

**chapter 6 – metabolic and vascular insulin sensitivity
in obesity and hypertension**

Obesity and hypertension are independently associated with microvascular insulin sensitivity.

to be submitted

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Abstract

Impaired insulin-induced glucose disposal and capillary recruitment (i.e. metabolic and microvascular insulin resistance, respectively) are characteristics of coexisting conditions obesity and hypertension. Whereas hypertension is considered a metabolic insulin resistant state in itself, it is presently unclear to what extent microvascular insulin resistance is independent of adiposity in hypertensive individuals. We addressed this question in a four-corner model, using four distinct phenotypic groups of individuals: non-obese normotensive (NN), non-obese hypertensive (NH), obese normotensive (ON), and obese hypertensive (OH). In a cross-sectional study 21 individuals with hypertension (12 lean and 9 obese) and 23 age- and BMI-matched normotensive controls (11 lean and 12 obese) were included. We examined capillary density in skin by capillary videomicroscopy at baseline and during a 120-min euglycemic-hyperinsulinemic clamp. Blood pressure was assessed using 24-h ambulatory blood pressure monitoring. Compared to NN individuals, metabolic insulin sensitivity decreased gradually from NH, ON to OH individuals (8.2 ± 2.4 , 6.4 ± 2.2 , 3.9 ± 1.8 , and 2.8 ± 1.9 $\text{mg}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, p for trend <0.001). Obesity showed a more profound decrease in metabolic insulin resistance (non-obese vs. obese 7.27 ± 2.38 vs. 3.42 ± 1.82 $\text{mg}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, $p<0.001$) than the presence of hypertension (normotensive vs. hypertensive 5.98 ± 2.93 vs. 4.84 ± 2.67 $\text{mg}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, $p=0.23$). Compared to NN individuals, insulin-augmented capillary recruitment decreased gradually from NH, ON to OH individuals (13.1 ± 15.9 , 4.4 ± 10.9 , 2.8 ± 4.7 , and -6.5 ± 12.0 percent-points, respectively, p for trend <0.0001). Both obese and hypertensive individuals displayed a significantly lower insulin-augmented capillary recruitment when compared with their respective controls (non-obese 8.6 ± 13.6 %-points vs. obese -1.2 ± 9.3 %-points, $p<0.01$ and normotensive 7.7 ± 12.1 %-points vs. hypertensive -0.26 ± 12.1 %-points, $p<0.05$). Obesity and hypertension have compounding detrimental effects on metabolic and microvascular insulin sensitivity. Obesity seems to be of greater impact than hypertension on metabolic insulin-sensitivity, whereas both have a similar impact on microvascular insulin sensitivity.

Introduction

The rising prevalence of overweight and obesity has reached pandemic proportions (1). The tendency of obesity to cluster with other cardiovascular risk factors such as hypertension and dyslipidemia in the metabolic syndrome has led to the suggestion for a common causal origin. Insulin resistance has received wide attention as a possible underlying combining factor explaining this clustering (2). Classically thought to be primarily a metabolic characteristic of insulin-target tissues like skeletal muscle, the liver and adipose tissue, insulin receptors and their downstream signaling cascade have been found to play an equally important role in the vasculature (3,4,5). The ensuing entity of vascular insulin resistance has since been proposed as an alternative clustering factor (6,7,8). By affecting both flow resistance and tissue perfusion, obesity-related microvascular dysfunction (e.g. impaired vasoreactivity) seems an important contributor in the development of hypertension and metabolic insulin resistance (7,9,10). Often found clustered together, obesity and hypertension are both regarded to be insulin-resistant states in their own right (8,11,12,13). However, this clustering with obesity has hampered previous studies investigating insulin sensitivity in hypertensive individuals (12,13). A substantial number of people with hypertension are not obese. Therefore, the question arises whether such individuals are also at a greater risk of metabolic and vascular insulin resistance, i.e. whether hypertension is associated with these characteristics independently of the presence of obesity. Similarly, in obese individuals with hypertension, the question remains whether the risks conferred by obesity and hypertension are additive. Although one can statistically correct for variables such as BMI (14), a 'four-corner' model featuring all possible combinations of hypertension and obesity would be best suited to address these questions. Our aim in the present study was therefore to characterize both metabolic and microvascular insulin-sensitivity in four groups of individuals with high and low blood pressure and high and low BMI as defining variables. We hypothesize that microvascular and metabolic insulin-sensitivity are decreased in both hypertensive and obese individuals.

