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The effect of a shift in sodium intake on renal hemodynamics is determined by body mass index in healthy young men

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A body mass index (BMI) $\geqslant 25\,kg/m^2$ increases the risk for long-term renal damage, possibly by renal hemodynamic factors. As epidemiological studies suggest interaction of BMI and sodium intake, we studied the combined effects of sodium intake and BMI on renal hemodynamics. Glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) were measured in 95 healthy men (median age 23 years (95% confidence interval: 22–24), BMI: $23.0 \pm 2.5\,kg/m^2$) on low (50 mmol Na^+, LS) and high (200 mmol Na^+, HS) sodium intake. Mean GFR and ERPF significantly increased by the change to HS (both $P<0.001$). During HS but not LS, GFR and filtration fraction (FF) positively correlated with BMI ($R=0.32$ and $R=0.28$, respectively, both $P<0.01$). Consequently, BMI correlated with the sodium-induced changes in GFR ($R=0.30$; $P<0.01$) and FF ($R=0,23$; $P<0.05$). The effects of HS on GFR and FF were significantly different for BMI $\geqslant 25$ versus $<25\,kg/m^2$, namely 7.8 ± 12.3 versus 16.1 ± 13.1 ml/min ($P<0.05$) and -0.1 ± 2.2 and $1.1 \pm 2.3\%$ ($P<0.05$). FF was significantly higher in BMI $\geqslant 25$ versus $<25\,kg/m^2$, (22.6 ± 2.9 versus $24.6 \pm 2.4\%$, $P<0.05$) only during HS. ERPF was not related to BMI. Urinary albumin excretion was increased by HS from 6.0 (5.4–6.7) to 7.6 (6.9–8.9). Results were essentially similar after excluding the only two subjects with BMI $>30\,kg/m^2$. BMI is a determinant of the renal hemodynamic response to HS in healthy men, and of GFR and FF during HS, but not during LS. Consequently, HS elicited a hyperfiltration pattern in subjects with a BMI $\geqslant 25\,kg/m^2$ that was absent during LS. Future studies should elucidate whether LS or diuretics can ameliorate the long-term renal risks of weight excess.

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Excess body weight is a risk factor for loss of kidney function in different renal disorders.[1–3] Recent studies showed that a body mass index (BMI) above $25\,kg/m^2$ in young adults is associated with an increased risk for end-stage renal disease on long-term follow-up, not only in subjects with a specific renal parenchymal disorder, hypertension, or diabetes, but also without those conditions.[4–8] The mechanisms underlying the predisposition to renal damage associated with a higher BMI are incompletely understood. In overt obesity, the mechanisms are assumed to involve hypertension,[9] insulin resistance,[10] as well as an unfavorable hemodynamic profile with renal hyperperfusion and hyperfiltration.[9,11–13] As a higher BMI is associated with a renal hyperfiltration profile also in healthy subjects without overt obesity, renal hemodynamics could be relevant in the renal effects of an extent of weight excess that does not amount to overt obesity yet.[12]

In population studies, a high BMI was strongly associated with a higher urinary albumin excretion (UAE).[14,15] Interestingly, an interaction was observed between high dietary sodium intake (estimated by urinary sodium excretion) and excess body weight as risk factors for UAE.[15] The renal mechanisms underlying this interaction would be of interest. Studies in essential hypertensive subjects have shown that a high sodium (HS) intake can elicit albuminuria,[16] with an unfavorable renal hemodynamic profile.[17] This raises the hypothesis that renal hemodynamic factors are involved in the interaction between sodium intake and BMI on UAE. Whereas the renal response to HS has been addressed in various populations,[12,14,15,17–21] the effect of BMI on the renal hemodynamic response to a HS intake has not been established so far.

Therefore, in the present study we investigated the influence of BMI on the renal hemodynamic response to a shift in sodium intake in healthy young male adults. They were studied during a period of low sodium (LS) (50 mmol/day) and an HS (200 mmol/day) intake, that is, a sodium intake reflecting the lower and upper boundaries of a normal intake.

RESULTS

Median age was 23 years (95% confidence interval: 22–24) and mean BMI $23.0 \pm 2.5\,kg/m^2$. The distribution of BMI values in our population is shown in Figure 1. The

distribution of BMI was somewhat skewed, with overt obesity (BMI $\geqslant$ 30 kg/m^2) in two subjects and overweight (BMI $\geqslant$ 25 kg/m^2) in 16 out of 95 subjects.

Subject characteristics on LS versus HS diet are given in Table 1. It shows that the differences in diet resulted in the expected differences in sodium excretion (U_{Na24}). HS intake caused a significant increase in body weight, consistent with a positive volume balance. Potassium excretion (U_{K24}) was similar during both diet periods. Blood pressure was slightly higher during HS ($P = 0.06$). In the study group as a whole, there were significant increases in effective renal plasma flow (ERPF) and glomerular filtration rate (GFR) in response to a change from LS to an HS diet, without a change in filtration fraction (FF). Fasting plasma glucose and insulin levels were in the non-diabetic range on both diets, with no differences between LS and HS intake. The UAE was below the threshold for detection in 23 and 34 out of 95 subjects on LS and HS intake, respectively. As a consequence, paired comparison of UAE between the diets was possible in only 53 subjects. In these subjects, UAE was significantly higher on HS intake. Active plasma renin concentration and aldosterone levels were significantly higher during the LS diet.

On univariate analysis, BMI was significantly associated with GFR and FF (Figure 2, middle panels) during HS intake but not during LS (Figure 2, upper panels). As a consequence, BMI was positively and significantly correlated with sodium-induced changes in GFR and FF (Figure 2, lower panels).

