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SUMMARY

Any healthy person can develop anorexia nervosa. Prolonged dieting causes reversible endocrine changes that emerge to combat starvation, the main threat to survival. Animals have evolved to develop strategies to cope with this challenge, assisted by hormonal systems that facilitate food hoarding, but which can also inhibit eating, reinforcing the anorexic state. However, a simple machine that provides feedback on how to eat can allow patients to escape from anorexia and restore their health.

To eat or not to eat? When energy stores are replete, leptin from fat cells encourages animals to reproduce, but this priority changes when food is in short supply. Fat depletion reduces leptin and up-regulates "hunger" hormones, such as neuropeptide Y (NPY), in the brain. Once thought to simply make you eat, NPY and other "orexigens" encourage the search for food at the expense of sex and even eating itself.

Recovery from anorexia nervosa by machine

Machine eating

The personal computer was developed because, faced with too much information, people need a machine to help them think. Today there is so much food that we need a machine to help us eat. Or else, as Albert Einstein said: "...we suffer in health or we suffer in soul or we get fat", because as he noted: "The devil has put a penalty on all things we enjoy in life."

We developed machine-assisted eating because an anorexic patient told us: "I don't know how to eat. Can I use a machine to practice?" She had lost her ability to eat normally, yet, despite being hungry, she maintained a stable, low body weight by eating the same small amount of food every day. Anorexics are clearly in a state of equilibrium, although an undesirable equilibrium. This, it turns out, is not a paradox and has a potential evolutionary explanation.

Adaptations to starvation

We now recognise the hypothalamus is intimately involved in appetite. 100 years ago, clinicians noted that patients with tumors that injured the hypothalamus became obese. This clinical phenotype was replicated by damaging a part of the hypothalamus in experimental animals; the so-called "satiety centre" was discovered. One neuroscientist aimed for, but missed, the satiety centre, the rats stopped eating and he had found the so-called "hunger centre".

Thus, the idea was born that opposing hypothalamic centres control eating, maintaining body weight homeostasis. Today, genetically-engineered mice grow twice as big as normal mice because their hypothalamus does not produce signals for satiety ("anorexigens"). Normally, the hypothalamus responds to



hormones released from the pancreas (insulin), fat (leptin), and the gastrointestinal tract (cholecystokinin) to ensure maintenance of a stable body weight. However, despite these feedback systems, a large number of people are getting dangerously overweight! Overeating is normal in today's food-rich environment. Tasty energy-dense foods are available at a low cost and our internal satiety mechanisms seem unable to prevent us from overeating when eating is so easy.

So how do anorexic patients manage to maintain a low weight? A clue is provided by studying the behaviour of rats. Among many other things, rats do two things very well: they reproduce and they eat. In order to reproduce, they have to eat; when energy stores are depleted, in females the reproductive cycle hibernates, but it can be activated by leptin – the hormone that normally signals that energy stores are replete. Similarly, the menstrual cycle is restored in female anorexic patients by treatment with hypothalamic hormones or leptin. When food is scarce, the rat's priorities change.

*“anorexic patients,
can eat big meals,
but don't”*

Unsurprisingly, the search for food increases, but more interestingly, when rats are given restricted access to food but are also given access to a running wheel, eating actually decreases. Hypothalamic orexigens become anorexigens. Hungry humans also do not eat a lot when offered the chance. In fact, women eat less food if they skipped dinner the day before; but are more likely to hoard the food than eat it. This makes sense, we have evolved to tolerate starvation; the ability to store, rather than eat food has been favoured. However,

starved people, including anorexic patients, can eat big meals, but don't.

Recovery from anorexia nervosa

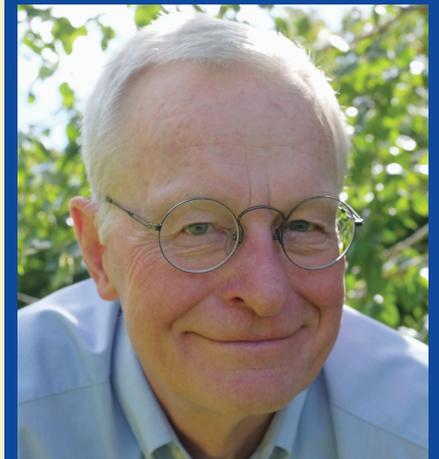
Dieting is the basis for all eating disorders and is associated with release of dopamine in the brain. Just like other pleasurable behaviour, such as eating and sex, dieting instills a feeling of “reward”, motivating a woman to continue eating little food. Eating then becomes dependent upon the rewarding situations, because the brain's system for learning is also engaged. As fat stores decrease, leptin levels decrease, and the drive for foraging increases. Just like a rat, the patient increases her physical activity, which represents a displacement activity for searching for food. Eventually, she is caught in a dangerous situation, with a low body weight and a high level of physical activity.

And so, what is the machine our patient wanted to use to escape from anorexia? It is simply a scale connected to a computer. Eating from a plate on the scale, the patient can follow a training curve on the screen of the computer to learn how to eat normally. Her own speed of eating emerges on the screen while she eats. And as eating normalizes and the patient is guided to resume her social activities, her body weight and the other consequences of starvation, including the psychological effects, normalize.

Exploring the basics

Albert Einstein also said: “... the goal of all theory is to make the irreducible basic elements as simple and as few as possible”. Managing eating behaviour is simple enough and has restored the health of hundreds of patients, but many “basic elements” remain to be discovered. Even though healthy men can develop the symptoms of anorexia nervosa in

semi-starvation, why are 95% of anorexia patients female? Women manage starvation much better than men, but the mechanisms that underlie these marked sex differences are unknown. The neuroendocrinology of eating is a virtual goldmine of “basic elements” waiting to be explored.



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