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Reducing the health risks of obesity without serious side effects

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The drug rimonabant was developed as a treatment for obesity and its myriad of serious health consequences (for example, type 2 diabetes). Despite having its desired effects on weight, which it decreased, and on levels of glucose and fats in the blood, rimonabant was never approved for use in the US because of serious neurological side effects including depression and anxiety.

Now, a team of researchers, led by George Kunos, at the National Institutes of Health, Bethesda, and Alexandros Makriyannis, at Northeastern University, Boston, have developed a drug that has the same positive effects in mice on levels of glucose and fats in the blood as rimonabant but none of the neurological side effects.

Rimonabant targets the protein CB1R, the same molecule that mediates the effects of marijuana. CB1R is expressed in the brain and in organs such as the liver, pancreas, and fat tissue. The team developed a drug that inhibited CB1R in peripheral mouse organs but could not access the brain. This drug did not cause weight loss or neurological side effects, which rimonabant does, but did have effects on levels of glucose and fats in the blood that should reduce the risk of the serious health consequences of obesity.

The authors therefore hope that this approach of targeting only peripheral CB1R can be translated into the clinic to reduce health risks in obese patients. However, in an accompanying commentary, Mary-Elizabeth Patti, at the Joslin Diabetes Center, Boston, cautions that it will

be important to ensure that such drugs really do not access the brain to mediate neurological effects.

More information: www.jci.org/articles/view/4255 … 6ce2dad54fc6a996740c

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