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MEETING ABSTRACT

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Presynaptic NPY Y_2 receptors reduce GABAergic neurotransmission within the central extended amygdala

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Background: Neuropeptide Y (NPY) is an evolutionarily conserved neuropeptide that is widely expressed throughout the mammalian brain and modulates the function of brain circuits involved in feeding, learning and memory, and survival behaviors. NPY and NPY receptors are expressed throughout the central extended amygdala and pharmacological interventions of this network have demonstrated that NPY signaling has an important role in influencing affective behaviors including fear and anxiety. Thus, modulating NPY signaling within the central extended amygdala may have therapeutic potential in the treatment of anxiety disorders. We have found that the NPY Y_2 receptor is highly expressed in a projection between the medial subdivision of the central amygdala (CeM) and bed nucleus of the stria terminalis (BNST). Thus, we investigated how the Y_2 receptor modulates neurotransmission in this projection.
Methods: Spontaneous and evoked GABAergic neurotransmission was measured by performing whole-cell patch clamp recordings of neurons of the CeM and BNST in the presence and absence of the Y_2 agonist, $PYY_{3–36}$.
Results: In wild-type mice, selective activation of the Y_2 receptor using the Y_2 receptor agonist $PYY_{3–36}$ reduced the frequency but not amplitude of GABA-mediated spontaneous inhibitory postsynaptic currents (sIPSCs) in neurons of both the CeM and BNST. Whole-cell recordings of paired-pulse-evoked inhibitory postsynaptic currents in the BNST and CeM indicated that $PYY_{3–36}$ reduces the presynaptic release probability of GABA. We next explored how NPY signaling modulates GABAergic neurotransmission within the central extended amygdala by performing electrophysiological recordings in brain slices from NPY knockout and NPY Y_2 receptor knockout mice. Interestingly, the basal frequency of spontaneous inhibitory postsynaptic currents in the CeM was elevated in both NPY knockout and NPY Y_2 receptor knockout mice, however this was not observed in the BNST.
Discussion: Taken together, these results indicate that the NPY Y_2 receptor modulates GABAergic neurotransmission within the central extended amygdala and mice lacking key components of the NPY system exhibit alterations in basal inhibitory neurotransmission.
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