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SEMINAR

DOPAMINE REGULATION OF THE RAS HOMOLOG ENRICHED IN STRIATUM

Laura Harrison, Ph.D.
Assistant Professor/Research, Department of Psychology
University of New Orleans
New Orleans Louisiana

Rhes (the *R*as *H*omolog *E*nriched in *S*triatum) is a small G protein that is highly expressed in brain regions receiving dopamine input, such as dorsal striatum, nucleus accumbens, and olfactory tubercle. This anatomical localization suggests that Rhes may be regulated by dopamine and involved in dopamine-mediated signaling. We have investigated dopaminergic regulation of *rhes* mRNA in adult and neonatal rats. In adults, *rhes* mRNA is decreased after removal of dopamine input to the striatum by either surgical denervation or pharmacological depletion, manipulations which result in profound dopamine receptor supersensitivity. The decrease in *rhes* mRNA occurs within 2 weeks of surgical denervation and lasts up to 7 months post-surgery, but is transient if animals are allowed to recover from pharmacological depletion. However, r*hes* mRNA is unchanged after chronic dopamine receptor antagonist treatment, which causes receptor up-regulation but not profound supersensitivity. Thus, changes in *rhes* mRNA expression are strictly correlated with receptor supersensitivity, perhaps as a result of continuous removal of dopaminergic input. Developmentally, *rhes* mRNA is detectable with *in situ* hybridization by day 4 and increases to adult levels between days 10 and 15. In addition to expression in striatum, high levels of mRNA are also detected developmentally in hippocampus, cerebellum, and several thalamic nuclei. A decrease in both protein and mRNA is detected in aged versus adult rats. Removal of dopamine input neonatally does not affect *rhes* mRNA expression in adulthood. Although the functions of Rhes are not yet known, its homology to AGS1/Dexras1 suggests that it may affect signaling through certain G protein-coupled receptors. Future studies will use *rhes*$^{-/-}$ mice to investigate the role of Rhes in striatal signaling.

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