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Physical Activity Improves Glucose Tolerance Independent of Weight Loss in Severe Obesity

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Abstract

Background: Impaired glucose tolerance, a risk factor for the development of type 2 diabetes, has a very high prevalence in obese subjects. This study aims to explore the contributions of changes in weight, physical activity (PA), sleep efficiency (SE) and excessive daytime sleepiness (EDS) to changes in glucose tolerance in severely obese subjects during a commercial lifestyle modification programme.

Methods: At intake, after 3 and 6 months of treatment, 33 subjects (28.2% male, age: 42.7 ± 12.3 years, weight: 118.1 ± 23.8, BMI: 40.0 ± 7.3 kg/m^2) were subjected to an oral glucose tolerance test (OGTT), wore an accelerometer for 6 consecutive days and weight and body composition were measured.

Results: After 6 months of treatment there was a significant reduction in weight -11.1 kg, BMI -3.8 kg/m^2, waist circumference -10.8 cm, %Body fat -4.7% and fat mass -10.2 kg (all values p at least <0.001). Glucose tolerance (2 h glucose during OGTT) (0.8 mmol/L, p=0.042) showed a significant improvement. PA, SE and EDS did not change significantly. Changes in weight and PA contributed significantly to the change in glucose tolerance (weight 16%, p=0.021; PA 11%, p=0.049).

Conclusion: We conclude that this commercial lifestyle modification programme significantly reduced weight, waist circumference, %body fat and fat mass and improved glucose tolerance after 3 and 6 months of treatment. The improvement in glucose tolerance was partly explained by the changes in weight and PA, but not by SE or EDS. This study reveals that severely obese subjects benefit from an increase in physical activity independent of weight loss with regard to improvements in glucose tolerance.

Keywords: Obesity; Lifestyle modification; Glucose tolerance; IGT; Physical activity; Sleep efficiency; Excessive daytime sleepiness; Weight loss

Abbreviations: %BF: Percentage Body Fat; EDS: Excessive Daytime Sleepiness; ESS: Epworth Sleepiness Scale; FM: Fat Mass; IGT: Impaired Glucose Tolerance; NGT: Normal Glucose Tolerance; OGTT: Oral Glucose Tolerance Test; PA: Physical Activity; SE: Sleep Efficiency; WC: Waist Circumference

Introduction

Overweight and obesity present a serious health risk, by increasing the risk of several diseases like type 2 diabetes mellitus and cardiovascular disease [1-3]. Reducing the risk of these co-morbidities and maintaining clinically meaningful weight loss should be the goal of any obesity treatment programme. Obesity treatment can consist of an increase in physical activity, reduction of energy intake and/or more healthy eating habits, behavioural change, pharmacological treatment, surgery or a combination of these methods [2-4].

Impaired glucose tolerance, a risk factor for the development of type 2 diabetes, has a high prevalence in obese subjects [5,6]. Weight loss, be it by bariatric surgery or by more conservative methods, has been shown to be associated with improvements in glucose tolerance in obese individuals [7-9]. In addition, it is well-known that exercise training may improve insulin sensitivity and glucose tolerance [10]. Research on this topic has primarily been done in heterogeneous groups, and studies specifically in obese subjects, and even more so in severe obesity, are scarce [11]. In recent years, sleep efficiency (SE) and excessive daytime sleepiness (EDS) have been shown to be associated with both glucose tolerance and obesity [12-15]. But a clear cause-effect relationship has not yet been established.

The aim of the present study was to explore the independent contributions of changes in weight, physical activity, sleep efficiency and EDS to changes in glucose tolerance in obese subjects during treatment in a commercial lifestyle modification programme.

Methods

Subjects

60 subjects from a local commercial obesity treatment centre (CO-EUR, Heerlen, The Netherlands) were recruited. Subjects were at least 18 years old and had a BMI >30 kg/m^2. Insulin-dependent diabetics and subjects that were not able to participate in the physical activity programme were excluded. The study protocol and informed consent document were approved by the Medical Ethical Committee of Maastricht. All subjects gave written informed consent before being enrolled into the study.

