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Cocaine Preference in the Drosophila melanogaster Genetic Reference Panel

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Studies on the genetic basis of susceptibility to cocaine addiction in human populations are challenging due to limited sample sizes, heterogeneity of genetic backgrounds, and environmental variability. Drosophila present a powerful model system for investigation into the genetic underpinnings of cocaine addiction, using preference for cocaine as a proxy for addiction behavior. Utilizing the Microplate Feeder Assay (MFA), we quantified cocaine preference for over 80,000 flies across 450+ distinct genetic backgrounds of the Drosophila melanogaster Genetic Reference Panel (DGRP). We provided individual flies with a choice between a control food and food supplemented with cocaine. The consumption of each solution was quantified for each individual fly using a plate reader following a 22-hour exposure. We found significant, naturally occurring genetic variation for cocaine preference across these DGRP lines with significant sexual dimorphism, where male flies on average exhibit higher cocaine preference than female flies of the same line. Estimates of broad sense heritability of consumption were calculated using individual level data, as well as using DGRP line means, and were found to be $H^2 = 0.24$ and $H^2 = 0.98$, respectively. Six genetic lines representative of both high cocaine preference and mean cocaine preference were selected for single-nuclei multiomics investigation. These data will facilitate future genome-wide association analyses and describe the transcriptomic and conformational changes specific to different cocaine preference predispositions. Our observations that innate cocaine preference is dependent on genetic background and sex will likely also apply to genetic risk susceptibility for cocaine addiction in human populations.