# Brain imaging insight into cannabis as a pain killer

December 20 2012

The pain relief offered by *cannabis* varies greatly between individuals, a brain imaging study carried out at the University of Oxford suggests.

The researchers found that an oral tablet of THC, the psychoactive ingredient in cannabis, tended to make the experience of pain more bearable, rather than actually reduce the intensity of the pain.

MRI brain imaging showed reduced activity in key areas of the brain that substantiated the pain relief the study participants experienced.

'We have revealed new information about the neural basis of *cannabis*-induced pain relief,' says Dr Michael Lee of Oxford University's Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB).

He adds: 'Our small-scale study, in a controlled setting, involved 12 healthy men and only one of many compounds that can be derived from *cannabis*. That's quite different from doing a study with patients. My view is the findings are of interest scientifically but it remains to see how they impact the debate about use of *cannabis*-based medicines. Understanding *cannabis*' effects on clinical outcomes, or the quality of life of those suffering chronic pain, would need research in patients over long time periods.'

The researchers report their findings in the journal *Pain*. The study was funded by the UK Medical Research Council and the National Institute

for Health Research (NIHR) Oxford Biomedical Research Centre.

Long-term pain, often without clear cause, is a complex healthcare problem. Different approaches are often needed to help patient manage pain, and can include medications, physiotherapy and other forms of physical therapy, and psychological support. For a few patients, *cannabis* or *cannabis*-based medications remain effective when other drugs have failed to control pain, while others report very little effect of the drug on their pain but experience side-effects.

'We know little about *cannabis* and what aspects of pain it affects, or which people might see benefits over the side-effects or potential harms in the long term. We carried out this study to try and get at what is happening when someone experiences pain relief using *cannabis*,' says Dr Lee.

The Oxford research team carried out a series of MRI scans with each of the 12 volunteers at the FMRIB centre in Oxford.

Before a scan, participants were given either a 15mg tablet of THC or a placebo. THC, or delta-9-tetrahydrocannabinol, is the active psychotropic compound in *cannabis* – the ingredient that's responsible for the high that drives recreational use of the drug.

To induce a certain level of pain, the volunteers also had a cream rubbed into the skin of one leg. This was either a dummy cream or a cream that contained 1% capsaicin, the ingredient of chillis that causes a hot, burning and painful sensation.

Each participant had four MRI tests to cover each combination of THC or placebo, and chilli pain-inducing cream or dummy cream.

'The participants were asked to report the intensity and unpleasantness of

the pain: how much it burned and how much it bothered them,' says Dr Lee. 'We found that with THC, on average people didn't report any change in the burn, but the pain bothered them less.'

While this average effect was statistically significant, there was great variability among the participants in THC's effect on the pain they experienced. Only six out of the 12 reported a clear change in how much the pain bothered them, for example.

The brain imaging results substantiate the reports of the participants. The change in unpleasantness of pain was matched with a suppression of activity in the part of the brain called the anterior mid-cingulate cortex. This structure sits in a deep part of the brain and is involved in many functions, and has previously been implicated in the emotional aspects of pain.

There were also changes in activity of the right amygdala that correlated with the lessening in the unpleasantness of the pain with THC. It is already known that the right side of the amygdala can be 'primed' by pain.

Of most interest to the researchers, however, was the strength of the connection in individuals between their right amydala and a part of the cortex called the primary sensorimotor area. The strength of this connection in individual participants correlated well with THC's different effects on the pain that that volunteer experienced.

This is suggestive that there might be a way of predicting who would see benefits from taking *cannabis* for pain relief.

'We may in future be able to predict who will respond to *cannabis*, but we would need to do studies in patients with chronic pain over longer time periods,' says Dr Lee.

He adds: '*Cannabis* does not seem to act like a conventional pain medicine. Some people respond really well, others not at all, or even poorly. Brain imaging shows little reduction in the brain regions that code for the sensation of pain, which is what we tend to see with drugs like opiates. Instead *cannabis* appears to mainly affect the emotional reaction to pain in a highly variable way.'

**More information:** The paper 'Amygdala activity contributes to the dissociative effect of cannabis on pain perception' by Michael C. Lee, Markus Ploner, Katja Wiech, Ulrike Bingel, Vishvarani Wanigasekera, Jonathan Brooks, David K. Menon, Irene Tracey (DOI: 10.1016/j.pain.2012.09.017) will appear in *PAIN*, Volume 154, Issue 1 (January 2013)

Provided by Oxford University

Citation: Brain imaging insight into cannabis as a pain killer (2012, December 20) retrieved 2 May 2024 from https://medicalxpress.com/news/2012-12-brain-imaging-insight-cannabis-pain.html

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