TABLE 1
Summary of results of studies in humans that investigated the effects of CCK, or CCK-receptor blockers on appetite, that is, food intake and subjectively rated appetite; IV = intravenous, ID = intraduodenal, CCK, 8, 9, 33 = cholecystokinine with 8, 9, 33 amino-acids

First author, and year of publication	Design and stimuli used	Number and type of subjects	Results with respect to food intake	Results with respect to appetite
Exogeneous				
Kissilef, 1981 (1)	Counterbalanced, cross-over -IV saline -IV.CCK8, 3.6 pmol/kg min infusion: 0 min before–12 min after end; ad libitum liquid testmeal (yogurt + fruit) 12 min before test meal, appetizer was served (0.9 MJ)	12 non-obese men, on average 105% of average desirable weight; age (mean ± sd): 25 ± 4 y	Mean test meal intake: saline = 644 g CCK 8 = 522 g (= −19%) difference = −122 ± 50 g (s.e.d)	No differences in hunger and satiety ratings
Pi-Sunyer, 1982 (2)	Double blind, randomized, cross-over -IV saline -IV CCK8, 3.6 pmol/kg min infusion: 0 min before–12 min after end; ad libitum liquid test meal (yogurt + fruit) 12 min before testmeal, appetizer was served (0.9 MJ)	8 obese men, on average 137% of average desirable weight; age (mean ± sd): 25 ± 4 y	Mean test meal intake: saline = 977 ± 423 g CCK-8 = 852 ± 472 g (= −13%) difference = −126 ± 65 (s.e.d)	No differences in hunger and and satiety ratings
Muurahainen, 1988 (3)	Counterbalanced, double blind, cross-over -IV saline -IV CCK8, total dose 2025 pmol (203 pmol/min) infusion: 6 min before start–4 min after start; ad libitum test meal (macaroni+ beef) 20 min before test meal, soup preload of 500 g (0.8 MJ)	12 non-obese men within 15% of desirable weight age (mean ± sd): 21 ± 3 y	Test meal intake (mean) saline = 602 g CCK8 = 362 g (= −40%) difference = −240 ± 81 g (s.e.d)	Not measured
Schick, 1991 (4)	Double blind, randomized, cross-over -IV-saline -IV CCK9, 1.6 pmol/kg min -IV CCK9, 8 pmol/kg min infusion: 15 m before–45 m after start; ad libitum test meal (sandwich quarters)	18 normal weight men age range: 21–26 y	Test meal intake at end infusion (mean ± s.e.m): saline = 32 ± 2 sandwich quarters CCK9-100 = 28 ± 2 (= −13%) CCK9-500 = 12 ± 3 (= −63%)	Not measured
Muurahainen 1991 (5)	Counterbalanced, cross-over -IV saline + 100 ml preload -IV saline + 500 ml preload -IV CCK8 (203 pmol/min) + 100 ml preload -IV CCK8 (203 pmol/min) + 500 ml preload infusion: 5 min before start–5 min after test meal (macaroni-beef) preload (tomato soup): 20 min before start testmeal	12 normal weight men, age range: 18–35 y weight within 15% of desirable body weight	Test meal intake (means ± s.d.): saline/100 = 778 ± 274 g saline/500 = 721 ± 352 g (−7%) CCK/100 = 709 ± 288 g (−9%) CCK/500 = 494 ± 300 g (−36%)	Hunger lower in CCK condition compared to saline condition Hunger ratings lower after 500 ml preload compared to 100 ml preload
Melton et al, 1992 (6)	Double blind for CCK/saline -IV CCK8, 98 pmol/min, 500 ml gastric balloon -IV saline, 500 ml gastric balloon -IV CCK8, max tolerated balloon volume -IV saline, max tolerated balloon volume infusion with 500 ml balloon: for 25 min starting 5 min before balloon inflation; infusion with maximum tolerated volume: started 22 min before inflation, and lasted until balloon deflation	4 normal weight women, age range: 23–28 y BMI range: 18–25 kg/m^2	Not measured	Higher mean fullness rating with CCK vs. saline at 500 ml (6.0 vs. 4.7 on 10-point scale). With 500 ml volume, no differences in hunger, satiety ratings. CCK enhanced effect of gastric pressure on fullness

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TABLE 1 (*Continued***)**

First author, and year of publication	Design and stimuli used	Number and type of subjects	Results with respect to food intake	Results with respect to appetite
Lieverse, 1993 (Chapter IV PhD-thesis) (7)	Double blind, randomized, cross-over -IV saline -IV CCK33, 0.2 pmol/kg ideal weight min infusion: for 60 min, leading to physiologically relevant CCK levels, i.e., 10–15 pMol in plasma	32 subjects, 14 obese women, age (mean ± sd): 41 ± 3 y, BMI: 40 ± 2 kg/m2 18 normal weight (4m, 14 f), age: 34 ± 2 BMI: 22 ± 0.3 kg/m2	Not measured	CCK vs. saline reduced hunger, desire to eat, prospective consumption, and increased fullness. Difference was about 10 mm on 100 mm VAS scale. No differences between lean and obese.
Lieverse, 1993 (8)	Double blind, randomized, cross-over -IV saline -IV CCK33 0.2 pmol/kg ideal weight min infusion: for 150 min leading to physiologically relevant CCK levels, i.e., 10–15 pMol in plasma 60 min after start infusion ad libitum testmeal (bananas)	18 subjects, 9 normal weight (5f, 4m) age range: 22–36 y, BMI range: 20–25 kg/m2 9 obese (9f), age range: 30–59, BMI range 33–49 kg/m2	Test meal intake (mean ± s.e.m) saline = 553 ± 55 g CCK = 486 ± 52 g (= −12%) (intakes were not significantly different; $P = 0.09$)	CCK vs. saline reduced hunger slightly more than saline (NS), no differences in desire to eat, prospective consumption. No differences between obese and normal weight
Lieverse, 1995 (9)	Double blind, randomized, cross-over -IV saline -IV CCK33 0.2 pmol/kg ideal weight min infusion for 165 min leading to physiologically relevant CCK levels, i.e., 10–15 pMol in plasma. 60 min after start infusion: 300 ml shake containing 100 g (132 kcal) bananas, 75 min after infusion ad libitum test meal (bananas)	18 women, 10 normal weight, age (mean ± sd): 41 ± 2 y, BMI: 22 ± 3 kg/m2; 8 obese, age: 41 ± 3 y, BMI: 39 ± 2 kg/m2	Test meal intake (mean ± s.e.m): saline = 346 ± 31 g CCK = 282 ± 29 g (−18%)	CCK vs. saline reduced hunger, desire to eat, prospective consumption, and increased fullness. Difference was about 10 mm on 100 VAS scale. No difference between obese and normal weight
Ballinger, 1995 (10)	Single blind, randomized, cross-over -IV saline -IV CCK8 0.54 pmol/kg min infusion for 40 min, leading to physiological relevant CCK levels, i.e. 6–8 pMol in plasma 20 min after start infusion: 200 ml water 25 min after start infusion: ad libitum testmeal (mixed attractive buffet)	6 normal weight (4m, 2f) mean age: 31 y range BMI: 21–25 kg/m2	Test meal intake (mean ± s.e.m): saline = 6.4 ± 0.7 MJ CCK8 = 5.1 ± 0.7 MJ (= − 21%)	Not measured
Gutzwiller, 2000 (11)	Double blind, randomized cross over -IV saline, IV saline -IV saline, IV CCK: 67.5 pmol/min -IV loxiglumide 10 mg/kg h, IV saline -IV loxiglumide 10 mg/kg h, IV CCK Infusion 1 from 0–125 min, after 45 min 400 ml 0.6 MJ banana preload, from 60–70 min infusion 2, 65–125 min ad libitum mixed test meal	32 normal weight men, age range: 21–33 y	Test meal intake (mean ± sem): Saline-sal: 7.5 ± 0.3 MJ Saline-CCK: 7.0 ± 0.3 MJ (−7%) Loxiglumide -sal: 8.3 ± 0.2 MJ (+10%) Loxiglumide-CCK: 7.3 ± 0.2 MJ (−3%)	Hunger reduced in saline-CCK condition by 3 units on 10 pts. scale Other condition produced similar hunger ratings, i.e. loxiglumide counteracted CCK effect
MacIntosh 2001 (12)	Double blind, randomized, cross over -IV saline milkshake (744 KJ, 375 g). -IV CCK8 0.9 pmol/kg min (Low Dose)	24 normal weight subjects 12 (6 m, 6 f) young age 18–33 y, mean BMI = 23.8 kg/m2 12 (6 m, 6 f) elderly age 67–83 y, mean BMI = 24.1 kg/m2	Energy intake at test meal Young: -saline: about 4 MJ -CCK8 LD = 4MJ (−0%) -CCK8 HD = 2.8 MJ (−35%) Elderly:	Lower hunger ratings in elderly vs. young No effect of treatment on hunger ratings

