

ORAL 3 [ID#7]

Neurotoxic Effects of Mephedrone, a Synthetic Derivative of Cathinone, Against Embryonic Neural Stem/Progenitor Cells

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OBJECTIVE: Mephedrone (meph, drone, bubbles) is a synthetic derivative of cathinone, the natural psychostimulant alkaloid found in the plant Khat. In recent years, the abuse of mephedrone has increased among adolescents and young adults in many countries. This study aimed to investigate the in vitro and in vivo neurotoxicity of mephedrone.

METHODS: Neural stem/progenitor cells derived from embryonic rats were incubated for 24 h in the presence of mephedrone and the cell viability was determined using the thiazolyl blue tetrazolium bromide assay and propidium iodide staining. For in vivo study, the pregnant mice received mephedrone during gestation (50 mg/kg, sc) and the hippocampus tissue of delivered pups were subjected to immunohistochemistry, real-time PCR, and TUNEL assay to evaluate proliferation and apoptosis.

RESULTS: In the cell culture condition, mephedrone significantly decreased the viability of neural stem/progenitor cells. In the hippocampus tissue of delivered pups, a significant inhibition of cell proliferation and an increase of apoptosis was observed. This effect was associated with decreased expression of the anti-apoptotic Bcl-2 gene and increased expression of the pro-apoptotic Bax gene. In addition, mephedrone caused an impairment of learning and memory in offspring born from litters received this compound.

CONCLUSION: These findings suggest that mephedrone induces cytotoxic effects on neural stem/progenitor cells and use of this compound during the gestational period may impair development of fetal nervous system.