Haemodynamic effects of eating: the role of meal composition

Department of Clinical Physiology and Nuclear Medicine and Ultrasound laboratory, Herlev Hospital, and Department of Medicine B, Rigshospitalet, University of Copenhagen, Denmark

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INTRODUCTION

Although it is well recognized that food intake leads to considerable haemodynamic changes, the underlying mechanisms controlling the postprandial increase in cardiac output are poorly understood [1–3]. Previous studies have demonstrated that the cardiovascular reactions to food intake depend both on the size and composition of the meals, although the role of carbohydrate, fat and protein contents on changes in intestinal blood flow has not been clarified [1, 4, 5]. Haemodynamic changes seem to be more pronounced after diets high in protein [6], whereas the intestinal hyperaemia after carbohydrate intake has a more rapid onset and lasts longer than after fat intake [7]. Although some association has been demonstrated between changes in cardiac output and flow in the superior mesenteric artery [8], the concept that the primary source of the central haemodynamic changes is to be found in the intestinal vascular bed involved in digestion, remains to be established.

Infusion of vasoactive peptides causes vascular effects similar to the food-induced haemodynamic changes, strongly suggesting but not proving that hormones released in conjunction with digestion play a major role in the postprandial cardiovascular response [9–11]. The plasma insulin concentration, being highly dependent on changes in plasma glucose and possibly responsible for a certain amount of the increased sympathetic nervous activity after a glucose load, has also been suggested to be an important mediator of cardiovascular changes [12–14].

The purpose of the present study was to investigate the role of meal composition on postprandial left ventricular volumes, splanchnic blood flow and skeletal muscle flow, to evaluate a possible intercorrelation between blood flow in these major vascular beds and to evaluate the impact of constituent parts of the food on plasma concentrations of catecholamines and insulin in healthy subjects.

SUBJECTS AND METHODS

We studied eight healthy non-obese male subjects aged 20 to 27 years (median 22 years) with a median weight of 75.5 kg (range 68–88 kg), median height 1.85 m (range 1.68–1.88 m) and median body mass index 22.8 kg/m² (range 21.1–24.8 kg/m²). The
Table I. Test meals. *Dry weight. **Total energy content 60 kJ per kg of body weight in three weight intervals: S (small), 60 kg or less; M (medium), 61–70 kg; L (large), 71 kg or more.

<table>
<thead>
<tr>
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<th>Fat</th>
<th>Carbohydrate</th>
<th>Protein</th>
<th>Control</th>
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<tr>
<td></td>
<td>Weight distribution* (g)</td>
<td>Energy content (kJ)**</td>
<td>Weight distribution* (g)</td>
<td>Energy content (kJ)**</td>
</tr>
</tbody>
</table>
| Fat            | S 69  | 80           | 10      | 12      | 10      | 11      | 0       | —
|                | M 86  | 83           | 11      | 11      | 10      | 10      | 0       | —
|                | L 98  | 80           | 12      | 10      | 14      | 12      | 0       | —
| Carbohydrate   | S 21  | 11           | 156     | 81      | 9       | 4       | 0       | —
|                | M 21  | 9            | 185     | 81      | 6       | 3       | 0       | —
|                | L 21  | 8            | 218     | 81      | 20      | 8       | 0       | —
| Protein        | S 18  | 9            | 15      | 8       | 166     | 83      | 0       | —
|                | M 18  | 8            | 19      | 8       | 195     | 85      | 0       | —
|                | L 18  | 11           | 20      | 8       | 205     | 79      | 0       | —