Methods

Participants

Forty-four healthy volunteers participated in this study (table 1). They were recruited by local advertisements. None had a history of cardiovascular events and all were non-diabetic according to ADA criteria (15). Participants were of Caucasian origin and non-smokers. Nine individuals were taking antihypertensive medication at the time of inclusion. Two were treated with an ACE inhibitor, alone (n=1) and in combination with a calcium channel blocker (n=1); two individuals were treated with an angiotensin II receptor blocker, alone (n=1) and in combination with a thiazide diuretic (n=1); three individuals were treated with beta-blockers, alone (n=2) and in combination with a thiazide diuretic (n=1); two individuals were treated with a thiazide diuretic alone. No medication was used during 4 weeks leading up to the day of study. After 4 weeks cessation of medication, and before the study, all participants underwent a 24h ambulatory blood pressure measurement. Individuals were categorized according to body mass index (BMI) and daytime systolic blood pressure (SBP) into 4 groups: non-obese normotensive (NN) (BMI < 30 kg·m⁻², SBP < 135 mmHg), non-obese hypertensive (NH) (BMI < 30 kg·m⁻², SBP ≥ 135 mmHg), obese normotensive (ON) (BMI ≥ 30 kg·m⁻², SBP < 135 mmHg) and obese hypertensive (OH) (BMI ≥ 30 kg·m⁻², SBP ≥ 135 mmHg). The study protocol was approved by the local Ethics Committee and in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants.

Study design

All individuals underwent the study protocol as shown in figure 1. Measurements were conducted in a fasting state on an outpatient basis in a quiet, temperature-controlled room (23.0±1.0°C) after 30 minutes of acclimatization. Participants had abstained from caffeine, alcohol and meals overnight. The microvascular measurements were performed in the supine position.

Measurements

Blood pressure

24-h ambulatory blood pressure monitoring (Spacelabs 90207, Redmond, Washington, USA) was performed during the screening period (and again after discontinuation of antihypertensive medication when applicable) at the non-dominant arm with appropriately sized cuffs at 20-minute intervals from 8.00 to 22.00 hours and at 30-minute intervals from 22.00 to 8.00 hours. The readings were individually edited into daytime and nighttime periods according to participants' activity diaries.

Capillary videomicroscopy

Nailfold capillary studies were performed as described in detail elsewhere (16). Briefly, nailfold capillaries in the dorsal skin of the third finger of the left hand were visualized by a capillary microscope (Zeiss), linked to a television camera (Philips LDH 070/20). A 3.2x objective (Zeiss 3.2/0.07) was used with a total system magnification of 99x. The number of perfused capillaries was counted off-line by an experienced investigator (M.P.d.B.) from a videotape. Capillary density at baseline was defined as the number of capillaries per square millimeter which were continuously perfused for 15 seconds during an observation-period of 30 seconds. Capillary density after post occlusive reactive hyperemia (PRH) was determined by counting all visible capillaries after four minutes of arterial occlusion. Capillary recruitment was calculated as the relative increase in capillary density from the continuously filled fraction to capillary density after PRH. Insulin-augmented capillary recruitment (percentage-points) was defined as the increase in capillary recruitment during hyperinsulinemia from capillary recruitment during saline infusion. The day-to-day coefficients of variation (CV) of continuously perfused capillary density and peak capillary density were $3.4\pm 2.0\%$ and $3.9\pm 1.6\%$ respectively, as determined in 10 individuals on separate days (16).