Study design

This study was a longitudinal observational study. The researchers

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did not intervene in the treatment programme performed at the obesity treatment centre. At the start (intake) of the treatment in the obesity treatment centre and after 3 and 6 months of treatment, we performed an oral glucose tolerance test (OGTT), a 6-day physical activity (PA) and sleep measurement and we measured weight, height, waist circumference (WC), percentage body fat (%BF) and fat mass (FM). Subjects filled out the Epworth Sleepiness Scale (ESS) at intake and at 3 and 6 months.

Measurements

Oral glucose tolerance test: A standardized OGTT was performed after an overnight fast. At t_0 a capillary blood glucose measurement was performed with a capillary blood glucose meter (Ascensia Breeze® meter, Bayer Healthcare LLC). Capillary blood was obtained by finger prick. The results of this blood glucose meter correlate well with laboratory blood glucose measurements (r=0.97) [16]. Directly thereafter subjects consumed a standard 300 ml glucose drink containing 75 g of glucose dissolved in water. During the next 2 hours, the subjects were not allowed to eat, drink or be physically active. Two hours after consumption of the drink (t_{2h}) capillary blood glucose was measured again. The capillary glucose concentration 2 hours after ingestion of the glucose drink was used to assess glucose tolerance and its change during treatment.

Anthropometric measurements: Body height was measured with a fixed stadiometer (Seca 222, Hamburg, Germany). Body weight was measured with a digital scale (Omron HBF-500E, Omron Healthcare Europe) to the nearest 0.1 kg. Body composition was determined by bioelectrical impedance analysis (Omron HBF-500E, Omron Healthcare Europe). Waist circumference was measured with a flexible tape (Seca 201, Hamburg, Germany).

Physical activity: Physical activity was measured during 6 days at each time point. For this measurement we used a uni-axial accelerometric device: the Sensewear Pro 2 Armband (HealthWear Bodymedia, Pittsburgh, PA). The Sensewear Pro 2 armband was positioned around the right upper arm and worn 24 hours per day except during bathing or water activities. Physical activity was described as a minimum of 2 consecutive minutes at ≥ 3 MET (1 MET (Metabolic Equivalent Task) is the Resting Metabolic Rate (RMR) obtained during quiet sitting. MET values of activities are multiples of RMR and range from 0.9 (sleeping) to 23 (running at 22.5 km/h or a 4:17 mile pace) [17].

Sleep efficiency: The Sensewear Pro 2 Armband measures sleep efficiency (SE) by calculating sleep time as percentage of lying down time. Sleep/wake is assessed per minute. In a recent study by O'Driscoll, the authors compared the Sensewear Pro 3 with polysomnography (PSG). They conclude that the Sensewear was reliable for determining sleep, but was not reliable for determining wakefulness. This reduces its ability to determine sleep versus wake when SE decreases and thus the SE measurement is less reliable than PSG [18].

Epworth sleepiness scale: The Epworth Sleepiness Scale (ESS) [19] is a simple questionnaire consisting of 8 questions on how likely a person is to fall asleep in 8 different situations. These questions generate a numerical score from zero (0) to 24. A score below 10 indicates that the person has an average daytime sleep propensity, a score of ten or higher indicates an above normal sleep propensity, which may for instance be related to the presence of sleep apnea.

Obesity treatment programme

All subjects were enrolled in the commercial obesity treatment programme. This programme consists of an 18-month multi-disciplinary programme targeting lifestyle modification. The programme includes a physical activity programme, psychological counseling and nutritional advice to promote a healthy lifestyle. For the physical activity part there is one group sport session (Nordic walking, swimming or medical training therapy) a week and the subjects are encouraged to implement two additional exercise sessions in their weekly routine. The psychological and nutritional group meetings are scheduled once a week initially, with individual meetings every two to four weeks, depending on the individual needs. In the course of the program the number and frequency of the group meetings is redefined, based on the individual subject's requirements and developments.

Statistical analysis

To analyze the effect of treatment on glucose tolerance, body weight and composition, physical activity and sleep, repeated measures ANCOVA was used. Baseline values were compared to the values after 3 and 6 months of treatment. An explorative stepwise multiple linear regression analysis was performed to elucidate the contributions of changes in body weight, physical activity, sleep efficiency and EDS to the change in glucose tolerance after 6 months. The significance threshold was set at $p \leq 0.05$.