<table>
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<tr>
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<th>Weight (g)</th>
<th>Energy content (kJ)**</th>
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<td>3278</td>
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<td>3286</td>
<td>860</td>
<td>3379</td>
<td>1150</td>
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<tr>
<td></td>
<td>M 375</td>
<td>3896</td>
<td>1085</td>
<td>3882</td>
<td>925</td>
<td>3880</td>
<td>1250</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>L 435</td>
<td>4496</td>
<td>1235</td>
<td>4488</td>
<td>1191</td>
<td>4472</td>
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<tr>
<td>Water added</td>
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<td>175</td>
<td>175</td>
<td>300</td>
<td>150</td>
<td>—</td>
<td>—</td>
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<tr>
<td>(ml)</td>
<td>M 850</td>
<td>175</td>
<td>175</td>
<td>300</td>
<td>150</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>L 900</td>
<td>125</td>
<td>125</td>
<td>300</td>
<td>150</td>
<td>—</td>
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Fig. 1. Investigation schedule. RBC, red blood cells (erythrocytes); MUGA, multigated radionuclide cardiography (including measurement of blood pressure)

study protocol was approved by the local ethics committee and informed consent was obtained from each subject.

**Study design**

The subjects were studied after an overnight fast of 12 h duration. Baseline measurements were performed after 30 min of supine rest. The subjects were then randomly assigned (by the throw of a dice) to consume a test meal rich in one of the main energy sources or water (control study) (Table 1). All subjects were investigated before and after any of the four different test meals, i.e. four times in total with an interval of at least 2 weeks. The meals were ingested within 30 min, and postprandial measurements were started 15 min after the end of the meal according to the schedule designated in Fig. 1.

**Test meals**

The meals, consisting predominantly of one energy source (80–85% of total energy), contained isocaloric amounts (60 kJ per kg of body weight) of carbohydrate, fat, protein or water (non-caloric) according to Table 1. Water was given as a supplement to make the meals isovolumic normalized to the most voluminous meal type, the carbohydrate meal, whose volume corresponded to 16–18 g per kg of body weight. All subjects were sitting at the time...
of the meal ingestion, which lasted approximately 30 min.

Measurements

All measurements were performed in the supine position. Observers performing the following observations were blinded to the sequence of meal compositions. Heart rate was registered by a three-lead ECG and calculated from the average R–R interval obtained during the sample period of the radionuclide cardiography. Blood pressure was measured with a standard mercury sphygmomanometer. Venous plasma concentrations of adrenaline and noradrenaline were determined by isotope derivative assay [15] and plasma insulin by radioimmunoassay [16].

Multiple gated radionuclide ventriculography was performed with 16 frames per cardiac cycle after labelling of autologous erythrocytes in vitro with 740 MBq of $^{99m}$Tc [17]. Left ventricular ejection fraction and volumes were determined by two independent observers by delineation of left ventricular end-diastolic, end-systolic and background regions as previously described [18]. Data were acquired in the left anterior oblique projection with a 5 to 10° caudal tilt to optimize separation of the left ventricle. The inter- and intra-observer variability of this procedure has been described previously [18]. Stroke volume was calculated as left ventricular end-diastolic volume × left ventricular ejection fraction, and left ventricular end-systolic volume as left ventricular end-diastolic volume – stroke volume. Cardiac output was calculated as stroke volume × heart rate [18].

Forearm blood flow

The blood flow of the right forearm was measured by venous occlusion plethysmography [19]. The room temperature was kept at 20 to 24°C. The strain gauge was placed at the largest girth of the right forearm and the hand was elevated above heart level supplied with a wrist cuff inflated to suprasystolic pressure. A cuff pressure of 40 mmHg was applied proximal to the strain gauge after calibration, and the procedure was performed at least four times to obtain reproducible measurements by one investigator and analysed by another observer, unaware of the identity of the meal ingested.

Portal vein flow

The portal vein flow was determined using a Duplex system combining ultrasonic B-mode imaging with pulsed-wave Doppler flow measurement, type 3555 with a 3.5 MHz curved-array transducer (B & K Medical, Gentofte, Denmark) [20]. The subjects were examined in the supine decubitus or left lateral position from the subcostal or intercostal approach. The portal vein was localized and its internal diameter measured on a longitudinal B-mode scan. The insonation angle of the pulsed Doppler line was kept as small as possible, and the Doppler sample volume was adjusted to contain the total vein lumen. Using a low filter constantly (100 Hz), an average of the flow velocity was measured and multiplied by the cross-sectional area of the vein to obtain flow in ml/min. The mean value of five measurements was used as the portal vein flow. The measurements were performed by an investigator unaware of the identity of the ingested meal.

