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TITLE

Barriers to physical activity in children and adults living with type 1 diabetes: a complex link with real-life glycemetic excursions.

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Key messages:

What is already known about this subject?

- Physical activity (PA) induces glucose fluctuations that are difficult to manage in everyday-life and fear of hypoglycemia is a main perceived barrier to PA.

What is the new information?

- Children/adolescents who spend more time in hypoglycemia on nights following PA see more hypoglycemia as a barrier while in their parents this link does not appear.
- Surprisingly, adults with type diabetes having more exercise events associated with a drop in glycemia were less afraid of exercise-related hypoglycemia.

Keywords: Barriers to physical activity, Exercise, Hyperglycemia, Hypoglycemia, Outpatient study, Type 1 diabetes

Word counts:

Abstract: 247 words

Main text: 3998 words

1 figure and 2 tables

1 table as supplementary material

ABSTRACT

Objective

Ever since the first research on barriers to physical activity (PA) highlighting fear of hypoglycemia as a major barrier, many studies have attempted to understand their demographic and behavioral determinants. However, no research has been conducted on whether these perceived barriers towards PA are based on real life-experienced adverse glycaemic effects of exercise.

Research design and methods

Sixty-two adults, and 53 children/adolescents living with type 1 diabetes along with their parents, completed the BAPAD-1 questionnaire on barriers to PA. Continuous glucose monitoring data were collected during one week of everyday life for 26 adults and 33 children/adolescents. Multiple linear regressions were used to explore links between BAPAD-1 scores and glycaemic excursions experienced during and after everyday life self-reported PA sessions, controlling for behavioral (accelerometry) and demographic confounders.

Results

In children/adolescents, the more time spent in hypoglycemia on nights following PA sessions, the more they reported hypoglycaemic risk as a barrier ($\beta = +0.365$, $P = 0.034$). Conversely, in adults, the higher the proportion of PA sessions accompanied by a drop in blood glucose, the less hypoglycemia was a barrier ($\beta = -0.046$, $P = 0.004$). In parents, BAPAD-1 scores were unrelated to children/adolescents' everyday life exercise-induced hypo/hyperglycemia.

Conclusions

In children/adolescents, fear of hypoglycemia was predominant in those exposed to nocturnal hypoglycemia associated with PA sessions. In adults, fewer barriers may mean they accept a bigger drop in their glycaemia during PA. This shows the importance of finding and promoting age specific solutions to prevent exercise-induced hypoglycemia.

MAIN TEXT

INTRODUCTION

Regular physical activity (PA) is a key component of type 1 diabetes management [1]. Regular PA is associated with improved quality-of-life, HbA_{1c} levels, lipid profile, BMI, cardiovascular fitness and reduction in insulin requirements [2-5]. To obtain these benefits, children/adolescents and adults with type 1 diabetes are encouraged to engage respectively in ≥ 60 min/day or ≥ 150 min per week of aerobic moderate-to-vigorous physical activity (MVPA), to practice resistance exercise two or three days per week, and limit sitting time [6]. Unfortunately, a significant proportion of children/adolescents and adults with type 1 diabetes do not follow these guidelines [7, 8]. Individuals with type 1 diabetes seem less engaged in MVPA than those without diabetes [9, 10], most likely because of diabetes-specific barriers to PA [11, 12] in addition to general barriers. Type 1 diabetes and insulin treatment can indeed alter physiological responses to exercise, and trigger large glycemic variations outside the target range [1]. Several diabetes-specific barriers to PA have been identified with the major ones being fear of hypoglycemia and loss of control over diabetes [10-13].

However, whether or not these fears are based on the real life-experienced adverse effects of PA on actual glucose fluctuations has never been investigated. This is nevertheless an important issue, even in the current context of rapid development of new technologies (*e.g.* continuous glucose monitoring – CGM – systems) [14]; the latter indeed represent a financial burden on healthcare systems, thus making their access difficult in many countries [15]. In addition, some patients are reluctant to wear diabetes-related devices on their bodies [16]. If blood glucose variations are linked to perceived barriers to PA, it will be worth directing research towards elaborating effective strategies to reduce the likelihood of hypoglycemic and/or hyperglycemic risks related to exercise. Otherwise, it will be important to focus on therapeutic education in order to reduce the distortion between patients' subjective fears and

blood glucose variations in everyday life. In adults with type 1 diabetes, Brazeau *et al.* showed that the number of severe hypoglycemic episodes in the previous year (assessed through patients' recall) was significantly associated with the score of hypoglycemia fear as a barrier to PA [11]. Another study found that parents whose children had experienced a severe hypoglycemic event, assessed by the Clarke questionnaire, had a higher fear of hypoglycemia score (assessed without reference to PA) [17]. In contrast, for Jabbour *et al.*, those children and adolescents with type 1 diabetes who had a higher hypoglycemia survey score (assessed overall, without reference to PA) reported fewer hypoglycemic episodes in the previous 12 months [18]. The complexity of linking scores of hypoglycemia fear to retrospective subjective recall of true hypoglycemic episodes is clearly illustrated in a study outside of the context of exercise [19]. In this study, 43% of 469 adults with type 1 diabetes consistently indicated low perceived hypoglycemia fear scores together with low frequency of reported severe hypoglycemia (over the 12 previous months), while another 32% surprisingly had low fear of hypoglycemia scores with high frequency of reported severe hypoglycemia episodes [19]. It is difficult to infer whether these controversial results come from patients' specific characteristics or difficulties in accurately reporting hypoglycemic episodes over relatively long retrospective periods.

Given the ambiguity of available data, the aim of this study is to explore whether children/adolescents (and their parents) and adults with type 1 diabetes who report having more barriers to PA are those who experience the greatest variations in blood glucose levels (hypoglycemic and hyperglycemic excursions and glycemic variability) in everyday life and/or during PA.

