by the Ethics Committee of the Hospital District of Southwest Finland.

2.2. Measurements of PA and SB

The accelerometers with the instructions for their use were mailed to the participants who provided consent. The participants were instructed to use the accelerometer during their waking hours for 1 week. After this, the accelerometer was mailed back to the UKK Institute in a prepaid envelope for analysis. A recent study from the UKK Institute showed that the mean amplitude deviation of the resultant acceleration during a 6-s epoch is a valid metric for analyzing the raw triaxial data from different accelerometer brands to describe

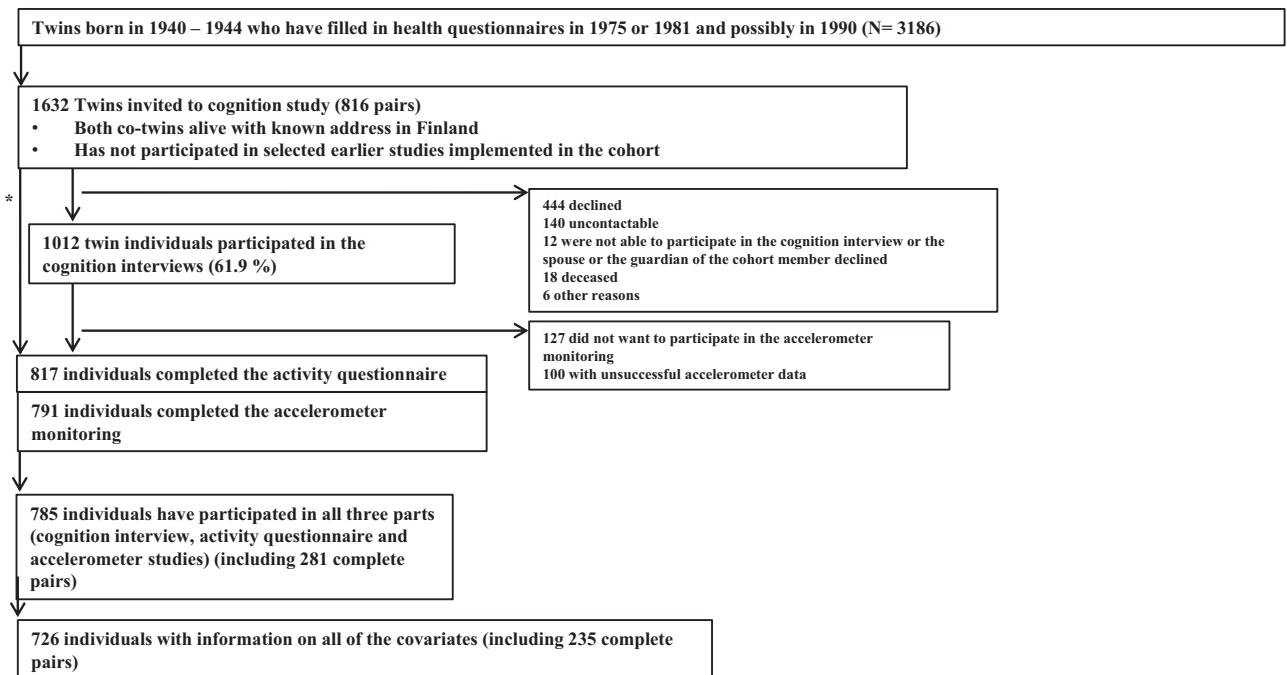


Fig. 1. Flowchart of the study. Six individuals did not finish cognition interview but participated in the accelerometer study (represented by the asterisk “*”).

PA and SB in a consistent manner [17]. The incident mean amplitude deviation values are strongly related to incident VO_2 during locomotion over a wide speed range on a flat surface [18]. Each mean amplitude deviation value was converted to metabolic equivalents (METs), and 1-minute exponential moving averages of these MET values were calculated for each epoch. Ambulatory activities were classified as LPA and MVPA according to the estimated MET level. Stationary activities were classified as lying, sitting, and standing using the recent validated method based on angle for posture estimation [19].

Different variables describing daily activity profile are the total time spent sitting or lying down (SB), LPA (1.5–2.9 MET), MVPA (≥ 3 MET), daily step count, and the mean daily MET describing the mean intensity of PA during the whole day. We required that there were accelerometer data on at least 10 hours for at least 4 days to be included in the analyses (Fig. 1).