Statistical analysis

Non-parametric analysis of variance (Friedman's test modified for multiple comparison) was applied to detect significant changes in any measured variable over time after a given meal. The same analysis was applied to compare changes in the variables induced by different meal compositions [21]. We rejected the null hypothesis at the 5% level, when our test statistic exceeded that of the $F$ distribution with (measurements−1) and (4−1)×(8−1) (measurements−1)×(subjects−1) degrees of freedom (0.95 quantiles). The critical rank sum difference was chosen from the $t$ distribution with (measurements−1)×(subjects−1) degrees of freedom (0.975 quantiles). Correlation between maximal changes in cardiac output and portal vein flow was determined by Spearman’s rank correlation [22].

RESULTS

Left ventricular volumes and derived parameters

Cardiac output increased by 35–40% after all the energy-containing meals. Stroke volume increased by 18–22% and heart rate by 11–16% (Fig. 2 and Table 2). All these haemodynamic changes were significantly more pronounced for the energy-containing meals than for the control studies. Maximum heart rate response after the carbohydrate-rich meal was significantly higher than heart rate after the fat-rich meal, but no other significant differences between haemodynamic changes after the various meal compositions were found. Fat-induced increments in heart rate and stroke volume tended to set in later and to be more short-lived, and the increase in cardiac output tended to last longer after the protein-rich meal (Fig. 2 and Table 2). A small but significant 12% increase in cardiac output was even found after water intake. The mean systolic blood pressure varied between 114 and 121 mmHg and the diastolic blood pressure between 67 and 73 mmHg with no significant changes after the meals (or water).

Left ventricular end-diastolic volume increased with a maximum response significantly more pronounced after carbohydrate and protein than after
fat and water. Left ventricular ejection fraction essentially remained at pre-meal values for all meal types, although a temporary decrease was recorded after protein ingestion. Stroke volume increased after all energy-containing meals. Left ventricular end-systolic volume only increased after carbohydrate and protein ingestion (Fig. 3 and Table 3).

**Forearm blood flow**

By analysis of variance no significant changes over time were detected in forearm blood flow after the meals (including the control), and no difference was observed between the forearm flows after different meal compositions. However, regarding only the early change in forearm blood flow 30 min after the meal compared with the basal state, the flow increased significantly more after carbohydrate than after fat and water (mean increase 14%). The change in forearm blood flow 30 min after the protein-rich meal was also different from the tendency towards a fall induced by water intake (Fig. 4).

**Portal vein flow**

Portal vein flow increased after each of the energy-containing meals, compared with the resting state ($P<0.05$), with a most pronounced mean increase of 107% (range 30–136%) after fat, 62% (32–110%) after carbohydrate, and 52% (−8–152%) after the protein-rich meal. Unexpectedly, the blood flow in the portal vein also increased after water ingestion by 15% (−11–53%), and only the fat and carbohydrate-induced increments were significantly greater than this control value (Fig. 5). A weak but significant association was detected between maximal changes in portal vein flow and maximal changes in cardiac output ($r=0.395, P<0.05$).

**Hormone analyses**

No significant changes were observed within or between serial analyses of concentrations of plasma adrenaline and noradrenaline after each meal (Table 4). Plasma insulin increased almost 6-fold after the carbohydrate-rich meal. This increase was significantly higher than that after fat (1.9) and protein (1.8), which in turn was higher than that after the control meal (Table 4). There was no association between changes in cardiac output and plasma concentrations of either hormone.

**DISCUSSION**

Haemodynamic changes after ingestion of the various meals in the present study are consistent with previous findings [23, 24] showing an increase in cardiac output, the prominent feature being a rise in stroke volume achieved by dilatation of the (left) ventricle as previously described after a mixed meal in healthy subjects [24, 25].

