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Editorial

Re-Setting the Gravitostat; An Environmental Theory of Obesity

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Illustration

Figure 1

https://www.thesun.co.uk/tv/19487821/thomas-the-tank-engine-fat-controller/

1954 was my first year at school, a Presbyterian establishment which built large numbers of doctors, lawyers and civil servants. Of around 2000 boys, only one had a weight problem. His name was Thomas so naturally we called him the Fat Controller, from the Thomas the Tank Engine books. The rest of us had body shapes more like this:

Figure 2

Thomas seemed out of place but he was, in retrospect, one of the first over-sized swallows of an endless summer.

The fat pandemic, which started around 1980 [1], continues unabated to this day. Despite vast sums of research funds wasted on finding ways of combatting obesity, with equally daunting amounts frittered away on public health campaigns, diets and drugs, the world continues to wax. It is happening everywhere [2] and the trend to fatness is accelerating [3]; within 6 years, half of U.S. adults will be not just overweight but obese [4].

Are ultra-processed foods to blame? Let me say, definitively, yes and no.

If you eat too many of these food-like products, you will gain weight. These supernormal stimuli [5] combine unnaturally high calorie density, addictive organoleptics and reduced satiety cues after all. And they undoubtedly cause a great deal of non-communicable degenerative disease. But are they solely responsible for the obesity pandemic? These products started to appear during the 2nd world war, a full generation before 1980, so the timelines do not fit particularly well.

Are we consuming more calories than we used to? Seemingly not, in the USA at least, since 2000 [6]:

Are we becoming less physically active? We are probably the least physically active generation of all time, but available data do not show an on-going decline; we have bottomed out and our activity levels may even be rising slightly [7]. Ring Fit Adventure and other exergames are probably in there somewhere.

Are we lacking in moral, as well as dietary fiber? Have we become more self-indulgent, less willing to diet?

Maybe, but that would be hard to prove. The diet industry continues to prosper, although it has never actually worked. Multiple clinical trials show that while diets can achieve short-term weight loss, they don't work in the long term [8]. The weight tends to return, as the global fat stats show.

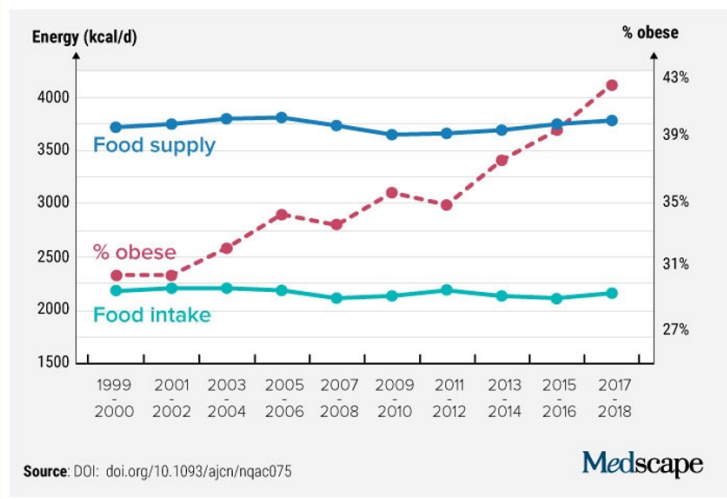

Figure 3

The most effective weight-loss treatments so far are the GMP-1 agonist Wegovy/Ozempic and the GMP-1/GIP agonist Mounjaro. These are injectables, require refrigeration, are far too expensive for the bulk of the population and come with some nasty side-effects. At the public health level they are simply irrelevant - and their effects, too, are temporary. Once you leave the shooting gallery, the weight creeps back [9].

But it is not just humans with a weight problem. Primates and rodents in research colonies, the rats that infest our cities and the cats and dogs that infest our homes have been expanding too [10] and so have horses [11].

This tends to argue against changing diet and levels of physical activity being the universal causes of our weight problem, so we should at least consider other potential drivers.

One possible explanation for so many different species getting larger might be an environmental contaminant, introduced into the environment circa 1980, which is re-setting a mechanism variously referred to as the ponderostat, lipostat, adipostat or gravitostat. This supposedly works like a thermostat, keeping an individual's body weight and amount of body fat within a narrow range despite variations in diet and activity.

To avoid or at least minimise confusion, I will refer to the gravitostat from here on.

The idea of an environmental toxin re-setting the gravitostat to a higher value, leaving us helplessly caught up in a rising tide of flab, is made explicit in a consensus statement given at the 2nd International Workshop on Obesity and Environmental Contaminants held in Uppsala, Sweden, on 8 - 9 October 2015 [12]. 'The findings from numerous animal and epidemiological studies are consistent with the hypothesis that environmental contaminants could contribute to the global obesity epidemic'.

The gravistat is, effectively, the fat controller. Various lines of evidence cumulatively suggest that it is located in the hypothalamus, receives weight-related input from the mechano-transducer cartilage protein Piezo1 in the knee and ankle joints, and affects both eating and exercise behaviors [13].

Legs talking to brain might seem a little too woo, but there is precedent; walking increases brain-derived neurotrophic factor (BDNF), executive mental function and mod [14-16]. BDNF increases memory, learning and brain plasticity, which presumably helped us to find our way from the cave to the hunting ground and back. Readers who keep up with the scientific literature may know that the most recent meta-analysis was negative [17]; but this paper did not differentiate between cognitive exercise (i.e. dancing, contact sports, hunting and foraging) and repetitive gym work, and is therefore, in my view, deeply flawed.

