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Timing of objectively-collected physical activity in relation to body weight and metabolic health in sedentary older people: a cross-sectional and prospective analysis

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BACKGROUND: Little is known about the impact of timing as opposed to frequency and intensity of daily physical activity on metabolic health. Therefore, we assessed the association between accelerometery-based daily timing of physical activity and measures of metabolic health in sedentary older people.
METHODS: Hourly mean physical activity derived from wrist-worn accelerometers over a 6-day period was collected at baseline and after 3 months in sedentary participants from the Active and Healthy Ageing study. A principal component analysis (PCA) was performed to reduce the number of dimensions (e.g. define periods instead of separate hours) of hourly physical activity at baseline and change during follow-up. Cross-sectionally, a multivariable-adjusted linear regression analysis was used to associate the principal components, particularly correlated with increased physical activity in data-driven periods during the day, with body mass index (BMI), fasting glucose and insulin, HbA1c and the homeostatic model assessment for insulin resistance (HOMA-IR). For the longitudinal analyses, we calculated the hourly changes in physical activity and change in metabolic health after follow-up.
RESULTS: We included 207 individuals (61.4% male, mean age: 64.8 [SD 2.9], mean BMI: 28.9 [4.7]). Higher physical activity in the early morning was associated with lower fasting glucose (−2.22%, 95% CI: −4.19, −0.40), fasting insulin (−13.54%, 95%CI: −23.49, −4.39), and HOMA-IR (−16.07%, 95%CI: −27.63, −5.65). Higher physical activity in the late afternoon to evening was associated with lower BMI (−2.84%, 95% CI: −4.92, −0.70). Higher physical activity at night was associated with higher BMI (2.86%, 95% CI: 0.90, 4.78), fasting glucose (2.57%, 95% CI: 0.70, 4.30), and HbA1c (2.37%, 95% CI: 1.00, 3.82). Similar results were present in the prospective analysis.
CONCLUSION: Specific physical activity timing patterns were associated with more beneficial metabolic health, suggesting particular time-dependent physical activity interventions might maximise health benefits.

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INTRODUCTION

Insufficient physical activity, which occurs frequently in our ageing and sedentary society [1–3], can aggravate misalignment of circadian rhythms that might consequently lead to obesity, diabetes mellitus, cardiovascular disease, cognitive decline, and premature mortality [3–8]. In 2020, the prevalence of overweight and obesity was 50.0% and 13.9% respectively in Dutch adults and even 58.1% and 16.5% respectively in adults aged 65 years and older [9]. Therefore, many current guidelines and interventions aim to increase physical activity to promote healthy living and decrease the obesity-associated disease burden.

Currently, many studies are focussed on duration, intensity and frequency of physical activity, and international guidelines recommend 150–300 min of moderate-intensity physical activity per week to maintain good health [10]. However, emerging evidence underlines a possible influence of timing of physical activity on weight control and (cardio)metabolic health [8, 11]. Although timing of physical activity is an aspect yet to be explored in further detail, studies comprising timing of other Zeitgebers (e.g. timing of nutritional intake and light exposure) have shown associations with weight loss [8, 12–15]. These studies particularly demonstrate that the impact on weight loss and perhaps on other aspects of metabolic health is not limited to the (average) amount of nutritional intake but also takes into account timing of behaviour. For example, de Cabo et al. showed the temporal effects on timing of meals across the day by intermittent fasting

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e.g. consuming all meals in an 8 h period [16]. The very few studies examining the impact of physical activity timing on health show that for example women who are less active in the morning, have an increased risk of obesity compared to women who were most active before noon [11].

As a result of evolving technology of accelerometery, more extensive analysis on for example timing of physical activity has been enabled [17–21]. However, recent studies are mainly focused on weight loss leaving other parameters of metabolic health uncharted [8, 11, 22]. Moreover, these studies applied a cross-sectional design which limits the validity of the findings. We hypothesised that particular timing of physical activity is associated with a more beneficial adiposity level and metabolic health status. Therefore, in the present study, we assessed the association between timing of physical activity and (changes in) weight and measures of metabolic health in a post-hoc analysis in relatively sedentary older people who were encouraged to increase their physical activity levels over a 3-month follow-up period [23].

METHODS

Ethical considerations

The Medical Ethical Committee of the Leiden University Medical Centre approved this study. Written informed consent was obtained from all study participants. The Active and Healthy Ageing (AGO) study was registered in the Dutch Trial Register (http://www.trialregister.nl) as NTR3045.