2.3. Cognition and covariates

We used the total cognitive score to assess cognition [20], which was, a combination of the telephonic assessment for dementia and the Telephone Interview for Cognitive Status notwithstanding the converging items. Higher points indicated better cognition. Telephonic assessment for dementia and Telephone Interview for Cognitive Status are designed to differentiate between subjects with dementia and those with healthy cognition. They include questions testing orientation, serial subtraction, word recall, semantics, sentence repetition, linguistic skills, and attention. Both have been

validated in the Finnish population and correlate well with the results of the Mini Mental State Examination [21].

The covariates were age, sex, average daily wearing time of the accelerometer, education level, body mass index, and whether the subject was living alone or not at the time of the accelerometer study. The participants were instructed to wear the accelerometer during waking hours but to remove it during showers, saunas, or aquatic sports and when sleeping. The mean wearing time was the average wearing time per day when more than 30-minute periods without any measured movement of the accelerometer were excluded. The mean wearing time was 14 h 1 min, which is in line with the mean wearing time of about 14 h in a recent population-based study of Finnish adults [22]. The mean wearing time was used as a covariate only in the analyses of SB and the mean daily MET because some participants forgot to remove the device at night. A maximum of 20-hour recording per day was analyzed for these participants. Years of education were based on the data from the questionnaire answered in 1981 and 1975 [20]. The information on living conditions was asked in conjunction with the cognition interview and categorized as those who lived alone and those who lived with someone (a spouse, children or grandchildren, relatives, siblings, or other). The height (cm) and the weight (kg) of the participant were asked in a questionnaire mailed with the accelerometer.

In the comparison analysis of the study participants and the cohort members who did not participate, self-report data from the 1981 questionnaire were used [20]. Heavy drinkers consumed at least six drinks on one occasion at least

monthly [23,24]. The midlife PA level was compared using an index of metabolic energy expenditure (MET), which is based on self-report data of the intensity, frequency, and duration of PA participation [20].

2.4. Statistical analysis

We used linear regression analyses in between-family analyses (twins treated as individuals) and fixed-effect conditional linear regression analyses in the within-family analyses (twins compared with their co-twin; ergo intrapair differences in PA were regressed on intrapair differences in cognition). We reported regression coefficients with 95% confidence intervals for cognition according to the objectively measured PA and SB. Family structure of data was taken into account in all analyses of individuals (robust variance estimator for clustered twin data [25]). Within-twin pair analyses were controlled for environmental (in dizygotic and monozygotic twins) and shared genetic (in monozygotic twins) unmeasured factors shared by twins from the same family. We ran two models. Model 1 was adjusted for age, sex, and the daily wearing time of the accelerometer (for SB and the mean daily MET). Model 2, the final fully adjusted model, was further adjusted for education, body mass index in 2016, and living conditions in addition to the covariates used in model 1. Additional models were adjusted for the covariates from model 1 and for either body mass index in 2016 or for education level (results not shown for the purpose of clarity and because the main associations did not change).

The assumptions of linear regression were met. Interactions between PA and SB measures and sex were tested, and there were none. Post hoc analyses of the correlations

between education and objectively measured PA and SB were studied using Spearman's correlation. These additional analyses were performed because of interesting and different results between models 1 and 2. All the analyses were performed using the Stata 14.2 version software program.

3. Results

3.1. Cohort characteristics

The characteristics of the study sample and the study participants' time used in total MVPA, LPA, and SB; the mean daily MET; and the average daily step count are shown in Table 1 and Supplementary Table 2. The participants were usually community dwelling, ambulatory, older adults (mean age, 72.9 years; range, 70.3–75.0 years). The average cognitive score was 42.7 (SD, 3.7). The scatter plots and Spearman's correlation coefficients are shown for the total cognitive score and continuous variables in Fig. 2.

In comparison to the baseline characteristics of the cohort born between 1940 and 1944 (N = 3186, of whom 893 had died, emigrated, an unknown address, a duplicate record, or were revealed not to be a biological twin before the cognition study), the participants of the cognition study (n = 1012) were better educated and slimmer during midlife, and fewer were heavy drinkers or smokers during midlife. The twins who participated in the accelerometer study (n = 791) were also better educated, and fewer were heavy drinkers in midlife than the twins who completed the cognition interviews but did not participate in the accelerometer study (n = 221). No difference was seen between midlife PA levels between the participants of the accelerometer study (n = 791) and the baseline cohort (N = 3186).

