Implications of amphetamine psychostimulants abuse in brain aging

Funding country: Portugal
Project starting year: 2010
Project ending year: 2013
Area(s) of research:
- Prevention responses
- Treatment responses
- Harm reduction responses
- Consequences of drug use
- Mechanism of drug use and effects

Objectives:
1. Investigate how chronic exposure to amphetamines and their metabolites may affect the number and fate of rat embryonic cortical neurons
2. Exposure of embryonic cortical neuron cultures from the rat to amphetamines and their metabolites (1 µM, 10 µM and 100 µM) on the day of seeding and the latter evaluation of the number of precursor cells and neurites, as well as study the intracellular proteins involved in these mechanisms.
3. Cell death model of primary cortical neurons and astocytes of rat that mimick an amphetamine's chronic exposure.
4. Exposure of adolescent wistar rats (aged between post-natal day (PD) 35 to PD 60) to amphetamines (10 mg/kg/dose X 2 every 5th day), the neurotoxic effects will be evaluated six months after the last exposure.

Scientific discipline(s) involved:
- Neuroscience, Pharmacology, Other medical sciences, Toxicology

Initial identified needs:
- Cellular brain aging process has been proved to be correlated with an accumulation of free radicals to which cells cannot cope with, leading to an increase cellular damage (Halliwell, 2006), with mitochondrial damage playing a leading role (Weissman et al., 2007). Interestingly, amphetamines promote free radical production and oxidative stress in the brain, as our group and others have established. We showed that amphetamine (AMPH) and MDMA can elicit an increase in oxidative stress, promote apoptotic neuronal death and produce mitochondrial DNA (mtDNA) deletions in both cultured neurons and animal brains (Carvalho et al., 2001; Capela et al., 2006a; Alves et al., 2007; Capela et al., 2007b).
- Therefore, both brain aging and amphetamine neurotoxicity share common features, namely oxidative stress, mitochondrial damage and neuronal cell death. HYPOTHESIS Does the use of amphetamines accelerate the process of brain aging? This problem is yet unanswered by current data, and is not evaluated by current laboratory paradigms of animal or cell culture by the exposure to amphetamine psychostimulants.

Performed by:
- Institute of Sciences and Agrarian and Agriculture-alimentary Technologies- Porto (ICETA-Porto/UP)
- Faculdade de Medicina da Universidade de Coimbra (FM/UC)
- Fundação da Faculdade de Ciências e Tecnologia (FFCT/FCT/UNL)

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Summary references:
- Neuroscienc 139:1069-1081.
- Krasnova IN, Ladedh BMW and Cadet JL (2005) Amphetamine induces apoptosis of medium spiny striatal projection neurons via the mitochondria-dependent

Website: Not applicable

Published reference(s):