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RESEARCH LETTER

Daily unstructured physical activity affects mean glucose, occurrence of hypoglycaemia and glucose variability in people with type 1 diabetes

Linda C. A. Drenthen MD[1] | Mandala Ajie MSc[1] | Esmée A. Bakker PhD[2,3] | Evertine J. Abbink PhD[1] | Dick H. J. Thijssen PhD[2,4] | Cees J. Tack PhD[1] | Bastiaan E. de Galan PhD[1,5]

[1]Department of Internal Medicine, Radboudumc, Nijmegen, The Netherlands

[2]Department of Physiology, Radboudumc, Nijmegen, The Netherlands

[3]Department of Physical Education and Sports, Faculty of Sport Sciences, Sport and Health University Research Institute (iMUDS), University of Granada, Granada, Spain

[4]Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, Liverpool, UK

[5]Department of Internal Medicine, Maastricht UMC+, Maastricht, The Netherlands

Correspondence
Linda C. A. Drenthen, MD, Department of Internal Medicine, Radboudumc, Nijmegen, The Netherlands.
Email: linda.drenthen@radboudumc.nl; lcadrenthen@gmail.com

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1 | INTRODUCTION

Because structured physical activities, also called sports activities, may cause substantial glycaemic disturbances in people with type 1 diabetes, specific management strategies are advised and used.[1–4] Little is known about glycaemic responses to daily unstructured physical activities, such as gardening, household maintenance and snow shovelling.[5] The daily amount of unstructured physical activity is highly variable within individuals and not reliably assessed by questionnaires. Moreover, most studies focus on moderate-to-vigorous-intensity physical activities (MVPA).[6–8] However, most daily-life (unstructured) physical activities are light-intensity physical activities (LIPA), but few studies have evaluated LIPA in relation to glucose homeostasis. This study examined the association between daily unstructured physical activities and glucose control in adults with type 1 diabetes under free-living conditions, objectively measured by state-of-the-art continuous measuring devices.

2 | METHODS

This was a post hoc analysis of the ADREM trial (clinicaltrialsregister.eu, EudraCT Number: 2019-004222-22) of insulin degludec dosing after structured exercise in 18 adults with type 1 diabetes (12 men, mean ± standard deviation [SD] age 38 ± 13 years, body mass index 25.0 ± 2.7 kg/m^2, glycated haemoglobin 56 ± 8 mmol/mol [7.3 ± 0.8%], duration of diabetes 12 ± 11 years, maximum rate of oxygen consumption 40.2 ± 9.6 mL•kg^{-1}•min^{-1}).[9] All participants wore a blinded continuous glucose monitoring device (Dexcom G6; Dexcom Inc., San Diego, California) and accelerometer (activPAL3 micro; PAL Technologies Ltd, Glasgow, UK) for 24 hours daily.[10] For the current post hoc analysis, we excluded the experimental days with structured exercise, so that we included three periods of 6 days per participant. The outcome variables are defined in the Supplemental Methods 1. Participants were

Linda C. A. Drenthen and Mandala Ajie share first authorship.

