Impact of methamphetamine on the blood-brain barrier: unmasking the underlying mechanisms and the role of neuroinflammation

Funding country: Portugal
Project starting year: 2010
Project ending year: 2013
Area(s) of research: Consequences of drug use, Mechanism of drug use and effects

Objectives:
The aim of the present project is to clarify the effect of METH on the BBB since it may be crucial for both decompensation of brain functions and cell injury following drug consumption. Since the molecular and cellular mechanisms underlying increased BBB breakdown associated with the consumption of psychostimulants remain unknown, we propose to clarify this issue by looking at the effect of methamphetamine on: 1) BBB permeability taking particularly attention to changes in tight junction proteins; 2) Levels and activity of matrix metalloproteinases (MMPs); 3) Crosstalk between endothelial cells and astrocytes; 4) Adhesion and migration of leukocytes. A protective strategy will be also evaluated by looking at: 5) The role of a nonsteroidal anti-inflammatory drug

Scientific discipline(s) involved: Neurosciences, Pharmacology

Initial identified needs:
Methamphetamine (METH) is a powerful stimulant drug of abuse that has steadily gained popularity worldwide. On average, 3.3% of all European adults report having used amphetamines at least once. In Portugal the consumption of METH has also increased during the last few years not only as a recreational drug, but also as a "treatment" to lose weight. This costly pandemic presents an enormous challenge to the government, the pharmaceutical industry, and the drug abuse research community. It is known that METH is a neurotoxic addictive drug that causes irreversible damage of neuronal and non-neuronal brain cells leading to neurological and psychiatric abnormalities. However, in contrast to the multiple factors contributing to chronic METH neurotoxicity, the mechanisms underlying life-threatening effects of acute METH intoxication remain less clear. Very recently, a few studies have suggested that METH-induced neurotoxicity may also result from its ability to compromise the function of the blood-brain barrier (BBB). Thus, given the limited understanding of the effect of METH on the BBB, the purpose of the present project is to clarify the molecular and cellular mechanisms underlying the BBB dysfunction associated with the consumption of METH, and the possible involvement of neuroinflammation.

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Summary references:
Website:
Published reference(s):