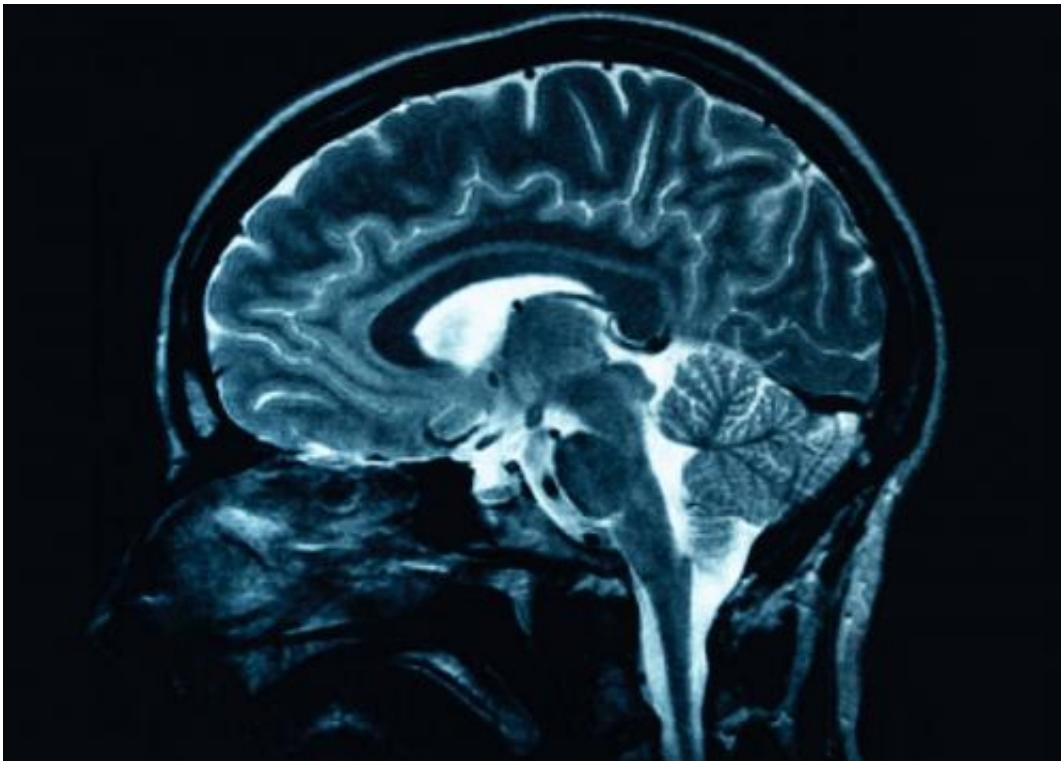


## 'Cannabis' receptor discovery may help understanding of obesity and pain

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(Phys.org)—Researchers have discovered that a genetic difference in a 'switch', which causes over-activity in parts of the brain, may explain why some people could be more susceptible to conditions such as obesity and addiction, and may play a role in chronic pain and psychosis.

Aberdeen scientists believe that the findings—published in the [Journal of Biological Chemistry](#)—might help our understanding of these conditions and also be a step towards the development of personalised therapies to help treat them.

The team from the University's Kosterlitz Centre for Therapeutics studied [genetic differences](#) around the gene CNR1. This gene produces what are known as cannabinoid receptors, which are found in the brain, and which activate parts of the brain involved in memory, mood, appetite and pain.

[Cannabinoid receptors](#) activate these areas of the brain when they are triggered by chemicals produced naturally in our bodies called [endocannabinoids](#).

Chemicals found in the drug cannabis mimic the action of these endocannabinoids and there is growing evidence that cannabis has pain relieving and anti-inflammatory properties which can help treat diseases such as [multiple sclerosis](#) and arthritis.

However, developing drugs from cannabis to treat these conditions is hampered by the fact that such drugs will have psychoactive side effects, and smoked cannabis can cause addiction and psychosis in up to 12% of users.

In order to understand more about these side effects and the [genetic factors](#) which determine how people respond, the scientists studied genetic differences around the CNR1 gene.

Dr Alasdair MacKenzie, who helped lead the team, said: "We chose to look at one specific genetic difference in CNR1 because we know it is linked to [obesity](#) and addiction. What we found was a mutation that caused a change in the genetic switch for the gene itself—a switch that is

very ancient and has remained relatively unchanged in over three hundred million years of evolution, since before the time of the dinosaurs.

"These genetic 'switches' regulate the gene itself, ensuring that it is turned on or off in the right place at the right time and in the right amount.

"It is normally thought that [mutations](#) cause disease by reducing the function of the gene, or the switch that controls it.

"In this case however, the mutation actually increased the activity of the switch in [parts of the brain](#) that control appetite and pain, and also—and most especially—in the part of the brain called the hippocampus, which is affected in psychosis.

Dr Scott Davidson, who played a key role in the discovery of this genetic difference in the switch added: "Further analysis of this mutation will help us to understand many of the side effects which are associated with cannabis use such as addiction and [psychosis](#)."

Professor Ruth Ross, Head of the Kosterlitz Centre and an internationally recognised expert in cannabis pharmacology, added: "Previously in drug research, attempts to detect the causes of adverse drug reactions have focused on the genes themselves.

"Our study is one of the first to explore the possibility that changes in gene switches are involved in causing side effects to drugs. We believe this approach will be crucially important in the future development of more effective personalised medicine, with fewer side effects."

One question that is intriguing the research team is why this overactive genetic switch evolved in the first place.

Dr MacKenzie explains: "We know that this overactive switch is relatively rare in Europeans, but is quite common in African populations. But we were all once African, so something must have decreased it in our early ancestors who left Africa and migrated through Central Asia towards Europe and the north.

"One possibility we are keen to explore is that once in Central Asia these early migrants came into contact with the cannabis plant, which we know was endemic across that area at that time. It is possible that the side effects of taking cannabis were such that people with the mutation were not so effective in producing and raising children. Therefore, over the generations the numbers of people with the mutation decreased.

"This work is at a very early stage however, and there are likely to be more exciting discoveries—not only on how these differences came about, but also about the role of this [genetic switch](#) in health and disease."

Provided by University of Aberdeen

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