Study setting and population

This post-hoc study embedded in the AGO-study, was conducted between 2011 and 2012. Originally, this randomised controlled trial was designed to study the effect of a 3-month web-based intervention program which was designed to increase physical activity levels in sedentary older adults. A more detailed description of the study setting and selection of study population is published elsewhere [23]. In short, individuals were eligible for the study inclusion when they were [1] between 60 and 70 years of age [2], had no history of diabetes mellitus or use of glucose-lowering medication [3], had no disabilities compromising increase in physical activity, and [4] were in the possession of a personal computer with access to the internet. All eligible individuals were screened for the presence of a sedentary lifestyle with the General Practice Physical Activity Questionnaire (GPPAQ). Individuals within the GPPAQ categories 'inactive', 'moderately inactive', and 'moderately active' were grouped together as 'inactive' which was defined as having <3 h of exercise and cycling combined weekly [23]. Only inactive individuals were included in the study after meeting the respective inclusion criteria. In total, 235 individuals were successfully included and randomly assigned to either the intervention program or the control arm of the AGO study in which they were randomly allocated. Individuals in the intervention arm received a commercially available web-based physical activity program (DirectLife, Philips, Consumer Lifestyle, Amsterdam, the Netherlands) [23]. The control group was put on a waiting list and did not receive any specific instructions regarding daily physical activity.

In the present study, all participants with more than or equal to three (≥3) consecutive days of valid and complete wrist accelerometer data at baseline and after 3-month follow-up, and data on outcomes of interest to this study available in either the intervention or control group were included. Of the 235 participants that were included in the AGO intervention study, 14 participants were excluded in the present analyses due to missing accelerometery data either at baseline or at follow-up. After further (visual) inspection of the accelerometer output data, 12 participants who did not meet the criterium of either ≥3 measurement days ($n = 5$), an interrupted measurement period ($n = 1$), or a non-correctable mislabelling of body location of the accelerometer ($n = 6$) were excluded. Finally, we removed two participants without any clinical data, leaving a total of 207 participants (intervention group: $n = 105$) for analyses.

As the effect of the intervention on daily mean physical activity was minimal [23], and no meaningful differences were observed in timing at follow-up between the intervention and control arm (Supplementary Figs. 1 and 2), no distinction was made between the intervention and control group in the main analyses. We are aware of the role of confounding factors that might cause differences between participants from the intervention and control group (i.e. change of diet due to the intervention). Nonetheless, since our group is rather small, we analysed all participants that met acceleration wear time criteria jointly for sake of power, and performed sensitivity analyses of the prospective data in the intervention and control group separately.

Physical activity assessment

Physical activity was objectively measured at baseline and after 3-month follow-up using a wrist- and ankle-worn tri-axial accelerometer (GENEActiv, Kimbolton, Cambs, United Kingdom) for an average of 6 consecutive days. During this measurement period, the devices were worn for 24 h per day on the right wrist and ankle. For this study, the ankle data was not used since the used data extraction program is validated for wrist-worn accelerometers [20], Wearing time started on a random weekday and the device was returned to the research centre by standard mail. Measurement frequency on the devices was set at 85.7 Hz and raw acceleration values in "g" were recorded continuously.

Raw acceleration from the GENEActiv was then processed with the GGIR package (v. 2.0-0, https://cran.r-project.org/web/packages/GGIR/index.html) which is a validated and commonly used tool to process raw accelerometery data from wrist-worn accelerometers [20, 24]. This package includes automatic calibration, abnormality detection and multiple data smoothening steps. Acceleration was summarised with metric Euclidean Norm Minus One with values set to zero (ENMO) and is shown in milligravity (*mg*) (1 $mg = 0.00981$ m/s $-$ ^{2}). 24 hourly means were calculated based on all measurement days for both baseline and after 3-months follow-up. In addition, minutes spent in activity intensities were calculated to give insight in activity levels of the study population. Daytime physical activity was defined as physical activity during waking hours as calculated by GGIR. Wake time activity was defined as all waking activity during a 24 h period (daytime activity + waking activity during sleep period time). Thresholds for activity intensities were: inactivity, <30 mg; light, 30–99 mg; moderate, 100–399 mg; vigorous, ≥400 mg.

Body composition assessment

Data on anthropometrics was collected at baseline and after 3-months follow-up. Body height (in meters) was measured without shoes using a stadiometer and body weight (in kilograms) was assessed without shoes using a measurement scale. Body mass index (BMI in kg/m^2) was calculated from body weight and height and fat percentage (in kg) was assessed by bio-electrical impedance (BIA) analysis using a commercial portable device with hand-to-foot single frequency measurement (Biostat 1500, Euromedix, Leuven, Belgium) [23].

Measurements of metabolic variables/biochemical assessments

Fasting blood samples were drawn from each participant at both visits in the morning. Samples were transferred to the laboratory within 2 h, divided into single-use aliquots, and frozen at −80 °C. All serum measurements were performed in one batch after completion of the entire study with fully automated equipment. Fasting glucose (mmol/L) was determined using the Modular P2 analyser (Roche, Almere, the Netherlands), fasting serum insulin (mU/L) using immunoassay by Immulite 2500 (DPC, Los Angeles, CA, USA), and glycated haemoglobin (HbA1c in mmol/mol Hb) was determined by high performance liquid chromatography (Primus Ultra2, Trinity Biotech Company, Kansas City, MO, USA). The homeostatic model assessment for insulin resistance (HOMA-IR) was calculated by multiplying fasting glucose in mmol/L with fasting serum insulin in mU/L and dividing by 22.5 [25]. For the longitudinal analysis, the changes in all outcome variables were used as dependent variables.