METHODS

This cross-sectional study is based on a secondary analysis of pooled data available from studies conducted in our laboratory, granted approval by the Lille University Ethics Committee (N°2018-319-S67), the North Western IV Regional Ethics Committee (no.EudraCT2009-A00746-51), and the Academic Ethical Committee Brussels Alliance for Research and Higher Education (N°B200-2017-039). Fifty-three children/adolescents ($n=13$ children aged 6-10, $n=40$ adolescents, aged 10-17 years [20]) and their parents, as well as 62 adults were included in this study. The inclusion criteria were age ≥ 6 years, diagnosis of type 1 diabetes for >1 year and no change in insulin delivery method (*i.e.*, multiple daily injections, MDI or continuous subcutaneous insulin infusion, CSII; none of the participants were treated with closed loop insulin delivery) over the last 3 months. Written consent was obtained from the three target groups (adults, children/adolescents, and their parents) before their inclusion in the study. Participants attended the laboratory once, during which anthropometric measurements were taken and questionnaires as well as devices (CGM sensor and accelerometer) provided. While the questionnaire on barriers to PA (BAPAD-1) was given to all participants and to children/adolescents' parents, a total of 39 adults and 34 children/adolescents agreed to wear a CGM sensor to follow glycemic excursions during one week of everyday life (Figure 1). Throughout the week of CGM recording, participants were asked to write a diary to report their PA sessions including PA at sports clubs, leisure time PA, and PA just getting around (Figure 1). They were asked to indicate the exact type of PA, its time, duration and subjective intensity (light, moderate, or intense). We then estimated energy expenditure in MET-hours (Metabolic Equivalent-hours) for each PA session by multiplying the duration (in hours) by the METs estimated from PA type and subjective intensity [21, 22]. Thirty-nine adults and 32 children/adolescents also accepted to wear an accelerometer to measure everyday life PA data for a period of one week (Figure 1).

Barriers to physical activity

Perceived barriers to PA were assessed using the BAPAD-1 questionnaire [23], which has 11 questions, 4 of which specific to diabetes (loss of control over diabetes, risk of hypoglycemia, fact that you have diabetes, risk of hyperglycemia). Participants were asked to rate, using a 7-point Likert scale, the likelihood that each of the items would keep them from practicing regular PA (with 1 = extremely unlikely and 7 = extremely likely). The team was available if the children did not understand any questions. The BAPAD-1 total score (mean of the 11 questions) and the sub-scores related to glycemic excursions or variability induced by PA (*i.e.*, loss of control over diabetes, risk of hypoglycemia, risk of hyperglycemia) were taken into consideration.

Everyday life and exercise-induced glycemic excursions

Fourteen adults and 29 children/adolescents agreed to wear, during one week of everyday life, a professional masked CGM sensor (Enlite iPro2, Medtronic, Inc; with a value every 5min) and to measure capillary blood glucose levels at least four times per day for subsequent CGM sensor calibration. Twenty-five other adults and 5 children/adolescents agreed to provide data from their intermittently scanned CGM sensor (FreeStyle Libre Flash, Abbott Diabetes Care; with a value every 15min) during one week of everyday life. Data from both types of sensors were combined in statistical analyses [24]. Glycemic excursions and variability were calculated from CGM recordings over several specific periods: (*i*) from the beginning to the end of the week (*i.e.*, ‘week’); (*ii*) all day long each day (*i.e.*, ‘days’); (*iii*) from bedtime until waking up each day (*i.e.*, ‘nights’); (*iv*) during each reported PA session ≥ 1.5 MET-hours; (*v*) for 2 hours after each reported PA session ≥ 1.5 MET-hours and (*vi*) the nights subsequent to each reported PA session ≥ 1.5 MET-hours. The threshold of 1.5 MET-hours was chosen as an energy expenditure equivalent to at least a minimum of 30 min at moderate intensity [6]. Only data

from participants with CGM values obtained over a minimum of 5 days out of 7, with at least 70% data for each day, were considered in the analyses [25]. Glycemic excursions taken into consideration were the percentage of time spent in range (between 3.9 and 10.0 mmol/L), the hypoglycemia alert glucose values <3.9 mmol/L¹, clinically significant hypoglycemia <3.0 mmol/L¹ and clinically significant hyperglycemia >13.9 mmol/L¹ [25, 26]. Glycemic variability was assessed through coefficient of variation (%CV) [25]. Hypoglycemia awareness was also assessed in all participants using the visual analogue scale of Gold *et al.* [27].

Usual physical activity levels

As a possible confounder of the impact of everyday life glycemic variations on perceived barriers to PA, usual PA levels were objectively measured using an Actigraph GT1M or GT3X accelerometer (only accelerations in the vertical axis were extracted [28]), worn on the right hip for one week, from the moment participants got up to the moment they went to bed (times recorded in a diary). The acceleration signal was sampled at 30 Hz. For a day to be valid, the accelerometer had to be worn for at least 10 hours a day for a weekday, or 8 hours a day for a weekend day [29]. Only participants wearing the accelerometer for a total of at least 4 valid days were included in the analysis [29]. Data were analyzed using ActiLife version 6.13.3 with periods of non-wear time defined using the algorithm proposed by Choi *et al.* [30] for the adults, and Troiano *et al.* [31] for the children/adolescents. Activity level thresholds chosen were those from Troiano *et al.* [31] for the adults, and from Evenson *et al.* [32] for the children/adolescents.

