

Major new appetite regulator successfully manipulated in mice

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Credit: Martha Sexton/public domain

Researchers from Imperial College London and colleagues have found a potential way to target the receptors that specifically control appetite in mouse brains, potentially without causing other side effects.

Thyroid [hormone](#) receptors (TRs) are spread widely throughout the body

and interact with circulating [thyroid](#) hormones to regulate functions such as appetite, the nervous system, body temperature, and cholesterol levels. Thus, any [drug](#) targeting thyroid hormones and their receptors needs to be specific to avoid affecting other body systems.

However, they are difficult to target individually due to their high numbers and so there are currently no anti-obesity drugs that target them.

Now, researchers from Imperial and colleagues have found a potential way to target specific TRs located only in the hypothalamus, an area of the brain that regulates appetite. The authors say the findings might lead to developing a new type anti-obesity drug in the future.

Dr James Gardiner, lead author of the research from Imperial's Department of Medicine, said: "Our hope is that these findings could ultimately lead towards drugs that target thyroid hormones as a way to reduce someone's appetite and help them control their weight. We haven't been able to target these hormones before without lots of side effects, but in this study we've been able to be very specific about which hormones we're targeting, which should greatly lessen potential side effects. We are excited to see where this might lead in the future fight against obesity."

In this [early stage](#) research, the authors divided 21 mice, who weighed roughly 20g each, into two groups. They injected mice in the first group with viruses that inactivated the brain TRs, but did not inject the second group. They then let both groups eat as much as they chose. Afterwards, the researchers examined the brains of the mice to confirm the virus had in fact inactivated the targeted receptors.

They found that the group of mice with the inactive TRs ate much more food and doubled in weight on average, doubling in size from the

baseline of 20 grams to 40 grams over six weeks. The mice with active TRs maintained a stable body weight at 20 grams.

The authors say this is evidence that when targeting drugs to a specific, local, receptor in the correct [brain](#) area, they can alter appetite in these mice without causing other side effects. This could potentially be applied to humans in the future, where a drug might decrease a person's [appetite](#) by activating TRs in the hypothalamus, without causing effects in other parts of the body. Dr Gardiner said: "If our findings can be applied to humans, then we may have a new target for obesity medication."

Humans with lowered thyroid receptor activity in their brains have previously been found to be on average more obese than others. If this research continues into testing drugs on human subjects, there would be no simple test to measure levels of receptor activity and adjust medication accordingly. Rather, treatment would be based on a system of trial and error with regard to whether the drug worked for specific individuals.

However, the authors warned that this research is at an early stage and the results should be taken with caution. Dr Gardiner added: "Due to the justifiably long and complex process of drug discovery, any potential treatment that could result from this will be far off in the future. However, the strength of our results, and the doubling in body size of these [mice](#), shows there's that the role of [thyroid hormones](#) and their [receptors](#) are definitely worth exploring further in the fight against obesity."

Provided by Imperial College London

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