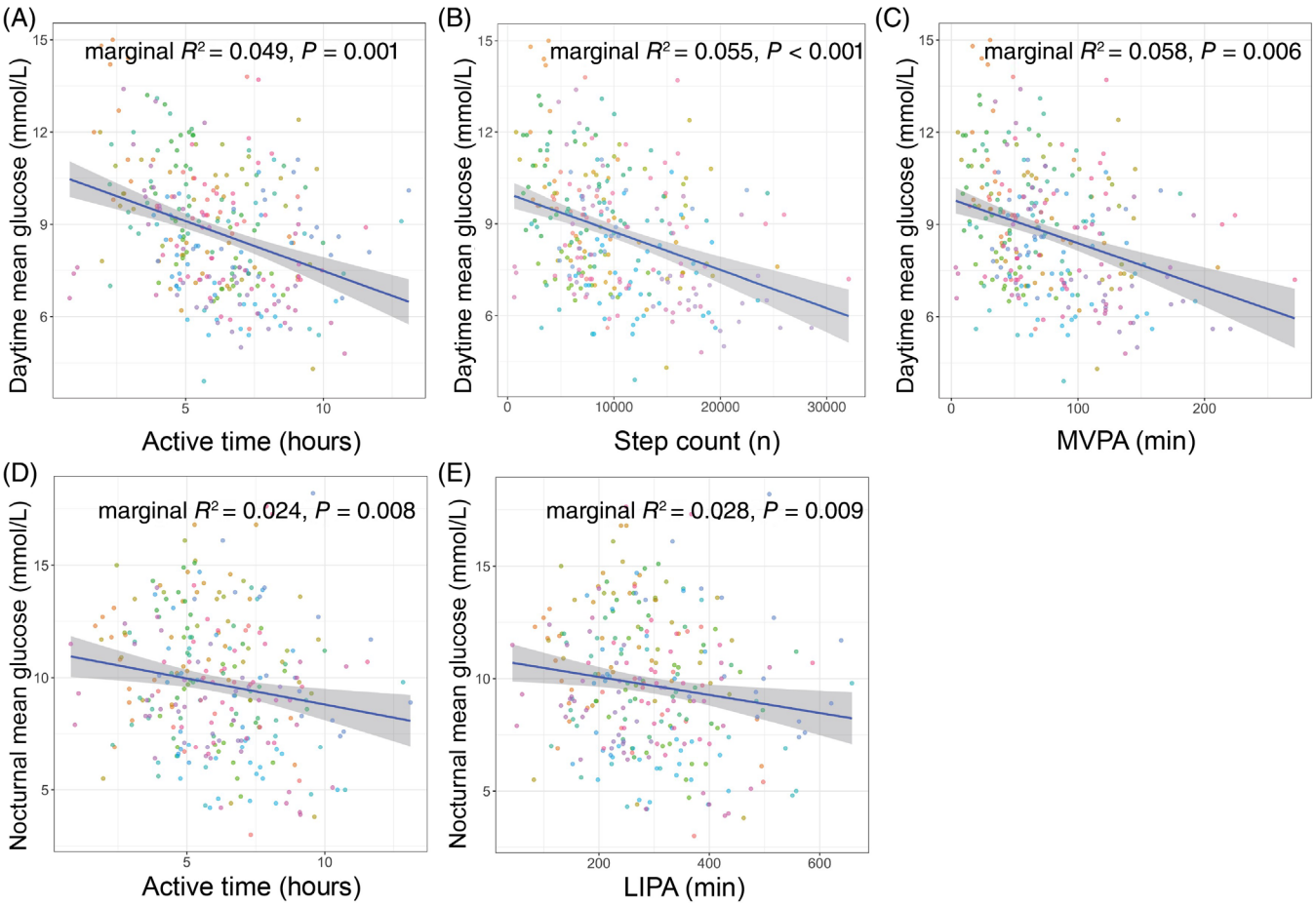

FIGURE 1 Correlation between active time (A), step count (B) and moderate-to-vigorous-intensity physical activity (MVPA) (C) with the mean glucose concentration on the awake period of the same day, and the correlation between active time (D) and light-intensity physical activity (LIPA) (E) with the mean glucose concentration during the subsequent night. Each different-coloured dot represents one participant. The line and grey area present the mean ± SEM of all participants together.

requested to refrain from strenuous exercise during the wearing periods and recorded sleep and wake times in a diary.

2.1 | Statistical methods

We determined the association between daytime unstructured physical activity and glucose parameters during: (i) the awake period of the same day; (ii) the subsequent night (sleep period); and (iii) the next-day awake period, using mixed-regression models (Supplemental Figure S1). A linear mixed model was used for analysing continuous variables and a logistic random-effects model was used for binary outcomes. We constructed two models: Model 1, in which activity parameters were used as predictors for the glucometrics outcome (Supplemental Tables S1–S4), and Model 2, in which the associations were adjusted for demographics. We performed an additional analysis, whereby we divided total-day physical activity into early-day (ie, from wake time to 3:00 PM [awake$_{WT\text{-}15}$]) and late-day (ie, from 3:00 PM to sleep time [awake$_{15\text{-}ST}$]) and we correlated these parameters with nocturnal glucose levels. Further details on the statistical analyses can be found in the Supplemental Methods 2. All data are expressed as mean ± SEM, coefficient (*B*) with 95% confidence interval (CI), or odds ratio [OR] and 95% CI, unless otherwise specified. Data were analysed using R version 4.1.2. *P* values <0.05 were taken to indicate statistical significance.

