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CONTROL OF HUMAN APPETITE: Implications for The Intake of Dietary Fat

J.E. Blundell, C.L. Lawton, J.R. Cotton, and J.I. Macdiarmid
BioPsychology Group, Psychology Department, University of Leeds, Leeds, LS2 9JT, United Kingdom

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ABSTRACT

The human appetite system contains central and peripheral mechanisms that interact with environmental features, especially with the physical and nutrient composition of the food supply. Foods varying in nutrient composition exert different physiologic effects, some of which function as satiety signals. High-fat diets (low food quotient) lead to high levels of energy intake. This effect is termed passive overconsumption and overcomes fat-induced physiological satiety signals. High-fat foods exert a weak effect on satiation (intra-meal satiety), and fat has a weaker effect, joule for joule, on postingestive satiety than do other macronutrients. The frequency of obesity is greater among high-fat than low-fat consumers. However, the development of obesity on a high-fat diet is not a biological inevitability. The investigation of people who resist the weight-inducing properties of high-fat diets is a key research strategy. Understanding the appetite control system suggests behavioral, nutritional, and pharmacologic strategies for modifying dietary fat intake.

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APPETITE, NUTRITION, AND ENERGY BALANCE

For the past 20 years or so, the study of appetite has been driven, in part, by the need to understand the problem of, and to develop strategies to treat and prevent, human obesity. A number of epidemiologic studies have indicated a positive relationship between the proportion of fat in the diet and the prevalence of overweight or obese people (see Table 1). Consequently, there is an urgent need to examine the relationship between the intake of dietary fat and the mechanisms that control human appetite.

SYSTEMS APPROACH TO APPETITE

In the past, the study of appetite was approached through single-concept models such as the glucostatic, lipostatic, or aminostatic hypotheses, or through the so-called hypothalamocentric view. Each approach sought to explain appetite by reference to a restricted physiological mechanism or neural component. Currently, appetite is studied through a systems approach (4, 9), with each single concept incorporated into a broad framework

The strength of a systems approach lies in its capacity to integrate variables that otherwise would be isolated from each other, for example, with regard to appetite control, being able to consider simultaneously qualitative aspects such as behavioral pattern with the quantitative notion of spontaneous energy intake. Moreover, a central aspect to the systems view is that adjustments in one domain will influence, or be influenced by, the state of components elsewhere in the system. This view seems particularly appropriate for considering the relationships between appetite, nutrition, and energy balance. Appetite is a phenomenon arising out of, and maintained by, a complex sequence of interactions among elements that form part of a biopsychological system with regulatory properties, and with interrelationships between particular domains, including the external environment (cultural and nutritional), the behavioral profile (quantitative and qualitative), the storage and utilization of energy, the brain mechanisms implicated in the control system, and the mediating subjective states such as attributions and cognitions. Thus, it seems unlikely we are dealing with biological or environmental imperatives, i.e. factors that invariably lead to an identical outcome. Nutritional manipulation may provoke a behavioral response (e.g. change in meal size) only in the presence of certain physiological conditions (e.g. low glycogen levels) in particular types of individuals (e.g. postobese). The same is true for control of fat intake; it seems unlikely that a simple unitary relationship exists between dietary fat and appetite control.

Table 1 Summary table of studies linking dietary fat with obesity[a]

Ref.	Study design	Manipulation	Subjects	Outcome	Conclusion
95	2-y LF dietary intervention trial	Dietary & behavioral program to lower F intake from 39 to 20% of energy; 4-d food diaries & FFQ were obtained at 6, 12, & 24 mo	276 f ≤ 159% ideal body wt by MLIC tables; 105 control grp; 171 intervention grp	Intervention grp lost more wt than control grp, max wt lost in first 6 mo	Changes in % energy from F were more strongly predictive of wt loss than changes in total EI
81	Outpatient feeding trial to investigate the effect of LF, HC diet on body wt, composition, and EI	4-wk baseline (37% F), then 20 wk on LF diet (20%); all foods provided by the lab; energy adjustments made in order to maintain body wt; body composition measured at end of 2 test periods	18f; 12 nonob; 6 ob	Both ob & nonob subjects exhibited a decrease of 2.8% body wt, 11.3% fat wt, & 2.2% increase in lean body wt; at end of LF period energy intake 119% of HF intake	Macronutrient composition appears to play a role in energy requirement
69	Retrospective study of the energy needs of 16 subjects fed liquid diets of precisely known composition for an average of 33 d	Subjects lived on a metabolic ward & received fluid formulas in quantities to maintain wt; the F content of the diets varied from 0–70%; P kept constant, C varied reciprocally with F	13 adults (10 m, 3 f), 3 children	No effect of diet composition on energy requirements was seen in either adults or children	Variations of F intake from 0–70% produced no signif. change in body wt
59	29 wk within subjects trial	LF diet (20–25% F) or control diet (35–40% F) for 11 wks followed by a 7-wk washout period then other diet for 11 wks; EI and body wt monitored	13 lean f, unrestrained	EI on the LF diet gradually increased by 0.092 kJ/wk; at end of 11 wks LF diet resulted in deficit of 1.22 kJ/d and a wt loss of 2.5 kg	Incomplete, 35% compensation

Table 1 (*continued*)

Ref.	Study design	Manipulation	Subjects	Outcome	Conclusion
64	Dietary intake; energy & macronutrient intakes & meal pattern studied	Dietary records, diet history, & 24-h recall	150 f (50 lean, 100 ob)	Dynamic phase of ob daily intake 2000 kJ higher than static ob; meal regularity much greater in the lean	No signif. diff. in energy or macronutrients but marked diff. in meal patterns
93	Investigation into EI & other determinants of relative weight	4 1-wk weighed food diary records, one every 3 mo for 1 y; activity questionnaire completed	141 f (wt stable)	Ob women reported higher intakes of total F & relative wt was signif. correlated with intakes of total F & SFA	F intake may play a role in obesity that is independent of total EI
28	Comparison of nutrient intakes & body composition	7-d food diary records; VO_{2max} & RMR measured; body density determined	155 m (moderately ob)	% body fat correlated signif. & + with total F, SFA, & MUFA when expressed as g/1000 kcal; same nutrients were correlated with BMI; total energy unrelated to wt or body fat	Diet composition may contribute to the etiology of or be concomitant to obesity in men
78	Comparison of diet composition, EI & exercise with body fat	Body fat determined by hydrostatic weighing; eating- & exercise-behavior questionnaire, 2-d food diary, & 24-h recalls completed	107 m, 109f	Adiposity + related to dietary F content in both m & f; no relationship with EI but leanness & exercise related	Ob subjects derived a greater % of their energy from F
42	The relationship between dietary F intake, adiposity, & regional subcutaneous fat distribution	Subcutaneous fat determined using skinfold thicknesses; body density determined by the underwater weighing technique; 3-d food diary records	337 m, 328 f	m & f with a higher % energy as fat weighed signif. more & had higher subcutaneous adiposity indexes; no difference in EI between HF & LF intake groups	Evidence of a relationship between dietary F intake & total adiposity

Table 1 (*continued*)

Ref.	Study design	Manipulation	Subjects	Outcome	Conclusion
109	A multivariate study of dietary F & body fat	Lifestyle and diet questionnaire; adiposity assessed by skinfold thickness measurements	205 f	Intake of dietary F was related signif. with adiposity with & without control for multiple confounding variables, e.g. total EI	Dietary F related to % body fat
108	Study 2—performed to determine the relationship between diet composition & various indicators of adiposity	3-d dietary records; subcutaneous skinfold measurements taken; body density assessed by hydrostatic weighing technique	244 m (only 133 weighed hydrostatically)	Significant + correlations between % energy as F & body fat mass. HF consumers had higher levels of fat mass, % body fat, & EI and greater trunk skinfold thicknesses	Dietary composition appeared to play a role in obesity
62	Longitudinal analysis of impact on dietary F intake & physical activity on wt change	Ht & wt, cigarette & alcohol consumption, familial risk for obesity, dietary intake using FFQ, & physical activity were assessed	142 m, 152 f	For f, high energy & F as well as increase in total EI were related to wt gain & increases in work activity related to decreased wt gain; for m, wt gain predicted by increases in F intake	F intake is important to wt loss efforts

[a] d, Day; wk, week; mo, month; y, year; m, male; f, female; HF, high fat; HC, high carbohydrate; LF, low fat; EI, energy intake; C, carbohydrate; F, fat; P, protein; SFA, saturated fatty acid; MUFA, monounsaturated fatty acids; UFA, unsaturated fatty acids; kJ, kilojoule; kcal, kilocalories; wt, weight; Ht, height; RMR, resting metabolic rate; MLIC, metropolitan life insurance company; FFQ, food frequency questionnaire; ob, obese; grp, group.

