The effects of MC4R activation on behavioral activity in transgenic mice

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Background: Melanocortin receptors are a family of 5 classical GPCRs that activate the adenylyl cyclase pathway in cells leading to production of the secondary messenger cAMP. The melnocortin-4 receptor (MC4R) is abundantly expressed in the hypothalamus. The MC4R has been implicated in regulating various physiological processes, including energy homeostasis, cachexia, cardiovascular function, glucose and lipid homeostasis, reproduction, and sexual function. Drugs have been developed to treat eating conditions as well as sexual hypoactivity disorders, although the full role of melanocortin signaling in behavior is.

Objectives: The objective of this study was to characterize how an exogenous melanocortin affected grooming behavior and potential signaling pathways involved.

Methods: Wildtype mice were treated with the MC4R agonist bremelanotide and its impact on grooming behavior was studied. We administered i.p. bremelanotide at 0.01mg/kg, 0.1mg/kg, 1mg/kg and 10mg/kg or vehicle was administered, and grooming was recorded for 1 hour for blinded analysis. In situ hybridization was used to determine whether x- expressing neurons colocalize with the melanocortin receptor in the PVH and SON of the hypothalamus.

Results: Bremelanotide treatment induced an increase anogenital grooming and total time spent grooming in the 1mg/kg treatment group and the 10mg/kg treatment group. Vasopressin neurons were found to colocalize with the MC4R in the PVH and the SON.

Conclusion: Bremelanotide induces a dramatic increase in grooming behavior that correlates with dosage. This effect could be mediated through the MC4R expressed in vasopressin neurons of the PVH. Additional studies to test the receptor type and location that induces bremelanotide's grooming effects are needed. A future study will test the effects of the knocking out MC4Rs present on arginine vasopressin neurons on grooming and other behaviors.

