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Gene X Exposome for Impulsivity

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Impulsivity is affected by the interplay of genetic and non-genetic (exposome) risk factors; however, its underlying mechanism remains poorly understood. We found that social context at the time of task performance interacts with dopamine signaling for impulsivity in Drosophila. To delineate the cellular and molecular mechanism, we conducted unbiased genetic screens and found fifteen novel impulsivity loci that include the genes coding for synaptic adhesion molecule Kekkon 5, cell adhesion molecule alpha-Integrin, neuronal calcium sensor Frequinin1 (NCS ortholog), multifunctional mitochondria enzyme Scully (HSD17B10 ortholog) and transketolase (associated with Wernicke-Korsakoff syndrome). All these loci contribute to impulsivity only in the presence of the heterozygous mutation in dopamine transporter as well as in the presence of same sex peers. The functional neural site of Kekkon 5 is the mushroom body alpha/beta neurons while that of Scully is the mushroom body gamma neurons. The mushroom body neurons are highly innervated by dopamine neuronal axons and have all D1 and D2 dopamine receptors. We are currently investigating the link between dopamine signaling and the newly identified impulsivity molecules, and additional exposome risk factors contributing to impulsivity. Our study underscores the impact of gene x exposome interaction on task performance and provides a unique opportunity to uncover the mechanism for the gene x exposome influence on impulsivity.