Role of age and caffeine consumption in MDMA-induced neuroinflammation and neurotoxicity in mice

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Preclinical studies in mice have reported that 3,4 methylenedioxymethamphetamine (MDMA, 'ecstasy'), an amphetamine-related drug largely consumed by adolescent and young adults, has the ability to induce neuroinflammation and neurotoxicity in substantia nigra *pars compacta* (SNc) and in caudate-putamen (CPu). On the basis that the use of amphetamine-related drugs is often combined with beverages containing a high quantity of caffeine, we investigated the effect of the combined administration of MDMA+caffeine on neuroinflammatory and neurotoxic processes, in adolescent and adult mice. Moreover, as clinical reports suggest that amphetamine-related drugs contribute to Parkinson's disease (PD), we evaluated whether consumption of MDMA during adolescence might influence the neuroinflammatory and neurotoxic effects of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), a toxin known to induce PD.
Adolescent and adult mice were treated with MDMA either acutely or chronically, alone or in combination with caffeine. MPTP was administered in adult mice treated during adolescence with MDMA.
In CPu of adolescent mice, caffeine potentiated MDMA-induced GFAP (astroglia), IL-1β, TNF-Î±, and TH (dopamine neuron degeneration), whereas in CPu of adult mice, caffeine potentiated MDMA-induced GFAP, IL-1β, TNF-Î± and CD11b (microglia). Moreover, in mice that were chronically treated with MDMA, administration of MPTP induced an increase in GFAP and CD11b levels and decrease TH-positive neurons in both CPu and SNc. The results demonstrate that the utilization of caffeine in association with MDMA during adolescence may worsen the neuroinflammation and the neurotoxicity elicited by MDMA and that chronic administration of MDMA during adolescence exacerbates both the neuroinflammation and the neurotoxicity caused by MPTP.