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Variation in Mushroom Body Morphology in Cocaine Preferring *Drosophila* Genetic Reference Panel Lines

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Previous studies revealed natural genetic variation in cocaine consumption and preference among the wild-derived, inbred lines of the *Drosophila* Genetic Reference Panel and implicated the mushroom bodies, brain structures that mediate experience-dependent behavior (Highfill et al., *PLoS Genet.* (2019) 15, e1007834). Previous studies also showed correlations between variation in mushroom body structure and aggression (Zwarts et al., *Nat. Commun.* (2015) 6, 10115). To assess whether variation in mushroom body morphology is correlated with variation in cocaine preference, we selected DGRP lines in which at least one sex showed preference for a cocaine-supplemented sucrose solution and control lines with mean aversion scores for cocaine preference. We dissected brains and stained mushroom bodies from males and females separately with an anti-fasciclin-II antibody. We quantified morphological measurements of lengths and thicknesses of the alpha and beta lobes by three-dimensional confocal microscopy. We also observed the absence of lobes, bilateral asymmetry, and anatomical abnormalities. Our initial studies on a small set of six lines, three cocaine-preferring lines and three lines with mean aversion scores, showed variation in mushroom body morphology and suggested a correlation of cocaine preference with alpha lobe structure. To consolidate these observations with statistical significance, we will expand this initial study to a larger sample of 48 lines. Based on evolutionary conservation of fundamental biological processes, correlations between variation in mushroom body morphology and cocaine preference in the fly brain raise the possibility that subtle variations in neural circuitry in the human brain could contribute to risk for cocaine use disorder.