Central and Peripheral Mechanisms

The concept of a biopsychological system tends to minimize the traditional distinction between central and peripheral mechanisms because it shows that both contribute to the expression of appetite. Moreover, peripheral factors do not act independently of central mechanisms, because peripheral actions eventually influence output by being routed through the brain. In turn, some central mechanisms influence behavior by adjusting the response of peripheral physiology to ingested nutrients. However, it is worth drawing attention to some important peripheral and central mechanisms that may be implicated in the response to dietary fat.

Smith et al proposed that "afferent information from ingested food acting in the mouth provides primarily positive feedback for eating; that from the stomach and small intestine primarily negative feedback" (100). Initially, the brain is informed about the amount of food ingested and its nutrient content via afferent input. The gastrointestinal tract is equipped with specialized chemo- and mechanoreceptors that monitor physiological activity and relay information to the brain mainly via the vagus nerve (77). This afferent information constitutes one class of satiety signals and forms part of the postingestive (preabsorptive) control of appetite.

Fat-Related Satiety Signals

Much interest in peripheral sites of action for the control of appetite has focused on peptidergic inhibition of food intake. Many peripherally administered peptides lead to an anorectic response, and good experimental evidence for a natural roles exists for cholecytokinin (CCK), pancreatic glucagon, bombesin, and somatostatin (98). Recent research has now confirmed the status of CCK as a hormone that mediates satiation and early phase satiety. The consumption of protein or fat stimulates the release of CCK, which activates CCK-A type receptors in the pyloric region of the stomach. This signal is transmitted via vagal afferents to the nucleus of the tractus solitarius, where it is relayed to the medial zones of the hypothalamus, including the paraventricular nucleus and the ventromedial hypothalamus. The anorectic effect of systemically administered CCK can be blocked by vagotomy (101) and by the selective CCK-A receptor antagonist, devazepide (MK-329) (27). Significantly, many reports now demonstrate that the CCK-A-type antagonist administered alone leads to an increase in food intake in experiment animals (52). Interestingly, trypsin inhibitors that block the inactivation of CCK produce a suppression of food intake in animals (75) and in humans (56).

A serotonin link in the mediation of CCK satiety has been proposed (20), and this probably depends on the 5-HT_{2C} subtype (82). Indeed, metergoline attentuates CCK-induced anorexia whereas devazepide antagonizes 5-HT-in-

duced inhibition of feeding (49). These mechanisms indicate ways in which the ingestion of dietary fat could trigger neurochemical responses that mediate satiety.

Another route by which dietary fat could induce a behavioral response is via enzyme systems responsible for the digestion of fat. In particular, pancreatic procolipase is a cofactor for lipase that is necessary for optimal fat digestion in the intestine during a meal. In rats, the 100 amino–acid procolipase is cleaved by trypsin to colipase and a pentapeptide, Val-Pro-Asp-Pro-Arg. This peptide, VPDPR or enterostatin, decreases food intake in rats (30). Moreover, enterostatin appears to selectively reduce intake of a high-fat diet (31). Enterostatin, with the suggested structure Val-Pro-Gly-Pro-Arg, also is increased after high-fat feeding and after administration of CCK-8 (76). These data suggest ways in which peripheral satiety signals could be generated by fat consumption.

Another class of satiety signals is believed to arise during the absorptive or postabsorptive phase. The products of food digestion may be metabolized in peripheral tissues or organs, or they may enter the brain directly. It has been argued that the degree of oxidative metabolism of glucose and free fatty acids in the liver constitutes a significant source of information useful for the control of appetite (38). If oxidative metabolism is a satiety signal for fat, it is important to recognize that, according to this hypothesis, the oxidative signal could arise from the metabolism of ingested fat or from fuels derived from internal adipose stores (36). The oxidation of fat may constitute a signal for the suppression of eating. Experimental evidence indicates that the inhibition of fat oxidation by methyl palmoxirate (37) or 2-mercapto acetate (66) causes an increase in feeding. It follows that any suppression of appetite arising from this mechanism need not be tightly synchronized with the ingestion of fat.

In principle, many products of digestion and humoral peptides that activate the enzymes that metabolize those products could bind to specific receptors or alter some aspect of neuronal metabolism. In each case, the brain is informed about some aspect of the metabolic state resulting from food consumption. One interesting possibility concerns the glycoprotein apolipoprotein A-IV, which is produced exclusively by the human small intestine (96). The output of A-IV into intestinal lymph increases as a result of feeding fat (e.g. 51). The intravenous administration of apolipoprotein A-IV decreases meal size in rats (40), and A-IV may constitute a physiological signal for satiation after the consumption of fat (39). Although apolipoprotein A-IV levels do respond to dietary fat in humans, the hypothesis that A-IV is a metabolic signal is weakened by the observation that concentrations are subject to a rapidly acting autoregulatory mechanism (114).

One additional source of peripheral satiety signals in the blood would be specific substances that reflect the state of depletion or repletion of energy

reserves, and that directly modulate critical brain mechanisms. These substances include satietin (63); adipsin (19), which is now thought more likely to be a regulator of fat metabolism than of appetite; and the sugar acids, 3,4-dihydroxybutanoic acid-{γ}-lactone, 2-buten-4-olide, and 2,4,5-trihydroxy pentanoic acid-γ-lactone (79). In addition, a putative anorectic factor has been extracted from the adipose tissue of overfed rats (57). More recently, the identification of a protein expressed by the ob-gene (117) of the mutant ob-ob mouse has revived interest in a long-term lipostatic regulator. This protein, leptin, is produced in adipose tissue, and decreases food intake (and increases energy expenditure) when administered to obese or lean animals (16, 50). This protein appears to be a modulator of both behavior and metabolism, but because plasma levels are actually increased in obese animals and humans (18), its role in the control of body weight is unclear.

The peptide galanin may be of particular importance in the central control of fat intake. Feeding is stimulated by injections of galanin into the paraventricular nucleus (65). Initially, it was shown that galanin, like neuropeptide Y, promoted carbohydrate intake but had no effect on protein intake (103). However, galanin also stimulated fat intake, an effect that was particularly strong at the end of the nocturnal cycle (70). These findings raise the possibility that there is a specific system in the brain that mediates a biological drive for dietary fat. In addition, galanin may be implicated in the vagal component of the pathway through which eating is initiated after blockade of fat oxidation by 2-mercapto acetate (84).

HUMAN APPETITE AND THE SATIETY CASCADE

The human appetite involves increases and decreases in the subjectively perceived urge to eat (usually termed hunger) and in the episodic intake of discrete units of food (usually termed meals and snacks). To determine how nutrients affect appetite, it is necessary to understand both subjective motivation and the eating pattern.

Hunger

Hunger refers to a drive or state of motivation that impels animals to search for food. Humans use the word "hunger" to express a subjective experience or feeling that is associated with the desire to obtain and eat food. From a functional point of view, hunger, as that nagging feeling whose presence constantly serves to stimulate thoughts about food and eating, achieves a purpose: It reminds us that the body needs food. Thus, hunger has a clear biological function.