Table 1
Characteristics of study cohort

Variable	The whole cohort (n = 726)	Men (n = 352)	Women (n = 374)
Age (y), mean (SD)	72.9 (1.0)	73.0 (1.0)	72.9 (0.9)
BMI (kg/cm ²), mean (SD)	26.1 (3.9)	26.1 (3.5)	26.1 (4.3)
Height (cm), mean (SD)	168.0 (8.9)	174.8 (6.4)	161.7 (5.7)
Weight (kg), mean (SD)	73.9 (13.4)	80.0 (12.3)	68.3 (11.9)
Total score, mean (SD)	42.7 (3.7)	42.3 (3.6)	43.0 (3.7)
Zygosity			
Monozygotic, n (%)	267 (35.9)	126 (35.8)	141 (37.7)
Dizygotic, n (%)	412 (57.8)	204 (58.0)	208 (55.6)
Zygosity unknown, n (%)	47 (6.2)	22 (6.3)	25 (6.7)
MVPA (min:s), mean (SD)	39:55 (28:04)	43:58 (30:12)	36:07 (25:22)
LPA (h:min), mean (SD)	2:55 (1:02)	2:53 (1:00)	2:58 (1:35)
SB (h:min), mean (SD)	8:57 (1:42)	9:23 (1:39)	8:51 (1:44)
The mean daily MET, mean (SD)	1.4 (0.1)	1.4 (0.2)	1.4 (0.1)
Daily step count, mean (SD)	6383 (3157)	6667 (3124)	6116 (3168)
Education (y), mean (SD)	8.7 (3.4)	8.6 (3.5)	8.9 (3.4)
Living			
Alone, n (%)	186 (25.6)	46 (13.1)	140 (37.4)
With a spouse, relatives, or friends, n (%)	540 (74.4)	306 (86.9)	234 (62.6)
Average wearing time of the accelerometer (h:min), mean (SD)	14:16 (1:20)	14:44 (1:22)	13:56 (1:19)

Abbreviations: BMI, body mass index; MVPA, moderate to vigorous physical activity; LPA, light physical activity; SB, sedentary behavior; SD, standard deviation.