Statistical analyses

Characteristics of the study population were presented as median (with interquartile range, IQR) for numerical data or N (%) for categorical data.

A principal component analysis (PCA) was performed to reduce the number of dimensions (e.g. define periods instead of separate hours) of hourly physical activity. This analysis produces uncorrelated summary variables of hourly physical activity capturing periods of physical activity. These new 'compatibility' scores characterise an individual's behaviour. For the cross-sectional analysis, we used the hourly mean acceleration data from the first visit. For the longitudinal analysis, we calculated the change of hourly mean acceleration between baseline and 3-months follow-up by subtracting the follow-up means from the baseline means ($\Delta = ENMO_{visit2} - ENMO_{visit1}$).

Moreover, change in all outcome variables (BMI, fat percentage, fasting glucose, fasting insulin, HbA1c, and HOMA-IR) was calculated by subtracting the follow-up measurement from the baseline measurement ($\Delta = \text{Value}_{\text{visit2}} - \text{Value}_{\text{visit1}}$). Principal components with an Eigenvalue ≥1 were considered relevant. The rotated component matrix (rotation method: Varimax, Kaiser Normalisation) was examined and clusters were established by interpreting this matrix. We considered the hours that had a factor loading of ≥0.4 in the interpretation of the component.

Subsequently, multivariable linear regression analyses were carried out to assess the associations between the calculated physical activity clusters and all outcome variables. All associations were adjusted for age and sex. This analysis was done for the cross-sectional data as well as the longitudinal data. For the longitudinal analysis, the changes in the outcome variables were used as dependent variables. All outcome variables, baseline variables and changes, were log transformed prior to the analysis to approximate a normal distribution. Subsequently, data was retransformed into a percentage difference in order to facilitate the clinical interpretation of the results. Additionally, to examine whether the found associations were explained by weight or weight loss after 3 months of follow-up, we corrected for BMI in the analyses for fasting glucose, fasting insulin and HOMA-IR. The longitudinal analyses were performed for the total study population as well for the intervention and control group separately, but we acknowledge that sample size became limited.

All statistical analyses were performed with SPSS Statistics v24 (IBM Corp, Armonk, NY, USA). Results were reported as the difference in outcome measure per SD increase in the principal component with accompanied 95% confidence interval (CI).

RESULTS

Participant characteristics

Participant characteristics are shown in Table 1. The median age of the total population was 65 (IQR: 62.2–67) years. The majority of participants were men (61.4%). On average, participants were overweight with a median BMI of 28 (IQR: 25.7–31.1) kg/m^2, and spent approximately 660 (SD: 89.6) minutes inactive.

Cross-sectional examination of physical activity timing and metabolic health characteristics

Based on the baseline hourly physical activity assessments, five largely nonoverlapping, correlated (>0.4) components with an Eigenvalue ≥1 were identified with consecutive periods of hourly physical activity (Supplementary Table 1). Notably, between 0:00 and 5:00 (defined as 'night'), between 4:00 and 9:00 (early morning), between 8:00 and 16:00 (morning and afternoon), between 15:00 and 22:00 (late afternoon to evening), and between 22:00 and 1:00 (late evening) (Fig. 1a).

Results of the baseline analyses are presented in Fig. 2. Higher physical activity at night was associated with higher BMI (2.86%, 95% CI: 0.90, 4.78), higher fasting glucose (2.57%, 95% CI: 0.70, 4.30), and higher HbA1c levels (2.37%, 95% CI: 1.00, 3.82). We found that six participants were active at night (defined as having one hourly average acceleration between 0:00 and 5:00 higher than or equal to 30 mg). To ensure these participants did not influence the latter results, we did additional sensitivity analyses in which these participants were excluded (Supplementary Table 2). This analysis showed that the results did not change notably. Furthermore, participants who were more active in the early morning had a lower fat percentage (−2.33%, 95% CI: −4.19, −0.50), lower fasting glucose levels (−2.22%, 95% CI: −4.19, −0.40), lower fasting insulin (−13.54%, 95% CI: −23.49, −4.39), and lower insulin resistance (−16.07%, 95% CI: −27.63, −5.65). Higher activity in the morning and afternoon, was associated with a lower BMI (per 1 SD increase in physical activity component: −2.22%, 95% CI: −4.29, −0.20), lower fasting insulin (−9.97%, 95% CI: −19.72, −1.01), and lower HOMA-IR (−10.96%, 95% CI: −22.02, −0.80). However, the association with fasting insulin diminished after adjusting for BMI (Supplementary Table 3). Higher physical activity in the late afternoon and evening was associated with lower BMI and fat percentage (−2.84%, 95% CI: −4.92, −0.70; −1.82%, 95% CI: −3.77, 0.00, respectively), but not with insulin, Hb1Ac and HOMA-IR. Similar results were observed for higher physical activity in the late evening (BMI: −2.02%, 95% CI: −3.98, 0.00, fat percentage: −1.82%, 95% CI: −3.67, −0.10). The association observed with fasting insulin remained after adjusting for BMI (Supplementary Table 3).

