## Associations of physical activity and sedentary time with indices of beta cell function and insulin resistance in type 2 diabetes

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**Background and aims:** The aim of this study was to investigate the associations between levels of total and intensity-specific physical activity and sedentary time with HOMA indices of beta-cell function and insulin resistance in persons with newly diagnosed type 2 diabetes (<2 years). To study the associations further, we divided the study sample into predefined pathophysiological sub-phenotypes according to beta-cell function and insulin resistance.

**Materials and methods:** We measured physical activity and sedentary time by dual monitor accelerometry in 765 persons with type 2 diabetes. We calculated HOMA indices and defined groups of sub-phenotypes according to low HOMA- $\beta$ /high HOMA-S (insulinopenic), low HOMA- $\beta$ /low HOMA-S (classic) and high HOMA- $\beta$ /low HOMA-S (hyperinsulinaemic).

**Results:** We conducted multiple linear regression analysis with measures of time spent in total, light, moderate and vigorous physical activity and time being sedentary as explanatory variables while controlling for age and sex. An additional 10 minutes/day of light and moderate to vigorous physical activity was associated with a 0.6% (95% CI 0.3%; 0.9%) and 1.9% (95% CI 1.3%; 2.6%) higher insulin sensitivity, respectively. For each additional 1,000 steps/day insulin sensitivity was 2% (95% CI 1.0%; 3.0%) higher. Conversely, a higher physical activity level was associated with lower betacell function (-1.2%;-2.9%, p<0.01), while more sedentary time was associated with higher beta-cell function (0.7%, 95% CI 0.3%; 1.0%). We further regressed our predefined groups of sub-phenotypes on physical activity and sedentary time. Compared with the classic group (reference), the hyperinsulinaemic group was significantly more sedentary (24.0 min/day 95% CI 8.8; 39.2) and spent less time in light (-14.6 min/day, 95% CI -23.5; -5.8) and moderate to vigorous physical activity (-6.1 min/day, 95% CI -10.4; -1.8). The insulinopenic group was significantly more active than the other two groups (p<0.01). When we further adjusted our regression models for awake time, physical and mental well-being, comorbidities, smoking and BMI, we found that the hyperinsulinaemic group was no longer different from the classic group with respect to activity level, whereas the insulinopenic group remained less sedentary and more active than both the classic and the hyperinsulinaemic group (p<0.01).

**Conclusion:** These findings suggest that a higher degree of insulin resistance/hyperinsulinemia is associated with more sedentary time and lower physical activity levels independent of physical and mental health, current smoking and BMI. The observed inverse association between physical activity and beta-cell function might support evidence stressing that beta-cell function is less affected by exercise. Although, a different disease etiology or genetic profile in combination with healthier lifestyle might as well explain the high physical activity level in persons with very low beta-cell function.

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