The impact of a BMI $\geqslant$ 25 kg/m^2 on the renal hemodynamic response to HS is shown in Table 2, providing mean values of blood pressure and renal hemodynamics by a break-up by a BMI $<$ or $\geqslant$ 25 kg/m^2. First, it shows that mean arterial pressure and ERPF, and their sodium-induced changes were not affected by BMI on either sodium intake. Second, during LS intake GFR was similar for both groups as well. However, the change in GFR (ΔGFR) elicited by the rise

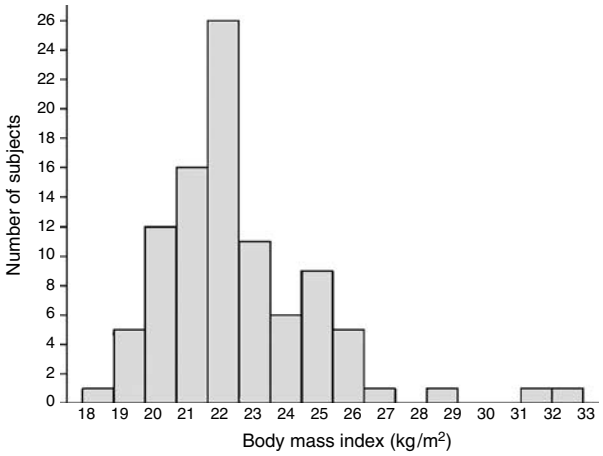

Figure 1 | Distribution of BMI.

Table 1 | Urinary electrolytes, body weight, blood pressure, renal hemodynamics, and metabolic parameters during LS versus HS intake

	Sodium intake		
	50 mmol/24 h	200 mmol/24 h	*P*-value for difference
U_{Na24} (mmol/24 h)	39 ± 27	251 ± 77	< 0.001
Body weight (kg)	78.7 ± 10,3	80.0 ± 10.3	< 0.001
U_{K24} (mmol/24 h)	83 ± 32	82 ± 28	NS
MAP (mm Hg)	87 ± 7	88 ± 7	0.06
ERPF (ml/min)	563 ± 101	602 ± 115	< 0.001
GFR (ml/min)	127 ± 18	136 ± 20	< 0.001
FF (%)	22.8 ± 3.0	23.0 ± 2.9	NS
Glucose (mmol/l)	4.7 ± 0.7	4.6 ± 0.6	NS
Insulin (mE/l)	8.9 (8.2–10.0)	9.0 (7.6–10.0)	NS
UAE (mg/24 h)*	6.0 (5.4–6.7)	7.6 (6.9–8.9)	< 0.01
APRC (ng ang-I/ml/h)	5.8 (5.2–7.1)	2.2 (1.8–2.6)	< 0.001
Aldosterone (ng/l)	130 (112–138)	40 (32–46)	< 0.001

APRC, active plasma renin concentration; ERPF, effective renal plasma flow; FF, filtration fraction; GFR, glomerular filtration rate; HS, high sodium; LS, low sodium; MAP, mean arterial pressure; NS, not significant; UAE, urinary albumin excretion; U_{Na24}, 24-h urinary Na^+ excretion; U_{K24}, 24-h urinary K^+ excretion.
Data are expressed as mean (± s.d.) or median (95% CI for the median).
*LS: *n*=72, HS: *n*=61, paired test in 53 subjects.

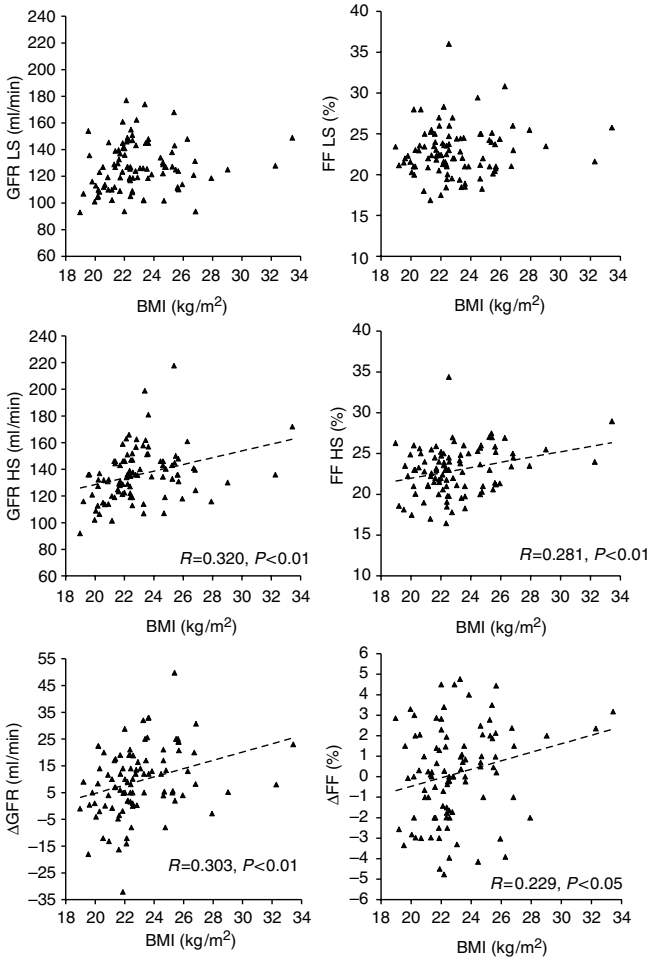

Figure 2 | Scatterplot describing the correlation between BMI and GFR during LS and HS and the sodium-induced change in GFR (ΔGFR): left panels. Correlations between BMI and FF during LS and HS, and sodium-induced change in FF ($\triangle$FF): right panels.