Statistics

Statistical analyses were performed using the IBM SPSS v. 27.0 software. The quantitative data are described as the mean \pm SD. Multiple linear regressions (barrier scores as dependent

variable) were used to evaluate the impact of everyday life glycemic excursions (covariate) on barriers to PA. All models were adjusted (by including covariates) for everyday life PA (MVPA) and sedentary time from accelerometry, as well as for participant characteristics (*i.e.*, age, gender, BMI in adults or Z-score BMI – calculated using WHO charts – in children/adolescents, HbA_{1c}, diabetes duration, and treatment method ‘MDI vs. CSII’). For analyses performed during reported PA sessions ≥ 1.5 MET-hours, 2 hours after or during the night subsequent to these PA sessions (*i.e.*, analyses involving only participants practicing at least one reported PA session ≥ 1.5 MET-hours per week), MVPA and sedentary time were replaced by the number of reported PA sessions ≥ 1.5 MET-hours. The residuals of the estimated linear regressions were analyzed, with the normality assumption always being met. We also conducted unpaired and paired *t* tests or, in cases of non-parametric data (normality tested using the Shapiro-Wilk test), Mann-Whitney U and Wilcoxon tests for comparing non-matched target groups (*i.e.*, adults vs. children/adolescents) or subgroups (*e.g.*, participants meeting PA guidelines vs. those not meeting PA guidelines...) and for comparisons between children/adolescents and their parents, respectively. Pairwise correlations between BAPAD-1 scores in children/adolescents and BAPAD-1 scores in their parents were tested using Pearson’s *r* or, for nonparametric data, Spearman’s ρ . *P* value < 0.05 was considered statistically significant.

RESULTS

Of the participants who wore a CGM sensor, 13 CGM datasets from adults and 1 from children/adolescents could not be analyzed either because there were insufficient valid recording days or the sensor failed. Among participants with CGM data, 16 adults and 25 children/adolescents reported one or more PA session(s) ≥ 1.5 MET-hours in their diary. Only 1 adult was excluded from analyses including accelerometry data because he did not strictly

follow recommendations to wear the accelerometer during all waking hours (Figure 1). Participant characteristics are presented in Table 1.

Barriers to physical activity (Figure 2, Supplementary Table 1)

In all target groups, the risk of hypoglycemia was the most prevalent perceived barrier to PA. The second and third barriers were weather conditions and location of a gym/physical health status (equally placed) in adults, loss of control and fear of hyperglycemia ranked equal in children/adolescents, and loss of control and location of a gym in their parents. The factors least considered to be barriers to PA were the fear of suffering a heart attack for adults and for children's parents, and a low fitness level for children. Diabetes-specific barrier scores did not differ significantly between children/adolescents and adults, between children and adolescents, nor between children/adolescents and their parents. Fear of hypoglycemia score among children/adolescents positively correlated with fear of hypoglycemia score in their parents ($r=0.39$, $P=0.005$).

Influence of anthropometric and demographic participant characteristics on barriers to PA (results of regressions without glycemic excursions as covariates)

In adults, women had higher total BAPAD-1 scores (women 3.2 ± 0.8 , men 2.4 ± 0.8 , $\beta=+0.861$; $P=0.010$) as well more fear of hyperglycemia ($\beta=+1.171$; $P=0.029$) and of loss of diabetes control ($\beta=+1.670$; $P=0.008$) as compared with men. In children/adolescents, girls had higher fear of hypoglycemia scores (girls 4.3 ± 2.1 , boys 3.7 ± 2.1 , $\beta=+10.132$; $P=0.021$). Diabetes duration influenced barriers to PA only in adults, with a longer duration being associated with a lower total BAPAD-1 score ($\beta= -0.050$; $P=0.008$) and with lower fear of hypoglycemia score ($\beta= -0.106$; $P=0.003$). Adults using MDI had lower total BAPAD-1 scores than those using CSII ($\beta= -0.639$; $P=0.034$).

Influence of usual PA levels and sedentary time on barriers to PA (results of regressions without glycemic excursions as covariates)

In children/adolescents, the most active participants (time spent at MVPA $\text{min} \cdot \text{day}^{-1}$) were those who most see fear of hypoglycemia as a barrier to PA ($\beta=+0.071$; $P=0.002$). Moreover, among the 29 children/adolescents who reported one or more PA session(s) ≥ 1.5 MET-hours in their diary, as the number of reported PA sessions increased, they had a higher BAPAD-1 total score ($\beta=+0.164$, $P=0.005$) and higher fear of hyperglycemia ($\beta=+0.262$, $P=0.002$) and fear of loss of diabetes control ($\beta=+0.191$, $P=0.013$). Accordingly, Mann-Whitney U tests showed that children/adolescents who meet PA guidelines [7, 8] were more likely to mention fear of hypoglycemia ($P=0.001$).

Conversely, the parents of the less active children/adolescents had a higher fear of hyperglycemia score ($\beta= -0.057$; $P=0.012$). However, higher fear of hyperglycemia ($\beta= -0.010$; $P=0.037$) and total BAPAD-1 ($\beta= -0.009$; $P=0.006$) scores were simultaneously observed for the parents of the less sedentary children/adolescents.

In adults, no significant links between barriers to PA and usual PA levels or sedentary time were detected.

Association between barriers to PA and everyday life glycemic excursions/variability

Fear of hyperglycemia score was not significantly influenced by glycemic excursions in everyday life or in response to reported PA sessions ≥ 1.5 MET-hours in all target groups. In addition, no influence of everyday life hyperglycemic excursions on barriers to PA were detected, except for children/adolescents who reported higher total BAPAD-1 scores in cases of more everyday life hyperglycemia (Table 2).

Among children reporting PA sessions ≥ 1.5 MET-hours, the more time spent < 3.0 mmol/L on nights subsequent to these PA sessions, the more barriers to PA they reported, particularly for the fear of hypoglycemia (Table 2).

In parents, BAPAD-1 scores were not related to everyday life exercise-induced hypoglycemia. However, when looking at all days of the week, even those without reported PA sessions, parents whose children spent less time in hypoglycemia are those who reported more barriers to PA for their child (Table 2). Similarly, parents reporting more barriers to PA and especially the fear of loss of diabetes control had the children with the least glycemic variability in everyday life (BAPAD-1 total score: $\beta = -0.063$, $P = 0.033$; fear of loss of diabetes control score: $\beta = -0.174$, $P = 0.001$).