There is good evidence that in most cases hunger is positively related to

food intake (11, 54). For example, after tracking diurnal rhythms of hunger and eating, Mattes noted that the "correlation using hunger ratings and intake during the same hour of the day was $r = 0.5$ ($p < 0.02$). That is, hunger ratings at the start of each hour were correlated with reported intake in the hour following each hunger rating" (73). Other researchers measuring spontaneous feeding in humans have concluded that "subjective hunger represents an intermediary step in the cause-effect sequence between gut filling and cessation of meal termination" (25). Consequently, the identification and management of hunger appear to be important factors underlying appetite function and in assessing the effect of fat on appetite control.

How is hunger related to the overall control of human appetite and food consumption? Feeling hungry is an important component in determining what, how much, and when we eat. However, it must be seen in a context of social and physiological variables. On one hand, eating patterns are maintained by certain enduring habits, attitudes, and opinions about the value and suitability, as well as by an overall liking or disliking, for the various foods. These factors, derived from the cultural ethos, largely determine the range of, and sometimes the timing for, foods consumed. So, too, the intensity of hunger experienced may be determined, in part, by the culturally approved appropriateness of this feeling. However, normal hunger is more importantly associated with the events surrounding meals—the so-called periprandial circumstances—and with the periods between them. Therefore, hunger can be considered to arise from an interaction between the physiological requirement of the body for food (or particular nutrients) and the capacity of food to satisfy these requirements. Hunger will therefore be successively stimulated and suppressed, giving rise to a diurnal rhythm. This rhythm, and the relationship between hunger and eating, may be modulated by certain social factors (e.g. distressing psychological events) or interrupted by some disease states. Indeed, in anorexia nervosa (80) or bulimia nervosa (85), hunger can be dissociated from the act of eating.

The Satiety Cascade

When food consumption reduces hunger and inhibits further eating, two processes are involved. For technical precision and conceptual clarity, it is useful to describe the distinction between satiation and satiety (3), terms that can be defined by measurable events. Satiation develops during the course of eating and eventually brings the period of eating to an end. Accordingly, satiation is defined by the measured size of the eating episode (volume, weight, or caloric value of food). Hunger declines as satiation develops and usually reaches its lowest point at the end of a meal. Satiety is the state in which further eating is inhibited and follows the end of an eating episode; it arises as a consequence of food ingestion. The intensity of satiety is measured by the duration of time

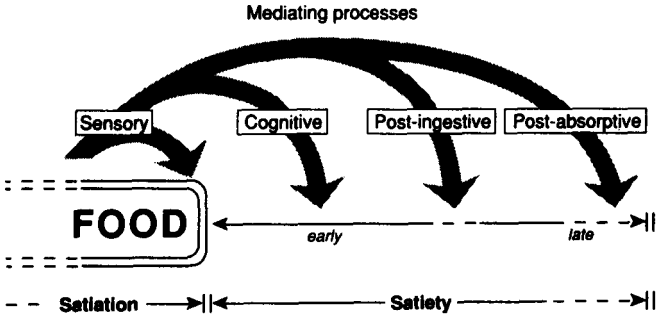


Figure 1 The satiety cascade, indicating the distinction between satiation and satiety and illustrating the major mediating processes contributing to satiety.

that elapses until eating is recommenced, or by the amount consumed at the next meal. The strength of satiety is also measured by the duration of the suppression of hunger: as satiety weakens, hunger is restored.

In the view of some researchers, satiation and satiety are intra- and intermeal satieties, respectively (112). What mechanisms are responsible for these processes? It is clear that the mechanisms involved in reducing hunger and in maintaining the suppression over hunger range from those that occur when food is initially sensed to the effects of metabolites on bodily tissues following digestion and absorption (across the wall of the intestine and into the blood stream). By definition, satiety is not an instantaneous event but occurs over a considerable time period. Four mediating processes have been identified that normally maintain inhibition over hunger and eating during satiety (Figure 1). These processes, called the satiety cascade, are: sensory, cognitive, postingestive (preabsorptive), and postabsorptive. (The physiological and neurochemical mechanisms that mediate these processes were described earlier.) A key factor in understanding the effects of nutrients on appetite control is the relative strength of pre- and postabsorptive processes.

Nutrients, Satiation, and Satiety

The concept of the satiety cascade implies that foods of varying nutritional composition will engage differently with the mediating processes and will therefore exert differing effects on satiation and satiety. There is considerable interest in whether or not the macronutrients (protein, fat, and carbohydrate) differ in satiating efficiency.

A procedure widely used to assess the action of food on satiety is the preload strategy. Precisely prepared foods (identical in taste and appearance but varying in energy and/or nutrient composition) are consumed in the preload. Effects

of consumption are then measured over varying periods by visual analogue rating scales (to assess hunger and other sensations), food checklists, accurately monitored test meals, and, if necessary, food diaries. The experiment needs to be carefully controlled and designed to prevent incidental features from interfering with the monitoring process, e.g. to prevent the occurrence of appetite-modulating stimuli during the interval between preload and test meal that would contaminate the evaluation of the satiating efficiency of the preload.

With the preload strategy and related procedures, it is possible to assess the satiating power of a wide variety of foods varying in macronutrient composition. Foods exerting only a weak effect on satiety would not be expected to provide effective appetite control.

There appears to be widespread agreement that protein is the most satiating of all the macronutrients (53, 89). It has been argued that "calorie for calorie, amino acids contribute more than carbohydrate and fat to the suppression of hunger in the post-absorptive period" (14). In addition, de Castro (24) has demonstrated a similar effect and has argued that protein contributes to satiety by a mechanism independent of its energy value.

One clear finding with carbohydrates is that they are efficient appetite suppressants. That is, they contribute markedly to the satiating efficiency of food and exert a potent effect on satiety (86, 87). This evidence is consistent with studies showing that an analogue of glucose, 2-deoxy-D-glucose (which blocks the utilization of glucose), actually increases hunger when given to human subjects (105). On the basis of studies on rats, it was argued some years ago that "if the cumulative inhibitory effects of carbohydrate on feeding are indeed energostatic... then any substance which can readily be used by the animal to provide energy should produce an appropriate food intake compensation over a period of several hours after loading" (13). Studies have shown that this is similar to what happens in humans. A variety of carbohydrates, including glucose, fructose, sucrose, and maltodextrins, induce such effects when given in a preload : They suppress later intake by an amount roughly equivalent to their caloric value, although the time course of the suppressive action may vary a little based on the rate at which the carbohydrate loads are metabolized (see 8).

DIETARY FAT AND ENERGY INTAKE

Little is known about the action of dietary fat on the processes underlying satiation and satiety in humans. However, there is widespread belief that high-fat diets are responsible for an elevated energy intake, which in turn leads to weight gain through fat deposition. To what extent does a high proportion of fat in a meal contribute to satiety by suppressing hunger and reducing subsequent energy intake? Does the reduction of dietary fat (or its replacement

by a fat substitute) weaken satiety and lead to a compensatory increase in subsequent intake? If compensation occurs, does it provide evidence for a fat-specific appetite (a drive to consume fat)? The answers to these questions are urgently needed if appropriate strategies are to be adopted to ensure that people can reduce their dietary fat intake to 35% of food energy (~30% of total energy), as proposed by health-advisory bodies. If people lower their fat consumption to meet dietary guidelines, will this engender a compensatory increase in appetite and/or a drive to eat more fat?