Insulin sensitivity

Insulin sensitivity was assessed by the hyperinsulinemic, euglycemic clamp technique (17). Briefly, insulin (Actrapid, Novo Nordisk, Bagsvaerd, Denmark) was infused in a primed ($0.4 \text{ U}\cdot\text{ml}^{-1}$) continuous manner at a rate of $1 \text{ mU}\cdot\text{kg}\cdot\text{min}^{-1}$. Euglycemia (5 mmol/L) was maintained by adjusting the rate of a 20% glucose infusion based on plasma glucose measurements performed at 5-10 minute intervals using an YSI 2300 STAT Plus analyzer (YSI, Yellow Springs, USA). Whole body glucose uptake (M-value) was calculated from the glucose infusion rate during steady state of the clamp and expressed per kilogram of body weight.

Laboratory data

Blood was collected before and during insulin infusion (figure 1). All serum samples were immediately centrifuged at 4°C and stored at -80°C . Insulin was measured by using an immunometric assay with luminescence (Siemens Healthcare Diagnostics Inc. Tarrytown, NY, USA). The inter-assay CV was below 7% and the intra-assay CV was below 4%. Glucose was measured with the hexokinase method (Roche Diagnostics, Mannheim, Germany). The inter- and intra-assay CV were both below 2%. Total cholesterol, high-density lipoprotein (HDL)-cholesterol and triglycerides were measured with an enzymatic colorimetric assay (Roche Diagnostics). The low-density lipoprotein (LDL)-cholesterol level as calculated according to the Friedewald formula. Free fatty acids were measured with an enzymatic colorimetric test (NEFA-C, WAKO chemicals, Neuss, Germany). Adiponectin was determined by radioimmunoassay (Linco Research, St.Charles, USA). The inter- and intra-assay CV were 9 and 5% respectively. All laboratory assays were performed in the clinical chemistry/endocrine laboratory of the VU University Medical Center.

Statistical analyses

All variables were first tested for normality of distribution. Data are presented as mean±SD or median and inter quartile range when applicable. One-way analysis of variance with the Bonferroni post hoc test (Kruskal Wallis for non-normally distributed data) was used to investigate differences in characteristics of interest between the 4 groups. We used two-way analysis of variance with the Bonferroni post hoc test to compare insulin sensitivity and microvascular function between obese versus non-obese and hypertensives versus normotensives. A one-way analysis of variance post-hoc test for trend was performed across the 4 groups for insulin sensitivity and microvascular function. Insulin sensitivity was hypothesized to decrease from lean normotensive individuals towards obese hypertensive individuals. Based upon previous results from our group, we expected to find the largest decrease in insulin sensitivity in the obese individuals (18,19). The 4 groups were ordered accordingly. Finally, multivariable linear regression analysis was performed to investigate to what extent microvascular insulin sensitivity determines metabolic insulin sensitivity for both the hypertensive and obese groups. The regression analyses were corrected for sex. A two-tailed P-value of <0.05 was considered significant. All analyses were performed using the statistical software package SPSS (version 18.0, SPSS, Inc., Chicago, USA).

Results

Characteristics of the study groups

Baseline characteristics of the study groups are shown in [table 1](#). Forty-four healthy individuals (35 women, 9 men) were included in this study. The mean age did not differ between the 4 groups. Mean blood pressure values were comparable between the two normotensive groups and between the two hypertensive groups. Mean BMI was comparable between the two non-obese groups and between the two obese groups. All 4 groups had comparable fasting glucose levels. Fasting insulin was higher in the obese groups as expected. The normotensive obese group had a relatively favorable lipid profile with a higher HDL-cholesterol, and a lower LDL-cholesterol compared to the other groups ([table 1](#)).