In the case of adults, those who reported less the fear of hypoglycemia as a barrier to PA surprisingly displayed a higher percentage of PA sessions ≥ 1.5 MET-hours involving a drop in blood glucose levels (Table 2). Accordingly, a lower total BAPAD-1 score was associated with more time spent < 3.0 mmol/L during their reported PA sessions ≥ 1.5 MET-hours (Table 2).

In all target groups, there was no relationship between barriers to PA and hypoglycemia awareness score of the Gold questionnaire.

DISCUSSION

This study sheds new light on the understanding of barriers to PA in individuals with type 1 diabetes. To our knowledge, this work is the first of its kind to explore the link between barriers to PA with actual everyday life glycemic excursions, especially during PA. In all the target groups (adults, children, parents), the fear of hypoglycemia was the top barrier to PA in line with the literature [10-12, 33-35]. We show that the more time children/adolescents spent in hypoglycemia on the nights subsequent to everyday life PA sessions ≥ 1.5 MET-hours, the more they reported fear of exercise-induced hypoglycemia as a barrier. Conversely, in adults, the

higher the proportion of PA sessions with a drop in blood glucose levels, the less they perceived hypoglycemia as a barrier.

Influence of participant characteristics on barriers to PA

Adults with a shorter duration of diabetes perceived more barriers compared with those with a longer duration. This shows the importance of working to reduce barriers to PA from the onset of the disease.

As in a recent study [36], women perceived more barriers to PA than men. It is worth noting that gender-related differences may appear from childhood, with the current study underlying, for the first time, a higher fear of hypoglycemia score among girls.

Adults using CSII reported more barriers to PA than MDI users. CSII users may in fact have more barriers to PA than those not on insulin pumps because of the distorted expectation that pumps should address all types of glycemic control challenge in relation to exercise. In children and adolescents, scores for PA barriers did not differ between both insulin delivery methods in accordance with Michaud et al. [37].

Influence of usual physical activity levels and sedentary time on barriers to PA

In addition to the characteristics of participants in our study, the exploration of the link between barriers to PA and everyday life glycemic excursions was also adjusted for PA level, as objectively assessed by accelerometry. This is crucial, since being more active (MVPA or reported PA sessions ≥ 1.5 MET-hours) in children/adolescents appeared to be associated with having more barriers related to exercise-induced glycemic variations. This result confirms the study of Jabbour et al. [18] showing that children with higher hypoglycemia fear survey behavior scores were those who engaged in more vigorous PA. It is therefore probably encouraging to find high barriers to PA scores among children/adolescents, since this reveals

that children practice PA and are aware of potential related difficulties. It would be worth testing, in future interventional studies, whether by lowering the barriers to PA in active children we could still further increase their level of PA. Of note, the link between children/adolescents' sedentary and active lifestyles and the barriers to PA reported by their parents seems more complicated to understand. Our results were indeed contradictory depending on whether one is interested in MVPA or sedentary time, and also differed from recent literature on younger children (≤ 6 years old) [38]. In adults, no relationship between barriers to PA and PA level was found, whereas in the study of Keshawarz *et al.* [10] participants who reported more diabetes-specific barriers to PA were those who spent less time in MVPA. Our participants were probably more active than those in Keshawarz *et al.* [10] with a mean of 341.8 vs. 209 min/week of MVPA. Moreover, more than half (55,3%) of the adults in the current study met the international PA recommendations, unlike participants in other studies (*e.g.* 33% [39] ; 32% [33]). It is thus possible that the number of participants with low PA levels in our study was too small to highlight the link between low levels of PA and high scores of barriers to PA as detected by Keshawarz *et al.* [10]. Further studies will be needed to confirm the possibility that the relationship between commitment and barriers to PA develops from a rather positive relevance in childhood (*i.e.*, more barriers as a manifestation of being more active) to a negative impact of barriers on behaviors in adulthood.

Association between barriers to PA and everyday life glycemic excursions/variability

Whether or not diabetes-specific barriers to PA are triggered by glycemic excursions experienced by the participants when performing exercise in everyday life had never been investigated.

It is noteworthy that children/adolescents who experienced more clinically significant hypoglycemia on the nights subsequent to PA saw more hypoglycemia as a barrier to PA, and

also perceived more general barriers. In the case of parents, we did not find any significant association between barriers to PA and exercise-induced glycemic excursions experienced by their children/adolescents. However, when everyday life glycemic excursions were regarded without reference to PA sessions, the parents stating more barriers were those whose children experienced less weekly time in hypoglycemia, and less glycemic variability. This result may illustrate the possibility that parents who are more careful about preventing hypoglycemia and glycemic variability in their children in everyday life are also those who pay more attention to other general healthcare issues, including those related to PA practice.

Overall, it would appear clinically relevant to provide adapted therapeutic patient education sessions for children to help them acquire individual strategies for minimizing the risk of nocturnal hypoglycemia. Other teams of researchers are currently implementing work in this direction [40]. In addition to therapeutic education, new technologies, and specifically continuous-glucose monitoring systems with alarms, may represent promising solutions for reducing barriers to PA related to glycemic excursions while lightening the mental burden. The use of artificial pancreas is even suggested as effective for reducing the risk of hypoglycemia during exercise and especially at night [41, 42].

Contrary to our results in children/adolescents, the adults mentioning fewer barriers to PA (*i.e.*, total BAPAD-1 score and fear of hypoglycemia score) were those who experienced more hypoglycemia and decrease in glycemia during PA sessions ≥ 1.5 MET-hours. This initially rather odd association raises some points. It is possible that people who experience more glycemia drops during exercise get used to this type of adverse event and subsequently their fear of hypoglycemia falls over time. Besides, this association could also show that adults who are less afraid of suffering from hypoglycemia feel less stressful about an exercise-induced decrease in glycemia. A somewhat comparable association had been suggested in a recent study, in which adults with greater awareness of strategies for hypoglycemia prevention – a

correlate of fewer barriers to PA [11] – mentioned more hypoglycemic episodes during exercise (subjectively reported, not measured with CGM) [43]. Our results raise the clinical issue of striking a balance between reducing barriers to PA in order to increase PA commitment [10] but at the expense of a certain risk-taking behavior towards glycemia management.