3 | RESULTS

All participants used multiple-dose injection as their diabetes treatment with insulin degludec as their basal insulin. Physical activity and glucose characteristics during the study period are shown in Table 1. In total, 280 measurement days were included in the analyses.

3.1 | Mean glucose concentration

More active time, higher step count, and more MVPA were associated with a lower mean glucose concentration in the same-day awake period (*B* −0.35 [95% CI −0.56, −0.14], $p = 0.001$; *B* −0.41 [95% CI −0.63, −0.18], $p < 0.001$; *B* −0.33 [95% CI −0.56, −0.09], $p = 0.006$

TABLE 1 Daily physical activity and glucose characteristics*

Characteristics	n = 18
Awake time, hours	15.4 ± 0.9
Sleep time, hours	8.0 ± 1.0
Active time, hours	6.1 ± 1.3
Step count, n	9916 ± 3452
LIPA, minutes	293 ± 72
MVPA, minutes	75 ± 27
Coefficient of variation, %	29.5 ± 4.9
SD, mmol/L	2.7 ± 0.6
Mean glucose concentration, mmol/L	9.1 ± 1.5
Hypoglycaemic events, n per week	4.9 ± 4.2

Note: Data are presented as daily mean ± SD.
Abbreviations: LIPA, light-intensity physical activity; MVPA, moderate-to-vigorous-intensity physical activity; SD, standard deviation.
*Only the number of hypoglycaemic events is presented as mean per week.

[Figure 1A–C, Supplemental Table S5]). More active time and more LIPA were associated with a lower mean glucose concentration during the subsequent night (*B* −0.45 [95% CI −0.78, −0.12], $p = 0.008$; *B* −0.49 [95% CI −0.85, −0.12], $p = 0.009$ [Figure 1D,E]). More early-day active time (active $\text{time}_{\text{WT-15}}$) and more $\text{LIPA}_{\text{WT-15}}$ were associated with a lower mean glucose concentration during the subsequent night (*B* −0.60 [95% CI −0.96, −0.24], $p = 0.001$; *B* −0.81 [95% CI −1.20, −0.41], $p < 0.001$), whereas late-day active time (active $\text{time}_{\text{15-ST}}$) and $\text{LIPA}_{\text{15-ST}}$ were not. No association was found between physical activity parameters and next-day mean glucose concentration.

3.2 | Hypoglycaemic events

More active time and higher step count were associated with higher risks of hypoglycaemia in the same-day awake period (OR 1.56 [95% CI 1.11, 2.21], $p = 0.011$; OR 1.55 [95% CI 1.09, 2.21], $p = 0.014$ [Supplemental Figure S2A and Supplemental Table S6]). Also, more active time, higher step count, more MVPA and more LIPA were all associated with higher risks of nocturnal hypoglycaemia (OR 2.40 [95% CI 1.46, 3.96], $p = 0.001$; OR 2.05 [95% CI 1.30, 3.21], $p = 0.002$; OR 1.71 [95% CI 1.07, 2.74], $p = 0.024$; OR 1.88 [95% CI 1.15, 3.07], $p = 0.012$ [Supplemental Figure S2B]). More active $\text{time}_{\text{WT-15}}$ and active $\text{time}_{\text{15-ST}}$, higher step $\text{count}_{\text{WT-15}}$, more $\text{MVPA}_{\text{WT-15}}$, and more $\text{LIPA}_{\text{15-ST}}$ were associated with higher risks of nocturnal hypoglycaemia (OR 2.08 [95% CI 1.30, 3.35], $p = 0.002$; OR 1.79 [95% CI 1.14, 2.83], $p = 0.012$; OR 1.86 [95% CI 1.22, 2.85], $p = 0.004$; OR 1.85 [95% CI 1.15, 2.99], $p = 0.012$; OR 1.80 [95% CI 1.13, 2.87], $p = 0.014$). Both active time and LIPA were positively associated with the occurrence of next-day hypoglycaemia (OR 1.59 [95% CI 1.12, 2.24], $p = 0.009$; OR 1.46 [95% CI 1.00, 2.11], $p = 0.048$ [Supplemental Figure S2C]).