Subjects deliberately exposed to a high-fat diet consume more calories and gain more weight than subjects obliged to eat from a range of low-fat foods (71). When food choice is unrestricted, the gain in body weight is greater when the dietary intake is high in fat (low food quotient) (108). These findings suggest that fat has a low satiating efficiency (60, 61), that the consumption of fat has only a weak suppressive effect on subsequent food intake. However, short-term studies that have sought to measure satiating efficiency have produced equivocal results: Some appear to demonstrate that fat has a satiating action equivalent to carbohydrate (113, 33, 90); others find that fat leads to a partial satiating effect (55) or exerts a weaker action than either carbohydrate (111) or protein and starch (89). Such differences in outcome could depend on the choice of experimental parameters and not on intrinsic differences in the metabolic properties of the macronutrients themselves. However, because inappropriate dietary advice may be given on the basis of experimental outcomes, it is important that the issue be subjected to further investigation. Studies on fat manipulations and appetite are summarized in Table 2.

Responses to the overconsumption or underconsumption of fat may differ. These have been termed the fat-minus and fat-plus manipulations (5), and experiments should be designed to investigate both phenomena. There is some evidence that the compensation for a reduction in dietary fat energy is incomplete in normal-weight subjects (55). In addition, intravenous infusion of a fixed amount of energy provided as fat suppressed subsequent oral energy intake to a lesser degree than did an equienergetic infusion of amino acids and carbohydrate (35). Consequently, joule for joule, fat may be less satiating than other macronutrients. Indeed, "since the volume and caloric [or, energy] value of the preloads given in this experiment were kept constant, it appears that foods high in protein and starch were more satiating than equicaloric [or, equienergetic] amounts of foods high in fat ..." (89). It has also been reported that tomato soup (78% carbohydrate) is more satiating than cheese and crackers (81 and 46% fat, respectively) (88). These and other studies raise the possibility that energy derived from dietary fat may not be as precisely monitored as is energy derived from other dietary constituents.

Table 2 Summary of studies investigating the effects of dietary fat on appetite control[a]

Ref.	Study design	Manipulation	Subjects	Outcome	Conclusion
113	2 × 2-wk within-subjects crossover design to investigate the effect of the dietary C:F ratio on spontaneous EI	HC diet 24% F 58%C 18%P, HF diet 47%F 35%C 18%P; diet, liquid formula (75%) & snacks (25%); energy density, taste & appearance were similar	22 Trappist nuns	Mean daily intakes remained constant; small changes in body wt occurred but were not signif.	Subjects reguated EI in spite changes in the C:F ratio
41	Nutrient loads given after a 13-h fast, olfaction suppressed with nose clips & taste with topical anesthesia of the mouth; intake measured at test meal 70 min later	6 loads, 4 caloric loads of 283 kcal; egg albumin (63 g F), corn oil (31.5 g F), corn starch (67.4 g C), & a mixture containing isocaloric portions of P, F, & C; plus 2 noncaloric loads	12 m, healthy	Mean intakes after the 6 loads did not diff. signif.; signif. diff. in intakes between pooled intakes after caloric loads vs intakes after noncaloric loads	29% compensation for lack of calories
55	Within-subjects design comparing effects of 2 HE & 2 LE lunches on motivation to eat & food intake; food diary records kept for rest of day	HEL 1—504 kcal (2109 kJ) 25.1 g P, 30.9 g F, 31.4 g C HEL 2—368 kcal (1540 kJ) 22.0g P, 15.6g F, 35.0g C LEL 1—256 kcal (1071 kJ) 16.2 g P, 4.7 g F, 38.2 g C LEL 2—261 kcal (1092 kJ) 31.9 g P, 8.0 g F, 16.7 g C bulk similar	2 m, 7 f	No signif. effect of lunch type on total EI; subjects ate more in the first 2 h post-lunch after the LEL; hunger ratings were signif. greater after the LEL	Some compensation did occur

Table 2 (*continued*)

Ref.	Study design	Manipulation	Subjects	Outcome	Conclusion
111	Within-subjects design, 4 diff. lunches with diff. C:F ratios; energy content of lunch 40% of individuals' estimated daily intake; satiety and a number of indices of F & C metabolism measured	A: 59.3% C, 22.5% F 18.2% P, C:F ratio 2.64; B: 48.6% C, 33.6% F 17.7% P, C:F ratio 1.45; C: 38% C 44.2% F 17.7% P, C:F ratio 0.86; D: 27.3% C 54.7% F 18% P, C:F ratio 0.5	26 m, healthy	Higher hunger scores 4 h after HF lunches (C&D) compared to after HC lunches (A&B)	NA
110	Within-subjects 2 × 2 design investigating effect of 2 types & 2 sizes of lunch on postprandial variables	A 48% F, C:F 2.04 100%; B 48% F, C:F 2.04 70%; C 28% F, C:F 0.77 100%; D 28% F, C:F 0.77 70%; 100% lunch determined by subjects own ad lib consumption of HC meal	7 m, nonob	A highest degree of satiety was obtained after the 100% HC lunch & still detectable 4 h after consumption	NA
29	Within-subjects 2 × 5-d design; subjects given HED or LED and allowed to eat to satiety	LED energy density 0.7 kcal/g, fiber 7 g/100 kcal, HED energy density 1.5 kcal/g, fiber 1 g/100 kcal; manipulation not only fat but fiber and simple sugars	2 f, 8 m, lean; 8 f, 2 m, ob	Energy consumption on LED was about 52% of the HED; eating time longer on the LED; satiety ratings after, between, & before meals were higher on the HED	Incomplete, no tendency to increase energy intake on LED nor decrease on HED through d 1–5
71	Within-subjects 3 × 2-wk design	Subjects fed ad lib on HF, MF, or LF diets for 2 wk; foods similar in appearance and palatability; rotating menu; diets contained 45–50, 30–35, & 15–20% energy from fat	24 f, unrestrained	Mean daily intake on the LF, MF, & HF diets were 2087, 2352, & 2714 kcal, respectively; subjects consumed an 11.3% deficit on the LF and 15.4% surfeit on the HF diet	<37% complete

Table 2 (*continued*)

Ref.	Study design	Manipulation	Subjects	Outcome	Conclusion
74	2 × 2-wk within-subjects crossover design to investigate the effect of HE or LE lunch on intake; a 1-wk baseline recovery period was incorporated at the beginning, between the two conditions and at the end	HE & LE lunch 66% more or less calorie than the subjects customary midday meal; proportion of macronutrients constant, energy level altered	5 m, 5 f, unrestrained	Total EI did not differ during the 3 control wks or between any of these periods & when subjects were provided with LE meal; total EI was significantly greater when subjects ingested the HE meal	Compensation occurs more readily for decreases than increases in energy intake
59	See Table 1 for details				
17	5-wk within-subjects design; 1-wk baseline period, 4 experimental wks; HC, LC, HF, or LF lunch consumed for 5 consecutive d; free feeding intake measured in food diaries	HC meal—843 kcal, 5.3 g F, 180.2 g C; LC meal—253 kcal, 5.8 g F, 30.2 g C; HF meal—960 kcal, 79.6 g F, 41.0 g C; LF meal—310 kcal, 6.3 g F, 42.0 g C; protein constant	8 m, 8 f, unrestrained	Mean daily intake on the LC & LF conditions were 88 & 97% of baseline; responses to the HC & HF led to intakes 104 & 116% of baseline	Compensation stronger for covert dilution than to supplementation; individual responses variable
104	Within-subjects design, ad lib HF & HC diets for 1 wk each; subjects studied in whole room calorimeter on d7 of each experimental wk	1-wk baseline, usual diet; test diets individualized; for HF diet—subtracted 0.04 from baseline RQ & gave food with FQ of this value; for the HC diet—added 0.04 to baseline RQ & gave food with FQ of this value	6 m, 5 f, lean; 5 m, 5 f, ob (wt stable)	Total EI was higher on HF diet, for the m & for the ob; no diff. in EE was found between the 2 diets, but was greater in m & the ob + energy balance was greater on the HF diet	Incomplete

Table 2 (*continued*)

