Drugs that stimulate oxytocin release promote social bonding in an animal model relevant to autism

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Background: Oxytocin (OT) enhances prosocial behavior in animal models, and intranasal OT enhances some aspects of social cognition in humans, suggesting that the oxytocin system may be a viable target for pharmacological therapies in autism spectrum disorder. However the therapeutic potential of oxytocin is limited by its poor penetration of the blood-brain-barrier. An alternative approach to modulating the OT system is to pharmacologically enhance endogenous OT release. Here we use social bonding in the monogamous prairie vole to assess the prosocial effects of drugs known to stimulate OT release. Social bonding in voles is a complex social cognitive process which can be efficiently assayed in the laboratory using a partner preference paradigm. The formation of a partner preference in female prairie voles is dependent on OT. We propose that the partner preference paradigm in prairie voles may have face, construct, and predictive validity for screening drugs to enhance social cognition in disorders such as autism. Alpha-melanocyte stimulating (alpha-MSH) hormone and serotonin (5-HT) act on the oxytocinergic neurons of hypothalamus to stimulate OT release. To target these systems, we administered Melanotan I (MTI) and Melanotan II (MTII), which act on melanocortin 3/4 receptors, and busprione (BUS), a 5-HT1a receptor agonist, to female prairie voles. We hypothesized that administration of these drugs prior to pairing with a male would accelerate partner preference formation. If our hypothesis is correct, then we predict that a similar pharmacological approach may be useful to enhance social cognition in humans and potentially ameliorate some of the social deficits associated with autism.

Objectives: To determine the effect of drugs known to stimulate OT release on social bonding in prairie voles.

Methods: Melanotan I (MTI; 1 and 10 mg/kg), Melanotan II (MTII; 1 and 10 mg/kg), buspirone (BUS; 8 and 30 mg/kg) or vehicle were administered peripherally to female ovariectomized prairie voles. The non-receptive animals were cohabitated with a male partner for a period of time shorter than that typically necessary to stimulate a partner preference. Following the cohabitation, the females were tested for social bonding using the partner preference paradigm. Time spent in side-by-side immobile contact with the partner or a novel stimulus animal was quantified.

Results: Females receiving the high dose of MTII and the low dose of BUS formed robust partner preferences. MTI did effect partner preference formation in this paradigm.

Discussion: Drugs that targeted both the melanocortin and the serotonin systems via receptors on OT neurons induced partner preference formation under conditions in which bonding does not typically occur. As the receptors targeted by both of these compounds reside on OT neurons, we suggest that the prosocial effects of these drugs may be due to stimulation of endogenous OT release. Thus, targeting these receptor systems provides a potential mechanism to stimulate the OT system, which may have therapeutic value for
enhancing social cognitive function in disorders such as autism, circumventing the limitation of peripheral OT administration.