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TABLE 1 (*Continued***)**

First author, and year of publication	Design and stimuli used	Number and type of subjects	Results with respect to food intake	Results with respect to appetite
	-IV CCK8 2.7 pmol/kg min (High Dose) infusion for 25 min, 375 g 0.7 MJ banana shake preload after min, after 10 min ad libitum mixed test meal		-saline: about 2.7 MJ -CCK8 LD = 2.2 MJ (−18%) -CCK8 HD = 1.6 MJ (48%) correlation between EI-test meal and CCK 8 levels was −0.34	
Kissileff, 2003 (13)	Single-blind, randomized, cross-over Treatments: -IV CCK without gastric distension -IV CCK with gastric distension -IV saline without gastric distension -IV saline with gastric distension -150 min: breakfast (300 kcal) 0–10 min: balloon filling (300 ml) 10 min: start IV infusion 30 min: end infusion start ad libitum lunch consisting of a strawberry yogurt shake (1.04 kcal/g) 40 min: end meal 55 min: end test CCK-8 infusion: 112 ng/ml 1ml/min Saline infusion: 1.0 ml/min 0.9% saline	16 non-obese subjects (8 m, 8 f) age men: 25.7 ± 2.4 y BMI men: 22.3 ± 1.6 kg/m2 age women: 23 ± 3 y BMI women: 21.71 ± 1.96 kg/m2	Reduction food intake compared to IV saline without distension. CCK + distension: 200 ± 43 g CCK no distension: 96 g (SED) Saline + distension: 31 ± 43 g (ns) CCK no dis vs CCK dis: 104 g CCK distension vs saline distension: 169 ± 43 g	After balloon filling, and before CCK infusion begun, subjects were significantly more full than when the balloon was not filled. No effect of CCK was observed.
Endogeneous				
Wolkowitz, 1990 (14)	Double blind, randomized cross-over -Oral 10 mg MK-329 (CCK receptor blocker) -placebo -120 min after treatment, subjects ate a 614 kcal mixed meal	8 healthy normal weight men, age range: 23–44 y weight within 15% of ideal weight	Not measured	90 min after treatment, hunger ratings were 17 mm higher on 100 mm scale after MK329 vs. placebo. ($P < 0.05$) 155 min after treatment, hunger ratings were 8 mm higher after MK329 vs placebo (NS)
French, 1993 (15)	Subjects were given meal of 150 g beefburger, and could eat ad libitum from bacon, tomatoes, bread, butter, and orange juice. CCK levels, and hunger ratings were measured just before meal, and 12 times after meal at 30 m intervals	9 healthy non-obese subjects (no further specifications)	Not measured	Means over subjects, correlation over time (r with n = 13): r(CCK, hunger) = −0.64 r(CCK, fullness) = 0.68 Within subject correlations: r(CCK, hunger) <0 for 3 of 9 subjects r(CCK, fullness) > 0 for 4 of 9 subjects
French, 1994 (16)	Double blind, randomized cross-over -Oral Loxiglumide tablets 3 × 400 mg/d 15 min before meals, during 3 days -placebo	11 normal weight age range: 18–44 y BMI range: 20–25 kg/m2	Daily energy intake across 3 d according dietary records saline = 7.9 ± 0.6 MJ loxiglumide = 8.6 ± 0.6 MJ (+9%) differences in intake NS	No effects on hunger and satiety

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TABLE 1 (*Continued)*

First author, and year of publication	Design and stimuli used	Number and type of subjects	Results with respect to food intake	Results with respect to appetite
Lieverse, 1994 (17)	Single blind, randomized cross-over -IV infusion of saline for 210 min, after 60 min ID infusion of saline -IV infusion of saline for 210 m, after 60 m min ID infusion of fat (6 g/h) -IV infusion of loxiglumide (10 mg/kg h), after 60 m ID infusion of fat (6 g/h). After 150 m an ad libitum test meal (sandwiches with cheese and butter)	10 normal weight subjects, (5 m, 5 f) mean age = 26 y	Test meal intake (mean ± sem): IV saline, ID saline = 269 ± 37 g IV saline, ID fat = 206 ± 35 g (−24%) IV loxiglumide, ID loxiglumide = 245 ± 30 g (−9%) differences in intake NS	Hunger was about 10 mm lower on 100 mm scale after ID fat/ IV saline than after ID saline/ IV saline. ID fat/IV loxiglumide produced hunger ratings in between other two conditions
Maas, 1999 (18)	Double blind, randomized, cross-over -ID saline ate 0.4 ml/ kg h -ID fat at 13.6 kJ/ kg h -ID non-digestable fat (SPE) at same rate infusion for 160 min, after 90 min ad libitum test meal (cheese sandwiches)	18 normal weight (9 m, 9 f), age (mean ± sem) 24 ± 1 y, BMI: 22 ± 0.4 kg/m2	Test meal intake (mean) saline = 3.7 MJ fat = 3.1 MJ (−16%) SPE = 3.3 MJ (−7%) correlation between CCK increase and food intake was −0.27	Fat reduced hunger in women, but not in men. SPE effects in between saline and fat effects.
Matzinger, 1999, Study 1 (19)	Double blind, randomized, cross over -ID saline, 400 ml water preload -ID saline, 400 ml (0.6 MJ) banana preload -ID fat (41 g), 400 ml water preload -ID fat (41 g), 400 ml banana preload -ID infusion for 120 min; preload after 40 min, ad libitum mixed meal from 60–120 min	12 normal weight men, age range: 20–44 y	Test meal intake (mean ± sem) ID saline, water = 7.4 ± 0.4 MJ ID saline, banana = 6.3 ± 0.4 MJ (−16%) ID fat, water = 6.6 ± 0.3 MJ (−12%) ID fat, banana = 5.0 ± 0.5 MJ (−32%)	Hunger, fullness ratings in line with food intake data; ID-fat, and banana preload reduced hunger
Matzinger 1999, Study 2 (19)	Double blind, randomized, cross over -ID saline, 400 ml ban preload, IV saline -ID fat, 400 ml ban preload, IV saline -ID fat, 400 ml (0.6 MJ) banana preload, IV loxiglumide, 10 mg/ kg h -IV infusion for 150 min; ID infusion after 30 min, preload after 70 min, ad libitum mixed test meal after 90 min	12 normal weight men, age range: 20–44 y	Test meal intake (mean ± sem) ID saline, IV saline = 7.8 ± 0.8 MJ ID fat, IV saline = 6.1 ± 0.5 MJ (−23%) ID fat, IV loxiglumide = 8.1 ± 0.5 MJ (+3%)	ID fat resulted in 1 point on 10 point scale lower hunger rating; IV loxiglumide counteracted this effect
Beglinger, 2001 (20)	Double blind, randomized, cross over -IV saline -IV loxiglumide 22 u mol/ kg h -IV infusion for 120 min, after 60 min ad libitum mixed test meal	40 normal weight age 21–34	Test meal intake (mean ± sem) saline = 7.0 ± 0.2 MJ loxiglumide = 7.8 ± 0.2 MJ (+ 10%)	Loxiglumide reduced satiety 1 unit/ 10 point scale
Burton-Freeman, 2002 (21)	Randomized, cross over -Low fibre, low fat breakfast 3.6 MJ -High fibre, low fat breakfast 3.6 MJ -Low fibre, high fat breakfast 3.6 MJ 6 hours after breakfast an ad libitum meal was served	8 men and 7 women age range: 20–50 y BMI-range: 22–28 kg.m**2	No effects on food intake during test meal	Highly significant relation between measures of hunger and satiety and plasma CCK response. For every 1% CCK increase, the amount subjects wanted to eat declined 0.45 mm on 100 mm rating scale

