Regulation of Dopamine Signaling in the Modulation of Locomotion

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Although genes that encode dopamine receptors and other proteins involved in dopamine biosynthesis, uptake, and vesicle loading are known, we lack a clear understanding of how dopaminergic signaling is regulated. Genetic studies of the basal slowing response, a dopamine-mediated behavior of C. elegans, might elucidate mechanisms that regulate dopaminergic signaling.

When well-fed hermaphrodites encounter a bacterial lawn, they slow their locomotion by approximately 30%. This behavior is called the basal slowing response and requires dopaminergic signaling. However, if animals are food-deprived for 30 minutes, they slow their locomotion by about 70% upon entry into a bacterial lawn. Dopamine plays a minor role in execution of this behavior, called the enhanced slowing response, suggesting that food-deprivation might suppress dopaminergic signaling and promote the use of other neurotransmitters to mediate locomotory slowing. We hope to understand how sensory stimulation causes dopamine release and how dopaminergic signaling is regulated.

Screens for altered basal slowing responses might identify novel genes involved in processes such as sensory transduction; dopamine vesicle loading, priming, and fusion; and regulation of dopamine receptors or their downstream effectors. However, screens for animals with defects in basal slowing behavior are difficult because of the small magnitude of the response. For this reason, we first screened for mutants that exhibit an increased basal slowing response. We mutagenized cat-2 deletion mutants carrying cat-2 in an extrachromosomal array. This cat-2 mutant lacks the tyrosine hydroxylase needed for biosynthesis of dopamine and is defective in basal slowing behavior; however, the transgene rescues basal slowing behavior. Since this array is inherited by a fraction of the progeny, we can confirm that the increased basal slowing of isolates depends on cat-2 and endogenous dopamine. We are currently characterizing an isolate with a cat-2-dependent increased basal slowing response.

In the future, we will perform screens for animals with defects in basal slowing by mutagenizing strains with increased basal slowing responses. We will characterize mutants identified in these screens using in vivo electrophysiological recordings of dopamine-secreting neurons and dopamine-responsive cells.

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