Ref.	Study design	Manipulation	Subjects	Outcome	Conclusion
68	2 × 2 design, 6 subjects given a HEL & 6 a LEL followed by a HF or HC free selection meal 1 wk apart; subsequent intake was recorded in food diaries; each subject completed 2 test days	Hunger manipulated by 2 fixed lunches, LEL (527 kcal) & HEL (985 kcal); after lunch a HF dinner (all foods >50% energy from fat) or a HC dinner (all foods >50% C) was offered	12 f, ob	Intake at dinner after the LEL was 15% greater than after the HEL; intake from the HF foods was approx. 100% greater than intake from the HC foods; post-dinner intakes did not differ signif.	No compensation for the EI consumed at the HF dinner compared with intake at the HC dinner
44	2 × 2 fully repeated measures design; same lunches as above (68) followed by HF or H sucrose-free selection snacks 2 h later; subsequent intake recorded in food diaries	As above (68) except HF or H sucrose snacks instead of dinner meals	18 m, lean unrestricted	Intake at dinner after LEL was 25% greater than after the HEL; intake from the HF foods was 68% greater than intake from H sucrose foods; post-dinner intakes did not differ signif.	No compensation for the EI consumed at the HF snack compared to intake at the H sucrose snack
32	Subjects remained in residential lab for 14 d; free access to food; manipulation occurred on days 6–11	1/3 of food items covertly substituted with reduced calorie versions; on d 12 regular foods returned	6 m, unrestrained	Subjects compensated for loss of calories by increased consumption of nonmanipulated foods; in last 3 d subjects failed to reduce intake when regular foods returned	Accurate compensation for the caloric loss, but not for increases in caloric intake
33	14-d residential study with lunch manipulations; each lunch provided for 3 consecutive days; free access to food at all other times	4 lunch types, 2 with 431 kcal and 2 with 844 kcal; the extra energy was derived from F in one of the HE lunches & C in the other	6 m, unrestrained	No signif. diff. in total daily caloric intake across the 4 conditions	Compensation occurred on d 1 of each condition & did not change over 3 d

Table 2 (*continued*)

Ref.	Study design	Manipulation	Subjects	Outcome	Conclusion
90	Within-subjects HF & HC preload design; 3 intervals between preload and ad lib lunch, 30, 90, & 180 min	2 yogurts similar energy densities, HC (81% C) & HF (65% F); 357 kcal each; control condition no yogurt	14 f, 14 m, nondieters	In 30 min condition subjects accurately compensated for energy of preloads; no effect of type of preload found on subsequent intake or appetite ratings	100% compensation at 30 min but as time interval increased accuracy of compensation decreased
34	14-d residential study; covert macronutrient & energy manipulations at 3 required eating occasions, b'fast, lunch & dinner vs no required eating; 7 conditions each for 2 d; energy content of conditions varied from 3000–7000 kJ	LF meals 16.9% F, 56.0% C; MF meals 43.9% F, 36.1% C; HF meals 57.6% F, 26.5% C; LC meals 26.9% F, 60.9% C; MC meals 16.0% F, 76.9% C; HC meals 10.6% F, 83.2% C; no required eating	6 m	In comparison to the no required eating condition subjects compensated for the energy of the set meals except on the LC condition when intake was significantly lower; total energy intake on HF days was less than on HC; macronutrient intake from foods other than those of the required eating occasions was not affected by set meals	Evidence of caloric compensation but no macronutrient compensation
115	Expt 1—Effect of ileal infusion of lipid emulsion on food intake & satiety	Amount of food consumed while ileal infusion of 50% corn oil + 3% albumin cf when saline & albumin were infused; comparison of the effects fat & saline on GE; comparison of IV infusion of intralipid & saline on intake at ad lib meal	4 m, 2 f, norm wt	Corn oil reduced the amount eaten & total EI from food	Compensation occurred
	Expt 2—Effect of ileal infusion on GE		5 m, norm wt	Half-life for GE signif. prolonged during corn oil infusion	NA
	Exp 3—Effect of IV infusion of fat emulsion		6 m, norm wt	No effect on energy intake at meal 60 m after infusion	No compensation

Table 2 (*continued*)

Ref.	Study design	Manipulation	Subjects	Outcome	Conclusion
116	Paired study to compare the effects of ileal & jejunal infusion of corn oil & saline, respectively	50% corn oil & saline were infused into the ileum in 1 group & into the jejunum in a 2nd. Food intake & appetite feelings were monitored	12 m, non ob; 6 ileum, 6 jejunum	The quantity of food consumed at the meal was reduced signif. after the fat infusion into both ileum & jejunum; lipid in the jejunum also reduced hunger before the start of the meal & also rate of ingestion	Compensation occurred
94	Expt 1—Subjects given soup preload with & without 60 g margarine added; intake measured at ad lib meals 20 min later	150 ml soup diluted with 150 ml water (12 kcal) vs 150 ml soup diluted with 90 ml water & 60 g margarine (455 kcal); HF b'fast (927 kcal, 65 g F, 287 g wt); LF b'fast (418 kcal, 8.1 g F, 283 g wt); b'fasts similar in appearance, P & C; same b'fasts given labeled with technetium sulphur colloid	6 m, healthy	Ingestion of HF or LF soup had no effect on intake at ad lib meals	No compensation
	Expt 2—Studied the effect of a HF & LF b'fast on an ad lib lunch 4 h later		6 m, healthy	Ingestion of HF b'fast signif. reduced intake at lunch meal	67% compensation
	Expt 3—Studied the effect of the HF & LF b'fast on gastric emptying for 4 h		6 m, healthy	No diff. in half-life for GE	NA
2	Within-subjects design, to determine the effects of 4 snack preloads on lunch intake 2 h later. Snacks vary in fat & energy density; 4 conditions	Fat-free snack, 740 kJ, 0 g F, 40 g C, 4 g P; MF snack, 953 kJ, 12 g F, 26 g C, 4 g P; HF snack, 1150 kJ, 18 g F, 24 g C, 4 g P; all ice cream & weighed 113 g; baseline 334 kJ, 0 g F, 16 g C, 3 g P, 109 g serving	9f, 15m; preschool children	3 ice cream preloads produced signif. suppression of intake compared to the baseline; ad lib lunch intake following 3 ice cream preloads was identical	Compensation incomplete particularly when the preloads contained larger amounts of fat & energy
108	Study 1—Within-subjects design, 2 sessions with ad lib intake from either HF or control foods; similar foods for both conditions	HF foods all had FQ < 0.85; control foods all had FQ > 0.85	8 m, healthy	When given foods FQ < 0.85 subjects mean daily intake was 1148 kcal/d more than when subjects were offered foods with FQ > 0.85 (mean energy intake 2987 kcal/d)	HF foods induced hyperphagia

Table 2 (*continued*)

Ref.	Study design	Manipulation	Subjects	Outcome	Conclusion
107	Expt 1—Within-subjects design, 2 sessions of 2d where subjects had to eat in the lab; free access to a variety of foods Expt 2—As above with slight difference in experimental manipulation	HF foods all had FQ ≤ 0.85, 16% P, 48% F, 36% C; control foods all had FQ ≥ 0.85, 15% P, 26% F, 59% C HF foods all had FQ < 0.85, but also C content <25% of energy, 15% P, 65% F, 20% C; control foods had FQ > 0.85, 19% P, 32% F, 49% C	15 m, healthy 8 m, healthy	Expt 1—Energy consumed on HF diet was greater than on control (15.7 ± 3 vs 13.6 ± 2.5 MJ) Expt 2—Energy consumed on HF diet was greater than on control (15.1 ± 1.5 vs 13.2 ± 3.1 MJ)	HF foods induced hyperphagia
26	Within-subjects design, 10 b'fast conditions; subjects recorded intake for remainder of the day	10 550-ml solutions varied in energy & macronutrients; 1 zero condition, 9 (3 × 3) others; 3 energy levels 0.42, 1.05, & 1.67 MJ, composed of either P, F, & C; subjects consumed solutions wearing nose clips	29 f, normal wt	Neither energy nor macronutrient content had any effect on intake; appetite ratings showed increased satiating effect with increased energy content	No compensation for the energy consumed at the b'fasts
58	Within-subjects design, 9 diff. preloads, diff. in physical state & fat level; eating prohibited for 3.5 h after preload, then food diary records; appetite ratings completed for 3.5 h post-preload	Physical states: liquid, solid (locust bean gum), & solid (gelatin); energy levels: 0.42, 1.67, & 3.35 MJ, only alteration in fat 0, 33, & 77 g; each preload 550 ml	33 f, lean	Comparing phys. states, bean gum reduced appetite the most, then gelatin, then liquid; the HF preload reduced appetite the most, then the MF followed by LF; no diff. in EI at lunch, rest of day, & next day after the 9 preloads; an effect of energy levels found at lunch	Small degree of compensation for energy at lunch, effect lost over rest of day; solids more satiating than liquid