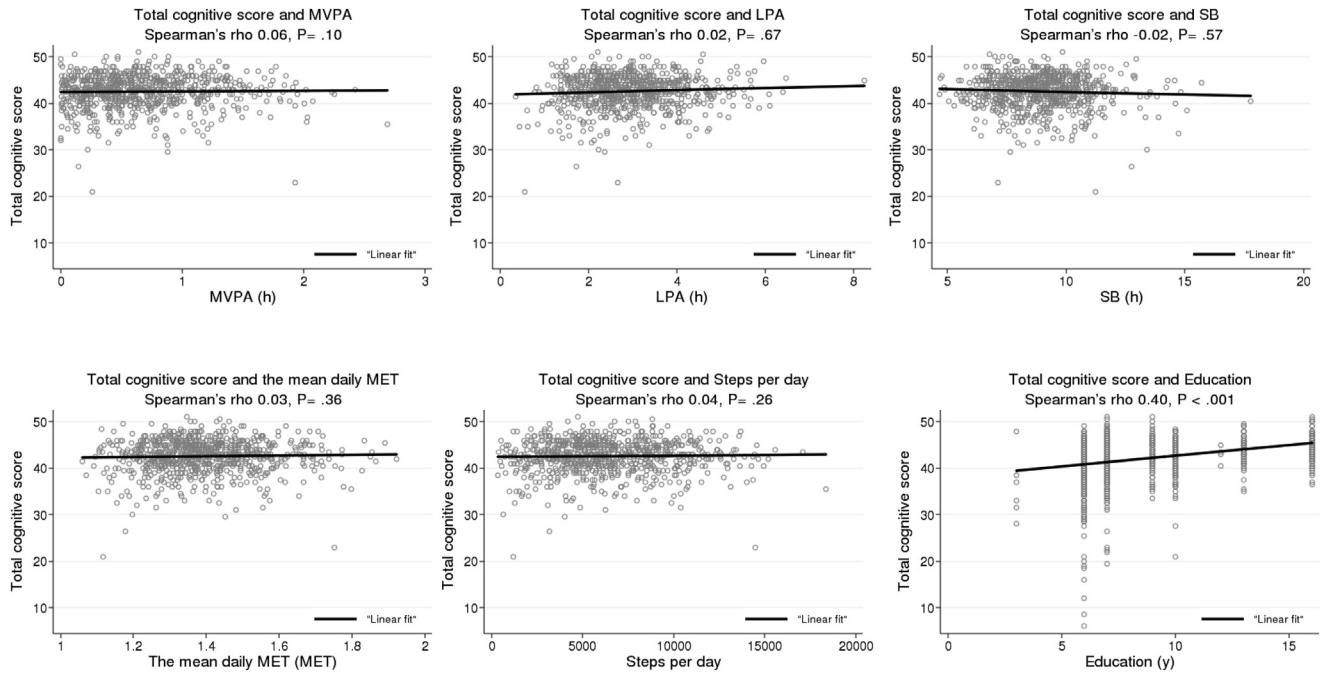


Fig. 2. Scatter plots and Spearman's correlation coefficients for total cognitive score and continuous variables. The y-axis represents total cognitive score on each plot, and the x-axis represents physical activity, sedentary behavior measurements, or information on education or BMI. Abbreviations: BMI, body mass index; MVPA, moderate to vigorous physical activity; LPA, light physical activity; SB, sedentary behavior; MET, metabolic equivalent.

3.2. Between-family analyses

In the between-family linear regression analyses of all individuals, the mean daily MET, MVPA, LPA, daily step count, and SB were not statistically significantly associated with cognition in model 1 (Table 2). In the final fully adjusted model (model 2), LPA and SB were significantly associated with cognition (LPA: β -estimate, 0.30 [95% confidence intervals, 0.02–0.58]; SB: β -estimate, -0.21 [95% confidence intervals, -0.42 to 0.003]).

3.3. Within-family analyses

In the within-family analyses of all twin pairs (adjusted for wearing time, SB, and the mean daily MET), MVPA,

LPA, SB, the mean daily MET, and daily step count were not significantly associated with cognition (Table 2) in either of the models. In separate within-family analyses of monozygotic or dizygotic twin pairs, no statistically significant results were found in the within-family models (Table 3).

3.4. Post hoc analyses

LPA had a significant negative correlation with education (ρ , -0.09; P = .02; Supplementary Table 1; n = 742). MVPA had a significant positive correlation with education. SB, the mean daily MET, and daily step count were not significantly associated with education.

Table 2
 β -Estimates for total cognitive score according to objectively measured PA

Level of PA	Between-family analyses		Within-family analyses	
	Model 1 (n = 726)	Model 2 (n = 726)	Age adjusted (n = 250 pairs)	Model 2 (n = 250 pairs)
All				
MVPA, h	0.18 (-0.51 to 0.88)	-0.30 (-1.00 to 0.39)	0.51 (-1.18 to 2.20)	0.20 (-1.64 to 2.04)
LPA, h	0.22 (-0.07 to 0.52)	0.30 (0.02 to 0.58)	0.60 (-0.21 to 1.42)	0.59 (-0.22 to 1.39)
SB, h	-0.20 (-0.41 to 0.01)	-0.21 (-0.42 to -0.003)	-0.42 (-1.00 to 0.15)	-0.40 (-1.00 to 0.19)
The mean daily MET	0.94 (-1.35 to 3.24)	0.21 (-2.15 to 2.57)	3.20 (-2.59 to 8.98)	2.40 (-3.98 to 8.51)
Daily step count (thousands)	0.04 (-0.07 to 0.15)	-0.002 (-0.11 to 0.10)	1.11 (-0.16 to 0.38)	0.08 (-0.19 to 0.35)

Abbreviations: MVPA, moderate to vigorous physical activity; LPA, light physical activity; SB, sedentary behavior; MET, metabolic equivalent; PA, physical activity.

NOTE: In between-family analyses, twin individuals were compared against each other. In within-family analyses, twins were compared to their co-twins, and intrapair differences in PA are regressed on intrapair differences in cognition. Model 1 is adjusted for age, sex, and the mean daily MET and SB also for the accelerometer wearing time. Model 2 is adjusted for age, sex, accelerometer wearing time (for SB and the mean daily MET), BMI in 2016, living condition, and years of education. The results written in bold are statistically significant.

