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## 3,4-Methylenedioxypropylamphetamine (MDPV), a major bath salt drug, reduces resting state functional connectivity in rat brain

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Synthetic cathinones represent an emergent hazard to public health. These are marketed on the streets as 'bath salts', 'plant food' or 'legal highs'. Bath salts are potent stimulant and hallucinogenic drugs, and their abuse has the potential to impair mental health. The various chemical constituents of bath salts share molecular features, biochemical actions, and behavioral effects with a range of other illegal stimulants such as cocaine, methamphetamine and methylenedioxymethamphetamine (MDMA, or 'Ecstasy'). Among the bath salts, 3,4-methylenedioxypropylamphetamine (MDPV) has been reported to exert powerful cocaine-like effects in rats (Baumann et al., *Neuropsychopharmacology*, 2012). MDPV produces strong craving and euphoria within a few minutes of intake that may last up to 4-5 hrs, or more. Importantly, MDPV consumption leads to a strong crash beginning around 6-8 hrs with varying degree of severity in terms of the negative affective outcomes. During this time, users experience hallucinations, excited delirium, severe depression, anxiety and panic attacks, and in many cases violent aggression and suicidal thoughts that may last hours, weeks, and even months. Despite the growing number of studies reporting the stimulant and reinforcing actions of bath salts there is still a knowledge gap with regard to their sites of action within the CNS and their effects on functional connectivity between brain regions. The present study was designed to investigate the dose dependent pharmacological actions of MDPV (in mg kg<sup>-1</sup>: 0.0, 0.3, 0.6 1.0, 3.0, and 6.0, ip) on BOLD activation across a number of corticostriatal, mesolimbic, frontal cortical and limbic subcortical circuits. Rats were imaged at 4.7T at the Advanced Magnetic Resonance Imaging and Spectroscopy (AMRIS) facility of the University of Florida. Analysis of intrinsic rsFC at 1 hr post-MDPV administration (doses in mg kg<sup>-1</sup>: 0, 0.3, 1, 3; n = 7-8 per dose) showed a dose-dependent reduction in rsFC between reward sites and memory regions. At the highest dose tested, however, we found once again that there is a significant increase in rsFC between frontal cortical areas and regions of the amygdala. The loss of synchronous BOLD activity between hippocampal and other memory regions along with greater BOLD synchrony between amygdala and prefrontal cortical sites could underlie part of the negative affective states elicited by binge consumption, especially at high dose. Similar functional connectivity changes have been reported in schizophrenia and have been linked with severity of cognitive dysfunction, hallucinations and negative affective states. This might represent an important signature of MDPV's mechanism of action in the CNS.

### Biography

Marcelo Febo is Assistant Professor of Psychiatry and Program Director of Translational Research Imaging at the University of Florida McKnight Brain Institute. His research laboratory uses MRI in mouse and rat models of neuropsychiatric and neurological disease. Magnetic resonance imaging studies are carried out at high fields to examine both functional and structural changes with chronic drug exposure. His main interests in the field of addiction research include the neural and behavioral consequences of chronic drug exposure on maternal-offspring interactions and social neural circuits. He also investigates the neural actions of the neuropeptides oxytocin and vasopressin in modulating social behavior and fear.

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