Table 2 (*continued*)

Ref.	Study design	Manipulation	Subjects	Outcome	Conclusion
23	Expt 1—Within-subjects design examining the effects of F or C suppl. added to a basic b'fast on appetite control	Subjects were given a 440-kcal (1841-kJ) b'fast, a 802-kcal (3356-kJ) F supp. b'fast, & a 803-kcal (3368-kJ) C supp. b'fast; subsequent energy & macronutrient intake & subjective appetite were monitored over the rest of the day	16 m, lean unrestrained	The F & C supps. had no effect on intake at lunch (41/2 h later), dinner (91/2 h later), nor over the full 24 h after b'fast; the F supp. had no effect on subjective appetite, however the C supp. exerted a suppressive effect on appetite in the period 1–3 h post-b'fast	No compensation
	Expt 2—Within-subjects design further investigating the effects seen in Study 1	Identical test meals, subjects offered an ad lib snack 11/2 h after b'fast; further intake recorded in food diaries	12 m, lean unrestrained	The F supp. exerted no effect on intake at the snack or over the whole day, however the C supp. signif. reduced intake at the snack (provided at the time the effects were seen in the VAS of the previous study)	No compensation occurred for the extra F & energy of F supp.; compensation did occur after the C supp. b'fast
7	A further examination of the effects of F & C supp. b'fasts on satiety	Identical b'fasts to those described above (23); 8 subjects were given an ad lib snack (11/2 h) after b'fast & the other 8 a lunch (41/2 h) after b'fast	16 m, lean unrestrained	Subjects who were given the ad lib snack ate signif. less at the snack after the C supp; intake after the basic & F supp. did not differ; no diff. in 24 h intakes; intakes at the ad lib lunch did not differ among the 3 conditions; EI over 24 h was greatest on the F supp. condition	No compensation was seen for the F supp. at either snack or lunch; some compensation for the C supp. was seen at the snack meal

Table 2 (*continued*)

Ref.	Study design	Manipulation	Subjects	Outcome	Conclusion
43	Total caloric intake measured when SPE covertly replaced conventional F in a single crossover study; a period of 7–14 d determined baseline caloric intake; this was followed by 2 × 20 test periods. SPE was substituted for F in 1 of these periods	60% of baseline intake was required intake, given at meals; a further 60% was allowed as free choice; in the SPE study period 40 g SPE replaced F for every 1200 kcal required intake; resulted in a 30% reduction in intake at meals	10 ob: 7 f, 3 m	Mean total EI fell 23% during SPE period; snack intake did not increase in order to compensate for the reduction in energy consumed	Very little compensation, 11%
15	Olestra was substituted for F at breakfast in this placebo-controlled, three condition crossover design study. Ad lib. intakes at lunch & dinner were measured. Food diaries were used to record intake for the remainder of the day	Conventional F was replaced by 36, 20, & 0 g of SPE at b'fast providing meals with 1189.5, 2425.8 & 3214.3 kJ, respectively	24 m, unrestrained	Intake over the three test manipulations did not differ	Compensation occurred for reduction in energy but not for F intake
92	Parallel study to above, identical design (15)	As above	24 m, nondieters	Intake at lunch did not differ across the conditions; a signif. greater amount (grams) was eaten after the 36-g SPE substitution at the dinner; no difference in total energy over the whole test period	As above

Table 2 (*continued*)

Ref.	Study design	Manipulation	Subjects	Outcome	Conclusion
1	Within-subject crossover design where 24-h food intake was measured over 4 2-d blocks in response to covert manipulations in the portion of energy from dietary fat; first 3 meals of d1 of each 2d block contained dietary fat or SPE; intake was measured over each 2-d period	Target fat substitution was 16 g of SPE for 16 g dietary fat; equivalent of removing 603 kJ; actual intake of SPE was 13.4 ± 1.4 g, energy replacement 516 kJ	12 f, 17 m; children 2–5 yr	Cumulative intakes end d1—SPE: 6740 ± 185, FAT: 7008 ± 196 kJ; cumulative intakes end d2—SPE: 13573 ± 346, FAT: 13676 ± 366 kJ	80% compensation at end of d2
97	Study 1—Within-subjects single-blind protocol to assess effects of IV infusions of F & C; subsequent intake measured at test lunch and dinner meals	IV infusions of F (20% intra lipid), C (20% dextrose), both 2092 kJ or saline (control) for 3.5 h	6 m, lean, healthy	No signif. effects of infusion condition on energy or % macronutrients consumed at lunch or dinner	No compensation
	Study 2—Within-subjects single-blind protocol to assess effects of IG infusionsof F & C; subsequent intake measured at test lunch and dinner meals	IG infusions of F (20% intralipid), C (20% dextrose), both 2092 kJ, or saline (control) for 15 min (rapid) or 3.5 h (slow)	6 m, lean, healthy	Rapid IG infusions of F or C and slow infusions of F signif. reduced EI at lunch; no effect of nutrient content or rate of infusion on macronutrient selection at lunch. No effect of infusion condition on dinner intakes	Accurate energy compensation at lunch for rapid IG infusion of F & C and slow IG infusions of F
	Both studies—Within-subjects design yogurt preloads followed by test lunch 30 min later	500 g preload of raspberry yogurt (2092 kJ) composed primarily of F (65%) or C (81%) vs no preload P and sensory properties constant	12 m, lean, healthy	Subjects receiving either F or C yogurt consumed less at lunch cf no load condition	Averaged across both studies compensation was 82% after F preload and 115% after C preload

Table 2 (*continued*)

Ref.	Study design	Manipulation	Subjects	Outcome	Conclusion
91	Balanced within-subject, repeated measures design to assess effects on satiety of preloads varying in F and C; subsequent intake measured at test lunch 30 min after preload	5 yogurt preloads varying in energy and macronutrient content; control: 674 kJ, 16% F, 45% C, 39% P; MC: 1098 kJ, 5% F, 74% C, 21% P; MF: 1098 K; 48% F, 29% C, 23% P; HC: 1494 kJ, 5% F, 81% C, 14P P; HF: 1494 kJ, 65% F, 20% C, 15% P	12 m lean unrestrained, 12 m lean restrained, 12 f lean unrestrained, 12 f lean restrained, 12 f ob unrestrained, 12 f ob restrained	In 5 of the 6 groups the HF preloads suppressed intake at lunch less than the HC preloads	Accurate compensation in 12 m who were lean and unrestrained but not in the other groups

[a] m, Male; f, female; HF, high fat; MF, medium fat; LF, low fat; HC, high carbohydrate; MC, medium carbohydrate; LC, low carbohydrate; F, fat; C, carbohydrate; P, protein; LE, low energy; HE, high energy; L, lunch; D, diet; H, high; SPE, sucrose polyester; d, day; wk, week; kcal, kilocalorie; kJ, kilo joule; MJ, mega joule; NA, not applicable; GE, gastric emptying; IV, intravenous; EI, energy intake; wt, weight; supp, supplemented; ob, obese; FQ, food quotient; RQ, respiratory quotient; b'fast, breakfast; IG, intragastric.

