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Genetic Evidence Supports a Relationship Between Locomotor Activity in a Novel Environment in Rodents a Human Externalizing Behavior

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Background, Rationale/significance, hypothesis: The locomotor response to a novel environment is widely studied in mice and rats. While the topic is not without controversy, studies of locomotor behavior have often argued that this trait is related to the susceptibility to substance use disorder-like behaviors, and numerous comparisons between locomotor behavior and human externalizing have been made. Using recently available genome wide association study (GWAS) data from almost 10,000 outbred rats and the results of a genome structural equation modeling study (effective $n \sim 1,500,000$) we have empirically evaluated the genetic relationship between these two traits.

Results: We performed network colocalization (NetColoc) using sets of genes identified by the two GWAS. Although there was only modest overlap between the gene lists themselves, NetColoc revealed highly significant overlap between the networks implicated by the two sets of genes. We used these data to highlight shared and unique subnetworks for both rats and humans.

Discussion: These data demonstrate, for the first time, that these two phenotypes probe common biological substrates and contribute to the ongoing quest for techniques capable of integrating polygenic signals across multiple species. Future studies will explore additional phenotypes that can be measured in model organisms and are relevant to substance use disorders.