It has been questioned whether different meal compositions and sizes would result in different postprandial changes [26]. Variable timing of haemodynamic reactions to food ingestion has been shown before with an earlier maximal rise in cardiac output after carbohydrate-rich meals compared with protein-rich meals [6]. Sidery et al. [7] found parallel initial increments in cardiac output after high-carbohydrate and high-fat meals. As in the present study, the rise in cardiac output was short-lived after fat ingestion compared with the carbohydrate meal. Avasthi et al. [28] found a longer lasting effect of high-protein meals on the increment in cardiac output compared with high-carbohydrate meals. Waaler and Eriksen [8] found a mean increase of approximately 30% in cardiac output after 4000 kJ fluid meals of different compositions. They also described somewhat parallel changes in the superior mesenteric arterial flow, substantiating the concept that the part of the splanchnic vascular circuit involved in digestion is the primary source of postprandial blood flow changes [27, 29]. However, there were considerable variations in the food-induced haemodynamic changes in their study.

The mechanism behind the integrated haemodynamic response to food ingestion is incompletely understood. Baron et al. [29a, 29b] recently found a
Postprandial haemodynamics

Table 2. Haemodynamic variables in relation to meal composition. Values are means (SDs). Response to fractional meal stimulation: $p < 0.05$ compared with baseline measurements; $p < 0.05$ compared with 30 min values; $p < 0.05$ compared with 60 min values. Difference in maximum response between meal studies: $p < 0.05$ compared with control study (water); $p < 0.05$ compared with fat study.

<table>
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<th>Heart rate (beats/min)</th>
<th>Stroke volume (ml)</th>
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<tr>
<td></td>
<td>56</td>
<td>60</td>
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<tr>
<td>Fat</td>
<td>4.42 (0.62)</td>
<td>5.25 (0.97)</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>4.28 (0.74)</td>
<td>5.75 (1.00)</td>
</tr>
<tr>
<td>Protein</td>
<td>4.56 (0.70)</td>
<td>5.40 (1.00)</td>
</tr>
<tr>
<td>Water</td>
<td>4.22 (0.80)</td>
<td>4.57 (0.73)</td>
</tr>
<tr>
<td>Time (h)</td>
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![Fig. 3. Radionuclide left ventricular volumes in relation to intake of various meal compositions. LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume. Figures indicate mean volumes](image)

dose-dependent increase in cardiac output secondary to increments in both heart rate and stroke volume in lean insulin-sensitive humans during steady-state hyperinsulinaemic euglycaemic clamp with a 60 min delay to maximal haemodynamic effect. At physiological plasma insulin concentrations, cardiac output increased approximately 15% and skeletal muscle vascular resistance decreased to a distinctly larger degree than systemic resistance. In our study the cardiac output response after physiological meal stimulation was measured at plasma insulin levels comparable to those of Baron et al. [29a, 29b]. The increase in cardiac output sustained after restoring plasma insulin to pre-meal values and cardiac output response after the protein meal showed no tendency towards decline when measurements were discontinued. Differences in cardiac output response could theoretically be caused by a sustained reaction due to a variable caloric component load caused by a potential local effect of food components on ventricular and intestine motility, transmucous uptake and release of local intestinal hormones. The cardiovascular action of insulin may explain some haemodynamic results in this study, but a direct extrapolation of the results during intravenous glucose–insulin stimulation (intestinal bypass) to the ingestion of physiological meals is questionable. The sustained reaction after caloric meals despite pre-meal insulin values and the surprisingly long-lived response to meals of water suggests that total caloric load and meal volume may play a major role.

Postprandial left ventricular end-diastolic and end-systolic volumes reached maximum values at 30 min after carbohydrate and protein. The fractional dilatation at end-diastole and end-systole was similar, leaving left ventricular ejection fraction unaffected by food ingestion apart from a minor temporary decrease after protein ingestion. Previous reports of postprandial haemodynamic changes in healthy subjects [23, 24] were thus confirmed. Patients with coronary artery disease and cardiomyopathy [30, 31] have been shown to exhibit a diverging response with an increased ejection fraction after ingestion of a rather small meal of approximately 3500 kJ. A more pronounced postprandial decrease in afterload in cardiac patients, especially those with heart failure and a high sympathetic nervous tone, may explain these discrepancies.