TABLE 2
Summary of results of studies in humans that investigated the effects of GLP-1 (Glucagon like peptide 1), on appetite, that is food intake and subjectively rated appetite; IV = intravenous, ID = intraduodenal

First author, and year of publication	Design and stimuli used	Number and type of subjects	Results with respect to food intake	Results with respect to appetite ratings
Exogeneous				
Flint, 1998 (22)	Double blind, randomized, cross-over -IV saline -IV GLP-1, 0.8 pmol/kg min infusion: from 0 min before start fixed breakfast–240 min after start breakfast, infusion was stopped 30 min before ad libitum lunch, infusion continued for 30 min during ad lib mixed lunch (pasta, meat, vegetables)	20 non-obese men, age = 20–31 y BMI = 20.3–25.7 kg/m2	Test meal intake (mean ± sem) saline = 4.2 ± 0.2 MJ GLP1 = 3.7 ± 0.3 MJ (−12%)	Hunger, satiety, prospective consumption ratings about 5–10 mm lower on 100 mm scale during GLP1 infusion vs. saline
Naslund, 1998 (23)	Double blind randomized, cross-over -IV saline -IV GLP1 0.75 pmol/kg min infusion: for 210 min, 0 min after infusion an ad libitum test meal was served (Swedish hash)	6 obese men age = 34.7 ± 3.3 y BMI = 35.6 ± 1.8 kg/m2 (mean ± sem)	Test meal intake (mean, range) placebo = 493 g (216–687 g) GLP1 = 464 g (207–685 g) (−5.9%)	After meal consumption, hunger ratings were lower during GLP1 infusion, at t = 240 m more than 30 mm difference on 100 mm scale
Gutzwiller, 1999a (24)	Double blind, randomized, cross-over -IV 5% glucose (placebo) -IV 5% gluc + GLP1, 0.375 pmol/kg min -IV 5% gluc + GLP1, 0.75 pmol/kg min -IV 5% gluc + GLP1, 1.5 pmol/kg min infusion: for 120 min, 60 min after start infusion, ad lib mixed test meal was served	16 non-obese men age = 23.6 ± 0.5 y (mean ± sem)	Test meal intake (mean ± sem) placebo = 6.8 ± 0.4 MJ 0.375 pmol GLP1 = 6.4 ± 0.4 MJ (−6.6%) 0.75 pmol GLP1 = 6.1 ± 0.4 MJ (−10.8%) 1.5 pmol GLP1 = 4.6 ± 0.3 MJ (−32.0%)	Hunger ratings dose-dependently lower after GLP1 vs placebo, with maximal difference of 3 points on 10 point scale, between placebo and 1.5 pmol GLP1 60 min after start infusion
Long, 1999 (25)	Single blind, randomized, cross-over -IV saline -IV 1.2 pmol GLP1/kg min infusion: for 60 min; 20 min after start infusion 400 ml water preload; 40 min after start infusion, ad libitum mixed test meal + 200 ml water	10 non-obese men age = 20–29 y BMI = 20–27 kg/m2	Test meal intake (mean ± sem) saline = 5.9 ± 0.4 MJ GLP1 = 5.5 ± 0.5 MJ (−7.1%) (NS; $P = 0.27$)	Hunger ratings were lower during GLP1 infusions, but differences were not statistically significant
Gutzwiller, 1999b (26)	Double blind, randomized, cross-over -IV saline -IV GLP-1 1.5 pmol /kg min infusion for 120 m, 60 m after infusion an ad libitum mixed meal was served	12 diabetic men, age (mean ± sem) = 55 ± 2y BMI = 29.4 ± 1.2 kg/m2	Test meal intake (mean ± sem) saline = 3.9 ± 0.4 GLP1 = 2.9 ± 0.3 (−26.5%)	Changes in hunger/satiety ratings compared to baseline about 1 point on 10 point scale less hungry/more, full on GLP1 vs. saline
Naslund, 1999 (27)	Double blind, randomized cross-over -IV saline -IV GLP-1 0.75 pmol/kg min infusion for 480 min, at t = 0 fixed breakfast at t = 240 ad libitum lunch (pasta dish), at t = 480 ad libitum diner (mixed meal)	6 obese men, age = 35 ± 4 y BMI = 46 ± 3 kg/m2 (mean ± sem)	Test meal intakes (mean - range) saline lunch = 4.3 (3.5–4.8) MJ GLP1 lunch = 3.8 (2.1–4.6) MJ (−12%) saline dinner = 3.1 (1.4–5.0) MJ GLP1 dinner = 2.3 (0.8–3.0) MJ (−26%) Reduction total intake: 21%	Hunger, desire to eat, prospective consumption ratings lower during GLP1 infusion, up to 4 points difference on 10 point scale (just before lunch)

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TABLE 2 (*Continued***)**

First author, and year of publication	Design and stimuli used	Number and type of subjects	Results with respect to food intake	Results with respect to appetite ratings
Flint, 2001 (28)	Single blind, randomized cross-over -IV saline -IV GLP-1 0.75 pmol/ kg fat free mass min infusion for 300 min minus a break for 30 m before lunch. At t = 0 a fixed breakfast, at t = 270 an ad libitum lunch (mixed meal)	18 obese men, age = 43 ± 2 y BMI = 34 ± 1 kg/m2 (mean ± sem)	Test meal intake (mean ± sem) saline = 2.92 ± 0.23 MJ GLP1 = 2.83 ± 0.28 MJ (−3.0%) NS	Hunger, prospective consumption ratings about 5 mm lower on 100 mm scale during GLP1 infusions; no differences in satiety, fullness ratings
Zander, 2002 (29)	Single blind, parallel -placebo -GLP1 4.8 pmol/ kg min infusion continuously subcutaneous for 6 weeks no food intake measured hunger, satiety measured for 2 h after fixed breakfasts and lunches at week 0, 1 and 6	GLP1 group: 10 diabetics (4 m/6 f) age = 55 ± 4 y BMI = 35 ± 6 kg/m2 placebo group: age = 54 ± 6 y BMI = 32 ± 4 kg/m2 (mean ± sem)	Body weight changes over 6 wks placebo = −0.7 kg GLP1 = −1.9 kg ($P = 0.16$)	AUC hunger, prospective consumption decreased more in GLP1 group than in placebo group; difference only significant in week 1 vs. week 0.
Endogeneous				
Kong, 1999 (30)	Single, randomized, cross-over -Oral 75 g glucose in 300 ml -Oral 75 g fructose in 300 ml -Oral 75 g glucose in 300 ml, followed by 75 g fructose in 300 ml, 60 min later; Glucose had much stronger effect on GLP1 Blood levels than fructose At t = 120 a ad lib mixed meal was served	8 men age = 27 ± 7 y BMI = 24 ± 3 y (mean ± sd)	Test meal intake (mean ± sem) glucose = 4.3 ± 0.9 MJ fructose = 4.3 ± 1.0 MJ gluc + fructose = 3.6 ± 1.0 MJ ($P < 0.005$ compared glucose and fructose)	No difference in hunger and satiety rating between three conditions
Rayner, 2000 (31)	Single blind, randomized, cross over -ID saline -ID glucose, 0.5 g /min -ID fructose, 0.5 g/ min infusion for 90 min, at t = 90 min, an ad libitum test meal was served GLP1 blood concentration were similar after glucose compared to fructose	10 subjects, 2 f, 8 m age = 25 y (19–37 y) BMI = 25 (21–28) kg/m2 (mean-range)	Test meal intake (mean; visually estimated from figure) saline ≈ 4.8 MJ glucose ≈ 4.7 MJ fructose ≈ 4.2 MJ (intake after fructose significantly lower)	Hunger lower after glucose and fructose compared to saline, about 10 mm on 100 mm scale ($P < 0.05$ glucose vs. saline $P = 0.08$ for fructose vs. saline)

TABLE 3
Summary of results of studies in humans that investigated the relationship between hunger and satiety and the responses of the human brain.

