

HORIZON

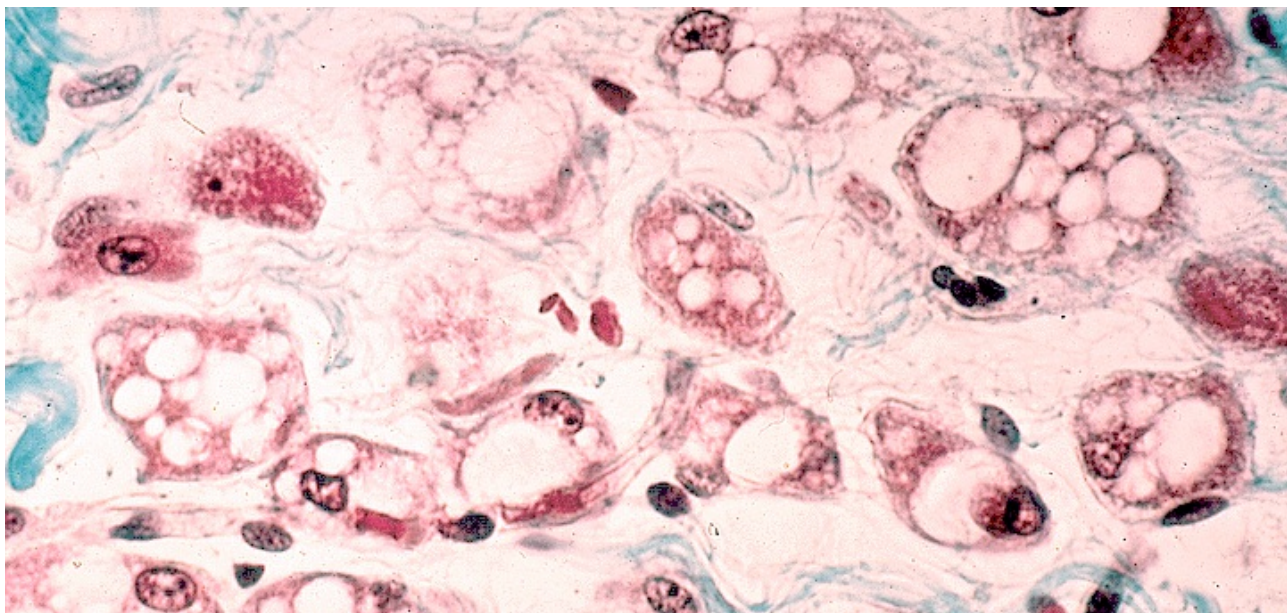
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HEALTH

Brown fat research opens up possibility of obesity tablets

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by Rex Merrifield



Calorie-burning brown fat cells typically turn on and off during the day, but finding a way to keep them working could help against obesity and diabetes. Image credit: 'Tecido adiposo multilocular brown adipose tissue' by Lucasmcorso is in the public domain

Keeping calorie-burning brown fat cells running throughout the day rather than allowing them to switch on and off, possibly via tablets or injections, could help our bodies cope better with a modern day abundance of food, according to researchers who are investigating the link between the body clock and obesity.

It's part of a growing field of research looking at how disruption to the body clock caused by lifestyle changes such as increased light exposure, shift work and plentiful food is contributing to problems including obesity and diabetes, and whether manipulating our internal timing could offer possible treatments.

The aCROBAT project, funded by the EU's European Research Council, is looking at how the body clock controls brown fat – a tissue that burns calories and uses up glucose from the blood to produce heat and dissipate energy in the body. The power of brown fat is tightly under the control of the body clock.

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‘For tens of thousands of years, our ancestors did not know when their next meal was coming. Therefore, we believe the body’s clock was programmed to turn off brown fat at times of day when it wasn’t needed,’ said aCROBAT coordinator Dr Zachary Gerhart-Hines, an associate professor at the University of Copenhagen, Denmark.

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But in societies such as Europe, where people can now eat whatever they want to, whenever they want to, this can lead to major health problems.

Dr Gerhart-Hines’ research is looking at ways to switch on brown fat and to keep it working for longer, to use up more of the excess of calories and blood glucose. ‘So essentially, can we keep brown fat turned on throughout the day?’

The idea is to identify pharmacological targets – enzymes or receptors – that play an essential role in how the body clock controls brown fat.

The researchers have already identified molecules both on the cell’s surface and interior that modulate brown fat at different points in the day. They now hope to design strategies that can unlock these ‘brake points’ to keep brown fat working.

Tablets and injections

The research has already turned up some promising candidates and depending on the process, this exploration could eventually lead to a tablet or injection-based therapy for clinical treatment of obesity or diabetes.

‘It’s fascinating to study how we as mammals have adjusted to become maximally efficient over tens of thousands of years and how we have managed to disrupt that elegant programming in less than a few hundred years,’ Dr Gerhart-Hines said.

‘Now what we hope to accomplish is really to figure out how we can use pharmacology and these different tools and techniques to help people by resetting the brown fat clock to modern times,’ he added.

In healthy people, the body clock – the internal timing that controls how different physiological functions turn on and off throughout the day – is broadly aligned with the day-night cycle so that we can be awake and active during the day and rest at night.

A group of researchers have been looking into how increased exposure to light could interfere with this alignment and contribute to obesity.

The EU-funded Obesity and Light project showed that under continuous light, zebrafish larvae developed many more fat cells than those living in a normal day-night cycle.

‘This was quite shocking to us,’ said Professor Juliette Legler from Brunel University London, UK, who coordinated the research. ‘They were on the same diet, but the light obviously regulates metabolism early in development and regulates how many fat cells differentiate.’

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The research, carried out by Dr Renate Kopp on a Marie Skłodowska-Curie fellowship at the Vrije Universiteit Amsterdam, the Netherlands, found a link between genes involved in fat cell differentiation and body clock genes, and that they regulate each other.

Essentially, exposing the fish larvae to light continuously was affecting the way that stem cells become fat cells. While the precise process is not yet clear, this was some of the very first evidence of a direct link between clock genes and genes involved in fat cell differentiation.

‘This was new and exciting for us, because it provides a biological mechanism for how an organism’s lipid metabolism is changed by changing day-night rhythms,’ Prof. Legler said.

‘We thought that if you draw the parallel to the human situation, nowadays we are exposed to more and more light and now true darkness is actually very rare,’ she added.

Two-way street

The research also showed that the relationship between the circadian clock and fat metabolism is a two-way street – environmental chemicals that can contribute to obesity also have the effect of disturbing body clocks.

So changes in the body clock affect how the fish stores fat, but chemicals that can cause obesity in zebrafish larvae can also lead to changes in the regulation of the body clock.

‘Our research provides a basis to look further in humans at the link between changes in day-night rhythm and metabolic disease,’ Prof. Legler said. ‘Because if we could understand that better and if we could provide advice (on) how important it is to have a regular sleeping pattern and to have complete darkness at some stage of the night, this could be a really simple way of preventing such important diseases as obesity.’

More info

[aCROBAT](#)

[Obesity and Light](#)