Serotonin and FLP-1 Neuropeptide Signaling Mediate the Enhanced Slowing Response

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Food-deprived *C. elegans* slow their locomotion upon encountering bacteria more than do well-fed animals. This behavior, called the enhanced slowing response, is partly dependent on serotonin (5-HT). Animals mutant for the 5-HT reuptake transporter gene *mod-5* slow even more than wild-type animals (the hyperenhanced slowing response), presumably because 5-HT signaling is potentiated. *mod-5* mutants are also hypersensitive to immobilization by exogenous 5-HT. To identify additional genes involved in 5-HT signaling and possibly in the enhanced slowing response, we screened for suppressors of the 5-HT hypersensitivity of *mod-5* animals. We also used a candidate-gene approach, testing the 5-HT resistance of strains containing deletions in metabotropic 5-HT receptor-like genes. We screened 105,000 genomes for suppressors of the 5-HT hypersensitivity of *mod-5* mutants. We isolated 26 mutants, which define at least eight genes. Nineteen of these mutants also suppress the hyperenhanced slowing response of *mod-5* animals. We identified alleles of two genes known to suppress the 5-HT hypersensitivity and the hyperenhanced slowing response of *mod-5* mutants: *goa-1*, which encodes an alpha subunit of a G-protein, and *mod-1*, which encodes a 5-HT-gated Cl- channel. We also identified alleles of *eat-16*, which encodes a Regulator of G protein Signaling (RGS) protein; *abts-1*, a bicarbonate transporter gene; and *flp-1*, a neuropeptide gene. Using a candidate-gene approach, we found that two deletion alleles of the gene ser-4 confer 5-HT resistance and defects in the enhanced slowing response. *ser-4* encodes a metabotropic 5-HT receptor (Olde and McCombie, *J. Mol. Neurosci.*, 1997). Like *goa-1* and *mod-1* mutations, *eat-16*, *flp-1* and *ser-4* mutations suppress the hyperenhanced slowing response of *mod-5* animals. Thus, these genes likely act downstream of or in parallel to one or more 5-HT synapse(s) that mediate(s) the enhanced slowing response. We found that the MOD-1 and SER-4 5-HT receptors act in parallel in the enhanced slowing response. We are currently testing genetic interactions with *flp-1* to determine how neuropeptide signaling relates to these two 5-HT signaling pathways. In addition, we are determining where these genes are expressed to identify the neural circuit(s) involved in the enhanced slowing response.

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