First author, and year of publication	Study design/stimuli	Measured parameters	Number and type of subjects	Central effects of food intake/stimulus
Tataranni, 1999 (32)	Satiety versus hunger in normal-weight men. 36h fast, liquid meal 50% of DEE* delivered over 25 min. Two 1-minute PET-scans at fasted baseline and two after feeding with 10–15 minutes between the two scans.	Plasma levels of glucose, insulin, leptin and FFA from blood samples collected immediately after each scan. Subjective ratings of hunger and satiety (VAS), recorded after each scan. rCBF*.	11 normal-weight men; 35 ± 8 yrs, 73 ± 9 kg, 19 ± 6% body fat.	Hunger was associated with increased rCBF near the hypothalamus, insular cortex and in the anterior cingulate cortex, parahippocampal and hippocampal formation, anterior temporal and posterior orbitofrontal cortex, thalamus, caudate, precuneus, putamen and cerebellum. Satiety was associated with increased rCBF bilaterally near the ventromedial prefrontal cortex, dorsolateral prefrontal cortex and the inferior parietal lobule. Postmeal insulin increase correlated negatively with postmeal rCBF changes near the insular cortex (LH: r = − 0.69, $P = 0.02$; RH: r = −0.57, $P = 0.06$) and the orbitofrontal cortex (LH: r = −0.72, $P = 0.01$; RH: r = −0.59, $P = 0.05$).
Gautier, 2000 (33)	Satiety versus hunger in obese and lean men. 36h fast, liquid meal 50% of DEE* delivered over 25 min. Two 1-minute PET-scans at fasted baseline and two after feeding with ~10 minutes between the two scans.	Plasma levels of glucose, insulin, leptin, FFA, gastrin, PP, and GLP-1 from blood samples collected immediately after each scan. Subjective ratings of hunger and satiety (VAS) recorded after each scan. rCBF*.	11 obese men; BMI* ≥35, 27 ± 5 yrs, 115 ± 11 kg, 38 ± 7% body fat, and 11 lean men; BMI* ≤25, 35 ± 8 yrs, 73 ± 9 kg, 19 ± 6% body fat.	Obese vs lean men in response to satiety: greater rCBF increase near the right dorsolateral and ventromedial prefrontal cortex and bilaterally in the dorsomedial prefrontal cortex, greater rCBF decrease in the right insular/anterior temporal region, right hippocampal formation, bilaterally in a large region including the orbitofrontal cortex and temporal pole and the cerebellum. rCBF decreases tended to be smaller in obese subjects in the hypothalamus, thalamus, and anterior cingulate. Negative correlation between changes in plasma insulin levels and changes in rCBF in various brain areas. Changes in hunger ratings correlated negatively with changes in rCBF in left and right prenuceus, in both lean and obese subjects.
Gautier, 2001 (34)	Satiety versus hunger in obese and lean women. 36h fast, liquid meal 50% of DEE* delivered over 25 min. Two 1-minute PET-scans at fasted baseline and two after feeding with ~10 minutes between the two scans.	Plasma levels of glucose, insulin, leptin, and FFA from blood samples collected immediately after each scan. Subjective ratings of hunger and satiety (VAS), recorded after each scan. rCBF*.	12 obese women; BMI* 41 ± 5, 30 ± 7 yrs, 110 ± 14 kg, 40 ± 2% body fat and 10 lean women; BMI* 23 ± 2, 32 ± 10 yrs, 61 ± 7 kg, 26 ± 6% body fat.	Obese versus lean women had a greater increase in rCBF in the ventral prefrontal cortex, greater decrease in the paralimbic areas and in areas of the frontal and temporal cortex. The correlation between postprandial changes in rCBF and plasma levels of FFA differed between obese and lean women in the right hippocampus/hippocampal gyrus, left ventral, and dorsomedial prefrontal cortex (group effect $P < 0.02$). Lean and obese women showed opposite correlations between plasma levels of glucose and FFA and postprandial changes in rCBF in the dorsomedial prefrontal cortex (glucose: lean women r = 0.77, obese r = −0.62; FFA: lean r = 0.07, obese women r = −0.72), and in the right hippocampus/parahippocampal gyrus (glucose: lean women r = 0.79; obese r = −0.31; FFA, lean r = − 0.58; obese r = 0.49).

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TABLE 3 (*Continued***)**

First author, and year of publication	Study design/stimuli	Measured parameters	Number and type of subjects	Central effects of food intake/stimulus
Del Parigi, 2002 (35)	Satiety versus hunger in men and women. 36h fast, liquid meal 50% of DEE* delivered over 25 min. Two 1-minute PET-scans at fasted baseline and two after feeding with ~10 minutes between the two scans.	Plasma levels of glucose, insulin, leptin, FFA, gastrin, PP and GLP-1 from blood samples collected immediately after each scan. Subjective ratings of hunger and satiety (VAS), recorded after each scan. rCBF*.	44 subjects; 22 males and 22 females, 31 ± 8 and 31 ± 9 yrs, 28 ± 12 and 34 ± 9 % body fat respectively.	Many similarities between men and women. In the fasted state men versus women showed greater rCBF in the fronto-temporal and paralimbic areas. In the satiated versus the fasted state women showed greater increases in rCBF in the dorsolateral prefrontal cortex, precuneus and the occipito-temporal cortex than men. Men versus women showed greater increases in rCBF in the ventromedial prefrontal cortex (all $P < 0.005$).
Matsuda, 1999 (36)	Satiation and satiety in obese and lean subjects. 12h fast, 75 g dextrose in 296 ml flavoured water/distilled water as control. Continuous fMRI of a midsagittal slice for 50 minutes, drinking after 10 minutes. Temporal resolution 12s per image (250 images).	Plasma levels of glucose, insulin and leptin from blood samples taken at 15 min intervals, starting 15 min before glucose ingestion. BOLD fMRI-signal*. For each ROI*: the time lag between the onset of stimulus intake and the maximum inhibition of the fMRI signal and the averaged inhibition over time.	10 obese subjects; 5 males and 5 females, BMI* 34.2 ± 1.3, 34 ± 2 yrs, 10 lean subjects, 5 males and 5 females, BMI* 22.0 ± 0.9, 32 ± 4 yrs.	Both lean and obese subjects showed an inhibition of the fMRI signal in the upper anterior (UAH) and lower posterior (LPH) hypothalamus (the paraventricular and ventromedial nuclei). Obese vs lean subjects showed a smaller (4.8 ± 1.3 vs 7.0 ± 0.6 % inhibition) and delayed (9.4 ± 0.5 vs 6.4 ± 0.5 min) decrease in fMRI signal in the UAH and LPH. The time taken to reach the maximum inhibitory response correlated with the fasting plasma glucose (UAH $r = 0.68$, $P < 0.01$, LPH $r = 0.75$, $P < 0.001$) and with plasma insulin concentrations (UAH $r = 0.43$, $P < 0.05$, LPH $r = 0.47$, $P < 0.05$) in all subjects.
Liu, 2000 (37)	Satiation and satiety in subjects of both sexes. 12h fast, 75 g dextrose in 296 ml flavoured water/distilled water as control. Continuous fMRI of a midsagittal slice for 48 minutes, drinking after 10 minutes. Temporal resolution 12s per image (240 images).	Plasma levels of insulin from blood samples taken at 15 min intervals, starting 15 min before glucose ingestion. BOLD fMRI-signal/fMRI activity index*.	21 subjects; 11 males and 10 females, 34 ± 3 yrs.	Temporal peaks around 1.9 min (signal increase) and 10.2 min (signal decrease) after the onset of drinking, in the sensorimotor cortex and the hypothalamus respectively. Significant negative correlation ($r = -0.68$, $P < 0.01$) between the fasting plasma insulin level and the fMRI activity* index in the hypothalamus 10 min after the onset of drinking the glucose solution.