Table 3
 β -Estimates for total cognitive score according to objectively measured PA in monozygotic and dizygotic twins

Level of PA	Within-family analyses	
	Model 1	Model 2
Monozygotic twins (n = 267 twins, 110 pairs)		
MVPA, h	0.29 (−1.98 to 2.56)	0.22 (−2.08 to 2.53)
LPA, h	0.95 (−0.30 to 2.20)	1.08 (−0.10 to 2.26)
SB, h	−0.74 (−1.63 to 0.15)	−0.77 (−1.61 to 0.08)
The mean daily MET	4.60 (−3.39 to 12.6)	4.82 (−2.62 to 12.3)
Daily step count (thousands)	0.06 (−0.26 to 0.38)	0.08 (−0.24 to 0.39)
Dizygotic twin (n = 412 twins, 125 pairs)		
MVPA, h	0.82 (−1.69 to 3.34)	0.56 (−2.35 to 3.46)
LPA, h	0.48 (−0.64 to 1.60)	0.39 (−0.74 to 1.53)
SB, h	−0.30 (−1.13 to 0.53)	−0.27 (−1.20 to 0.67)
The mean daily MET, MET	3.35 (−5.21 to 11.9)	2.66 (−7.94 to 13.3)
Daily step count (thousands)	1.12 (−0.31 to 0.57)	0.11 (−0.36 to 0.58)

Abbreviations: MVPA, moderate to vigorous physical activity; LPA, light physical activity; SB, sedentary behavior; MET, the metabolic equivalent of a task; physical activity.

NOTE: In within-family analyses, twins were compared to their co-twins, and intrapair differences in PA are regressed on intrapair differences in cognition. Model 1 is adjusted for age. For analysis of the mean daily MET and SB, model 1 also adjusts for the accelerometer wearing time. Model 2 is adjusted for age, BMI in 2016, living condition, and years of education. In addition, accelerometer wearing time was adjusted when analyzing SB and the mean daily MET.

4. Discussion

Our cross-sectional study of Finnish elderly twins shows that PA and SB are associated with cognition, but the association is attributable to genetic selection and environmental similarity between siblings. More LPA and less SB were significantly and linearly associated with better cognition in the individual-based analyses in the whole cohort. For example, a 1-hour increment of daily LPA augmented the total cognitive score by 0.30 points ($P = .036$; Cohen's $d = 0.08$). Thus, the effect can be considered small. The within-family analyses comparing each twin with their co-twin, however, showed no significant association between the objectively measured PA profile and cognition. This means that the association seen at an individual level is probably caused by selection—genetic, environmental, or a combination of both. The smaller number of participants in between-family analyses, however, might also explain the differing results in between- and within-family analyses to some extent. No association was seen for MVPA, mean daily MET, or daily step count and cognition in the between-family analyses or in the within-family analyses.

In between-family models of the whole cohort, SB and LPA had a significant association with cognition only in the final fully adjusted model (model 2) and in a model in which education alone was added to model 1 (adjusted for age, sex, and wearing time for SB). We checked the distribution of education in our data post hoc; the more educated participants engaged significantly less in LPA, but no significant difference was seen for SB between the more and less educated participants. This unexpected distribution is probably due to the different societal situations (after war) in Finland in the 1950s and 1960s when the cohort members

were of school age. Because the point estimates were also near the significance limit in model 1, the uneven distribution of education might explain the statistically nonsignificant results in model 1 of at least LPA.

Earlier cross-sectional studies on the objectively measured PA profile and cognition have showed varied results. Some studies have associated MVPA with better cognition [5,7] in the elderly, and one study associated LPA with better cognition [8]. Our study is in line with the study by Johnson et al. [8] because in our study, especially LPA intensities were also associated with better cognition. Johnson et al., however, tested executive function in distinction to our study assessing global cognition. Our study is unique in that we were able to show that the association is likely due to genetic and environmental selection.

Daily step count was not associated with cognition in any of the models in our study. This is in line with our finding that MVPA is not associated with cognition because all paces above 3 km/h fall into the category of MVPA, and thus, the daily step count can be considered to represent more MVPA than LPA, although it is a mixture of both. Previous cross-sectional studies with an objective measurement of PA did not report results regarding step counts [5–8].