High-Fat Foods and Overconsumption

Many studies have demonstrated that people who consume high-fat foods (either through personal choice or in experimental situations) tend to overconsume energy. The opposite occurs with high-carbohydrate foods. Interestingly, however, in some studies in which the proportions of fat and carbohydrate were varied, the results showed the two to have equivalent satiating power (32, 33, 90). However, because of the potent action of protein on satiety, it is clearly necessary when comparing fat and carbohydrate to keep protein constant. In one study in which fat displayed a satiety action similar to carbohydrate, the fat foods contained much higher amounts of protein (33). Consequently, the apparently strong satiating action of fat could have been due to the presence of the protein. However, the satiating power of dietary fat may be altered according to its association in a food with either protein or carbohydrate (21). Such an effect could explain instances where fat caused a potent inhibition of subsequent eating (e.g. 94).

There is another aspect, however, that may be more important when measuring effects of fat ingestion—the difference between satiation and satiety (Figure 1). Satiation is the process in operation while foods are being eaten; satiety is the state engendered as a consequence of consumption. Satiation controls meal size; satiety measures the capacity of a food to control subsequent hunger and eating, or satiating efficiency (60, 61). Dietary fat's most important action on appetite could be while it is being consumed rather than afterwards.

Interestingly, most experiments on fat and appetite have used some variation of the preload or fixed meal presentation in which subjects are required to consume an obligatory amount of fat (or fat mixture). The consequences of this mandatory consumption (determined by the researcher) are then measured. This procedure offers a measure of satiety (not satiation). It is likely that this procedure provides only limited information about the effect of fat on appetite and may preclude complete understanding of the effect dietary fat has on energy intake. An alternative procedure, sometimes called concurrent evaluation (60), can be used to assess the effect the fat content of foods has on the amount willingly consumed (satiation) when subjects are provided with a range of foods and allowed to eat freely to comfortable fullness. Use of this procedure has demonstrated that subjects consume much greater quantities of energy from a range of high-fat foods than from foods high in general carbohydrates (22) or sucrose (44). This effect, particularly strong in obese subjects (6, 67, 68), has been termed high-fat hyperphagia (102), or passive overconsumption (10). The effect is almost certainly due, in large part, to the high energy density of the high-fat foods, hence it can be regarded as a passive form of high consumption rather than as eating actively driven. However, it should be kept in mind that, in certain circumstances, ingested fat does stimulate food intake

(60) and that oral sensory effects of fat do appear to stimulate intake in rats (99, 106).

Although high-fat foods induce remarkably high levels of energy intake (mainly fat energy) in meals (21) or snacks (45), the experiment design still permits a measure of postingestive effects on satiety. Interestingly, these very high levels of fat energy consumed do not induce any noticeable intensification of satiety when compared with much lower energy intakes of high-carbohydrate foods. Therefore, high-fat foods can readily stimulate high intakes of fat energy with no proportionate increase in satiating power. Consequently, a single meal (or snack) of high-fat foods normally leads to a significant increase in that day's food consumption. These effects provide an explanation for the relationship of the eating pattern to the long-term overconsumption of energy on a high-fat (low food quotient) diet (71, 108).

The methodology outlined above is important in that it demonstrates overconsumption in connection with the intake of high-fat foods, as seems to happen in real life. Consequently, in considering the effect dietary fat has on appetite, it is necessary to measure the effects while fat is being consumed (satiation) as well as after consumption (satiety).

The Fat Paradox: Fat-Induced Satiety Signals and High-Fat Hyperphagia

In considering the relationship between fat and satiety, a paradox becomes apparent. On one hand, fat in the intestine appears to generate potent satiety signals (83). On the other hand, intake of high-fat foods leads to a form of passive overconsumption that suggests fat has a weak effect on satiety (68). The paradox can be expressed as the puzzle of fat-induced satiety and high-fat hyperphagia.

The infusion of corn oil into the intestine inhibits hunger and slows the rate of gastric emptying (115). However, intralipid infused intravenously has no inhibitory effect on appetite. Similar effects have been demonstrated in rats (47). Moreover, the inhibitory action of intralipid in the intestine can be blocked by lorglumide, an antagonist of CCK-A-type receptors (46). Taken together, these studies suggest that fat in the intestine generates potent preabsorptive satiety signals that are mediated, at least in part, by a CCK mechanism.

However, when rats are placed on high-fat diets or given fat supplements, they take in excessive amounts of energy and rapidly gain weight. Moreover, human subjects given a range of high-fat foods also increase their energy intake and gain weight compared with subjects eating a medium- or low-fat diet (see above). In addition, high-fat foods markedly increase meal size (measured in terms of energy), an effect particularly marked in obese subjects (68). What

is the explanation for the apparent contradiction between fat-induced satiety signals and the easy overconsumption of high-fat foods?

Although emulsified fat delivered to the intestine (duodenum or jejunum) produces prompt satiety signals, fat consumed orally takes some time to reach the intestine in similar form, and its action is likely to be diluted by other nutrients. Hence, consumed fat may engender more slowly arising satiety signals. Two features of fat favor the rapid consumption of energy: Fat produces potent oral stimulation, which facilitates intake; and high-fat foods normally have a high energy density, which means a large amount of fat energy can be consumed before fat-induced satiety signals become operative. The signals are apparently too delayed to prevent the intake of large amounts of this food. One of the consequences of a food supply containing readily available, very palatable high-fat foods is that the natural fat-induced satiety mechanism becomes overwhelmed.

This dietary override of physiological signals has a number of implications. First, it is clear that the effect of fat per se should be separated from the effects of high-fat foods. References to the effect of dietary fat and satiety should recognize that the effects of fat delivered in controlled amounts to the intestine may demonstrate effects that are still present but eclipsed when subjects eat large quantities of high-fat foods. Second, the recognition of this paradox suggests nutritional and pharmaceutical strategies for the reduction of fat consumption. Any technique that would advance or intensify fat-induced satiety signals or that would prevent the effects of high-fat foods on satiation would prevent the passive overconsumption of fat energy that hinders good control of appetite.

CHARACTERISTICS OF HIGH-FAT CONSUMERS

One way to advance understanding of the impact of dietary fat on appetite control is to study appetite within the context of natural eating patterns. This can be achieved either by modeling natural eating patterns in the laboratory or by characterizing the dietary habits of high- and low-fat consumers identified through large-scale surveys of epidemiologic studies. The Leeds High Fat Study (72) identified such individuals in the Leeds (United Kingdom) community. In addition, the data base arising from the Dietary & Nutritional Survey of British Adults (DNSBA) (48) was reanalyzed to define for that sample the relationship between dietary fat, food consumption, and body mass index (BMI).

High- and low-fat consumers were defined as consuming >45 or ≤35% of their food energy as fat, respectively. When nutrient intake is defined as percentage of total energy consumed, it can be seen that carbohydrate intake falls as fat intake increases (Figure 2). This reciprocal relationship is also apparent for fat and sucrose (12).

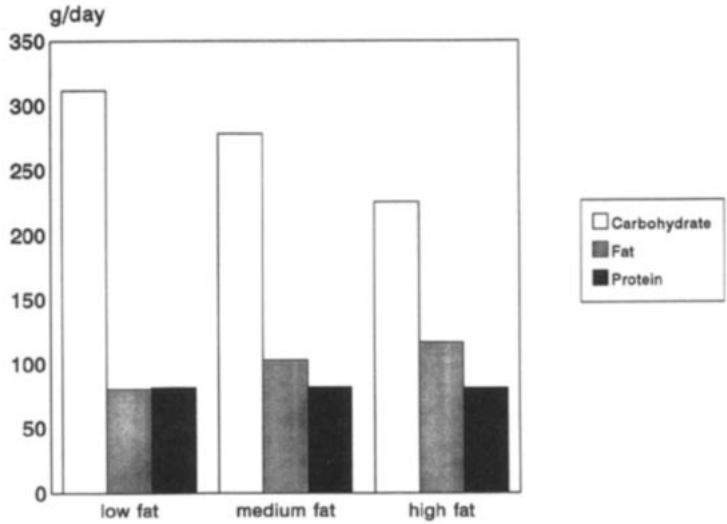


Figure 2 Average daily macronutrient intakes [in grams (g)] for subjects defined as low-, medium-, or high-fat consumers according to the percentage of energy consumed as fat (analysis of the DNSBA data base).