* Abbreviations in alphabetical order: BOLD-signal. Blood Oxygen Level Dependent signal, a measure for neuronal activity; BMI, Body Mass Index (kg/m2); DEE. Daily Energy Expenditure; fMRI activity index. Average normalized signal change in a region of interest (Liu et al 1999); rCBF, regional Cerebral Blood Flow, measure for neuronal activity; ROI, Region of Interest; VAS. Visual Analog Scale.

TABLE 4
Summary of design and results of studies in humans that investigated the effects of glucose on appetite, that is food intake and subjectively rated appetite; IV = intravenous, ID = intraduodenal.

First author, and year of publication	Design and stimuli used	Number and type of subjects	Results with respect to food intake	Results with respect to appetite ratings
Exogenous				
Thompson, (1977) (38)	Single blind, cross-over -IV saline -IV 2-deoxy-D-glucose (50 mg/kg) 0–20 min: infusion saline or 2DG 125 min: intensity + pleasantness rating of sucrose solutions 185–210 min: chocolate-flavored liquid lunch 240 min: end experiment	5 normal-weight men	Mean test meal intake: saline = 797 ml 2DG = 1170 ml (= + 47%) difference = + 373 ml	2DG increased hunger significantly from 30–180 minutes compared to saline
Welle, (1980) (39)	Single blind, cross-over Day 1: IV 2 deoxy-D-glucose (50 mg/kg) Day 2: IV saline (50 ml, 0.9% saline) Day 3: IV 2 deoxy-D-glucose (50 mg/kg) 0–20 min: infusion saline or 2DG 150–180 min:lunch consisting of four sandwiches, pie and a beverage	5 men, within 10% of ideal weight for height Age: 19–25 y	Mean test meal intake: 2DG day 1 = 1312 ± 228 kcal 2DG day 2 = 1345 ± 155 kcal saline = 981 ± 228 kcal	2DG increased hunger significantly ($P < 0.05$) at 90, 120, and 150 min, compared to saline
Gielkens, 1998 (40)	Single blind, randomized, cross-over -IV saline (normal glucose, normal insulin) -IV 20% glucose to maintain blood glucose at 15 mmol/L (high glucose/high insulin) -IV insulin (80–100 mU/L) + IV 20% glucose in order to maintain normal glucose levels, i.e. 4–5 mmol/L) (normal glucose/high insulin)	6 healthy subjects (1 m, 5f) BMI range: 20–25 kg/m^2 Age: 22 ± 1 y	Not measured	IV glucose significantly reduced feelings of hunger and prospective food consumption compared to control and insulin infusion (about 35 mm on a 100 mm scale). The wish to eat was not significantly ($P = 0.07$) reduced. No effects on fullness were found.
Chapman, 1998 (41)	Single blind, randomized, cross-over 25–170 min: IV 20% glucose to maintain glucose levels at baseline (5 mmol/L) in first three conditions 20–170 min: IV treatments -IV control, normal glucose, normal insulin -IV + 0.8 mU*kg^{-1}*min^{-1} insulin, normal glucose, high insulin -IV + 1.6 mU*kg^{-1}*min^{-1} insulin, normal glucose, high insulin -IV 25% glucose infusion as on 1.6 mU*kg^{-1}*min^{-1} insulin condition, high glucose/high insulin (12 subjects) 140-170 min: ad libitum test meal	14 healthy young subjects (12m + 2f) BMI: 23.6 ± 1.9 kg/m^2 Age range: 20–33 y Non-restrained eaters 12 subjects completed the fourth, glucose only condition.	Test meal intake (mean ± sem) Control = 4.4 ± 0.4 MJ Insulin 0.8 = 4.5 ± 0.4 MJ (+ 1%) Insulin 1.6 = 4.5 ± 0.4 MJ (+ 1%) Glucose + = 3.8 ± 0.4 MJ (−15 %) Intake glucose condition was significantly lower ($P < 0.05$), compared to the other three conditions.	Hunger ratings did not differ significantly between the four conditions.
Andrews, 1998b (42)	Single blind, randomized, cross-over 0-180 min: -IV 20% glucose, to maintain blood glucose at 5 mmol/L, normal glucose, normal insulin -IV 20% glucose, to maintain blood glucose at 8 mmol/L, high glucose, high insulin 90–180 min: -ID infusion of triglyceride emulsion (1.5 kcal/min, 82 ml/h)	10 healthy men BMI range: 22.5–29.6 kg/m^2 Age range: 19–40 y	Not measured	0–90 min.: fullness was greater, hunger was lower (about 10 mm at a 100 mm scale) at 8 mmol/l glucose infusion compared with 5 mmol/I infusion. 90–180 min.: appetite decreased with blood glucose levels of 8 mmol/I compared with 5 mmol/I. Fullness increased at blood glucose levels of 5 mmol/I, but not at 8 mmol/l leading to higher scores of fullness with 5 mmol/l glucose

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TABLE 4 (*Continued***)**

First author, and year of publication	Design and stimuli used	Number and type of subjects	Results with respect to food intake	Results with respect to appetite ratings
Exo/Endogenous				
Lavin, 1996 (43)	- ID 20% glucose (4 ml/min) + IV 0.9% saline (2 ml/min) (A) - ID 9% saline (4 ml/min) + IV 25% glucose (blood glucose matched concentrations after ID glucose) (B) - ID 20% glucose (4 ml/min) + IV octreotide (250 μg/h in 0.9% saline) (C) Infusion (A+B): t = 30 − t = 120 minutes Infusion (C): octreotide: t = 0–120 minutes, ID glucose: t = 30 − t = 120, IV glucose: t = 0 till absorption ID glucose. Octreotide inhibits release of insulin and GI-hormones After ID infusion a cold buffet-style meal was presented for 30 min	7 healthy men BMI range: 20–25 kg/m^2 Age range: 19–35 y Non-restrained eaters 5 subjects for condition C	Test meal intake at end infusion (mean ± sem ID glucose + IV saline: 907 ± 150 kcal ID saline + IV glucose: 1093 ± 152 kcal ID glucose + octreotide: + 30% compared to ID glucose	ID glucose decreased hunger and increased fullness and satiety compared with IV glucose (about 1.8, 1.5 and 1.0 res. on a 10 pt scale). Plasma glucose levels were the same although total amount of energy from ID infusions of glucose was greater (288 ~ 152 kcal) from 60–75 min after start of infusion.
Endogenous				
Campfield, 1996 (44) Study 1	Time-blinded After an overnight fast subjects had to request a meal when they felt hungry. Blood glucose was monitored for 2–6 hours	18 healthy subjects (9m, 9f)	Not measured	In 83% of the 18 subjects, changes in hunger ratings and spoken meal requests were preceded by, and significantly correlated with, brief transient declines in blood glucose. Unchanged hunger ratings were associated with stable blood glucose concentrations.
Campfield, 1996 (44) Study 2	Crossover, time-blinded Overnight fast, followed by either -IV saline (5 mU/kg) -IV insulin (5 mU/kg)	5 healthy subjects; examples of results of 2 subjects were reported	Not measured	Increased measures of desire to eat (about 37 mm on a 100 mm scale) and hunger (about 22 mm on a 100 mm scale) after insulin-induced transient declines in blood glucose concentration.
Andrews, 1998a (45)	Single blind, randomized, crossover Visit 1 0–90 min: ID glucose (2.9 kcal/min) or ID lipid (2.9 kcal/min) 90–180 min: ID saline (0.9%, 3 ml/m) 180–270 min: ID infusion of the alternate nutrient (glucose of lipid). ID-glucose lead to plasma glucose levels of 8.5–9 mmol/l After visit 1 subjects consumed 400 g glucose supplement per day for 7 days immediately before visit 2. Visit 2: same protocol as Visit 1	10 healthy men BMI range: 21.7–26.9 kg/m^2 Age range: 19–38 y	Not measured	Day 1: Lipid reduced the desire to eat (about 10 mm on a 100 mm scale) and increased fullness (about 15 mm on a 100 mm scale). ID glucose did not change appetite ratings Day 2: ID glucose did not change appetite ratings. ID lipid was not more satiating compared to glucose
Melanson, 1999a (46)	Blind, cross-over, time-blinded Oral preloads: - 350 g, high-carbohydrate, lemon-flavored drink (1000 kJ) - 350 g, high-fat lemon-flavored drink (999 kJ) First meal request: one of the preloads. Second meal request: ad libitum lunch	10 weight-stable men non-restrained eaters BMI: 22.2 ± 1.8 kg/m^2 Age range: 18–30 y	Ad libitum lunch intake (mean ± sem) Fat = 4519 ± 677 kJ; CHO = 4013 ± 789 kJ ($P > 0.05$)	71% of dynamic and transient declines in blood glucose were associated with meal requests. Of all meal requests, 72% were associated with a decline in blood glucose.

