

Genetic and social factors critical for inhibitory control

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The ability to suppress inappropriate behavior is a fundamental feature of executive function supporting flexible and goal-oriented behaviors. This inhibitory control is known as response inhibition and impaired response inhibition causes impulsivity or compulsivity underlying drug abuse, addiction and relapse. We identified that the fruit fly *Drosophila* displays response inhibition, which is the first demonstration in non-mammalian species. A go/no-go test is typically used to measure response inhibition in human subjects and requires subjects to produce a motor response when cued to do so (go) or otherwise withhold it (no-go). To study response inhibition in *Drosophila*, we developed a fly version of the go/no-go test and found dopamine as an important neuromodulator for inhibitory control. When subjected to a go/no-go test, the *fmn* mutants lacking dopamine transporter initially withhold movement but, within a minute, exhibit loss of inhibitory control. Notably, this maladaptive behavior is sensitive to social context, offering a useful system to study the mechanism by which genetic, social and environmental factors impinge on response inhibition and impulsivity. We conducted genetic interaction study and found the D1 receptor-mediated cAMP signal pathway as a key cellular mechanism underlying the social context-sensitive impulsivity. Anomalous response inhibition is associated not only with addiction but also with autism, ADHD and PTSD but its underlying cellular and molecular mechanisms are largely unknown. Our innovative study in a well-established model organism is likely to fill the knowledge gap.