The strength of the current study lies in its unique approach to exploring the association between subjective ‘*barriers to PA*’ and the objective measure of ‘*real-life interstitial glucose excursions*’. In addition, different target groups (children, adolescents and adults) were enrolled making our results potentially applicable to a wider population. A limitation of this study is the use, among children, of the BAPAD-1 questionnaire, which is normally destined for adults [23]. Our study indeed initially began in 2014, whereas Livny *et al.* [34] proposed an adapted version of the questionnaire in 2020. However, care was taken to adapt the terminology of two items of the adult version to child respondents. It should also be noted that this is the first study assessing barriers to PA both among children with type 1 diabetes and their parents. Children/adolescents as well as their parents assigned “fear of hypoglycemia” and “fear of loss of diabetes control” as the first barriers to PA, meaning that the possibility of parents passing on their fears to their children [44] merits further attention. Another limitation lies in the use of CGM rather than capillary glycemia during exercise bouts when lag-time between interstitial and capillary glucose is increased and glucose concentrations may be overestimated in cases of low values [1].

In conclusion, fear of hypoglycemia appears to be the main perceived barrier to PA among people living with type 1 diabetes whatever their age, and also among children’s parents. In children/adolescents fear of hypoglycemia as a barrier to PA was predominant in those actually exposed to nocturnal hypoglycemia in response to everyday life exercise. These results should

encourage healthcare professionals to propose, especially for children, practical individual strategies, and/or novel technologies, for preventing exercise-induced hypoglycemia and engaging safely in PA. In adults with type 1 diabetes, further studies will be needed to explore whether perceiving fewer barriers is a result of more knowledge about strategies for hypoglycemia prevention thus triggering conscious-risk taking towards glucose variations during exercise.

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Author contributions. E.H. designed the experiments. S.B. and R.R.L. contributed to the design of the experiments. C.P, E.L., S.T., C.T., and E.H. carried out the experiments. E.H., C.P., and E.L. collected and analyzed data. J.H. created algorithms for analyses of glycemic excursions and variability. P.F., C.S., I.G., C.B., B.K., J.W. recruited participants with type 1 diabetes. E.H. and C.P. wrote the manuscript, which was reviewed in detail by S.T. All the other authors were also involved in reviewing the manuscript. E.H. guaranteed the integrity of this study throughout its duration, and as such, had full access to data with responsibility for data integrity and the accuracy of the data analysis.

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TABLES

Table 1—Participant characteristics.

| | Adults (<i>n</i> = 62) | Children/Adolescents (<i>n</i> = 53) |
|---|---|--|
| <i>Anthropometric and demographic data</i> | | |
| Age (years) | 32.9 ± 10.9 (18.0-68.0) | 12.2 ± 2.9 (6.0-17.7) |
| Sex, <i>n</i> men/women | 42/20 | 29/24 |
| BMI (kg · m ⁻²) | 24.2 ± 3.6 (17.2-37.3) | NA |
| Z-score BMI | NA | 0.4 ± 1.1 (-1.9-3.2) |
| Fat mass (%) | 21.4 ± 9.9 (7.9-46.5) (<i>n</i> = 58) | 19.3 ± 5.3 (8.3-30.2) (<i>n</i> = 43) |
| HbA _{1c} (mmol · mol ⁻¹) | 57.6 ± 12.7 (33.0-95.0) | 60.7 ± 10.9 (43.0-92.0) |
| HbA _{1c} (%) | 7.4 ± 1.2 (5.2-10.8) | 7.7 ± 1.0 (6.1-10.6) |
| Diabetes duration (years) | 13.9 ± 9.5 (1.0-38.0) | 5.9 ± 3.8 (0.3-16.7) |
| Age at diabetes onset (years) | 19.0 ± 11.2 (1.3-56.0) | 6.3 ± 3.8 (0.5-14.0) |
| Insulin delivery (CSII/MDI) | 24/38 | 25/28 |
| Insulin dose (units · kg ⁻¹ · day ⁻¹) | 0.6 ± 0.2 (0.2-1.3) | 0.9 ± 0.4 (0.3-2.0) |
| <i>n</i> used to wearing a CGM sensor/not used | 35/27 | 8/45 |
| <i>N</i> with diabetes complications/no complications | 9/53 | NA |
| Gold score [% with a score <4] | 2.4 ± 1.2 [80.8] (<i>n</i> = 52) | 2.5 ± 1.4 [79.5] (<i>n</i> = 39) |
| <i>Weekly continuous glucose monitoring data</i> (% time spent at specific thresholds; [<i>n</i> meeting/not meeting the recommended targets] for each threshold) | | |
| <i>N</i> | N=26 | N= 33 |
| % time < 3.0 mmol/L | 3.7 ± 4.2 (0-13.5) [9/17] | 2.7 ± 3.1 (0-10.4) [16/17] |
| % time < 3.9 mmol/L | 8.1 ± 7.1 (0-28.5) [8/18] | 7.4 ± 5.8 (0-24.6) [12/21] |
| % time between 3.9-10.0 mmol/L | 55.3 ± 14.5 (14.5-88.1) [4/22] | 51.6 ± 12.8 (28.2-76.2) [3/30] |
| % time > 10.0 mmol/L | 36.5 ± 16.6 (6.4-72.0) [6/20] | 41.0 ± 16.0 (0.7-69.4) [4/29] |
| % time > 13.9 mmol/L | 12.7 ± 11.2 (0-37.5) [7/19] | 15.7 ± 10.5 (0-39.6) [4/29] |
| Coefficient of variation (%) | 40.2 ± 7.5 (25.6-56.2) [7/19] | 42.0 ± 7.2 (28.9-57.6) [7/26] |
| <i>Usual physical activity</i> | | |
| Total time in MVPA (min · week ⁻¹) | 341.8 ± 219.8 (33.0-1115.4)(<i>n</i> = 38) | NA |
| Total time in MVPA (min · day ⁻¹) | NA | 52.1 ± 22.6 (24.4-102.2) (<i>n</i> = 32) |
| Total time in intense PA (min · week ⁻¹) | 33.9 ± 62.2 (0-322.0) (<i>n</i> = 38) | 139.9 ± 87.5 (23.3-326.7) (<i>n</i> = 32) |
| Total sedentary time (hours · day ⁻¹) | 10.4 ± 2.1 (7.0-15.1) (<i>n</i> = 38) | 10.0 ± 1.8 (5.8-13.1) (<i>n</i> = 32) |
| <i>n</i> meet PA guidelines/no meet* | 21/17 (<i>n</i> = 38) | 10/22 (<i>n</i> = 32) |