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TABLE 4 (*Continued*)

First author, and year of publication	Design and stimuli used	Number and type of subjects	Results with respect to food intake	Results with respect to appetite ratings
Melanson, 1999b (47)	Blind, randomized, crossover, time-blinded Preload: - 350 g, simple carbohydrate, lemon-flavored drink (1000 kJ) - 350 g, high-fat lemon-flavored drink (999 kJ) - 350 g, aspartame, lemon-flavored drink (150 kJ) First meal request: one of the preloads. Second meal request: ad libitum lunch	10 weight-stable men BMI: 23.4 ± 1.9 kg/m^2 Age: 25.2 ± 4.0 y Non-restrained eaters	Ad libitum lunch intake (mean ± sem) Fat = 5617 ± 661 kJ; Aspartame: = 5861 ± 1652 kJ Sugar (CHO) = 6112 ± 910 kJ ($p > 0.05$)	Duration of blood glucose response until baseline is possitively correlated with the duration of the intermeal interval and post-drink satiety 81% of dynamic and transient declines in blood glucose were associated with meal requests. Of all meal requests, 73% were associated with a decline in blood glucose.
Melanson, 1999c (48)	Visit 1: max aerobic capacity and power output assessment Visit 2, 24-h time-blinded stay: Evening: Glycogen depletion exercise. After meal request; low-carbohydrate isoenergetic dinner. Next morning: 1st meal request: ad libitum high-carbohydrate and high-fat food and beverages (high-fat drink (999 kJ, 350 g), simple carbohydrate drink (1000 kJ, 350 g)	10 weight-stable men BMI: 21.9 ± 1.9 kg/m^2 Age: 23.1 ± 3.1 y Non-restrained eaters	Not measured	No effects of glycogen depletion on appetite ratings were found Postabsorptively (when glycogen buffer is depleted, before first meal), 8 of 10 meals were initiated during stable blood glucose. 77% of all postprandial (after meal) declines in blood glucose were associated with meal requests. Of all postprandial meal requests, 87% were associated with a decline in blood glucose
Kovacs, 2002 (49)	Randomized, cross-over, time-blinded Treatments: - 2-week diet; 3 times/day semi-solid meal without guar gum, 947 kJ - 2-week diet; 3 times/day semi-solid meal with guar gum, 947 kJ - 2-week diet; 3 times/day, solid meal, 947 kJ After treatment and overnight fast, time-blinded subjects could request a meal. 1st, 2nd and 3rd meal request: low energy meal provided the two weeks before 4th meal request: ad libitum standardized meal (pasta + tomato sauce)	15 overweight men BMI: 28.6 ± 1.8 kg/m^2 Age: 43.7 ± 9.3 y	Not measured	Post-absorptive transient declines before meal request were not associated with meal initiation. 48% of the postprandial dynamic declines were associated with meal initiation and all 4 postprandial transient declines were associated with meal initiation.

TABLE 5
Summary of design and results of studies in humans that investigated the effects of insulin on appetite, that is food intake and subjectively rated appetite; IV = intravenous, ID = intraduodenal.

First author, and year of publication	Design and stimuli used	Number and type of subjects	Results with respect to food intake	Results with respect to appetite
Exogenous				
Woo, 1984 (50) Study 1	Randomized, cross-over T = 0 minutes: breakfast T = 180 minutes: start infusion; - IV saline (0.15 M) - IV insulin (0.03 U/kg/h) and IV glucose (0.25 g/kg/h) as isotonic solution T = 210 minutes: *ad libitum* liquid meal infusion stopped 15 minutes after end meal	8 nonobese subjects (4m + 4f), age men (mean ± sd): 24.7 ± 2.2 y, average desirable weight men: 96.5 ± 11.1% Age women: 23.5 ± 1.7 y, average desirable weight women: 104.5 ± 13.7%	The insulin-glucose infusion (hyperinsulinemia + hyperglycemia) did not influence food intake.	Not measured
Woo, 1984 (50) Study 2	Randomized, cross-over T = 0 minutes: breakfast T = 168 minutes: appetizer T = 180 minutes: lunch and start infusion; - IV saline (0.15 M) - bolus injection insulin (12 mU/kg) + IV insulin (0.03 U/kg/h) and IV glucose (0.125 g/kg/h) as isotonic solution T = 210 minutes: *ad libitum* liquid meal infusion stopped 12 minutes after end meal	4 males, age (mean ± sd): 23.5 ± 6.8 y, average desirable weight: 96.6 ± 6.7%	Glucose concentrations were not different between the two types of infusion. No significant differences in food intake were observed between mean intake during saline infusion (1100 g) and during insulin infusion (1106 g)	Not measured
Rodin, 1985 (51)	Four experimental groups: - *Basal Insulin, euglycemia (control:* 120 minutes saline infusion (1 mL/min) - *Hyperinsulinemia, hypoglycemia:* insulin infusion (concentration maintained at 100 mU/mL) and glucose infusion (concentration decline from 90 to 59 mg/dL over 150-min study period) - *Hyperinsulinemia, hyperglycemia:* glucose infusion (concentration maintained at 125 mg/dL above fasting levels for 150 min) - *Euinsulinemia, hyperglycemia:* somatostatin infusion (9 μg/min) (inhibits endogenous insulin secretion) and insulin infusion (0.08 mU/kg/min). Glucose was maintained at 200 mg/dL for 150 minutes, starting 10 minutes after start somatostatin infusion.	20 healthy young subjects (7 f, 13 m), age range: 20–31 y	Mean fluid intake after infusion stopped: Control = 718 ml Hyperinsulinemia, hypoglycemia = 1110 ml Hyperinsulinemia, hyperglycemia = 1225 ml	Hyperinsulinemic conditions showed significant increased levels of hunger (4.8 and 5.2) compared to baseline (3.4 and 3.8) and euinsulinemic (3.7) conditions on a 7-point category rating scale. No significant differences between the hyper- and hypoglycemic conditions was observed. Hyperinsulinemia was also associated with enhanced palatability of sweet solutions
Lavin, 1996 (43)	- ID 20% glucose (4 ml/min) + IV 0.9% saline (2 ml/min) (A) ->high insulin - ID 9% saline (4 ml/min) + IV 25% glucose (blood glucose matched concentrations after ID glucose) (B) - ID glucose (4 ml/min) + IV octreotide (250 μg/h in 0.9% saline) (C) Infusion (A+B): t = 30 − t = 120 minutes Infusion (C): octreotide: t = 0–120 minutes, ID glucose: t = 30 − t = 120, IV glucose: t = 0 till absorption ID glucose. Octreotide inhibits release of insulin and GI-hormones) After ID infusion a cold buffet-style meal was presented for 30 min	7 healthy men, age range: 19–35 y, BMI range: 20–25 kg/m^2 Non-restrained eaters Condition C was carried with 5 of 7 subjects.	Test meal intake at end infusion (mean ± SE) ID glucose + IV saline: 907 ± 150 kcal ID saline + IV glucose: 1093 ± 152 kcal ID glucose + IV glucose and octreotide: + 30% compared to ID glucose	ID glucose, with corresponding high insulin levels, decreased hunger and increased fullness and satiety compared with IV glucose (about 1.8, 1.5 and 1.0 res. on a 10 pt scale). Octreotide infusion (with corresponding lower insulin levels) decreased hunger and increased fullness

