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3,4-Methylenedioxypyrovalerone (MDPV), a major bath salt drug, reduces functional connectivity in rat brain.

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Reports: Miami 'zombie' attacker may have been using 'bath salts'

The Drug That Never Lets Go

By Jonny Marder
Timeline of Bath Salt Effects on Behavior

- **Pleasure**
- **Empathy**
- **Sociable**
- **Crash:** Depressed mood, Anxiety/panic, Delirium/Paranoia, Hallucinations, Suicidal ideation
- **Aggressive behavior**

Abnormal behavioral pattern may continue

De Felice et al, Life Sciences, 2014
EXPERIMENTAL DESIGN

- 30 rats imaged at 4.7 Tesla under a combination of medetomidine/isoflurane anesthesia (0.5%).
- MDPV doses: 0, 0.3, 1.0, 3.0 mg/kg i.p. (n = 7-8 per dose group)
  - Doses are shown to increases in vivo striatal dopamine levels and increase locomotor activity and stereotypic behaviors (Baumann et al Neuropsychopharmacology, 2012; Marusich et al Neuropharmacology, 2014).
  - Doses have been shown to potently reduce intracranial self stimulation thresholds (ICSS thresholds). These are rewarding and show potential for abuse. (Bonano et al Psychopharmacology, 2013)
- Higher doses elicit prolonged anhedonia like actions lasting over 24 hrs (Merluzzi et al Developmental Psychobiology 2014), similar to what is reported in humans.
- Resting state fMRI datasets collected 1 hr following administration:
  - Images processed for seed based fMRI using various regions to examine functional correlated regions of the brain.
  - Model free independent component analysis was also used here to explore changes in network level changes in activity.
  - Behavioral tests were also carried out to confirm the actions of MDPV.
A. Saline treated

Component 1: Retrosplenial cortex/sensory-motor regions
Component 2: Anterior cingulate/insular cortex/striatum
Component 3: Dorsal hippocampus
Component 5: Prefrontal cortex/motor cortex/ventral striatum
Component 7: Anterior cingulate/dorsal cortex of inferior colliculus
Component 10: Cingulate/motor/somatosensory cortex
Component 11: Cingulate/retrosplenium/motor/sensory

B. MDPV 0.3 mg kg⁻¹

Component 1: Motor/Somatosensory cortex
Component 3: Anterior cingulate/2nd cerebellar lobule/PAG
Component 8: Cingulate/motor/sensory cortex
Component 12: Prelimbic/orbital areas
Component 13: Retrosplenial cortex/sensory-motor Regions
Component 14: dorsal cortex of inferior colliculus
Component 15: Retrosplenial cortex/visual cortex/sensory-motor regions
B. MDPV 1.0 mg kg\(^{-1}\)
Component 1: Disrupted
Component 2: visual cortex
Component 3: Disrupted
Component 4: Disrupted
Component 5: visual cortex
Component 7: Pontine nuclei
Component 14: Disrupted

B. MDPV 3.0 mg kg\(^{-1}\)
Component 1: Somatosensory trunk region
Component 2: Disrupted
Component 4: Brainstem
Component 5: Disrupted
Component 6: Disrupted
Component 8: Pontine nuclei
Component 11: VPL thalamus/somatosensory BF cortex
SUMMARY

- Low dose MDPV causes a slight increase in functional connectivity, particularly between striatal and prefrontal areas.
- High doses of MDPV (above 1mg kg⁻¹, i.p.) cause a severe reduction in functional connectivity.
- At the highest doses tested here (3 mg kg⁻¹, i.p.) an interesting pattern emerges in which there is an increase in connectivity between regions of the prefrontal cortex and the amygdala. These animals show also very prolonged and potent stimulant actions.
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