First trial—investigating magic mushrooms as a treatment for depression—delayed by UK and EU regulations

April 8 2013

The world's first clinical trial to explore the use of the hallucinogenic ingredient in magic mushrooms to treat depression is being delayed due to the UK and EU rules on the use of illegal drugs in research.

Professor David Nutt, president of the British Neuroscience Association and Professor of Neuropsychopharmacology at Imperial College London (UK), will tell the BNA's Festival of Neuroscience today (Sunday) that although the UK's Medical Research Council has awarded a grant for the trial, the Government's regulations controlling the licensing of illegal drugs in research and the EU's guidelines on Good Manufacturing Practice (GMP) have stalled the start of the trial, which was expected to start this year. He is calling for a change to the regulations.

He will tell the meeting at the Barbican in London, that his research has shown that psilocybin, the psychedelic ingredient in magic mushrooms, has the potential to alleviate severe forms of depression in people who have failed to respond fully to other anti-depressant treatments. However, psilocybin is illegal in the UK; the United Nations 1971 Convention on Psychotropic Substances classifies it as a Schedule 1 drug, one that has a high potential for abuse with no recognised medical use, and the UK has classified it as a Class A drug, the classification used for the most dangerous drugs. This means that a special licence has to be obtained to use magic mushrooms in research in the UK, and the manufacture of a synthetic form of psilocybin for use in patients is

tightly controlled by EU regulations.

Prof Nutt will say: "The law for the control of drugs like psilocybin as a Schedule 1 Class A drug makes it almost impossible to use them for research and the reason we haven't started the study is because finding companies who could manufacture the drug and who are prepared to go through the regulatory hoops to get the licence, which can take up to a year and triple the price, is proving very difficult. The whole situation is bedevilled by this primitive, old-fashioned attitude that Schedule 1 drugs could never have therapeutic potential, and so they have to be made impossible to access."

"The knock-on effect is this profound impairment of research. We are the first people ever to have done a psilocybin study in the UK, but we are still hunting for a company that can manufacture the drug to GMP standards for the clinical trial, even though we've been trying for a year to find one. We live in a world of insanity in terms of regulating drugs at present. The whole field is so bogged down by these intransient regulations, so that even if you have a good idea, you may never get it into the clinic."

He will say that the regulations need to be changed. "Even if I do this study and I show it's a really useful treatment for some people with depression, there's only four hospitals in this country that have a licence to hold this drug, so you couldn't roll out the treatment if it worked because the regulations would make it difficult to use," he said.

Prof Nutt and his team at Imperial College London (UK) have shown that when healthy volunteers are injected with psilocybin, the drug switched off a front part of the brain called the anterior cingulate cortex, which is known from previous imaging studies to be over-active in depression. "We found that, even in normal people, the more that part of the brain was switched off under the influence of the drug, the better

they felt two weeks later. So there was a relationship between that transient switching off of the brain circuit and their subsequent mood," he will explain. "This is the basis on which we want to run the trial, because this is what you want to do in depression: you want to switch off that over-active part of the brain.

"The other thing we discovered is that the major site of action of the magic mushrooms is to turn down a circuit in the brain called the 'default mode network', which the anterior cingulate cortex is part of. The default mode network is a part of the brain between the front and back. It is active when you are thinking about you; it coordinates the thinking and emotional aspects of you."

The researchers discovered that the 'default mode network' had the highest density of 5HT2A receptors in the brain. These are known to be involved in depression and are the targets for a number of existing anti-depressive drugs that aim to improve levels of serotonin – the neurotransmitter that gives people a sense of well-being and happiness. Psilocybin also acts on these receptors.

"We have found that people with depression have over-active default mode networks, and they are continually locked into a mode of thinking about themselves. So they ruminate on themselves, on their incompetencies, on their badness, that they're worthless, that they've failed; these things are not true, and sometimes they reach delusional levels. This negative rumination may be due to a lack of serotonin and what psilocybin is doing is going in and rapidly replacing the missing serotonin, switching them back into a mind state where they are less ruminating and less depressed," Prof Nutt will say.

The proposed trial will be for patients with depression who have failed two previous treatments for the condition. Thirty patients will be given a synthetic form of psilocybin and 30 patients will be given a placebo. The

drug (or placebo) will be given during two, possibly three, carefully controlled and prepared 30-60 minute sessions. The first session will be a low dose to check there are no adverse responses, the second session will give a higher, therapeutic dose, and then patients can have a third, booster dose in a later session if it's considered necessary. While they are under the influence of the drug, the patients will have guided talking therapy to enable them to explore their negative thinking and issues that are troubling them. The doctors will follow up the patients for at least a year.

"What we are trying to do is to tap into the reservoir of under-researched 'illegal' drugs to see if we can find new and beneficial uses for them in people whose lives are often severely affected by illnesses such as depression. The current legislation is stopping the benefits of these drugs being explored and for the last 40 years we have missed really interesting opportunities to help patients."

Ethical approval for the trial was granted in March and Prof Nutt says he hopes to be able to start the trial within the next six months – so long as he can find a manufacturer for the drug.

More information: Abstract title: "Can we use psychedelic drugs to treat depressions?" Symposium: "Treating depression with antidepressants: where are we now and where are we going?" at 11.30 hrs BST on Sunday 7 April, Frobisher Auditorium 2.

Provided by British Neuroscience Association

depressiondelayed.html