Microvascular variables at baseline

Both continuously perfused capillary density and total capillary density after PRH were lower in the obese normotensive individuals at baseline as compared to both non-obese groups. However, baseline capillary recruitment, expressed as percentage increase, was not different among the four groups ([table 2](#)).

Microvascular insulin sensitivity decreases when more cardiovascular risk factors are present

During insulin infusion, continuously perfused capillary density and total capillary density after PRH were again lower in the obese normotensive individuals as compared to both non-obese groups. Subsequent capillary recruitment was lower in the obese hypertensive group as compared to the non-obese normotensives ([table 2](#)). Both obese and hypertensive individuals displayed a significantly lower increase in insulin-augmented capillary recruitment when compared with their respective controls ([table 2](#)). Post-hoc analysis showed a trend in decreasing microvascular insulin sensitivity in the presence of hypertension, obesity and the combination of both ([figure 2](#)). The use of absolute changes in capillary density showed similar results (data not shown). There was no interaction between obesity and hypertension regarding insulin-augmented capillary recruitment (p-value for interaction-term = 0.89).

Metabolic insulin sensitivity decreases when more cardiovascular risk factors are present

The level of euglycemia during the hyperinsulinemic clamp did not differ between the groups (NN 4.8±0.4 mmol/l, NH 4.7±0.4, ON 4.9±0.2 and OH 4.6±0.4). The mean plasma insulin level during the steady state of insulin infusion was higher in the obese groups, and for the obese hypertensives significantly so, as compared with the

nonobese groups (ON 494±67 pmol/l, OH 554±92 pmol/l versus NN 455±47, NH 426±71), thus relatively overestimating the M-value for the obese group. Metabolic insulin-sensitivity was significantly lower in the obese and hypertensive individuals as compared with the non-obese and normotensive individuals respectively (table 2). The presence of hypertension was associated with a further decrease of insulin sensitivity within the obese and non-obese groups (figure 3). There was no interaction between obesity and hypertension regarding insulin-mediated glucose uptake (p-value for interaction-term = 0.67).

The association between microvascular and metabolic insulin sensitivity

In a multivariable linear regression analysis, we investigated whether the association between the presence of hypertension or obesity with whole body glucose uptake could statistically be explained, at least partly, by microvascular insulin sensitivity. The presence of hypertension decreased whole body glucose uptake by 1.59 milligrams of glucose per kilogram body weight per minute (95%-CI: -3.24 to 0.06; p=0.058). After adjustment for microvascular insulin sensitivity, the regression coefficient of the association between the presence of hypertension and whole body glucose uptake decreased by 57% (β -0.68, 95%-CI: -2.43 to 1.08; p=0.44). The presence of obesity decreased whole body glucose uptake by 3.73 milligrams of glucose per kilogram body weight per minute (95%-CI: -5.27 to -2.19; p<0.0001). After adjustment for vascular insulin sensitivity, the regression coefficient of the association between the presence of obesity and whole body glucose uptake decreased by 11% (β -3.32, 95%-CI: -4.79 to -1.84; p<0.0001).