Table 1. Characteristics of the study population at baseline.

Characteristics	Baseline	Changes after follow-up Δ
N	207	207
Age, (years)	65 (62.2–67)	
Women (n,%)	80 (38.6)	
Body composition		
BMI (kg/m^2)	28 (25.7–31.1)	−0.2 (−0.8–0.1)
Fat percentage (kg)	34.4 (30.1–42.5)	−0.3 (−1.6–1.1)
Biochemistry		
Fasting venous glucose (mmol/L)	5.6 (5.2–6.1)	−0.2 (−0.2–0.1)
Fasting insulin (mU/L)	11.1 (7.6–17.3)	−0.9 (−3.5–1.2)
HbA1c (mmol/mol Hb)	34.9 (33.1–36.8)	−0.2 (−1.1–0.6)
HOMA-IR	2.8 (2.8–4.4)	−0.3 (−1.1–0.3)
Physical activity		
Daytime		
Inactivity (min)	660 (89.6)	−1.6 (72.7)
Light (min)	238.1 (55.6)	4.8 (48.3)
Moderate (min)	82.3 (35.7)	10.7 (28.11)
Vigorous (min)	1.5 (0.6–2.9)	0.5 (3)
Wake time		
Inactivity (min)	712.3 (90.6)	−0.1 (71)
Light (min)	243.3 (55.6)	5.1 (48)
Moderate (min)	83.6 (36.2)	10.6 (27.9)
Vigorous (min)	1.5 (0.6–2.9)	0.5 (3.1)

Physical activity data represents the 24 h mean from the complete measurement period (3–6 days). Daytime physical activity was defined as physical activity during waking hours as calculated by GGIR. Wake time activity was defined as all waking activity during a 24 h period (daytime activity + waking activity during sleep period time). Thresholds for activity intensities were: inactivity, <30 mg; light, 30–99 mg; moderate, 100–399 mg; vigorous, ≥400 mg. Follow-up data are presented as the change of variables from baseline to follow-up ($\Delta = \text{Value}_{\text{visit2}} - \text{Value}_{\text{visit1}}$). Follow-up measurements were done 12 weeks after baseline. Data presented as number n proportion (%); mean (SD); median (25–75th percentile).

n number of participants, *BMI* body mass index, *HOMA-IR* homeostatic assessment model for insulin resistance.

Longitudinal examination of physical activity timing and metabolic health characteristics

Table 1 also shows the difference in characteristics after 3 months of follow-up. Notably, a median improvement in almost all metabolic parameters was seen after three months of follow-up (e.g. Δ Fasting insulin = −0.9 mU/L IQR: −3.5–1.2).

In the PCA on the change in physical activity, eight components with an Eigenvalue ≥1 were identified (Supplementary table 4). The values of the eight components correlated with changes in physical activity representing the following periods; between 0:00 and 4:00 (night), between 4:00 and 7:00 (late night/early morning), between 6:00 and 9:00 (early morning), between 8:00 and 12:00 (late morning), between 12:00 and 17:00 (afternoon), between 17:00 and