PA has been shown to be beneficial for brain health in many ways in animal models and in epidemiologic studies assessing PA with questionnaires; it increases cerebral perfusion, ameliorates synaptic plasticity, and prevents vascular deterioration [26–28]. Objectively measured PA has been shown to be positively associated with hippocampal and temporal lobe volumes [29,30] and negatively associated with white matter lesions [31]. Our study, however, showed no independent association for PA with better cognition. Certainly, a cross-sectional analysis is not an adequate

measure of life-long engagement in PA, but the two are associated [32]. One possibility is that there is an independent association between PA and cognition, but it was not seen in our cohort because there was a slight trend toward better educated individuals with healthier lifestyles (less midlife smoking and binge drinking) in our cohort. In an unselected cohort with a larger variance of people and where people with a lower education level and who engaged in smoking and binge drinking were better represented, the results could have been different. Another possibility is that there is no independent association between PA and cognition, or at least, the association is more complex or not as strong as hypothesized. The evidence from epidemiologic studies showing that PA protects subjects from dementia and cognitive decline and showing that this negative association is low to moderate [9] may in fact be inflated due to hidden genetic and environmental selection. A similar phenomenon was seen in the association between PA and reduced mortality [33]. No independent association of PA with cognition seems unlikely as, for example, brain morphology and functional differences are seen in young adult monozygotic pairs discordant for PA [34,35].

4.1. Strengths and limitations

This study is the first to look at the association between objectively measured PA and SB profile and cognition in elderly participants in Finland. Besides the unique twin design, one of the strengths is the use of an accelerometer, which enabled objective and valid measurement of several traits of PA and SB as well as the monitoring of PA in individuals with impaired cognition. The telephonic interviews used in this study to assess cognition have been validated in a Finnish population and have a good correlation with the Mini Mental State Examination [21]. We also took into account several important confounding factors.

Our study also has limitations. Although accelerometers have obvious advantages in measuring accurately absolute exercise intensity and PA that includes movement-induced and ground-impact-induced accelerations on even ground, activity levels for many popular Finnish sports and exercises cannot be measured exactly. These sports include forest work (chopping wood), working out at the gym, cross country skiing and bicycling, or aquatic sports. However, many of these are likely recognized as MVPA although the actual intensity remains underestimated. Walking is, however, the preferred type of PA for the elderly [36]. Although we had a validated measure of cognition, a telephonic interview does not compensate for a thorough clinical examination, laboratory tests, and a broad neuropsychological battery accompanied by neuroimaging studies. The older cohort of the FTC study represents the Finnish population generally well. There was a slight trend toward a selection of better

educated participants from a higher social class who were less likely to engage in cigarette smoking and binge drinking in the accelerometer study cohort. Compared to an earlier study of objectively measured PA and SB in Finnish adults aged 18 to 85 years, the PA and sedentary profile was quite comparable in the oldest age group of 70 to 85 years. The amount of LPA was a bit higher in our study (approximately 2 h 55 min vs. approximately 2 h), the amount of MVPA was a bit lower (40 min vs. approximately 55 min), and the amount of SB was a bit higher (8 h 57 min vs. approximately 8 h) [22].

4.2. Conclusion

Objectively measured LPA and SB are associated with cognition in the elderly in Finland, but the association is likely to be attributable to genetic and environmental selection. Especially, LPA and less SB were associated with better cognition in the elderly in analyses of individuals—LPA positively and SB negatively. In within-family analyses of all twin pairs and in monozygotic and dizygotic twin pairs separately, there were no significant associations, meaning that the association seen in the between-family analyses could be the influence of similarity in genetics and childhood environment. Our study cohort was selected slightly toward those with a higher education level and healthier lifestyle; greater variance in this aspect might yield more distinct associations. Whether the earlier observed association in the literature between midlife PA and cognition is inflated by genetic and environmental selection should be clarified in future research, for example, in larger multicenter studies.

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Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.trci.2018.06.007>.

RESEARCH IN CONTEXT

1. Systematic review: A PubMed search to look for articles addressing objectively measured physical activity (PA) and cognition was undertaken. Only few of the studies on PA and cognition have used an objective measure of PA.
2. Interpretation: To our knowledge, this study is the first to look at the association of objectively measured PA and cognition with a twin design taking into account genetic and environmental selection. Our findings suggest that genetics and environmental similarity explain partly the association of PA and cognition in the earlier literature.
3. Future directions: Our results underline the importance of genetic and environmental similarity in assessing PA and cognition. There is a need for larger multicenter studies using genetically informative data such as families, twins, or Mendelian randomization studies to establish in which extent the association of PA and cognition seen in the earlier literature is explained by underlying genetic and environmental factors common to both PA and cognition.