Discussion

The present study demonstrates that obesity and hypertension have compounding detrimental effects on metabolic and microvascular insulin sensitivity. In this study, obesity seems to be of greater impact than hypertension on metabolic insulin-sensitivity, whereas both have a similar impact on microvascular insulin sensitivity. To date, dedicated studies comparing hypertension and obesity have mainly focused on metabolic insulin-sensitivity, although various definitions of hypertension and obesity as well as methods to assess metabolic insulin-sensitivity have been used (11,12,13). To the best of our knowledge, this is the first study to evaluate the relative contributions of obesity and hypertension to microvascular and metabolic insulin-sensitivity in one study. Metabolic insulin sensitivity did not differ between the hypertensive and normotensive non-obese individuals nor between the hypertensive and normotensive obese individuals. This might be due to the relatively small number of individuals in the individual groups as there was a significant inverse trend across the groups for insulin sensitivity. Indeed, when comparing all hypertensive individuals with their normotensive counterparts, the M-value was significantly lower. Both obese groups were, on average, metabolically insulin-resistant and their M-value was significantly lower as compared to either of the non-obese groups. Overall, the presence of obesity seems to be a stronger determinant of metabolic insulin sensitivity, but not microvascular insulin sensitivity compared to the presence of hypertension in this study population. As skeletal muscle and the vasculature share an intracellular insulin signaling pathway, with its downstream PI3K/AKT/NO cascade leading to GLUT4 translocation and vasodilation respectively, we would have expected the inverse trends for metabolic and vascular insulin sensitivity to run in parallel (4,7,8,9). The fact that they do not in this study population suggests that there may be additional factors at play. In addition to stimulation of the PI3K/AKT/NO cascade, insulin also activates the mitogen-activated protein kinase pathway in endothelial cells, which enhances the generation of the vasoconstrictor ET-1 via ERK1/2 signaling (4). In healthy individuals, the vasodilatory signal predominates, but if the ET-1 pathway is stimulated, this can lead to impaired insulin-mediated vasodilatation or even insulin stimulated vasoconstriction. Compared to normotensive individuals (obese and non-obese), hypertensive individuals (obese and non-obese) have been shown to have enhanced activation of the ET-1 pathway (20). The presence of hypertension would thus tip the insulin-mediated NO/ET-1 balance further towards vasoconstriction than would obesity. Alternatively (and

perhaps in concert with effects on ET-1), site-specific (e.g. local effects of perivascular adipose tissue versus systemic effects of visceral adipose tissue) or dose-response effects of adipokines such as adiponectin and TNF- α might explain the difference in the insulin-sensitivity trends (8,21). These non-parallel trends suggest microvascular insulin sensitivity to be a more important determinant of whole body glucose uptake in the presence of hypertension than in the presence of obesity. Statistically, this seemed to be the case in the multivariable regression analyses with a change of nearly 60% in whole body glucose uptake when adjusting for microvascular insulin sensitivity in the presence of hypertension as opposed to an 11% change in the presence of obesity.

There are several strengths and limitations to this study. Often part of the obese metabolic syndrome-phenotype, hypertension per se is widely regarded as an insulin-resistant state after several showed impaired insulin-sensitivity in hypertensive individuals (11,12,13,19,22). Of note, in most of these studies the insulin resistant-state of hypertensive individuals is relative to their respective controls. In the study by Laine et al. for example, the hypertensive subjects were on average quite insulin sensitive with an M-value of 7.7 mg of glucose taken up per kg of skeletal muscle per minute (22). Several studies mentioned used the oral glucose tolerance test (12,13), a test more suited to study pancreatic beta cell function (23). Except for one study that used 24-h blood pressure monitoring (19), most studies have used the average of three office blood pressure measurements to establish the presence of hypertension. Finally, although their objective to study non-obese hypertensive subjects was met, the included participants were often still overweight (BMI > 25) (11,13). During the recruitment of participants for the present study, we were able to include on average normal weight hypertensive individuals. This enabled us to study clearly distinct groups (i.e. four corners). We have used state-of-the art and gold-standard methods to assess the variables of interest. Besides the use of the euglycemic hyperinsulinaemic clamp to assess metabolic insulin-sensitivity, blood pressure was assessed via 24-h ambulatory blood pressure monitoring, greatly improving accuracy over triplicate office measurements. Finally the video microscope is the only method capable of direct visualization of capillaries in skin. Recently, we were able to demonstrate a direct statistical relationship between capillary recruitment in skin and changes in microvascular blood volume in skeletal muscle, corroborating the use of skin as a proxy for microvascular function in skeletal muscle (16). The overall number of participants in this study and the number of men in particular was relatively small. The latter makes the findings less generalizable. Men were, however, relatively overrepresented in the non-obese hypertensive group, possibly underestimating insulin-sensitivity as compared to the (all) female subject-groups. The adipokine adiponectin, a well known insulin-sensitizer (24) for example was lower in men than women (data not shown). Another notable difference between the groups was the relatively favorable lipid profile of the obese normotensive women with higher HDL and lower LDL levels, possibly affecting the results. We have previously shown capillary recruitment as assessed with the video microscope to be similar throughout the different phases of the menstrual cycle (25).