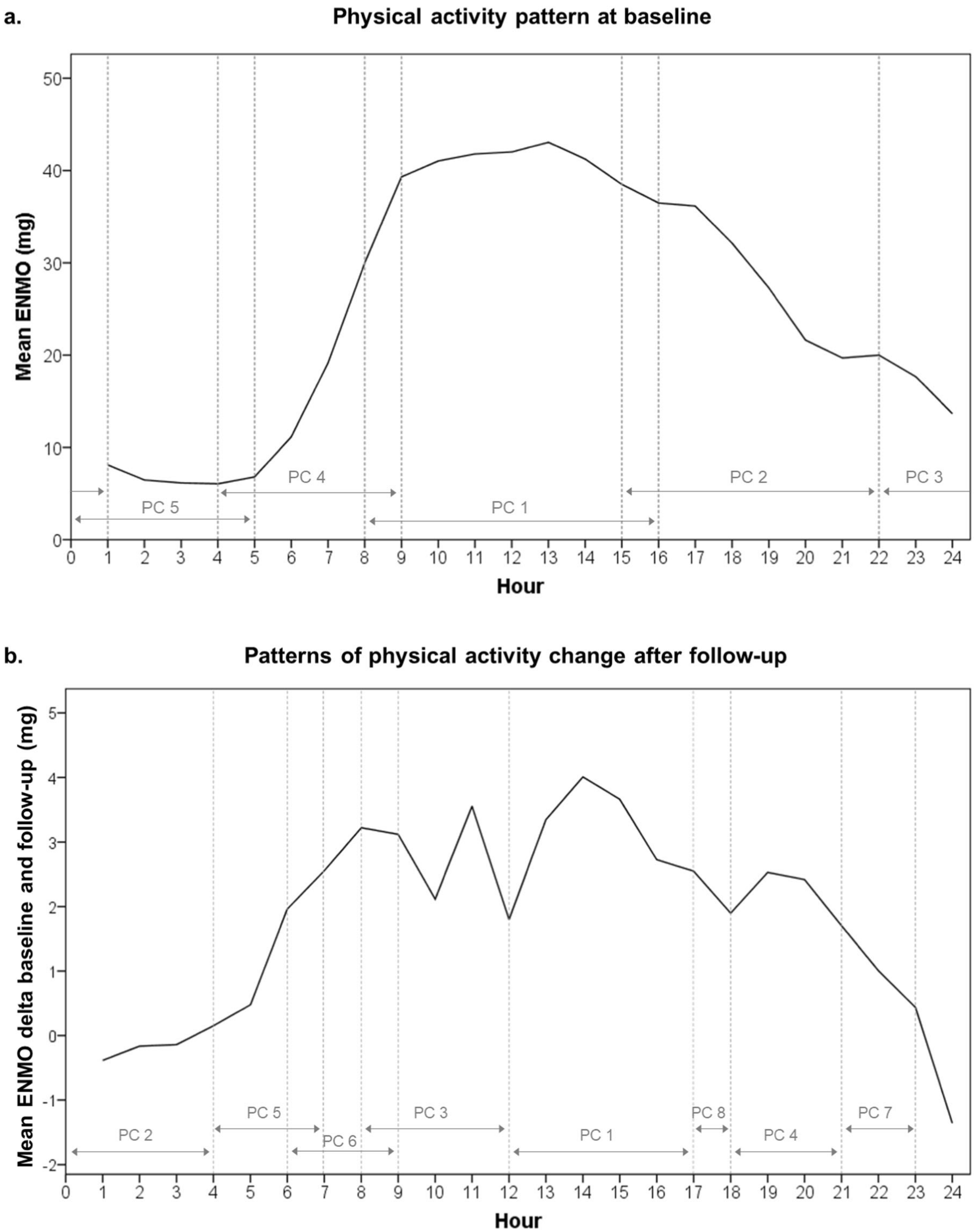

Fig. 1 Characteristics in (changes in) physical activity in the study population. a Shows the average pattern of acceleration at baseline accompanied by principal components (PC) of physical activity timing. **b** Shows the average pattern of physical activity change after 3 months of follow-up accompanied by principal components of change in physical activity timing. The *x*-axis presents the 24 daily hours (from midnight to midnight). The *y*-axis presents the mean acceleration calculated through euclidean norm minus one (ENMO) and presented as milligravity (mg).

18:00 (late afternoon), between 18:00 and 21:00 (early evening), and between 21:00 and 23:00 (late evening) (Fig. 1b).

Results from the multivariable-adjusted linear regressions are shown in Fig. 3. Participants with increased physical activity at night showed a higher increase in HbA1c levels after 3 months of follow-up (0.90%, 95% CI: 0.20, 1.59). Similar to the baseline analysis, these results were apparent in all outcome variables. Increased physical activity in the late night/early morning was associated with a greater decrease of BMI and fat percentage during follow-up (−0.40%, 95% CI: −0.80, 0.00, −1.41%, 95% CI: −2.53, −0.30). Participants who became more active in the late morning had a greater decline in levels of fasting insulin and insulin resistance (−7.68%, 95% CI: −14.22, −1.61), −7.90, 95% CI: −15.14, −1.01, respectively). The association with fasting insulin

