

CIRCADIAN STUDIES OF NPY DEFICIENT AND NPY Y2 RECEPTOR DEFICIENT MICE. [S.Hastings](#); [J.McKeon](#); [M.Ward](#); [S.Soscia](#); [P.C.Molyneux](#); [M.E.Harrington*](#)

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Neuropeptide Y (NPY) plays a role in modulating photic and non-photoc entrainment of circadian rhythms. Much of the prior work on NPY was conducted using hamsters. Last year at this meeting we reported that NPY knockout (KO) mice showed increased free-running periods in constant dark (DD) and decreased phase shifts to light at CT16 (Soscia et al., 2002). We have now compared levels of light-induced Fos-immunoreactivity (ir) in the NPY KO mice relative to wildtype controls. Mice were anesthetized with Nembutal and perfused with 0.9% saline and 4% paraformaldehyde 1 hour after the start of a light pulse at CT16. Brain sections were processed for Fos-ir (antibody: Santa Cruz, 1:10,000) and immuno-stain was quantified using Scion Image software. NPY KO and wildtype controls showed similar levels of Fos-ir after light exposure (average for NPY KOs: 103% of controls). We have also studied Y2 receptor KO mice (from Patrik Ernfors, PhD, Karolinska Institutet), using both electrophysiological and behavioral studies. Y2 receptor KO mice did not show subjective day NPY-induced resetting of the rhythm of spontaneous firing rate measured from the SCN slice in vitro. Wheel-running rhythms were measured to examine light-mediated entrainment. Mice (Y2 KO and controls) were housed for 10 days under LD 12:12 and then placed in DD for 18 days, with a light pulse (15 min, 12 lux) delivered at CT16 on the eighth day. The Y2 receptor KO mice showed a larger percent of their total activity (17%) in the light period of the LD cycle as compared to the wildtype controls (7%). Strains did not differ in free-running period in DD. Preliminary results indicate a difference in the magnitude of phase shifts to the CT16 light pulse. Our studies allow further understanding of the role of NPY in modulating circadian rhythms, and help to highlight the specific roles of the Y2 receptor in this action of NPY.

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