References

- [1] Koster A, Caserotti P, Patel KV, Matthews CE, Berrigan D, Van Domelen DR, et al. Association of sedentary time with mortality independent of moderate to vigorous physical activity. *PLoS One* 2012; 7:e37696.
- [2] de Rezende LF, Rodrigues Lopes M, Rey-López JP, Matsudo VK, Luiz Odo C. Sedentary behavior and health outcomes: an overview of systematic reviews. *PLoS One* 2014;9:e105620.
- [3] Lam LC, Ong PA, Dikot Y, Sofiatin Y, Wang H, Zhao M, et al. Intellectual and physical activities, but not social activities, are associated with better global cognition: a multi-site evaluation of the cognition and lifestyle activity study for seniors in Asia (CLASSA). *Age Ageing* 2015;44:835–40.
- [4] Middleton LE, Barnes DE, Lui LY, Yaffe K. Physical activity over the life course and its association with cognitive performance and impairment in old age. *J Am Geriatr Soc* 2010;58:1322–6.
- [5] Kerr J, Marshall SJ, Patterson RE, Marinac CR, Natarajan L, Rosenberg D, et al. Objectively measured physical activity is related to cognitive function in older adults. *J Am Geriatr Soc* 2013; 61:1927–31.
- [6] Barnes DE, Blackwell T, Stone KL, Goldman SE, Hillier T, Yaffe K. Study of Osteoporotic Fractures. Cognition in older women: the importance of daytime movement. *J Am Geriatr Soc* 2008;56:1658–64.
- [7] Zhu W, Howard VJ, Wadley VG, Hutto B, Blair SN, Vena JE, et al. Association between objectively measured physical activity and cognitive function in older adults—the reasons for geographic and racial differences in stroke study. *J Am Geriatr Soc* 2015;63:2447–54.
- [8] Johnson LG, Butson ML, Polman RC, Raj IS, Borkoles E, Scott D, et al. Light physical activity is positively associated with cognitive performance in older community dwelling adults. *J Sci Med Sport* 2016; 19:877–82.
- [9] Blondell SJ, Hammersley-Mather R, Veerman JL. Does physical activity prevent cognitive decline and dementia?: A systematic review and meta-analysis of longitudinal studies. *BMC Public Health* 2014; 14:510.
- [10] Middleton LE, Manini TM, Simonsick EM, Harris TB, Barnes DE, Tylavsky F, et al. Activity energy expenditure and incident cognitive impairment in older adults. *Arch Intern Med* 2011;171:1251–7.
- [11] Buchman AS, Boyle PA, Yu L, Shah RC, Wilson RS, Bennett DA. Total daily physical activity and the risk of AD and cognitive decline in older adults. *Neurology* 2012;78:1323–9.
- [12] Zhu W, Wadley VG, Howard VJ, Hutto B, Blair SN, Hooker SP. Objectively measured physical activity and cognitive function in older adults. *Med Sci Sports Exerc* 2017;49:47–53.
- [13] Johnson W, Deary IJ, McGue M, Christensen K. Genetic and environmental links between cognitive and physical functions in old age. *J Gerontol B Psychol Sci Soc Sci* 2009;64:65–72.
- [14] Kaprio J, Koskenvuo M. Genetic and environmental factors in complex diseases: the older Finnish Twin Cohort. *Twin Res* 2002;5:358–65.
- [15] Gatz M, Reynolds CA, John R, Johansson B, Mortimer JA, Pedersen NL. Telephone screening to identify potential dementia cases in a population-based sample of older adults. *Int Psychogeriatr* 2002; 14:273–89.
- [16] Brandt J, Spencer M, Folstein M. The telephone interview for cognitive status. *Neuropsychiatry Neuropsychol Behav Neurol* 1988;1:111–7.
- [17] Vähä-Yppä H, Vasankari T, Husu P, Suni J, Sievänen H. A universal, accurate intensity-based classification of different physical activities using raw data of accelerometer. *Clin Physiol Funct Imaging* 2015; 35:64–70.
- [18] Vähä-Yppä H, Vasankari T, Husu P, Mänttari A, Vuorimaa T, Suni J, et al. Validation of cut-points for evaluating the intensity of physical activity with accelerometry-based mean amplitude deviation (MAD). *PLoS One* 2015;10:e0134813.
- [19] Vähä-Yppä H, Husu P, Suni J, Vasankari T, Sievänen H. Reliable recognition of lying, sitting and standing with a hip-worn accelerometer. *Scand J Med Sci Sports* 2018;28:1092–102.
- [20] Iso-Markku P, Waller K, Vuoksima E, Heikkilä K, Rinne J, Kaprio J, et al. Midlife physical activity and cognition later in life: A Prospective Twin Study. *J Alzheimers Dis* 2016;54:1303–17.
- [21] Järvenpää T, Rinne JO, Riihä I, Koskenvuo M, Löppönen M, Hinkka S, et al. Characteristics of two telephone screens for cognitive impairment. *Dement Geriatr Cogn Disord* 2002;13:149–55.
- [22] Husu P, Suni J, Vähä-Yppä H, Sievänen H, Tokola K, Valkeinen H, et al. Objectively measured sedentary behavior and physical activity in a sample of Finnish adults: a cross-sectional study. *BMC Public Health* 2016;16:920.
- [23] Kaprio J, Koskenvuo M, Langinvainio H, Romanov K, Sarna S, Rose RJ. Genetic influences on use and abuse of alcohol: a study of 5638 adult Finnish twin brothers. *Alcohol Clin Exp Res* 1987; 11:349–56.
- [24] Sipilä P, Rose RJ, Kaprio J. Drinking and mortality: long-term follow-up of drinking-discordant twin pairs. *Addiction* 2016;111:245–54.
- [25] Williams RL. A note on robust variance estimation for cluster-correlated data. *Biometrics* 2000;56:645–6.
- [26] Boraxbekk CJ, Salami A, Wählin A, Nyberg L. Physical activity over a decade modifies age-related decline in perfusion, gray matter volume, and functional connectivity of the posterior default-mode network—A multimodal approach. *Neuroimage* 2016;131:133–41.
- [27] Kandola A, Hendrikse J, Lucassen PJ, Yücel M. Aerobic exercise as a tool to improve hippocampal plasticity and function in humans:

- practical implications for mental health treatment. *Front Hum Neurosci* 2016;10:373.
- [28] Kivipelto M, Rovio S, Ngandu T, K areholt I, Eskelinen M, Winblad B, et al. Apolipoprotein E epsilon4 magnifies lifestyle risks for dementia: a population-based study. *J Cell Mol Med* 2008;12:2762–71.
- [29] Varma VR, Chuang YF, Harris GC, Tan EJ, Carlson MC. Low-intensity daily walking activity is associated with hippocampal volume in older adults. *Hippocampus* 2015;25:605–15.
- [30] Dougherty RJ, Ellingson LD, Schultz SA, Boots EA, Meyer JD, Lindheimer JB, et al. Meeting physical activity recommendations may be protective against temporal lobe atrophy in older adults at risk for Alzheimer's disease. *Alzheimers Dement (Amst)* 2016; 4:14–7.
- [31] Burzynska AZ, Chaddock-Heyman L, Voss MW, Wong CN, Gothe NP, Olson EA, et al. Physical activity and cardiorespiratory fitness are beneficial for white matter in low-fit older adults. *PLoS One* 2014; 9:e107413.
- [32] Hamer M, Kivimaki M, Steptoe A. Longitudinal patterns in physical activity and sedentary behaviour from mid-life to early old age: a sub-study of the Whitehall II cohort. *J Epidemiol Community Health* 2012; 66:1110–5.
- [33] Karvinen S, Waller K, Silvennoinen M, Koch LG, Britton SL, Kaprio J, et al. Physical activity in adulthood: genes and mortality. *Sci Rep* 2015;5:18259.
- [34] Tarkka IM, Savi c A, Pekkola E, Rottensteiner M, Leskinen T, Kaprio J, et al. Long-term physical activity modulates brain processing of somatosensory stimuli: Evidence from young male twins. *Biol Psychol* 2016;117:1–7.
- [35] Rottensteiner M, Leskinen T, Niskanen E, Aaltonen S, Mutikainen S, Wikgren J, et al. Physical activity, fitness, glucose homeostasis, and brain morphology in twins. *Med Sci Sports Exerc* 2015;47:509–18.
- [36] Lim K, Taylor L. Factors associated with physical activity among older people—a population-based study. *Prev Med* 2005;40:33–40.