What foods contribute to the overall intake of dietary fat? The DNSBA data indicates that the greatest contributor to fat in the diet is meat and meat products, which provide 25% of the total intake of fat. Both men and women in the high-fat groups derived the greatest percentage of their fat intake from meat and meat products, whereas cereal and cereal products (including cakes, pastries, biscuits, and bread) contributed the most fat to the diet in the low-fat groups. Comparing high- and low-fat consumers, the male high-fat consumers ate significantly more high-fat meat products (bacon, lamb, meat pies, sausages, burgers, fried white fish), butter, whole milk, cheese, eggs, savory snacks (i.e. crisps), desserts, and alcohol. They also ingested less breakfast cereal (including high-fiber cereals), skimmed milk, low-fat spreads, chicken, yogurt, potatoes (not fried), fruit, and table sugar. The women's dietary patterns were similar to the men's, but there were fewer differences between high- and low-fat groups in terms of consumption of high-fat meat products. Bacon, meat pies, and sausages were the only meat products that differentiated the female high- and low-fat groups. One interesting feature was the lack of a significant difference in the reported intakes of high-fat sweet products such as pastries, cakes, chocolates, and biscuits for high- and low-fat consumers. Interestingly, men in the low-fat group tended to eat more of these products than did men in the high-fat group, whereas the inverse was true for the women. These differences were consistent with variations in food intake found between high-

and low-fat consumers in the Leeds study. These data show that, in general, high-fat consumers eat more meat products (sausages, pastries, pies, etc), butter, whole milk, cheese, and eggs and less carbohydrate, particularly sugar, than do low-fat consumers.

Clearly, a complete study of appetite control must embrace food preferences and selection, as well as quantitative changes in intake, and the mechanisms controlling satiation and satiety should be related to natural dietary patterns.

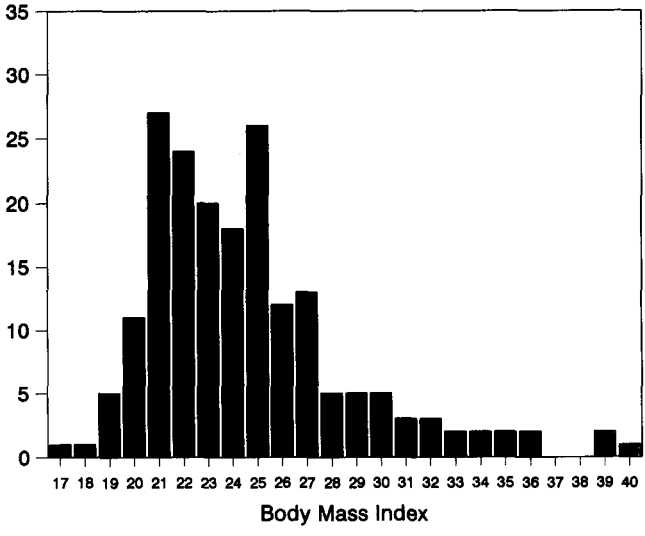
High-Fat Consumption and BMI

One way to assess the effect of consumption of high-fat foods on weight control is to compare BMIs for high- and low-fat consumers. This has been done with the national data base (DNSBA). The sample was defined according to the percentage and the absolute amount of fat consumed. To ensure the inclusion of valid data, subjects who reported being ill or who were dieting during the study period were excluded from the analysis. In addition, it is argued that a ratio of energy intake (EI) to basal metabolic rate (BMR) of less than 1.2 is not compatible with habitual intake and normally signifies underreporting of energy intake. Therefore, all subjects with an EI:BMR of less than 1.2 were excluded. Consequently, the analysis was carried out on those subjects most reliably identified as habitual high- and low-fat consumers.

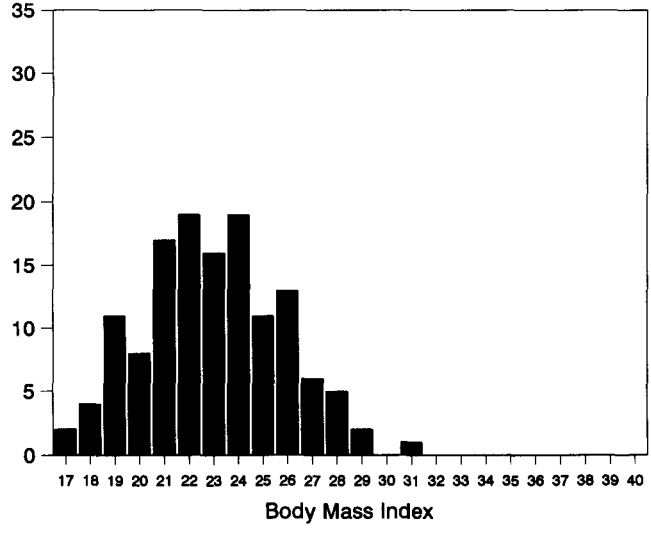
The most meaningful relationship is the distribution of BMIs for the high- and low-fat groups, classifed by fat grams consumed per day (Figure 3). There is a greater positive skew in the distribution of BMIs of high-fat consumers. Defining obesity as a BMI of more than 30, there were 19 times more obese subjects in the high-fat group than there were in the low-fat group. Indeed, among the sample of low-fat consumers, only one person was obese. Thus, a low-fat diet offers a good deal of protection against the development of obesity.

However, not everyone in the sample identified as eating a high-fat diet was obese. Indeed, there were many normal weight and even some underweight people among the high-fat consumers. This suggests that some people are able to resist the weight-increasing properties of high-fat diets. This resistance could be behavioral or physiological. For example, some individuals may expend extremely high levels of energy in physical activity, or they may have high BMRs or high rates of fat oxidation. Although a high-fat diet facilitates weight gain and promotes obesity, it does not appear to constitute a biological imperative that inevitably leads to obesity.

The only variable to distinguish between high and low BMIs for high-fat consumers was age, with high-BMI, high-fat consumers being an average of 11 years older (41.7 vs 30.6 years for high and low BMIs, respectively). It therefore appears that habitual consumption of high-fat foods enhances the possibility of weight gain reaching the threshold for obesity.



a.



b.

Figure 3 Distribution of BMIs for high-fat (*upper panel*) and low-fat (*lower panel*) consumers defined by the absolute amount of fat consumed in grams per day. The high-fat consumer group contains more subjects with BMIs greater than 30 (analysis of the DNSBA data base).

Formulation

Taken together, the above findings suggest a picture for understanding the importance of dietary fat. High-fat foods can overcome fat-induced satiety signals and facilitate overconsumption. Such foods are highly palatable and the fatty texture may arouse oro-sensory facilitation of eating. Once consumed, fat generates only a relatively weak effect on satiety. High-fat consumers normally have low intakes of carbohydrate, and their choice of foods and habitual pattern of intake appear to be quite different from that of low-fat consumers. In addition, high-fat consumers have a greater tendency to become obese than do people who eat a low-fat diet. This process is presumably helped by the reported preference of obese people for fatty foods. However, it is clear that the development of obesity on a high-fat diet is not a biological inevitability. Some people who eat high-fat diets remain slim. Analysis of the physioloca and behavioral properties of these high-fat-consuming, low-BMI individuals constitutes an important research strategy. The overall picture suggests clear strategies—behavioral, nutritional, and pharmacologic—for the modification of eating patterns in order to treat obesity and, more importantly, to prevent weight gain and to resist any further increase in the percentage of obese people in our society.

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