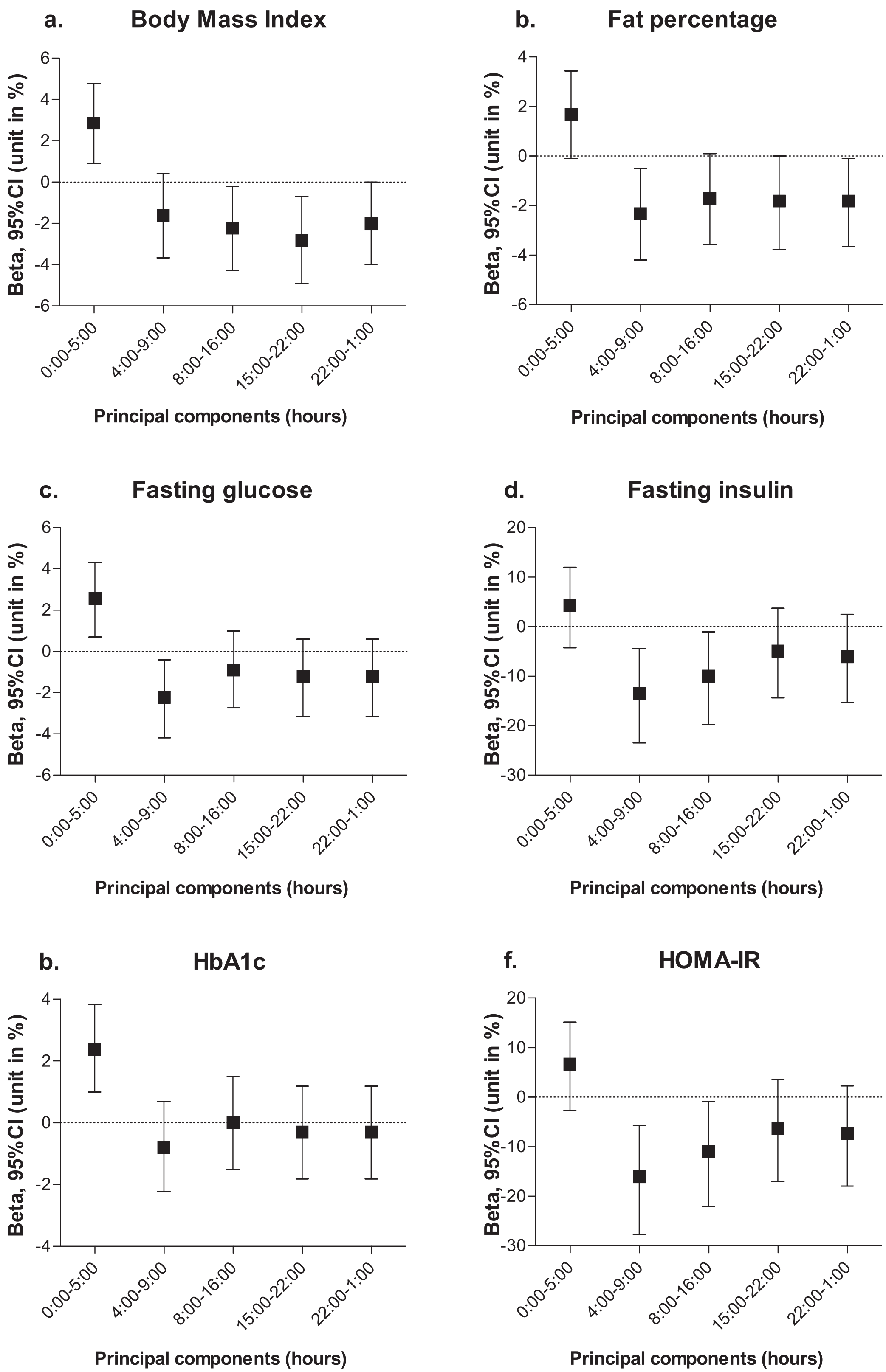

Fig. 2 The associations between the individual variables of metabolic health and the principal components (PC) representing the baseline physical activity. The associations between periods of timing of physical activity (derived with principal component analyses) and the individual variables of metabolic health results are displayed as the percentage difference in outcome (with accompanying 95% confidence interval) per SD increase in physical activity in the specific principal component (e.g. physical activity period). Definitions principal components: 0:00–5:00, night; 4:00–9:00, early morning; 8:00–16:00, morning and afternoon; 15:00–22:00 late afternoon to evening; 22:00–1:00 late evening. As outcomes, we studied: body mass index (**a**), fat percentage (**b**), fasting glucose (**c**), fasting insulin (**d**), HbA1c (**e**), and the homeostatic model assessment for insulin resistance (HOMA-IR, **f**).