The neuroendocrinology of the gravitostat is being explored [18,19] and its functionality has been more or less confirmed in mice [20], obese rats [21] and humans - at least, in obese humans [22], i.e. in those whose gravitostat had stabilized at a higher value.

It used to work in normal weight humans too.

If you research photos of folk from 1880 to 1980, they show a generally lean population. A number of clinical trials carried out before 1980 support the idea that the gravitostat used to work well enough in most people [23-26]. So, could our gravitostat have become misaligned? And if so, how did this happen?

Among the most eloquent exponents of this idea are a brother and sister team who blog as Slime Mold/Time Mold [27].

I was predisposed to like them because slime molds are among my favorite organisms.

They can solve quite complex problems. They can navigate (and remember) labyrinth mazes, discriminate between (and remember) a range of chemical substances, make informed decisions concerning these things and pass knowledge about what they have learned to other slime molds [28]. Their IQ is thus similar to Jedward, though they have no brain or even a nervous system.

But back to the scientific sibs. In their blog they make a very interesting and fun case for lithium as a driver of obesity, and they develop multiple lines of evidence to support their case. The three most important are:

1. Lithium, an established treatment for manic-depressive illness, has long been associated with weight gain. About a quarter of those who take it gain between 10 and 26 pounds [29]. Serotonin might be involved; lithium exerts serotonergic effects [30] and many SSRI drugs also promote weight gain.
2. Even at very low (environmental/nutritional) levels, lithium exerts a range of behavioral effects [31,32].
3. Due to developments in water extraction, brine extraction and lithium mining and manufacture, our exposure to lithium has increased since circa 1980 [33].

But there is another potential link that the Molds have missed. Recent evidence indicates that in obese individuals, the dopamine response to food is significantly impaired in the striatum, leading to a reduced reward response, reduced satiety and increased appetite [34]. Lithium interferes with specific aspects of dopamine neurotransmission in a way which inhibits dopamine-dependent behaviours [35] and may therefore mimic the obese dopamine response.

Am I convinced that environmental lithium is driving the obesity pandemic? Not entirely. The data are not all consistent, nor would you expect them to be when dealing with a clearly multi-factorial issue such as weight gain. A recent meta-analysis, for example, suggested that contrary to mainstream views, medical lithium might not cause weight gain at all [36].

Nevertheless, although the case against lithium cannot be said to be proven, I do think there may be something in it. Anyone interested in digging deeper into this topic should visit Slime Mold Time Mold [27] to review not only the main text but also the comments, which raise many interesting points and arguments.

If, after imbibing the lithiated Kool-Aid [37] you should decide to reduce your lithium intake, here are a few tips.

45% of public-supply wells and about 37% of U.S. domestic supply wells have concentrations of lithium that could, according to the US Geological Survey and the Environmental Protection Agency, present a potential risk to human health [38]. Those living in areas where the water contains high levels of lithium could consider water filtration.

The common water treatment systems for lithium include distillation, reverse osmosis, and strong acid cation exchangers such as AmberSep™ G26 H Resin. Despite manufacturers' claims, carbon filters do not seem to be very effective [39].

Consider dietary changes. Lithium does not accumulate in animals, so the primary dietary sources of lithium are plant foods [40]. Distribution in plant organs tends to be leaves > roots > stems > fruits. Leafy vegetables and root crops are therefore the main contributors of lithium to the diet [41].

Some plants have a higher tolerance to lithium than others, and tend to contain higher levels as a result. Others are lithium bio-accumulators. Some plants bioaccumulate Li so effectively that they are being considered for bio-extraction a.k.a agro-mining, specifically the *Brassica* species oleracea (wild cabbage) and napus (canola) [42].

Few eat wild cabbage, and I doubt that many lithium compounds partition into canola oil. However, in the two groups listed above you also find Goji berries [43] and various Solanaceae (potatoes, peppers, tomatoes and aubergines) [40,44]. Lettuce, a member of the Asteraceae family, is also good at taking up lithium [45,46], as is beetroot [47,48].

I don't think that you have to exclude all these foods, but some vegetables grown in lithium-rich (or contaminated) soils might pose a real problem. A 70 kg human would exceed the tolerable daily intake of lithium by consuming as little as 40 grams of beetroot, or 35 grams of lettuce, from contaminated soil, daily [48].

Another approach might be to increase your intake of cations such as sodium, potassium and magnesium which compete in the body, in some respects, with lithium [49,50]. Excess sodium consumption has its own problems [51,52], whereas increasing intakes of potassium and magnesium intakes are associated with lowered blood pressure and reduced mortality [53-55]. The choice is a relatively straightforward one, unless you are on a potassium-sparing diuretic.

You might decide to cut back on using lithium grease lubricants. There has been a recent trend for lithium batteries to be recycled into fertilizer [56] and perhaps we should be more cautious about that too.

In the final analysis, however, there is no final analysis. The lithium story is a fascinating one but the Molds themselves do not rule out the recently ubiquitous plasticisers, and neither do I [57]. The use of antibiotic growth promoters in animal husbandry, and their possible impact on the human microbiome, is another area the moldy siblings explore.

As a dog returns to its vomit so will I come back, predictably, to ultra-processed food. The evidence linking increased consumption of these delicious but frankly unethical products to weight gain is very strong indeed [58-61]. Cut down on lithium by all means, but cut out lollipops and Lucky Charms first.

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