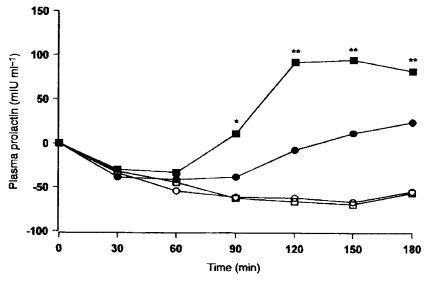
# Why is dieting so difficult?

Sir — Dieting for cosmetic or medical reasons is common in developed countries, but is surprisingly ineffective as a means of achieving sustained weight loss[1]. We have previously established that moderate dieting alters the activity of 5-hydroxy-tryptamine (5-HT), a brain neurotransmitter involved in regulating appetite and food intake[2]. Specific membrane receptors for 5-HT exist in many subtypes, possessing diverse functional roles. Tecott *et al.*[3] have shown that mutant mice lacking 5-$HT_{2C}$ receptors become obese through abnormal control of feeding behaviour, in agreement with other animal experimental data suggesting that 5-$HT_{2C}$ receptors in the hypothalamus are important for controlling food intake.

We studied the effect of moderate dieting in 12 healthy women (age 20–39 yr) on the prolactin responses to the 5-$HT_{2C}$ receptor agonist *m*-chlorophenylpiperazine (mCPP), a measure of the sensitivity of hypothalamic 5-$HT_{2C}$ receptors[4]. Subjects received a double-blind, randomized, placebo-controlled challenge with mCPP (0.25 mg per kg, orally) in the early follicular phase of their menstrual cycle, and one week later started a 1,000-kcal daily diet. The mCPP/placebo challenges were repeated 3 weeks later at the same stage of the menstrual cycle, by which time subjects had achieved a mean weight loss of 3.1±0.2 kg. Following dieting, the effectiveness of mCPP in increasing plasma prolactin levels was significantly enhanced, but plasma concentrations of mCPP were unaltered (data not shown). Consistent with our previous work[2], dieting significantly lowered plasma concentrations of tryptophan, the amino-acid precursor of 5-HT, which resulted in a decreased plasma ratio of tryptophan to branch-chain amino acids (leucine, isoleucine and valine; 0.032±0.003 as opposed to 0.026±0.001; $P = 0.014$).




Mean plasma prolactin (measured as change from baseline) in 12 female subjects before (circles) and after (squares) double-blind oral challenge with mCPP (0.25 mg per kg; solid symbols) or placebo (at time 0; open symbols). Subjects were tested on two occasions before (pre) and at the end (post) of a 3-week, 1,000-kcal diet. Analysis of variance showed a significant interaction of mCPP, diet and time ($F = 5.73$; d.f. = 6,66; $P<0.0001$); *, $P<0.05$; **, $P<0.01$ (Fisher's test of least significant difference).

A decrease in the ratio of tryptophan to branch-chain amino acids would be expected to lower the availability of tryptophan to the brain and reduce brain 5-HT synthesis[2]. Thus dieting lowers plasma tryptophan, thereby decreasing brain 5-HT and producing the compensatory upregulation in the responseiveness of 5-$HT_{2C}$ receptors which we have detected. Dieting therefore seems to decrease neurotransmission at hypothalamic 5-$HT_{2C}$ receptors by reducing the availability of their neurotransmitters. How might this affect dieting behaviour?

Just as the absence of hypothalamic 5-$HT_{2C}$ receptors causes mice to overeat, medications that antagonize 5-$HT_{2C}$ receptors, such as the antidepressant mianserin and the antipsychotic agent clozapine, cause troublesome weight gain in clinical use. Thus, during dieting subjects are likely to experience urges to overeat which will compromise efforts at continued food restriction. Indeed, dieting is well recognized as causing disordered eating patterns which may evolve into clinical eating disorders such as bulimia nervosa[5], a condition characterized by uncontrolled episodes of overeating. Humans have evolved powerful adaptive mechanisms for maintaining food intake. Trying to overcome these by voluntary food restriction is not only difficult but may be counterproductive in some individuals. On the other hand, appropriate manipulation of 5-$HT^{2C}$ receptor function may benefit those in whom weight loss is indicated for clinical reasons.

**P. J. Cowen**
**E. M. Clifford**
**C. Williams**
**A. E. S. Walsh**
**C. G. Fairburn**
*University Department of Psychiatry, Littlemore Hospital, Oxford OX4 4XN, UK*

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# Differential abortion in the yucca

Sir — Pellmyr and Huth[1] showed that the yucca *Yucca fillamentosa* can prevent over-exploitation by the yucca moth *Tegeticula yuccasella,* a pollinator/seed predator, through differential abortion of infested fruits. Our work on *Yucca whipplei typica* and *Tegeticula maculata* confirms these findings, but suggests that over-exploitation may be a minor selective pressure maintaining differential abortion.

At maturity, *Y. w. typica* produces a single inflorescence of 500–1,500 flowers[2]. *Tegeticula* females, the plant's sole pollinator, actively place pollen on yucca stigmas, usually after laying one or a few eggs in the flower's ovary. On average, a resulting larva consumes 7.7 of the 174 available seeds[3]. The consumed seeds are viewed as the plant's fitness cost to maintain the mutualism.

Typically, 50% of the initiated fruits are aborted early in development, apparently due to resource limitations[3,4]. Given the limited number of fruits that can be matured, retention of higher-quality (less infested) fruit should increase reproductive success and thus mitigate the cost of mutualism by shifting costs back onto the pollinator.

We compared abortion rates of fruits that received no oviposition (hand pollinated) with those exposed to oviposition (open pollinated) on each of seven plants. Retention of uninfested fruits was higher on six of the plants (no difference on the seventh; $P<0.02$, sign test). In another study, we counted eggs in 26 pairs of aborting and non-aborting fruits whichoccupied adjacent positions on racemes. Aborting fruits in the pairs had significantly more eggs (see figure).

Two questions arise. First, is differential abortion a special mechanism for coping with *Tegeticula,* or a general adaptation? Second, how effectively does differential abortion reduce the costs of mutualism?

Differential abortion is a viable strategy for *Y. w. typica* because of its apparent overproduction of flowers. Pollen export increases with inflorescence size more strongly than seed set, which indicates that the 'extra' flowers contribute to plant reproductive success through male function[3]. This makes the female organs in many of the flowers expendable, and gives the plant the opportunity to selectively mature those that will develop into the best fruits. Other *Yucca* spp. abort fruits with low seed set[1], and we found frequent abortion of fruits resulting from self-pollination (the plant is self-compatible)[3]. Thus, as with other species[5], differential abortion is a general adaptation in *Y. w. typica.*

Cost reduction achieved by selectively aborting infested fruits is small. Given observed abortion rates, numbers of eggs