In conclusion, the inverse trends of both microvascular and metabolic insulin sensitivity with compounding cardiometabolic risk factors corroborate a generalized disturbance in the insulin-signaling cascade found in both skeletal muscle and the microvasculature.

Tables

table 1 - characteristics of the study groups, mean±SD or median (interquartile range)

characteristic	low BMI	low BMI	high BMI	high BMI
	low BP (NN)	high BP (NH)	low BP (ON)	high BP (OH)
<i>n</i> (males)	11 (3)	12 (6)	12 (0)	9 (0)
age, yrs	45.2 ± 9.1	42.9 ± 11.0	42.2 ± 9.2	39.3 ± 9.4
BMI, kg·m ⁻²	23.4 ± 2.1	23.9 ± 2.4	36.9 ± 5.0	39.2 ± 8.3
waist, cm	84.1±6.7	86.5±11.2	111.1±14.6	104.1±8.2
SBP, mmHg	120.2 ± 6.2	148.3 ± 9.6	123.1 ± 7.5	145.7 ± 7.2
DBP, mmHg	78.3 ± 9.7	95.9 ± 10.5	73.6 ± 8.3	89.0 ± 7.2
MAP, mmHg	92.4 ± 8.8	113.3 ± 10.2	91.4 ± 7.4	108.0 ± 7.2
fasting plasma glucose, mmol/l	4.7 ± 0.4	4.9 ± 0.4	5.1 ± 0.5	5.0 ± 0.3
fasting plasma insulin, pmol/l	27.4 (23.8-35.1)	33.4 (26.2-57.9)	64.0 (38.9-92.2)	59.1 (47.3-132.2)
adiponectin, mg/l	15.0 ± 5.7	10.9 ± 5.2	10.9 ± 4.6	10.0 ± 3.2
fasting serum total cholesterol, mmol/l	4.8 ± 1.0	4.8 ± 0.5	5.0 ± 1.0	5.0 ± 0.9
fasting HDL-cholesterol, mmol/l	1.6 ± 0.3	1.6 ± 0.5	2.5 ± 0.9	1.4 ± 0.8
fasting LDL-cholesterol, mmol/l	2.8 ± 0.9	2.6 ± 0.5	2.0 ± 0.8	2.8 ± 0.9
fasting serum triglycerides, mmol/l	0.8 (0.5-1.4)	1.1 (0.8-1.5)	1.0 (0.8-1.3)	1.3 (0.9-2.3)
fasting plasma FFA's, mmol/l	0.4 ± 0.2	0.5 ± 0.2	0.6 ± 0.1	0.6 ± 0.2

BP indicates blood pressure, SBP indicates daytime 24hr systolic blood pressure, DBP indicates daytime 24hr diastolic blood pressure, MAP indicates daytime 24hr mean arterial pressure, HDL indicates high density lipoproteins, LDL indicates low density lipoproteins, FFA's indicates free fatty acids.

