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Study Helps Unravel Mysteries of Brain's Endocannabinoid System

NIDA research could lead to better treatment for pain and marijuana addiction

New research funded by the National Institute on Drug Abuse (NIDA), part of the National Institutes of Health, has identified a new mechanism for the processing of endocannabinoids, natural brain compounds similar to THC, the active ingredient in marijuana. The results of this study, led by researchers from Stony Brook University, were published March 16 in the Proceedings of the National Academy of Sciences.

Endocannabinoids are known to play a role in numerous physiological processes including appetite, memory, and pain. Researchers had long suspected that endocannabinoids needed a specific transporter that would ferry them to the location where they are broken down. This study successfully identified a couple of previously known fatty acid binding proteins (FABPs) as capable of carrying the endocannabinoid anandamide (also known as AEA) from the cell membrane, through the cell interior, to the location where it is destroyed.

"This finding is important because it significantly expands the range of potential targets for developing medications that could help fight pain, addiction, and other disorders," said NIDA Director Dr. Nora D. Volkow. "For example, the manipulation of the endocannabinoid system has the potential to provide sorely needed therapeutics for the management of severe pain that are devoid of the side effects of opiate analgesics."

The breakdown of AEA requires two factors. First, because AEA is a fatty compound and thus unable to move inside the watery cellular environment, there needs to be a mechanism for transporting AEA to the location where it is inactivated. Second, the cell must express an enzyme called FAAH, which is responsible for breaking down and inactivating AEA. In the laboratory, the researchers coaxed a non-neuronal cell type (Cos-7) to express FAAH. These FAAH-expressing Cos7 cells were able to break down AEA efficiently, indicating that the intracellular AEA transport mechanism was already present and operational in these cells. The researchers identified these carriers as two different, previously known fatty-acid binding proteins (FABPs). By specifically inhibiting FABPs, they were able to decrease the breakdown of AEA by about 50 percent.

"Inhibiting FABPs could potentially raise the levels of AEA in the brain's synapses," said Dr. Dale Deutsch, lead author of the study. "Naturally occurring AEA levels have been shown to curb pain without the negative side effects, such as motor coordination problems, of molecules like THC that can also bind the cannabinoid receptor. So it's advantageous to try and target AEA for therapeutic purpose."

"From a theoretical viewpoint, this approach could be used for treating marijuana addiction," said Dr. Volkow. "Compounds that inhibit FABPs could produce an effect similar to nicotine patches for smokers or methadone for opiate replacement. This line of research may also be important for other types of addiction, such as chronic alcohol abuse, which also affects AEA levels," she explained.

In addition to pain control, researchers are also examining manipulation of the endocannabinoid system for treating anxiety, obsessive-compulsive disorder, traumatic brain injury, and other substance abuse disorders.

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