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Novel genetic loci interacting with social environment for dysfunctional inhibitory control

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Inhibitory control is a core executive function for goal-directed behavior and anomalous inhibitory control is associated with drug use and addiction. Inhibitory capacity is not uniform in all individuals or circumstances but is affected by genetic and environmental interplay; however, its underlying mechanism remains poorly understood. We found that social context interacts with dopamine activity to impact inhibitory control in *Drosophila*. With a novel behavioral assay, we found that the flies with enhanced dopamine neurotransmission lost inhibition and exhibited impulsive movements only in the presence of peers. The social context-sensitive impulsivity requires the mushroom body D1 dopamine receptor and cAMP signaling. Strikingly, mushroom body activation is sufficient to provoke impulsivity without dopamine input nor social context. To delineate the cellular and molecular mechanisms, we conducted unbiased genetic screens and found several loci interacting with dopamine signaling for dysfunctional inhibitory control. One of the loci encodes the synaptic adhesion molecule Kekkon 5 whose expression is abundant in the mushroom body alpha/beta neurons. Consistently, the neural site of the kekkon5 and fumin genetic interaction is mapped to the mushroom body alpha/beta neurons and we are currently exploring the link between D1 signaling and Kekkon 5. Taken together, our study underscores the impact of social environment in task performance that is largely overlooked in human subjects research and rodent models, and further provides a unique opportunity for mechanistic study of social and genetic influence on inhibitory control.