Results

At the 6 months measurement there were only 33 subjects left from the initial 60 (Figure 1). The changes over the 3 and 6 months period will be reported for the subjects that did not drop out of the study (N=33).

Baseline characteristics

Of these 33 subjects 66.7% was female. The subjects could be distributed among the following BMI categories: BMI 30-35 (31.3%); BMI 35-40 (21.9%); BMI >40 (46.9%). 60% had normal glucose tolerance (NGT) and 40% had impaired glucose tolerance (IGT). Only 2 of the 60 subjects had an EDS score ≥ 10. Time spent in light activity (>1 to <3 MET) was 288 ± 97 min/day, in moderate activity (>3 to <6

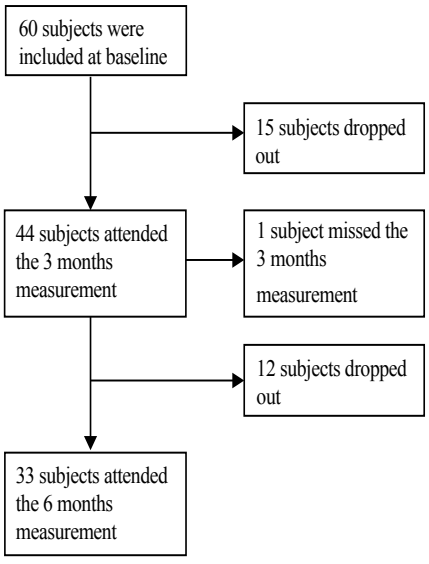

Figure 1: Flowchart of subjects from baseline to 6 months.

MET) was 68 ± 46 min/day and vigorous activity (>6 MET) was 1 ± 3 min/day.

Mean ± SD values of the tested variables at baseline can be found in table 1. No significant differences between completers and drop-outs were found at baseline.

Post-treatment characteristics

After 3 months of treatment weight, BMI, WC, %BF and fat mass (all values p at least <0.001) were significantly reduced. These improvements were sustained at 6 months (all values p at least <0.001). Glucose tolerance, presented as 2 h glucose concentration, improved significantly after 3 months and showed a slight rebound at 6 months, but was still significantly improved compared to baseline. At the 3 months OGTT measurement, 4 of the initial 13 IGT subjects transitioned to NGT. This number was unchanged at 6 months.

SE was significantly reduced within the first 3 months compared to baseline. At 6 months this reduction was no longer statistically significant. PA increased after the first 3 months, but this improvement was not seen after 6 months of treatment. The EDS score showed no significant changes (Table 1).

Linear regression analysis

To explore the independent contributions of the changes in weight, PA, SE and EDS to the changes in 2 h glucose concentration over the 6 months treatment period, a backward stepwise multiple linear regression analysis was performed.

This resulted in the following final model:

$\Delta_{0\text{-}6}$2h glucose (in mmol/L)=intercept + β_1*$\Delta_{0\text{-}6}$weight (in kg) + β_2*$\Delta_{0\text{-}6}$PA (in min/d), with: intercept=0.867; β_1=0.390 (p=0.021) and β_2=-0.322 (p=0.049).

The partial regression plots for changes in weight (Figure 2A) and changes in PA (Figure 2B) show that the changes in weight and PA account for a total of 27% (weight: 16%; PA: 11%) of the variation in the change in 2 h glucose concentration. Adding the baseline 2 h glucose value to the model did not influence the outcome.

Discussion

This commercial lifestyle modification programme significantly reduced weight, BMI, WC, %BF and fat mass and improved glucose tolerance after 3 months of treatment. For the anthropometric measurements, further improvements were found at 6 months of treatment. Glucose tolerance did not show further improvements, but was still significantly improved compared to baseline after 6 months. PA significantly increased in the first 3 months, but this increase disappeared again onto the 6 months mark. Sleep efficiency was significantly reduced in the first 3 months but no longer after 6 months of treatment. The main finding of this study was a positive association between the changes in physical activity with the changes in glucose tolerance, independent of changes in weight. We found no association between changes in sleep quantity and quality and changes in glucose tolerance. To date, this is the first study reporting such finding in an extremely obese population.

