Reversible biological adaptations in obesity

Christopher Ochner and colleagues address the very important issue of whether reversal of the neurohormonal adaptations associated with obesity is physiologically possible. They suggest that these changes are irreversible and thus prevent the possibility of designing successful strategies using lifestyle interventions. They argue that any treatment of obesity should include direct biological intervention.[1]

For example, weight loss induced by a 10-week low-calorie diet in obese patients has been reported to cause an increase in the concentration of ghrelin, a potent hunger hormone. Remarkably, this hormonal change, and other changes thought to increase hunger and decrease satiety, persist at 1 year after the intervention, providing an explanation for why diet-induced weight loss is so difficult to maintain.[2] We believe this argument is rather simplistic, and although we have replicated the long-term increase in the concentration of ghrelin after diet-induced weight loss in obese adolescents, this effect was reversed in patients who practiced eating less food at a reduced speed by use of real-time feedback on a computer screen that told them how much food and how rapidly they should be eating (figure).[3] Control of eating behaviour in this way also normalised some of the other neuroendocrine changes associated with obesity and was more effective at reducing bodyweight and improving health than was a standard diet intervention. These improvements persisted for 6 months after the intervention.[4] The speed of eating increases in obesity,[5] and by targeting this behavioural change gastrointestinal hormonal responses can be normalised. Ochner and colleagues noted that gastric bypass surgery also reverses the hormonal abnormalities of obesity.[1] The reduction in fasting ghrelin concentrations achieved by behavioural intervention is similar to that obtained by gastric bypass. Addressing eating behaviours, such as eating speed, directly through targeted behavioural modification might be a useful avenue to explore before resorting to surgery.

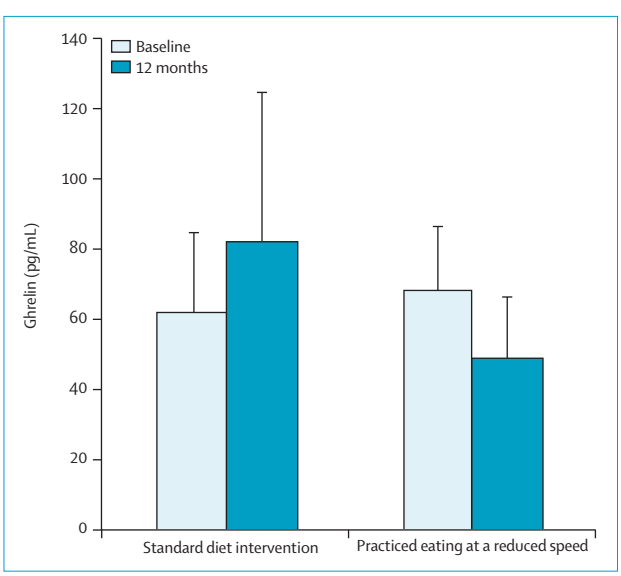

***Figure*: Fasting concentrations of ghrelin in obese adolescents[3]**
13 adolescents received a standard diet intervention for 12 months, and 14 practiced eating at a reduced speed for 12 months. Values are mean (SD).

PS and CB own stock in Mando Group AB, the company that treats underweight and overweight patients using the Mandometer. PS and CB own the intellectual property rights to Mandometer (a patented device). JS and SL declare no competing interests. We thank Björn Meister for his advice.

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Authors' reply

We thank Per Södersten and colleagues for their thoughtful commentary, and appreciate the contribution of their research.[1] However, its description primarily argues against contentions that were not made in our Comment,[2] which necessitates some clarification. We state that the neurohormonal adaptations to sustained obesity often persist indefinitely, but we do not suggest that is it not physiologically possible to reverse them. Further, the increased ghrelin following low-calorie diet described by Södersten and colleagues is an example of an adaptation to caloric restriction, which differs from biological adaptations to sustained obesity that serve to maintain or even increase an individual's adipose storage capacity.[3] It is only these latter adaptations to sustained obesity (*vs* caloric restriction) that we suggest often persist indefinitely. To be clear, this is not to suggest that such adaptations are not potentially reversible, but that there is no evidence of their reversal over any specific time period without surgery. We provide the example of adipocyte proliferation[4] to illustrate this point.

Even if it were possible to design efficacious lifestyle interventions that were able to reverse or reduce some of these biological adaptations to obesity in laboratory settings, it is important to bear in mind that there is a meaningful difference between efficacy and effectiveness. There is no evidence that such interventions would be practically effective in the