Data are means ± SD (minimum-maximum) or number of participants. The number of subjects is indicated for outcomes where some data is lacking. Fat mass was assessed from bioelectric impedance in adults and from bicipital, tricipital and subscapular skinfolds in children/adolescents. HbA_{1c} is the last one performed within the 3 months prior to the laboratory visit. * PA guidelines: 150 min/week of moderate to vigorous PA for adults and 60 min · day⁻¹ of moderate to vigorous PA for children/adolescents. CSII, continuous subcutaneous insulin infusion; MDI, multiple daily insulin injections; MVPA, moderate to vigorous physical activity; NA, not applicable; PA, physical activity.

Table 2— Association between barriers to physical activity (dependent outcome) with everyday life hypoglycemic and hyperglycemic excursions, adjusting for physical activity, sedentary time and participant characteristics as other covariates.

| Dependent variables: barriers to physical activity | Total score | Hypoglycemia score |
|--|---------------------------|---------------------------|
| Glycemic excursions as covariates: | | |
| <u>During or after PA sessions ≥ 1.5 MET-hours*</u> | | |
| <i>Effect of hypoglycemic excursions (% time)</i> | | |
| Adults | | |
| < 3.0 mmol/L, during PA | $\beta = -0.151; P=0.019$ | |
| Children/Adolescents | | |
| < 3.0 mmol/L, night subsequent to PA | $\beta = +0.158; P=0.023$ | $\beta = +0.365; P=0.034$ |
| <i>Percent of reported PA sessions ≥ 1.5 MET-hours involving a decrease in glycemia[†]</i> | | |
| Adults | | $\beta = -0.046; P=0.004$ |
| <i>Effect of normoglycemia (% time)</i> | | |
| Adults | | |
| 3.9-10.0 mmol/L, during PA | $\beta = +0.023; P=0.006$ | |
| 3.9-10.0 mmol/L, 2h after PA | $\beta = +0.031; P=0.043$ | |
| <u>During everyday life (without reference to PA sessions)</u> | | |
| <i>Effect of hypoglycemic excursions (% time)</i> | | |
| Parents | | |
| < 3.0 mmol/L, Week | $\beta = -0.187; P=0.003$ | |
| < 3.0 mmol/L, Week [‡] | $\beta = -0.840; P=0.021$ | |
| < 3.0 mmol/L, Days [‡] | $\beta = -0.848; P=0.024$ | |
| < 3.0 mmol/L, Nights | $\beta = -0.110; P=0.014$ | |
| < 3.9 mmol/L, Week | $\beta = -0.099; P=0.009$ | |
| < 3.9 mmol/L, Week [‡] | $\beta = -1.041; P=0.016$ | |
| < 3.9 mmol/L, Days | $\beta = -0.068; P=0.040$ | |
| <i>Effect of hyperglycemic excursions (% time)</i> | | |
| Children/Adolescents | | |
| > 13.9 mmol/L, Week | $\beta = +0.059; P=0.048$ | NA |

In this table, covariates are in rows and dependent outcomes are in columns.

Coefficients and corresponding *P*-values displayed in the table were estimated from multiple linear regressions, using $\text{mg} \cdot \text{dL}^{-1}$ as the unit for glycemic outcomes. Dependent outcomes are barriers to physical activity with everyday life or exercise-induced glycemic excursions/variability included as covariates. The results concerning the impact of other covariates included in the regressions (*i.e.*, physical activity, sedentary time and participant characteristics) are not shown in this table (their impact is already presented in the text, under the ‘Results’ section). The link between everyday life glycemic excursions and fear of hyperglycemia score is not presented in the table because the analyses appeared to be non-significant. An empty box means there is no significant effect.

* Analysis carried out on the subset of participants reporting physical activity sessions ≥ 1.5 MET-hours during the week of everyday life. † We counted the total number of reported physical activity sessions ≥ 1.5 MET-hours for each participant and the number of sessions ≥ 1.5 MET-hours during which blood glucose levels decreased. With this, we were able to calculate the percentage of sessions during which blood glucose levels dropped. ‡ Refers to

outcomes when hypoglycemic or hyperglycemic risk is expressed as achieving or not the international recommendations (SPSS software analyses compare those who don't achieve the international recommendations with those who did). The international recommendations are as follows: % time <3.0 mmol/L <1%; % time <3.9 mmol/L <4%; % time >13.9 mmol/L <5% [25].

Days, measured during the daytime period; Nights, measured during the nighttime period; Week, measured throughout the usual week, including daytime and nighttime; NA, Non-applicable.

FIGURE LEGEND

Figure 1—BAPAD-1 questionnaire score.

Legend.