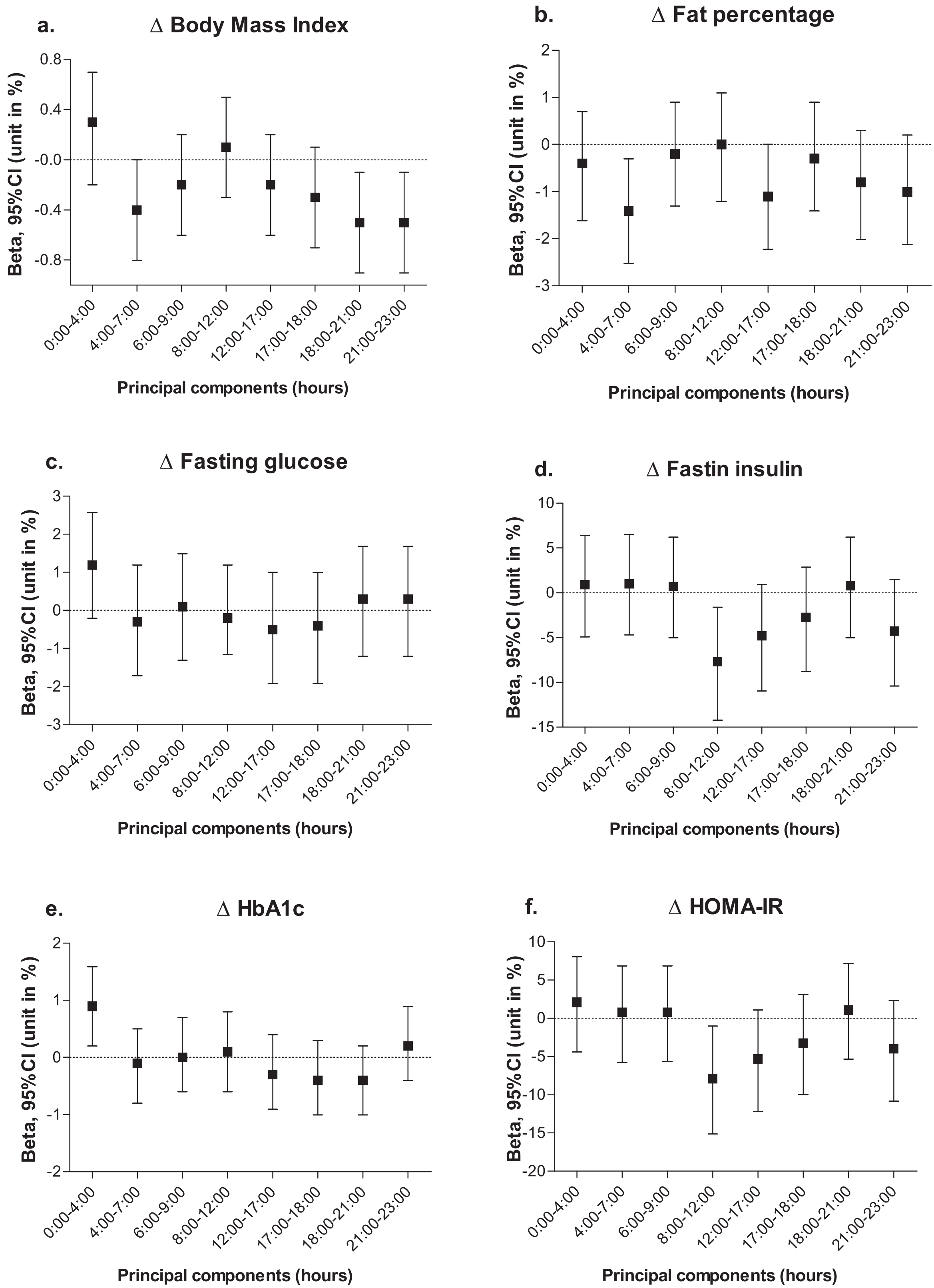

Fig. 3 The associations between the individual variables of metabolic health and the longitudinal principal components (PC) representing change in timing of physical activity. The represented timing periods are shown in the legend on the bottom. Results are displayed as SD (in %) with accompanying 95% confidence interval. Definitions principal components: 0:00–4:00, night; 4:00–7:00, late night/early morning; 6:00–9:00, early morning; 8:00–12:00, late morning; 12:00–17:00, afternoon; 17:00–18:00, late afternoon; 18:00–21:00, early evening; 21:00–23:00, late evening. As outcomes, we studied the changes in the following measures: body mass index (**a**), fat percentage (**b**), fasting glucose (**c**), fasting insulin (**d**), HbA1c (**e**), and the homeostatic model assessment for insulin resistance (HOMA-IR, **f**).

remained similar after adjusted for change in BMI (Supplementary table 5). Participants with a higher increase in physical activity in the afternoon between baseline and follow-up, had a greater decrease in the percentage of body fat (per 1 SD physical activity increase component: −1.11%, 95% CI: −2.22, 0.00). Furthermore, participants with higher increase in physical activity in the early evening (−0.50%, 95% CI: −0.90, −0.10) and late evening (−0.50%, 95%CI: −0.90, −0.10) had a greater decrease in BMI after 3 months of follow-up. No clear associations were found for increased physical activity in the early morning and in the late afternoon.

DISCUSSION

The overall aim of the present study was to examine the associations between the timing of objectively-collected physical activity and metabolic health measures in sedentary older people. This observational prospective cohort study identified principal components that reflect specific patterns of timing and change of timing of physical activity. Furthermore, we found that increased physical activity in the morning was associated with lower BMI, fasting glucose, fasting insulin, and insulin resistance. On the other hand, we found that increased physical activity at night was associated with higher BMI, fasting glucose, and HbA1c.