3.3 | Glucose variability

More active time was associated with a higher coefficient of variation in the same-day and next-day awake periods (*B* 1.14 [95% CI 0.02, 2.26], $p = 0.045$; *B* 1.22 [95% CI 0.09, 2.35], $p = 0.034$), but not with overnight coefficient of variation (Supplemental Table S7). No correlations were found between physical activity parameters and SDs of the same day, subsequent night or next day (Supplemental Table S8).

4 | DISCUSSION

We found that daily, unstructured, physical activity was associated with a lower mean glucose concentration during the same day and subsequent night, but also with greater glucose variability and higher risk of hypoglycaemia that persists until the next day. The association between unstructured physical activity versus mean glucose concentration and risk of hypoglycaemia during the subsequent night was largely independent of the time of the day at which physical activity was performed (early-day vs. late-day). Together, these results may indicate that, in addition to the widely known association between structured MVPA and glucose control,[2,11] unstructured physical activities, even those performed at low intensity, also affect glucose control.

We found that unstructured physical activity explains up to 19% of the variation in hypoglycaemic risk, which underscores the clinical relevance of our study. Our study particularly highlights the importance of LIPA with regard to a range of glucose parameters, including (nocturnal) hypoglycaemia. Indeed, a 113-minute increase in LIPA translated into a 0.5 mmol/L drop in mean nocturnal glucose, but at the cost of an almost twofold increased risk of hypoglycaemia (Supplemental Table S9). These associations were less prominent for MVPA, which may be explained by better awareness of the association between MVPA and blood glucose concentration.

Strengths of our study are the data collection under free-living conditions and the use of a continuous glucose monitor combined with a 24-hour-measuring, accurate, accelerometer specifically designed to evaluate LIPA.[12] Limitations include the relatively small sample size, although this is balanced by the high number of measurement days. Also, generalization to people who are less trained or who are using automated insulin delivery systems should be performed with caution. Lastly, participation in the ADREM study[9] could have made participants (more) aware of the impact of (unstructured) physical activity on glucose parameters. This may have led to underestimation of the actual association between physical activity and glucose parameters.

In conclusion, unstructured physical activity, even at low intensity and performed in the morning and early afternoon, is associated with lower mean glucose concentrations during the same day and subsequent night, and with increased risks for subsequent (nocturnal) hypoglycaemia in people with type 1 diabetes. These observations suggest

that daily unstructured physical activities may help to improve glucose control, provided that additional measures are considered to minimize the risk of hypoglycaemia.

AUTHOR CONTRIBUTIONS

Linda C. A. Drenthen, Cees J. Tack, and Bastiaan E. de Galan designed the study. Linda C. A. Drenthen recruited the participants and collected the data. Esmée A. Bakker modified the activity tracker script and Linda C. A. Drenthen applied this to the patient data. Mandala Ajie analysed the data. Linda C. A. Drenthen and Mandala Ajie wrote the first version of the manuscript. All authors discussed the results and implications, commented on the manuscript at all stages and approved the final version of the manuscript. The guarantor (Bastiaan E. de Galan) accepts full responsibility for the work and conduct of the study, has access to the data, and controlled the decision to publish.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts to disclose that are relevant to this manuscript.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/dom.15277.

DATA AVAILABILITY STATEMENT

The datasets generated during and/or analysed in the current study are available from the corresponding author upon reasonable request.

ORCID

Linda C. A. Drenthen https://orcid.org/0000-0002-3020-7948

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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