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Stimulants and Brain Cell Death

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Q Do methamphetamines cause any cellular damage or cell death in the brain?

A Yes, that's one of the things we've been finding in the lab. Serotonin cell death is reported for ecstasy but for methamphetamine we find dopamine, cell loss and system degeneration. Evidence of cell death can be found in the corpus striatum

Q What sort of things do you see in the post-mortem brain of a methamphetamine user?

A In the lab, when you cut the brain and perform histology stains, you can see cells that are dying; however, this must be done within a certain time frame, because after approximately two weeks, it is not seen. The optimal staining timeframe is somewhere between 24-72 hours. Ernst and others have used imaging to show evidence of cell death in humans. No question brain cells die. The only question is how you go about proving it in research studies.

Q What are the short-term/long-term effects of methamphetamine use?

A Short-term problems include cognitive, memory and decision problems. Motor system starts to be compromised and you see tremors. Long-term use can result in the development of problems with thinking and with reality testing. They can have the psychotic like symptoms of Schizophrenia.

Q How is MDMA (Ecstasy) different from methamphetamines?

A Ecstasy is different in that the cell death and damage occurs in the serotonergic system instead of the dopamine system. Cell death is evident and maybe irreversible. Culture experiments have shown that MDMA is more toxic than methamphetamine, but more studies are necessary. It differs from the DA release in methamphetamine use because of the production of free radicals that destroy neurons. Recognized long-term effects, or MDMA include, memory loss, sleep disorders and depression.

Q How do morphine and other opiates differ from methamphetamines?

A Opiates work through the opiate-receptor system. Opiates do not produce cell death like MDMA or Methamphetamine.

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A Morphine use cause immune system cell death.

Q Are there any treatments available to prevent cell death?

A No, we have not come to that stage yet. We have tried a number of medicines, but prevention of MDMA effects is not possible at this point. Right now, we are looking at the mechanisms that cause cell death. We must have an understanding of these mechanisms before the development of focused treatment.

Q Can the effects of methamphetamines be blocked by SSRI's?
A It can only give partial protection. Better protection would be from dopamine transporter blocker, or use dopamine antagonists. The best protection is not taking methamphetamine.

Q What are the cardiac findings of cocaine users?
A The vasculature of a 30 year-old cocaine user is the same as an individual in their 70's. The cocaine user has the same risk for stroke over time & continually gets worse. Both EEG and blood flow get worse. Cocaine is a major cardiac stress and risk factor.

Q Has there been evidence of cell death in amphetamine use?
A All of the amphetamines kill cells in vitro and in vivo. Of these, MDMA (Ecstasy) appears to be the worst. Nora Volkow's group has also found abnormalities in various regions of the human brain. The cell death that we see is permanent because cells will not come back. Ernst et al looked at markers of cell death using MRI and these are also increased.

Q What are the effects of prenatal exposure to amphetamines?
A Behavioral abnormalities, cell death and other abnormalities have been observed. Pregnant mothers who use Methamphetamine may cause damage to their fetuses. Methamphetamines show more toxicity in older animals.

Q What are some of the behavioral effects of methamphetamine use?
A Some behavioral studies have shown cognitive abnormalities, persistent paranoia and poor decision-making ability.

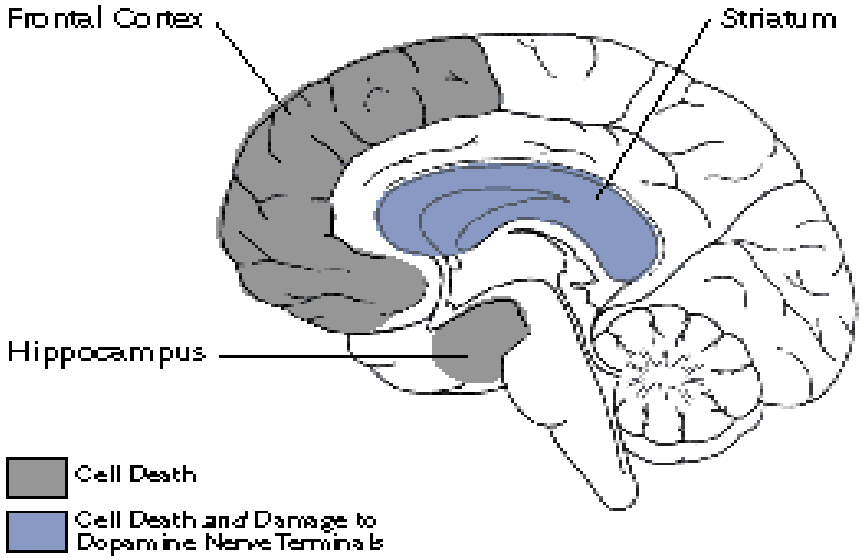
Q Do drugs used in the treatment of ADD/ADHD cause cell death?
A Ritalin does not kill the brain cells, but some other drugs used in ADHD treatment do.

Q What type of patients are methamphetamine/ MDMA users?
A Because these patients are destroying their brains, they may not be able to follow instructions when they are in a treatment program. I wouldn't say they were bad patients or even non-compliant. The brain damage might hinder their ability to follow through, however.

Q Is their any new data on marijuana?
A Similar neurophysiological findings to cocaine users when it comes to blood flow. A young marijuana user's vasculature looks like that of someone who is 60. Also abnormalities in the prefrontal cortex are evident. I do not think marijuana smokers know of or understand this data and what they mean.

Q What about caffeine and nicotine?
A Abnormalities in caffeine users have only been shown in withdrawal. If you're a coffee drinker, keep drinking it. Nicotine has proven positive in protecting against morphine-induced cell death. Nicotine does not kill immune cells.

Q What work are you presenting this year at the psychiatric and neuroscience meeting?
A We are presenting more data on the neurotoxicity of methamphetamine and MDMA.



Methamphetamine-induced damage to nerve terminals of dopamine-producing cells occurs primarily in a brain region called the striatum. Methamphetamine-induced apoptosis killed off different types of nerve cells in the frontal cortex, the hippocampus, and the striatum in mice.

Jean Lud Cadet, M.D. graduated from Columbia University, College of Physicians and Surgeons, in 1979. He is trained both as neurologist and psychiatrist. He compelled a residency in neurology at Mount Sinai and in psychiatry at Columbia University in New York City. He subsequently did a fellowship in neuropsychiatry at the National Institute of Mental Health at the National Institutes of Health (NIH), after which he joined Columbia University as an assistant professor of neurology and psychiatry. He joined the National Institute on Drug Abuse (NIDA) in 1992. He is presently Chief, Molecular Neuropsychiatry Section, and Clinical Director of the NIH/NIDA Intramural Research Program. His research interests include (1) clinical neurobiology of drug abuse and addiction, (2) cellular and molecular neurotoxicology of drug abuse, (3) the involvement of free radicals in neurodegeneration, (4) the role of cell death-related genes in the toxicity of drug abuse, and (5) the participation of catecholamines in neurodegenerative disorders.

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