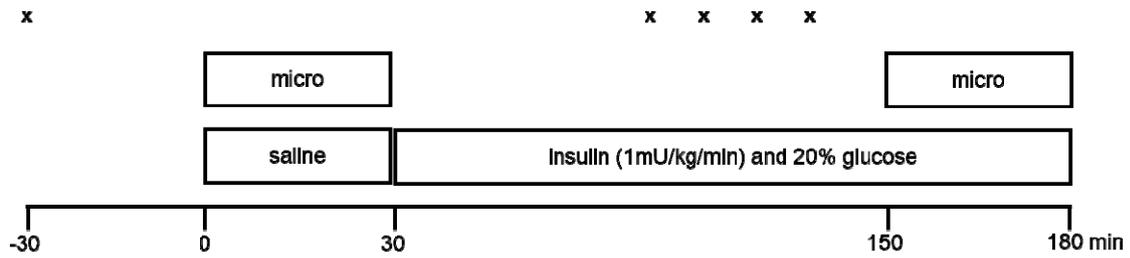
table 2 - insulin's vascular and metabolic effects, mean±SD

parameter	NN (n=11)	NH (n=12)	ON (n=12)	OH (n=9)	hypertensive versus normotensive, p difference	obese versus non-obese, p difference
saline continuously perfused capillaries, n/mm2	50.4 ± 6.2	50.4 ± 4.7	42.6 ± 5.6 [#]	44.8 ± 7.0 [*]	0.54	0.001
saline total capillary density, after PRH, n/mm2	71.9 ± 16.0	71.8 ± 9.3	54.2 ± 7.4 ^{***,##}	64.6 ± 10.8	0.14	0.001
saline capillary recruitment, %	43.0 ± 29.7	42.6 ± 15.8	27.8 ± 15.8	44.4 ± 11.1	0.18	0.26
insulin, baseline continuously perfused capillaries, n/mm2	50.0 ± 5.2	50.9 ± 6.0	42.0 ± 6.6 ^{*,#}	46.1 ± 8.7	0.23	0.003
insulin, total capillary density, after PRH, n/mm2	77.7 ± 12.7	74.6 ± 11.9	54.7 ± 9.3 ^{***,##}	63.1 ± 9.5 [*]	0.43	7*E-6
insulin, capillary recruitment, %	56.1 ± 24.9	47.1 ± 17.7	30.6 ± 15.6 [*]	37.9 ± 12.1	0.88	0.003
insulin-augmented capillary recruitment, %-points	13.1 ± 15.9	4.4 ± 10.9	2.8 ± 4.7	-6.5 ± 12.0 ^{**}	0.014	0.004
M-value, mg·kg ⁻¹ ·min ⁻¹	8.2 ± 2.4	6.4 ± 2.2	3.9 ± 1.8 ^{***,#}	2.8 ± 1.9 ^{***,##}	0.23	<1.0E-7

NN indicates non-obese normotensive, NH indicates non-obese hypertensive, ON indicates obese normotensive and OH indicates obese hypertensive. Column 1 through 4: one-way ANOVA analyses between the 4 groups * p<0.05 vs. column 1, ** p<0.01 vs. column 1, # p<0.05 vs. column 2, ## p<0.01 vs. column 2. Column 5 and 6: two-way ANOVA analyses as indicated. PRH indicates peak reactive hyperemia, M-value indicates metabolic insulin sensitivity as assessed with the hyperinsulinemic euglycemic clamp.