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TABLE 5 (*Continued***)**

First author, and year of publication	Design and stimuli used	Number and type of subjects	Results with respect to food intake	Results with respect to appetite
Chapman, 1998 (41)	Single blind, randomized, cross-over T = 25–170 min: treatment - IV control, normal; glucose, normal insulin - IV + 0.8 mU*kg^{-1}*min^{-1} insulin, normal glucose, high insulin - IV + 1.6 mU*kg^{-1}*min^{-1} insulin, normal glucose and high insulin - IV 25% glucose infusion as on insulin (1.6 mU*kg^{-1}*min^{-1}) condition, high glucose, high insulin (12 subjects) The glucose infusion rate was varied to maintain glucose levels at baseline. 140–170 min: ad lib. cold buffet meal	14 healthy young subjects (12m + 2f), age range: 20–33 y, BMI (mean ± sd): 23.6 ± 1.9 kg/m^2 Non-restrained eaters 12 subjects completed fourth condition, glucose only condition	Test meal intake (mean ± sem) Control = 4.4 ± 0.4 MJ Insulin 0.8 = 4.5 ± 0.4 MJ (+1%) Insulin 1.6 = 4.5 ± 0.4 MJ (+1%) Glucose + = 3.8 ± 0.4 MJ (−15%) Intake glucose condition was significantly lower ($P < 0.05$), compared to the other three conditions.	Hunger ratings did not differ significantly between the four conditions
Gielkens, 1998 (40)	Single blind, randomized, cross-over Treatments t = 0–240 min - IV saline - IV 20% glucose (15 mmol/L) (hyperglycemia + hyperinsulinemia) - IV insulin (80–100 mU/L) + IV 20% glucose (4–5 mmol/L) (hyperinsulinemia + euglycemia) 10 mmol KCl was added to 500 ml 20% glucose.	6 healthy subjects (1m, 5f), age (mean ± sd): 22 ± 1 y, BMI range: 20–25 kg/m^2	Not measured	Hyperinsulinemia without hyperglycemia did not influence appetite ratings. Hyperinsulinemia in combination with hyperglycemia significantly reduced feelings of hunger and prospective feeding intentions compared to control and insulin infusion (about 35 mm on a 100 mm scale). The wish to eat was not significantly ($P = 0.07$) reduced. No effects on fullness were found.
Endogenous				
Holt, 1996 (52)	Randomized, cross-over In total 38 foods separated in 6 categories were tested. At the start of each food group, subjects were given a 1000 kJ portion of white bread (reference food). Each test food was served as a standard 1000 kJ portion with 220 mL of water. Each food item was consumed within 10 minutes. An ad libitum test meal was served at 120 minutes.	41 healthy subjects, age (mean ± sd): 22.1 ± 2.9 y, BMI: 22.7 ± 0.4 kg/m^2 (11–13 subjects per food category) non-restrained eaters	A negative correlation (r = 0.40, $P < 0.01$) between insulin AUC responses and ad libitum food intake at 120 minutes was found.	No significant correlations between glucose and insulin measures (e.g. AUC, index, mean peak values) and subjective satiety measures were observed
Speechly, 2000 (53)	Randomized, cross-over - High fat preload meal, containing 20% of daily energy requirement - Low fat preload meal, containing 55% of daily energy requirement Ad libitum lunch 5 hours after preload meal	6 healthy lean men, age (mean ± sd): 26.67 ± 5.47 y, BMI: 22.50 ± 1.08 kg/m^2 6 healthy obese men, age: 39.83 ± 19.03 y, BMI: 39.05 ± 11.63 kg/m^2	Insulin levels immediately before lunch showed a significantly negative correlation with food intake at lunch in lean (r = −0.63) but not in obese subjects (r = −0.31)	Not measured
Verdich, 2001 (54)	Subjects were served a 2.5 MJ solid test meal (bread with ommelette), followed by an ad libitum lunch 190 minutes later.	12 healthy lean men, mean age: 34.2, age range: 28.7–39.6 y, mean BMI: 23.1, BMI range: 22.3–23.9 kg/m^2 19 healthy obese men mean age: 35.0, age range: 30.1–39.9 y, mean BMI: 38.7, BMI range 37.3–40.1 kg/m^2	In lean subjects energy intake was inversely related to; fasting insulin concentration prior to the fixed test-meal; insulin concentration immediately before the ad libitum test meal; $AUC_{total,\ insulin}$ and $AUC_{incremental,\ insulin}$ $AUC_{total,\ insulin}$ was found to explain 67% of the variation in ad libitum energy intake. No correlation between insulin and intake in obese subjects.	Not measured

