Acute behavioral and molecular effects of the cathinones MDPV and α-PVP in the mouse brain

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MDPV and α-PVP are the most popular cathinones available in the clandestine market. Pre-clinical studies indicate that MDPV and α-PVP induce psychomotor stimulation, affect thermoregulation and promote reinforcing properties in rodents. However, a direct comparative analysis on the effects caused by MDPV and α-PVP on behavior and neuronal activation in rodents is still lacking. Behavioral analyses revealed that both MDPV and α-PVP alter spontaneous and stimulated motor responses, with MDPV showing a greater psychomotor effect than α-PVP, in agreement with its higher potency to inhibit the dopamine transporter. Notably, MDPV was more effective than □-PVP in facilitating spontaneous locomotion, displaying a biphasic effect in contrast to the monophasically-stimulated locomotion induced by □-PVP. We also decided to investigate neuronal activation via the analysis of immediate early genes (IEGs) such as Arc/Arg3.1 and c-Fos. We also found a different modulation of these genes (IEGs) in the frontal lobe, striatum and hippocampus, indicating that MDPV and α-PVP cause changes in brain homeostasis following a specific regional and temporal pattern. In fact, in striatum and frontal lobe, both cathinones up-regulated IEGs expression 30 min after the injection but MDPV-induced increase in Arc/Arg3.1 and c-Fos lasted longer than □-PVP. Notably, a different situation was observed in the hippocampus, where MDPV significantly up-regulates Arc/Arg3.1 and c-Fos mRNA levels, whereas □-PVP is ineffective. These data represent the first evidence that MDPV and □-PVP alter neuronal activation after a single exposure and may contribute to explain, at least in part, their toxicity. Also, these findings suggest that a single exposure to MDPV or □-PVP alters baseline neuronal activity, an effect that may represent an early sign of altered homeostasis and that could be used to differentiate between these cathinones with different chemical structures as well as different pharmacodynamic properties.