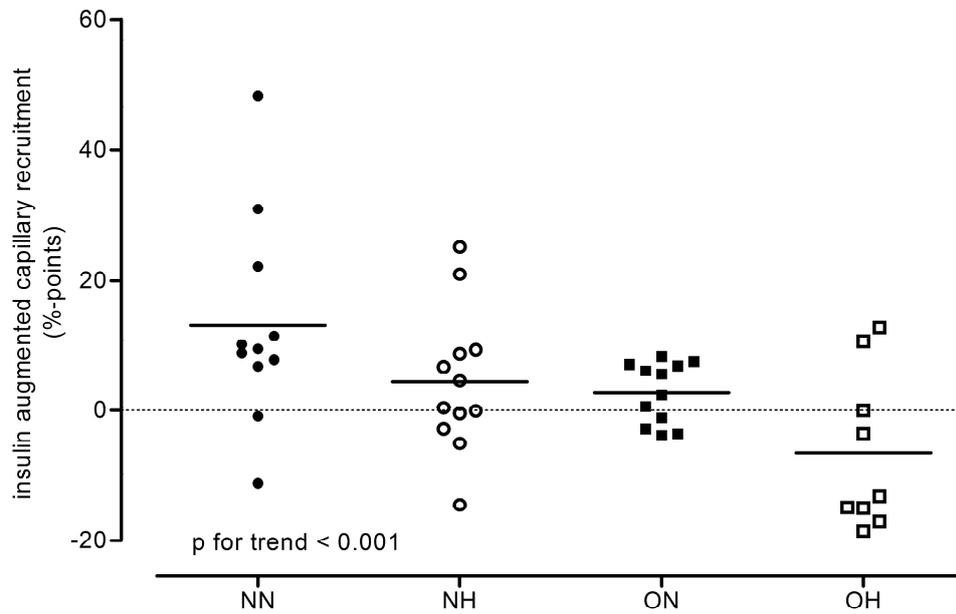
Figures

figure 1 – design of the study



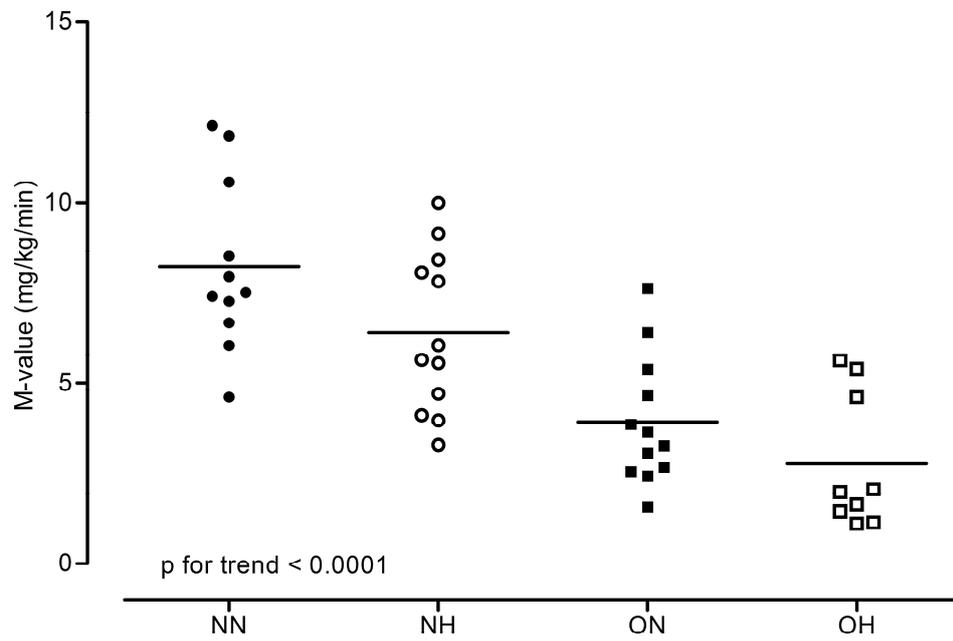
Micro indicates capillary videomicroscope; x, blood samples for fasting measurements and insulin concentrations.

figure 2 - insulin augmented capillary recruitment



Mean and scatter dot-plot. NN (black circles) indicates non-obese normotensive, NH (open circles) indicates non-obese hypertensive, ON (black squares) indicates obese normotensive and OH (open squares) indicates obese hypertensive.

figure 3 – M-value



Mean and scatter dot-plot. M-value indicates metabolic insulin sensitivity as assessed with the hyperinsulinemic euglycemic clamp. Mean and scatter dot-plot. NN (black circles) indicates non-obese normotensive, NH (open circles) indicates non-obese hypertensive, ON (black squares) indicates obese normotensive and OH (open squares) indicates obese hypertensive.

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