One of our findings was that most of the daytime components were associated with lower BMI. The majority of previous literature favours morning physical activity in relation to weight loss and body composition [8, 11, 26, 27]. Nonetheless, evidence is ambiguous. A study with a small sample size ($n = 29$) found that obese postmenopausal women that had a self-selected walk in the evening had a greater decrease in fat mass than women who walked in the morning [28]. Our results are most in line with the majority of evidence showing that increased activity in the morning has positive metabolic health outcomes [8, 11, 26, 27]. However, we did find associations between increased physical activity in the afternoon and evening in relation to reduced BMI and insulin resistance as well. An explanation for these differences is that the beneficial effects of certain timing on health and performance might differ between chronotypes [29, 30]. Early birds are possibly more inclined to perform and benefit more from higher physical activity in the morning than night owls and vice versa. This preference might be associated with other behavioural chronotype features, such as night-time snacking in night-owls [31]. Unpropitiously, we were unable to identify chronotypes to perform subgroup analyses as data on chronotypes was not collected in our study. Future studies on physical activity timing and metabolic health should consider chronotype and sleep patterns as possible interacting or confounding factors.

Moreover, our findings showed that increased physical activity at night brought inversed associations compared with high physical activity at daytime. The results indicated that participants with higher nightly physical activity at baseline or increased nightly physical activity during follow-up, had a higher BMI, higher fasting glucose levels and increased HbA1c. An explanation is that the observed increased physical activity at night time is merely an indicator for insomnia or poor sleep quality which is proven to have a causal relation with poor metabolic health and hormonal levels [32, 33]. An alternative explanation might be found in the extensive evidence on circadian rhythms and their influence on metabolic health. More recently, studies have focussed on how timing of certain behavioural exposures (i.e. Zeitgebers) including physical activity affects circadian rhythms [8, 30, 34]. These studies show that exposure to this behavioural factor late at night seems to alter the alignment between circadian rhythms in the suprachiasmatic nucleus and peripheral tissues, which can offset metabolic processes such as glucose metabolism and insulin resistance that can eventually lead to weight gain [7, 8, 29, 34, 35].

We were able to perform longitudinal analyses to examine the effect of change in physical activity timing on metabolic health. We found that participants who, after three months of follow-up, became more active in the morning had a substantial decrease in their fasting insulin levels and insulin resistance. A study on diurnal patterns of glucose metabolism in normo-glycaemic older individuals, showed that postprandial glucose response was lower in the morning compared to afternoon and, notably, evening glucose response [36]. This suggests higher insulin response efficiency and/or lower insulin resistance in the morning. Together with our findings, this might indicate that increasing physical activity in the morning, when insulin sensitivity is highest, is most beneficial for overall diurnal glucose homeostasis.

This study has a number of strengths and limitations to address. To our best of knowledge, this study was the first that was able to examine the longitudinal effects of physical activity timing and change of timing over the course of 3 months. In addition, we assessed timing of physical activity using objective measurement methods. A major limitation of previous research on physical activity behaviour is that conventional measurement methods have not been sufficiently enriched to be able to investigate all aspects of physical activity, including timing. Finally, we used a data-driven dimension reduction analysis to map timing in this specific data whereas previous studies have used predefined periods of timing (morning: 6:00–12:00, noon: 12:00–18:00 etc.) [11, 27, 37]. These predefined periods might not always correspond with daily life timing since this is highly dependent of one's occupational activities. Although this PCA adds statistical power which is beneficial when working with a smaller data set, the utilisation of such analysis can complicate the clinical interpretation of the result. A limitation of our study was that, since this was a post-hoc analysis some years after study inclusion, we were not able to collect additional data on health behaviours such as eating behaviour. Therefore, we were not able to control for possible important unmeasured confounding factors. However, we believe that the influence of residual confounders is minimalised due to the relatively short follow-up time of 3 months in the present study, especially in the prospective analysis. Nevertheless, we advise that future studies should take possible confounders and behavioural factors into account. Finally, we had a rather small and homogeneous sample with respect to health status and sedentary behaviour.

In conclusion, the present study contributes to the current knowledge in the literature indicating that timing of physical activity, more specifically, high physical activity in the morning, is associated with several measures of improved metabolic health. Furthermore, the present study provides novel insight on the effect of increased morning physical activity on fasting insulin and insulin resistance. Our results suggest that time-dependent physical activity interventions might be required to reach maximum health benefits. Advantageously, influencing this Zeitgeber by changing an individual's physical activity timing, is a rather effortless intervention to improve said individual's metabolic health.

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AUTHOR CONTRIBUTIONS

GA, MS, DvH, and RN conceptualised the study. GA performed the data analysis. GA, MS, DvH, and RN contributed to the interpretation of the data. CAW, SPM, FvdO, DvH, and PES contributed to the study design and CAW and SPM performed the data collection. PES, FvdO, SPM, DvH, and RN contributed to the funding acquisition. The drafting of the initial version of the paper was done by GA and RN. All authors critically revised the paper for important intellectual content. All authors read and approved the final paper.

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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