Dietary fats entering the brain may explain link between obesity and depression

May 10 2019

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Obesity and depression have long been linked, with previous clinical studies finding an association between these two conditions. However, until now, the mechanisms of how obesity affects depression and vice

versa have not been fully understood.

Now, in a new study led by the University of Glasgow in collaboration with the Gladstone Institutes, and published today in *Translational Psychiatry*, scientists have been able to demonstrate the links between the consumption of diets high in saturated fats that lead to obesity and the development of depression phenotypes. They have also found that by decreasing the expression of a specific enzyme called phosphodiesterase, symptoms of obesity-linked depression can be reduced.

In novel findings, shown in mouse models, researchers were able to see that saturated fatty acids were actually entering the brain via the bloodstream and thereafter accumulate and affect crucial brain signals related to depression. Mice fed a fat-dense diet (made up of 60% saturated and unsaturated fats) were shown to have an influx of dietary fatty acids in the hypothalamus region of the brain, an area related to the metabolic system and known to be linked with depression. These fatty acids were then able to directly affect the key signaling pathways responsible for the development of depression.

The relationship between obesity and depression is known to be complicated, with patients with obesity less likely to respond well to common antidepressant medication. Indeed, patients with obesity show a substantially slower response to antidepressant treatment, with less overall improvements.

Researchers in this study believe that their novel findings may now influence new targets for antidepressant medications that may be more suitable for overweight and obese individuals.

Professor George Baillie, lead author of the study from the University of Glasgow, said: "This is the first time anyone has observed the direct effects a high fat diet can have on the signaling areas of the brain related

to depression. This research may begin to explain how and why obesity is linked with depression and how we can potentially better treat patients with these conditions.

"We often use fatty food to comfort ourselves as it tastes really good, however in the long term, this is likely to affect one's mood in a negative way. Of course, if you are feeling low, then to make yourself feel better you might treat yourself to more fatty foods, which then would consolidate negative feelings.

"We all know that a reduction in fatty food intake can lead to many health benefits, but our research suggests that it also promotes a happier disposition. Further to that, understanding the types of fats, such as palmitic acid, which are likely to enter the brain and affect key regions and signaling will give people more information about how their diet can potentially affect their mental health."

In this study, researchers found that either dietary or genetically induced obesity in mice lead to depression phenotype, and that this phenomenon occurred via the disruption of the cAMP/PKA signaling pathway. In addition, they found that the consumption of a fat-dense diet led to an influx of dietary fatty acids specifically in the hypothalamus. These fatty acids could then directly modulate the PKA signaling pathway responsible for the development of depression. These findings suggest that the influx of saturated fatty acids due to the consumption of a high fat diet can alter the cAMP/PKA signaling process, which results in the development of depression phenotype.

More information: Eirini Vagena et al. A high-fat diet promotes depression-like behavior in mice by suppressing hypothalamic PKA signaling. *Translational Psychiatry*,volume 9, Article number: 141 (2019).

Medical Xpress

Provided by University of Glasgow

Citation: Dietary fats entering the brain may explain link between obesity and depression (2019, May 10) retrieved 20 March 2024 from https://medicalxpress.com/news/2019-05-dietary-fats-brain-link-obesity.html

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