1A. In adults

1B. In children/adolescents

1C. In children/adolescents' parents

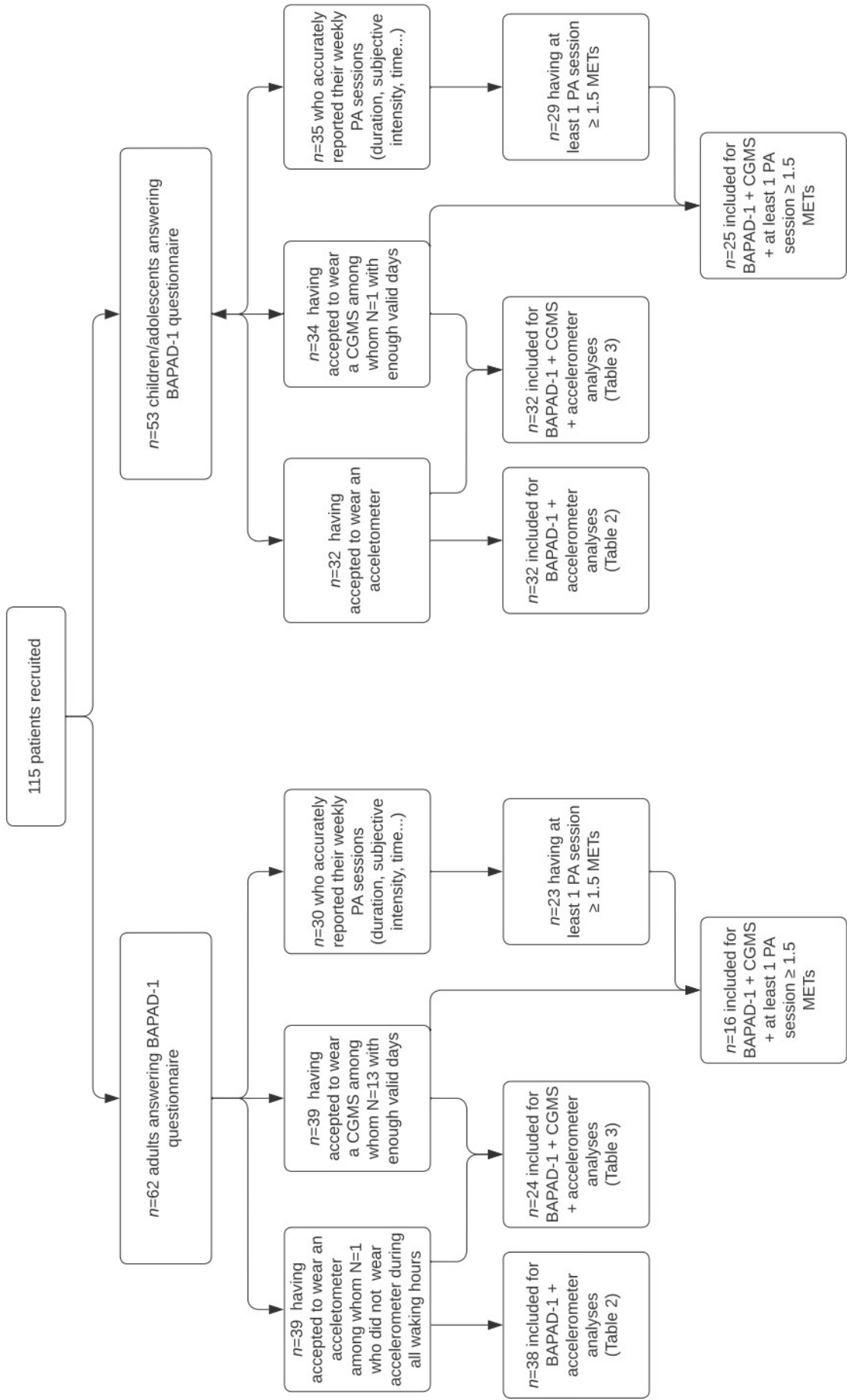
The likelihood that each item would keep the participants from practicing regular physical activity is rated on a scale of 1 to 7 (1 = extremely unlikely to 7 = extremely likely). Scores were grouped from 1 to 3 in black, and 4 to 7 in white.

