Drug shared by addicts seems to protect against HIV brain dementia

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To their surprise, researchers at Georgetown University Medical Center (GUMC) have discovered that morphine (a derivate of the opium poppy that is similar to heroin) protects rat neurons against HIV toxicity - a finding they say might help in the design of new neuroprotective therapies for patients with the infection.

The discovery, being presented at the annual meeting of the Society of NeuroImmune Pharmacology, also helps explain why a subset of people who are heroin abusers and become infected with HIV through needle sharing don't develop HIV brain dementia. This brain disorder includes cognitive and motor abnormalities, anxiety and depression.

"We believe that morphine may be neuroprotective in a subset of people infected with HIV," says the study's lead investigator, Italo Mocchetti, PhD, Professor of neuroscience at GUMC. "That is not to say that people should use heroin to protect themselves - that makes no medical sense at all - but our findings gives us ideas about designing drugs that could be of benefit.

"Needless to say we were very surprised at the findings," he added. "We started with the opposite hypothesis - that heroin was going to destroy neurons in the brain and lead to HIV dementia."

The researchers conducted the study because they knew that a number of HIV-positive people are also heroin abusers, and because of that, some are at high risk of developing neurological complications from the

infection. Others, however, never develop these cognitive problems, Mocchetti says.

Because little is known about the molecular mechanisms linking opiates and HIV neurotoxicity, Mocchetti and his team conducted experiments in rats. They found that in the brain, morphine inhibited the toxic property of the HIV protein gp120 that mediates the infection of immune cells. With further investigation, they concluded that morphine induces production of the protein CCL5, which they discovered is released by astrocytes, a type of brain cell. CCL5 is known to activate factors that suppress HIV infection of human immune cells. "It is known to be important in blood, but we didn't know it is secreted in the brain," says Mocchetti. "Our hypothesis is that it is in the brain to prevent neurons from dying."

They say morphine blocked HIV from binding to CCR5 receptors it typically uses to enter and infect cells. The researchers believe CCL5 itself attached to those receptors, preventing the virus from using it. In this way, it prevented HIV-associated dementia. This effect, however, only worked in the M-trophic strain of HIV, the strain that most people are first infected with. It did not work with the second T-trophic strain that often infects patients later.

"Ideally we can use this information to develop a morphine-like compound that does not have the typical dependency and tolerance issues that morphine has," says Mocchetti.

Provided by Georgetown University Medical Center