

Binge-like Acquisition of 3,4-methylenedioxypyrovalerone (MDPV) Self-administration Devalues Wheel Activity and Predicts Higher Subsequent Drug Intake in Rats.

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Supplemental Rationale, Results and Discussion

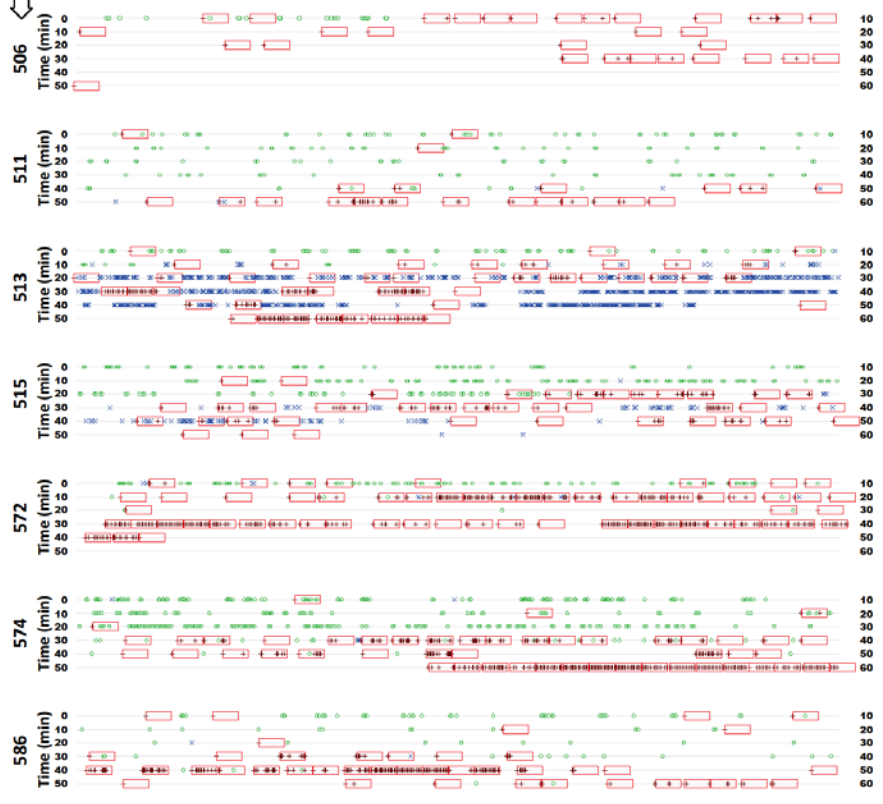
Individual Full-Resolution Response Records of Lever-Presses and Wheel Activity – Behavioral Microstructure of the “Binge” Session

Analysis of the infusion rate and wheel activity by 5-min bin (**Figure 4**) further elucidated the within-individual behavior depicted by session (**Figure 2**) which communicates a far different picture than provided by the group average data (**Figure 1**). Nevertheless the *drug seeking behavior*, i.e., pressing the drug-associated lever, was still potentially underestimated because of the imposed time-out period (20 seconds) after each infusion. These responses were recorded and as can be seen in the plots of all within-session behavioral events (drug-associated and inactive lever presses, *full* rotations of the wheel, and infusions) as a function of time within the session (**Figure 6**), lever-presses of the drug-associated lever continued at a high rate through the timeout intervals for 12 of the 13 binge-like acquisition pattern individuals (Unlocked-wheel rat #s 511, 513, 515, 572, 574 and 586; Locked-wheel rat #s 501, 507, 509, 510, 512, 514). Such intervals of continual responding, uninterrupted through the 20-second timeout, resulted in a series of infusions delivered at the maximum infusion rate. There were also some intervals in which the intrusion of *inactive*-lever presses and wheel rotations were observed between infusions as infusion rate accelerated; thus, wheel activity *per se* was not entirely prevented by drug taking. This analysis reinforces the observation that summary measures collapsed/averaged across individuals or across sessions, and *even across 5-min sampling intervals within individual*, can underestimate the intensity of behavior shaped by MDPV self-administration.

Finally, it is critical to note that inactive lever presses and wheel turns were observed to occur between MDPV infusions, including during the timeout intervals. Thus, although MDPV self-administration is associated with stereotypies, and drug-associated lever pressing could *possibly* be due to involuntary stereotypy, it was clear that during these binge-like sessions animals could still move to other locations within the operant chamber (e.g., the wheel on the wall opposite the drug-associated lever) and therefore could readily break away from drug-associated lever pressing and engage in alternate behaviors.

Event: ← 20 sec → = Infusion + Timeout + = Drug-Lever Press X = Inactive-Lever Press O = Wheel Turn

UNLOCKED WHEEL



LOCKED WHEEL

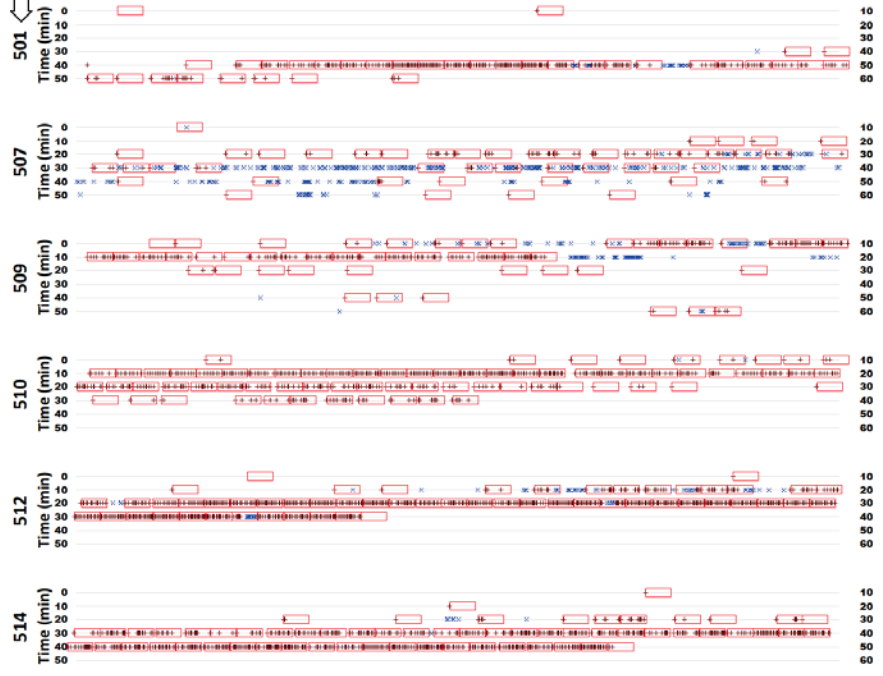


Figure 6: Microstructure of behavior during binge-like acquisition: Each event recorded during the session (+ = drug-paired-lever press; X = inactive-lever press; O = full rotation of the wheel; □ = MDPV infusion and timeout interval) is plotted as a function of time from the start of the session (in centiseconds resolution) for representative rats that exhibited a Binge-like acquisition pattern. **[See Below for a Full Resolution Version of the Figure]**

Event  = Infusion + Timeout  = Wheel Turn  = Drug-Lever Press  = Inactive-Lever Press

