

Characterization of a Novel *Drosophila* SERT Mutant: Insights on the Contribution of the Serotonin Neural System to Behaviors

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A better comprehension on how different molecular components of the serotonergic system contribute to the adequate regulation of behaviors in animals is essential in the interpretation on how they are involved in neuropsychiatric and pathological disorders. It is possible to study these components in "simpler" animal models including the fly *Drosophila melanogaster*, given that most of the components of the serotonergic system are conserved between vertebrates and invertebrates. Here we decided to advance our understanding on how the serotonin plasma membrane transporter (SERT) contributes to serotonergic neurotransmission and behaviors in *Drosophila*. In doing this, we characterized for the first time a mutant for *Drosophila* SERT (dSERT) and additionally used a highly selective serotonin-releasing drug, 4-methylthioamphetamine (4-MTA), whose mechanism of action involves the SERT protein. Our results show that dSERT mutant animals exhibit an increased survival rate in stress conditions, increased basal motor behavior, and decreased levels in an anxiety-related parameter, centrophobism. We also show that

4-MTA increases the negative chemotaxis toward a strong aversive odorant, benzaldehyde. Our neurochemical data suggest that this effect is mediated by dSERT and depends on the 4-MTA-increased release of serotonin in the fly brain. Our in silico data support the idea that these effects are explained by specific interactions between 4-MTA and dSERT. In sum, our neurochemical, in silico, and behavioral analyses demonstrate the critical importance of the serotonergic system and particularly dSERT functioning in modulating several behaviors in *Drosophila*. © 2017 American Chemical Society.

amine release

centrophobism

Drosophila

motor behavior

olfaction

SERT

4 methylthioamphetamine

amphetamine derivative

serotonin

serotonin transporter

unclassified drug

Drosophila protein

serotonin

serotonin receptor affecting agent

serotonin transporter

SerT protein, *Drosophila*

animal experiment

animal tissue

Article

brain tissue

chemotaxis

controlled study

Drosophila

locomotion

male

neurotransmission

nonhuman

priority journal

serotonin release

serotonergic system

survival rate

animal

animal behavior

brain

Drosophila melanogaster

drug effect

genetics

metabolism

mutation

Animals

Behavior, Animal

Brain

Drosophila melanogaster

Drosophila Proteins

Mutation

Serotonin

Serotonin Agents

Serotonin Plasma Membrane Transport Proteins