At baseline, 47% of the subjects had a BMI >40 kg/m^2 which makes them eligible for bariatric surgery [20]. 40% had impaired glucose tolerance (IGT). SE at baseline was comparable with reports from other studies in diabetics [12] and moderately obese [15] subjects, with 41% of our subjects having a SE in the normal range of >85%. On average, the subjects in our study performed moderate to high intensity (>3 MET) PA for 69 min/day. This is considerably less than the moderately obese (BMI approximately 32 kg/m^2) subjects in a recent study by Scheers et al. [21]. These subjects performed 127 min/day of moderate to high intensity PA [21].

Average percentage weight loss during the first 3 months is higher in our study (7.3%) compared to large population studies of other commercial treatment programmes (4-5%) [22-25]. Percentage weight loss at 6 months also exceeds previous reports of other commercial treatment programmes (9.4% vs. 4.6 to 5.1%) [26,27]. 31% of the initial 13 IGT subjects transitioned to NGT during the 6 months treatment.

Physical activity (>3 MET) increased with 30 min/day in the first 3 months, but at 6 months this increase was only 9 min/day compared to baseline. When looking at the advice given by the treatment centre (1 obligatory and 2 self-implemented exercise sessions per week for an approximate total of 180 minutes), the increase of 30 min/day in the first 3 months is just above the given advice (180 minutes per week=26 min/day). The difference of 9 min/day at 6 months compared to baseline could mean that the subjects only attended the obligatory exercise session (60 minutes per week=9 min/day). The 3 months measurement was mainly done in the summer, whereas the 6 months measurement was executed during winter. Therefore, seasonal variation in leisure time physical activity could also be an explanation

		Baseline		3 months		6 months	
Variable	**N**	**Mean ± SD**	**N****	**Mean (CI)**	**p-value***	**Mean (CI)**	**p-value***
Age (years)	33	42.7 ± 12.3					
Height (cm)	33	172 ± 1.0					
Weight (kg)	33	118.1 ± 23.8	32	-8.7 (-10.6 to -6.7)	<0.001	-11.1 (-13.5 to -8.6)	<0.001
BMI (kg/m^2)	33	40.0 ± 7.3	32	-2.9 (-3.6 to -2.3)	<0.001	-3.8 (-4.6 to -2.9)	<0.001
WC (cm)	33	124 ± 15.6	32	-6.5 (-7.8 to -5.1)	<0.001	-10. 8 (-12.7 to -8.9)	<0.001
Body fat (%)	31	46.7 ± 6.8	29	-4.3 (-5.3 to -3.3)	<0.001	-4.7 (-5.9 to -3.5)	<0.001
Fat mass (kg)	31	54.1 ± 12.6	29	-8.8 (-10.5 to -7.1)	<0.001	-10.2 (-12.3 to -8.1)	<0.001
Fasting glucose (mmol/L)	33	5.0 ± 0.9	31	-0.1 (-0.5 to 0.3)	0.648	0.6 (0.3 to 0.8)	<0.001
2h glucose (mmol/L)	33	8.2 ± 3.0	31	-1.2 (-2.2 to 0.2)	0.017	-0.8 (-1.5 to 0.0)	0.042
SE (%)	33	81.8 ± 6.9	27	-1.7 (-3.3 to -0.1)	0.035	-1.5 (-3.3 to 0.3)	0.095
ESS	33	3.4 ± 2.7	32	-0.3 (-0.8 to 0.3)	0.337	-0.5 (-1.1 to 0.1)	0.078
PA (min/day)	33	69 ± 49	27	30 (7 to 53)	0.011	9 (-8 to 26)	0.273

*Analysis by repeated measures ANOVA
**Number of subjects that had baseline, 3 and 6 months measurements for the analyzed variables in the repeated measures ANOVA

Table 1: Baseline characteristics and changes from baseline after 3 and 6 months of treatment (mean (CI, confidence interval)).