REFERENCES

1. Kissileff HR, Pi-Sunyer FX, Thomton J, Smith GP. C-terminal octapeptide of cholecystokinin decreases food intake in man. Am J Clin Nutr 1981;34:154–60.
2. Pi-Sunyer X, Kissileff HR, Thornton J, Smith GP. C-terminal octapeptide of cholecystokinin decreases food intake in obese men. Physiol Behav 1982;29:627–30.
3. Muurahainen N, Kissileff HR, Derogatis AJ, Pi-Sunyer FX. Effects of cholecystokinin-octapeptide (CCK-8) on food intake and gastric emptying in man. Physiol Behav 1988;44:645–9.
4. Schick RR, Schusdziarra V, Mossner J et al. Effect of CCK on food intake in man: physiological or pharmacological effect? Z Gastroenterol 1991;29:53–8.
5. Muurahainen NE, Kissileff HR, Lachaussee J, Pi-Sunyer FX. Effect of a soup preload on reduction of food intake by cholecystokinin in humans. Am J Physiol 1991;260:R672–R680.
6. Melton PM, Kissileff HR, Pi-Sunyer FX. Cholecystokinin (CCK-8) affects gastric pressure and ratings of hunger and fullness in women. Am J Physiol 1992;263:R452–R456.
7. Lieverse, R. CCK and bombesin and obesity. 61–73, 1993. Thesis/Dissertation.
8. Lieverse RJ, Jansen JB, van de ZA, Samson L, Masclee AA, Lamers CB. Effects of a physiological dose of cholecystokinin on food intake and postprandial satiation in man. Regul Pept 1993;43:83–9.
9. Lieverse RJ, Jansen JB, Masclee AA, Lamers CB. Satiety effects of a physiological dose of cholecystokinin in humans. Gut 1995;36:176–9.
10. Ballinger A, McLoughlin L, Medbak S, Clark M. Cholecystokinin is a satiety hormone in humans at physiological postprandial plasma concentrations. Clin Sci (Lond) 1995;89:375–81.
11. Gutzwiller J, Drewe J, Ketterer S, Hildebrand P, Krautheim A, Beglinger C. Interaction between CCK and a preload on reduction of food intake is mediated by CCK-A receptors in humans. Am J Physiol Regul Integr Comp Physiol 2000;279:R189–R195.
12. MacIntosh CG, Morley JE, Wishart J et al. Effect of exogenous cholecystokinin (CCK)-8 on food intake and plasma CCK, leptin, and insulin concentrations in older and young adults: evidence for increased CCK activity as a cause of the anorexia of aging. J Clin Endocrinol Metab 2001;86:5830–7.
13. Kissileff HR, Carretta JC, Geliebter A, Pi-Sunyer FX. Cholecystokinin and stomach distension combine to reduce food intake in humans. Am J Physiol Regul Integr Comp Physiol 2003;285:R992–R998.
14. Wolkowitz OM, Gertz B, Weingartner H, Beccaria L, Thompson K, Liddle RA. Hunger in humans induced by MK-329, a specific peripheral-type cholecystokinin receptor antagonist. Biol Psychiatry 1990;28:169–73.
15. French SJ, Murray B, Rumsey RD, Sepple CP, Read NW. Is cholecystokinin a satiety hormone? Correlations of plasma cholecystokinin with hunger, satiety and gastric emptying in normal volunteers. Appetite 1993;21:95–104.
16. French SJ, Bergin A, Sepple CP, Read NW, Rovati L. The effects of loxiglumide on food intake in normal weight volunteers. Int J Obes Relat Metab Disord 1994;18:738–41.
17. Lieverse RJ, Jansen JB, Masclee AA, Rovati LC, Lamers CB. Effect of a low dose of intraduodenal fat on satiety in humans: studies using the type A cholecystokinin receptor antagonist loxiglumide. Gut 1994;35:501–5.
18. Maas MI, Hopman WP, Gelder BV et al. Does intraduodenal administration of sucrose polyester (Olestra) cause satiation in humans? Appetite 1999;33:195–208.
19. Matzinger D, Gutzwiller J, Drewe J et al. Inhibition of food intake in response to intestinal lipid is mediated by cholecystokinin in humans. Am J Physiol 1999;277:R1718–R1724.
20. Beglinger C, Degen L, Matzinger D, D'Amato M, Drewe J. Loxiglumide, a CCK-A receptor antagonist, stimulates calorie intake and hunger feelings in humans. Am J Physiol Regul Integr Comp Physiol 2001;280:R1149–R1154.
21. Burton-Freeman B, Davis PA, Schneeman BO. Plasma cholecystokinin is associated with subjective measures of satiety in women. Am J Clin Nutr 2002;76:659–67.
22. Flint A, Raben A, Astrup A, Holst J. Glucagon-like peptide 1 promotes satiety and suppresses energy intake in humans. J Clin Invest 1998;101:515–20.
23. Naslund E, Gutniak M, Skogar S, Rossner S, Hellstrom PM. Glucagon-like peptide 1 increases the period of postprandial satiety and slows gastric emptying in obese men. Am J Clin Nutr 1998;68:525–30.
24. Gutzwiller J, Goke B, Drewe J et al. Glucagon-like peptide-1: a potent regulator of food intake in humans. Gut 1999;44:81–6.
25. Long S, Sutton J, Amaee W et al. No effect of glucagon-like peptide-1 on short-term satiety and energy intake in man. Br J Nutr 1999;81:273–9.
26. Gutzwiller JP, Drewe J, Goke B et al. Glucagon-like peptide-1 promotes satiety and reduces food intake in patients with diabetes mellitus type 2. Am J Physiol 1999;276:R1541–R1544.
27. Naslund E, Barkeling B, King N et al. Energy intake and appetite are suppressed by glucagon-like peptide-1 (GLP-1) in obese men. Int J Obes Relat Metab Disord 1999;23:304–11.
28. Flint A, Raben A, Ersboll AK, Holst JJ, Astrup A. The effect of physiological levels of glucagon-like peptide-1 on appetite, gastric emptying, energy and substrate metabolism in obesity. Int J Obes Relat Metab Disord 2001;25:781–92.
29. Zander M, Madsbad S, Madsen JL, Holst JJ. Effect of 6-week course of glucagon-like peptide 1 on glycaemic control, insulin sensitivity, and beta-cell function in type 2 diabetes: a parallel-group study. Lancet 2002;359:824–30.
30. Kong MF, Chapman I, Goble E et al. Effects of oral fructose and glucose on plasma GLP-1 and appetite in normal subjects. Peptides 1999;20:545–51.
31. Rayner CK, Park HS, Wishart JM, Kong M, Doran SM, Horowitz M. Effects of intraduodenal glucose and fructose on antropyloric motility and appetite in healthy humans. Am J Physiol Regul Integr Comp Physiol 2000;278:R360–R366.
32. Tataranni PA, Gautier JF, Chen K et al. Neuroanatomical correlates of hunger and satiation in humans using positron emission tomography. Proc Natl Acad Sci USA 1999;96:4569–74.
33. Gautier JF, Chen K, Salbe AD et al. Differential brain responses to satiation in obese and lean men. Diabetes 2000;49:838–46.
34. Gautier JF, Del Parigi A, Chen K et al. Effect of satiation on brain activity in obese and lean women. Obes Res 2001;9:676–84.
35. Del Parigi A, Chen K, Gautier JF et al. Sex differences in the human brain's response to hunger and satiation. Am J Clin Nutr 2002;75:1017–22.
36. Matsuda M, Liu Y, Mahankali S et al. Altered hypothalamic function in response to glucose ingestion in obese humans. Diabetes 1999;48:1801–6.
37. Liu Y, Gao J, Liu H, Fox P. The temporal response of the brain after eating revealed by functional MRI. Nature 2000;405:1058–62.
38. Thompson DA, Campbell RG. Hunger in humans induced by 2-deoxy-D-glucose: glucoprivic control of taste preference and food intake. Science 1977;198:1065–8.
39. Welle SL, Thompson DA, Campbell RG, Lilavivathana U. Increased hunger and thirst during glucoprivation in humans. Physiol Behav 1980;25:397–403.
40. Gielkens HA, Verkijk M, Lam WF, Lamers CB, Masclee AA. Effects of hyperglycemia and hyperinsulinemia on satiety in humans. Metabolism 1998;47:321–4.
41. Chapman IM. Effect of intravenous glucose and euglycemic insulin infusions on short-term appetite and food intake. Am J Physiol 1998;274:R596–R603.
42. Andrews JM, Rayner CK, Doran S, Hebbard GS, Horowitz M. Physiological changes in blood glucose affect appetite and pyloric motility during intraduodenal lipid infusion. Am J Physiol 1998;275:G797–G804.
43. Lavin JH, Wittert G, Sun WM, Horowitz M, Morley JE, Read NW. Appetite regulation by carbohydrate: role of blood glucose and gastrointestinal hormones. Am J Physiol 1996;271:E209–E214.
44. Campfield L, Smith F, Rosenbaum M, Hirsch J. Human eating: evidence for a physiological basis using a modified paradigm. Neurosci Biobehav Rev 1996;20:133–7.
45. Andrews JM, Doran S, Hebbard GS, Rassias G, Sun WM, Horowitz M. Effect of glucose supplementation on appetite and the pyloric motor response to intraduodenal glucose and lipid. Am J Physiol 1998;274:G645–G652.
46. Melanson K, Westerterp PM, Saris W, Smith F, Campfield L. Blood glucose patterns and appetite in time-blinded humans: carbohydrate versus fat. Am J Physiol 1999;277:R337–R345.
47. Melanson KJ, Westerterp-Plantenga MS, Campfield LA, Saris WH. Blood glucose and meal patterns in time-blinded males, after aspartame,

carbohydrate, and fat consumption, in relation to sweetness perception. Br J Nutr 1999;82:437–46.
48. Melanson KJ, Westerterp-Plantenga MS, Campfield LA, Saris WH. Appetite and blood glucose profiles in humans after glycogen-depleting exercise. J Appl Physiol 1999;87:947–54.
49. Kovacs EM, Westerterp-Plantenga MS, Saris WH et al. Associations between spontaneous meal initiations and blood glucose dynamics in overweight men in negative energy balance. Br J Nutr 2002;87: 39–45.
50. Woo R, Kissileff H, Pi SF. Elevated postprandial insulin levels do not induce satiety in normal-weight humans. Am J Physiol 1984;247:R745–R749.
51. Rodin J, Wack J, Ferrannini E, DeFronzo RA. Effect of insulin and glucose on feeding behavior. Metabolism 1985;34:826–31.
52. Holt SH, Brand Miller JC, Petocz P. Interrelationships among postprandial satiety, glucose and insulin responses and changes in subsequent food intake. Eur J Clin Nutr 1996;50:788–97.
53. Speechly DP, Buffenstein R. Appetite dysfunction in obese males: evidence for role of hyperinsulinaemia in passive overconsumption with a high fat diet. Eur J Clin Nutr 2000;54:225–33.
54. Verdich C, Toubro S, Buemann B, Lysgard MJ, Juul HJ, Astrup A. The role of postprandial releases of insulin and incretin hormones in meal-induced satiety—effect of obesity and weight reduction. Int J Obes Relat Metab Disord 2001;25:1206–14.