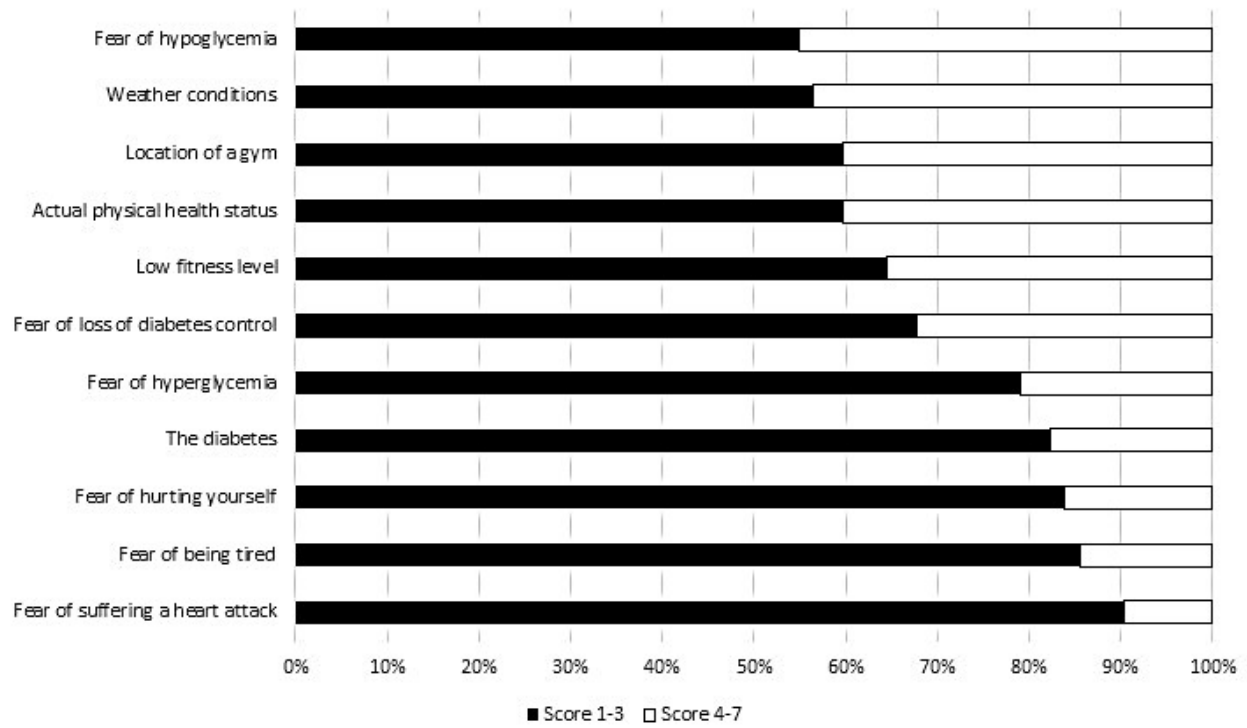
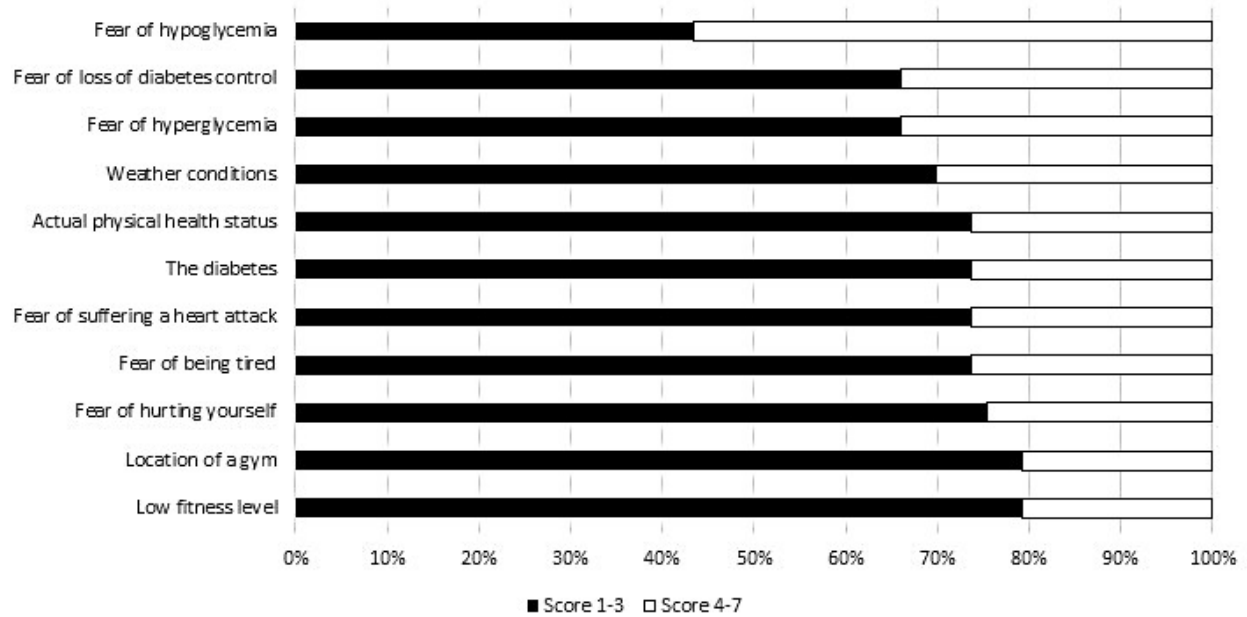
SUPPLEMENTARY MATERIAL

Supplementary Table 1 – Barriers to physical activity assessed by BAPAD-1 questionnaire.

| Barriers to active lifestyle | Adults | Children/Adolescents | Parents of children/adolescents |
|---|------------------|----------------------|---------------------------------|
| 1. The fear of loss of diabetes control | 2.9 ± 1.7 | 2.8 ± 1.9 | 3.2 ± 1.8 |
| 2. The fear of hypoglycemia | 3.5 ± 1.7 | 3.9 ± 2.1 | 3.8 ± 2.0 |
| 3. The fear of being tired | 2.2 ± 1.3 | 2.5 ± 1.9 | 2.8 ± 1.6 |
| 4. The fear of hurting yourself | 2.1 ± 1.5 | 2.3 ± 1.8 | 2.6 ± 1.7 |
| 5. The fear of suffering a heart attack | 1.7 ± 1.2 | 2.4 ± 2 | 2.2 ± 1.5 |
| 6. A low fitness level | 2.9 ± 1.7 | 2.2 ± 1.4 | 2.3 ± 1.7 |
| 7. The fact that you have diabetes | 2.2 ± 1.3 | 2.4 ± 1.7 | 2.6 ± 1.8 |
| 8. The fear of hyperglycemia | 2.4 ± 1.3 | 2.8 ± 2.0 | 2.6 ± 1.7 |
| 9. Your actual physical health status excluding your diabetes | 2.5 ± 1.6 | 2.3 ± 1.6 | 2.2 ± 1.6 |
| 10. Weather conditions | 3.1 ± 1.9 | 2.6 ± 1.8 | 2.6 ± 1.6 |
| 11. The location of a gym | 2.9 ± 1.7 | 2.3 ± 1.6 | 2.6 ± 1.9 |

Data are means ± SD. The likelihood that each item would keep the participants from practicing regular physical activity is measured on a scale of 1 to 7 (1 = extremely unlikely to 7 = extremely likely). PA, physical activity. In bold, the top two barriers (or 3 barriers if 2 are equally ranked) for each sub-group.



A**Adults****B****Children / Adolescents****C****Parents**