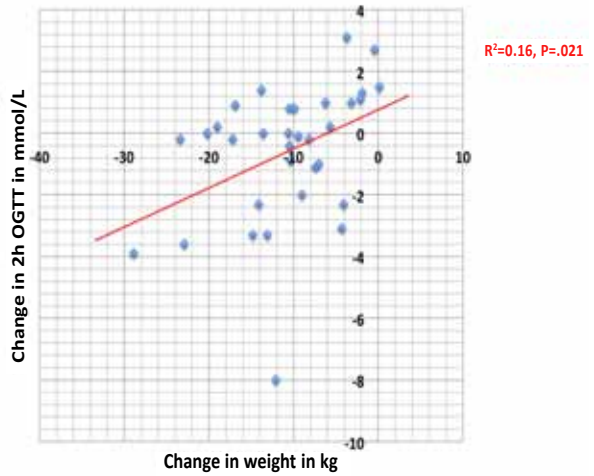

Figure 2A: Partial linear regression plot of the change in 2h glucose value and the change in weight.

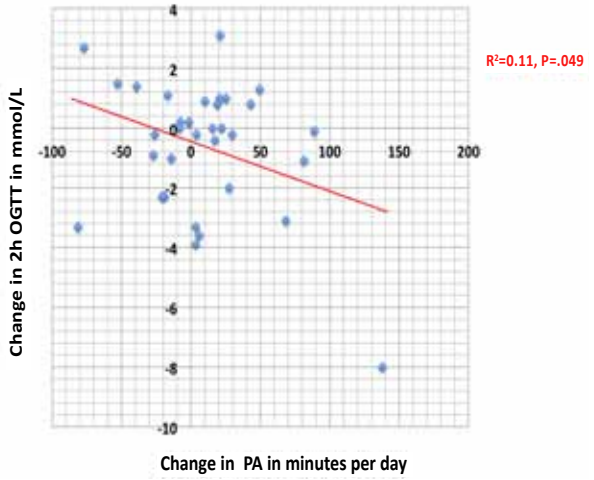

Figure 2B: Partial linear regression plot of the change in 2h glucose value and the change in PA.

for the decrease in PA at the 6 months measurement compared to the 3 months measurement. Data on seasonal variation in PA have been reported by Pivarnik et al. [28]. They report that in winter compared to summer, their participants perform fewer exercise sessions per week and the sessions have a shorter duration.

The most interesting finding of this study was the association between the change in glucose tolerance and the changes in weight and PA, whereas no association with changes in SE or EDS was found.

Previous studies by Katzel et al. have shown that weight loss but not aerobic exercise improved glucose tolerance in obese men after 9 months of weight loss vs. exercise [29,30]. Weight loss in these studies was comparable with our findings. There have been studies reporting on exercise-induced improvements in glucose tolerance [31,32]. But the subjects in these studies were overweight and had abnormal glucose regulation [32] and/or were at high risk for CVD [31]. The results from the above named studies show that weight loss and exercise can independently improve glucose tolerance. But, we did not find a comparable study that shows an independent effect of physical activity on glucose tolerance in a lifestyle modification programme where significant weight loss is achieved in severely obese subjects.

We did not find an association between changes in glucose tolerance and changes in SE or EDS. This may be due to the fact that there was no significant improvement in SE and EDS. EDS was within normal values (score<10) during the whole study period, we therefore conclude that EDS is not a big issue in this sample. Also, SE was significantly reduced at 3 months compared to baseline. Our hypothesis was that SE would improve with weight loss but maybe the weight loss was not large enough. Kalra et al. [33] found a significant improvement in SE after surgical weight loss of 66.4 ± 8.8 kg.

This study has some limitations. First we experienced a large drop-out of 45%. This is due to subjects not wanting to continue with the study, but also some subjects dropped out of the treatment programme and were therefore not eligible for inclusion in our study. In 5 subjects PA and SE was not measured correctly, probably because subjects did not clean the electrodes on the device. These electrodes can become obstructed by sebaceous matter and therefore fail to conduct signals from the skin of the arm. When cleaned properly every evening this is no problem, but some subjects forgot to do this. In 3 subjects we were not able to measure %body fat and fat mass with the bio-impedance scale, because of a %body fat >55%, the upper detection limit of the bio-impedance scale. Only 1 subject missed the 3 months measurement, but was present at the 6 month measurement, hence the missing weight, BMI and WC data.

We can conclude that this commercial lifestyle modification programme significantly reduced weight, waist circumference, %body fat and fat mass and improved glucose tolerance after 3 and 6 months of treatment. The improvement in glucose tolerance was partly explained by the changes in weight and PA, but not by SE or EDS.

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