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Evidence of Genetically-Driven Latent Factors in Longitudinal Oxycodone Self-Administration Data From the Hybrid Rat Diversity Panel

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Longitudinal rodent models of drug self-administration are often used to demonstrate the acquisition and escalation of drug seeking behaviors. Typically, rodents are presented with an active lever linked to the delivery of a drug and an inactive lever. The number of active and inactive lever presses and the resulting number of doses delivered per day are tracked over several days. We used this model to examine genetic influences on oxycodone self-administration in 13 inbred rat strains during acquisition and escalation periods. The full paradigm included 60 observations per rat (3 outcomes per day for 20 days). We used factor analysis to identify 11 interpretable latent factors to summarize self-administration behaviors, e.g., summary of number of correct lever presses across days 2 through 5 of acquisition (early correct). Broad sense genetic heritability within treatment group for individual factors ranged from 0.15 to 0.63. Eight of the 11 latent factors demonstrated a significant treatment effect, i.e., oxycodone vs. saline. Six of the 8 latent factors with a treatment effect had a significant three-way interaction between treatment, sex, and strain demonstrating that both sex and genetics can modify/alter oxycodone self-administration behaviors. By combining individual observations into meaningful latent factors, we can dramatically increase the power of our study by reducing our multiple testing burden, we can retain rats with a few missing observations, and we can increase interpretability of our findings. Finally, we validated several summary measures typically used with similar paradigms using a data-driven, unsupervised approach. Supported by NIDA (U01DA051937).