The consistent postprandial increase in cardiac output after each meal, together with the unchanged blood pressure, indicates that systemic vascular resistance is considerably reduced. We found only small differences in the initial forearm blood flows after food intake. A decrease in calf blood flow representing mainly muscle flow was also reported...
Table 3. Radionuclide left ventricular volumes and ejection fraction in relation to meal composition. Values are means (SDs). Response to fractional meal stimulation: *P < 0.05 compared with baseline measurements; **P < 0.05 compared with 30 min values; ***P < 0.05 compared with 60 min values. Difference in maximum response between meal studies: dP < 0.05 compared with control study (water); eP < 0.05 compared with fat study.

<table>
<thead>
<tr>
<th></th>
<th>Left ventricular end-diastolic volume (ml)</th>
<th>Left ventricular end-systolic volume (ml)</th>
<th>Left ventricular ejection fraction (%)</th>
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<tbody>
<tr>
<td>Fat</td>
<td>133</td>
<td>150</td>
<td>155†</td>
</tr>
<tr>
<td></td>
<td>143†</td>
<td>60</td>
<td>56</td>
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<td>Carbohydrate</td>
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<td>148†</td>
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after high-fat but not after high-carbohydrate meals in a previous study [7]. Yi et al. [23] found 10–15% increments in both forearm and calf blood flow after a mixed meal in healthy subjects, and concluded that no evidence exists of redirection of blood to the gastrointestinal vascular bed from other areas.

It was earlier hypothesized that the primary sources of postprandial haemodynamic alterations were changes in blood flow in those areas of the intestine engaged in digestion [1, 2]. Splanchnic blood flow, as measured by the indocyanine green method, increases after food intake [32], and experimental studies show that this increase can be measured by determination of the portal vein flow [9, 33]. In the present study, significant increments in Doppler estimated portal vein flow were recorded after food intake even in the control study. A significantly higher flow was measured after the fat-rich meal compared with the other meal compositions. Our results vary slightly from those of Moneta et al. [34], who found a similar increase in the Doppler estimated blood flow of the superior mesenteric artery 1 h after ingestion of small fat- and carbohydrate-containing meals with an earlier peak increase of the latter.

The mechanisms by which postprandial intestinal and central vascular changes are mediated is the subject of an ongoing discussion based on diverging theories. Our findings indicate that some connection exists between the magnitude of change in cardiac output and changes in portal vein flow. Several gastrointestinal hormones were recently rejected as significant determinants in the regulation of the postprandial mesenteric artery blood flow [35]. Our analyses could not detect any correlation between increments in cardiac output and plasma concentration of insulin. Vasoactive intestinal peptide has cardiovascular effects that mimic those recorded after a meal [11]. In accordance with previous findings no significant changes were recorded in the plasma concentration of catecholamines after any meal in our young healthy subjects, examined in the supine position. However, a certain role of the sympathetic nervous system in the regulation of
postprandial haemodynamics is indisputable, especially in the upright position and in elderly subjects [25, 36]. A significant increase in peripheral extraction of adrenaline may further conceal postprandial elevations of arterial blood levels of the hormone.

In conclusion, postprandial cardiovascular changes do not differ substantially in extent, but to some degree in timing after various isocaloric and isovolumic meal compositions. The increase in stroke volume is achieved by an increase in left ventricular volumes. The mechanisms by which the changes are mediated are incompletely understood. The present study indicates some role of gastric emptying. Since small but significant haemodynamic changes are recorded after the control meal. In addition, postprandial flow analyses of portal vein flow suggest a significant albeit weak impact of splanchnic flow on cardiac output.

REFERENCES


