

Abstract

Oxytocin has been proposed as a potential treatment approach in drug addiction, but little is known about the effects of oxytocin in translationally relevant models of addiction or the neurobiological substrates of the actions of oxytocin. This presentation highlights the ability of oxytocin to reduce drug taking and drug seeking in a rat model of methamphetamine (meth) addiction.

In the first set of experiments, we developed and applied a behavioral economics model of meth addiction to assess the effects of oxytocin on both meth demand and conditioned cue-induced reinstatement of meth seeking following a period of drug withdrawal. Systemic oxytocin treatment reduced both meth demand (determined by an increase in α , the downward acceleration of a demand curve) and reinstatement of cue-induced meth seeking. Notably, oxytocin had the highest efficacy to reduce reinstatement in those rats showing the highest motivation for meth.

A second set of experiments examined the central effects of oxytocin on meth demand and reinstatement. The effects of systemic oxytocin on meth demand were completely blocked by central infusion (icv) of an oxytocin receptor antagonist, while direct application of oxytocin in the nucleus accumbens (NAc) abolished the effects of oxytocin on both meth demand and reinstatement. Finally, oxytocin activity in the NAc was found to be necessary for enhanced meth demand, as central antagonism of oxytocin receptors in the NAc blocked the effects of systemic oxytocin.

Taken together, these results show a centrally mediated action of oxytocin in reducing demand for meth and cue-induced reinstatement of meth seeking. Future development of oxytocin-based pharmacotherapy may be beneficial for psychostimulant addiction.

References

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2. Zhou L, Sun WL, Young AB, Lee KH, McGinty JF, See RE (2014) Oxytocin reduces cocaine seeking and reverses chronic cocaine-induced changes in glutamate receptor function. *International Journal of Neuropsychopharmacology*; 18(1):1–11.
3. Cox BM, Young A, See RE, Reichel CM (2013) Sex differences in methamphetamine seeking in rats: Impact of oxytocin. *Psychoneuroendocrinology*; 38:2343–2353.

Speaker 2: Inga D Neumann, Germany

Title: Chronic effects of oxytocin: Are we ready for its therapeutic use?

Abstract

Due to its acute pro-social and anxiolytic properties, and the attenuation of stress responses the neuropeptide OXT has received substantial interest. We have recently shown that OXT promotes social preference behaviour and prevents social phobia induced by social defeat stress in rats and mice¹. Further, in a mouse paradigm for social fear conditioning², OXT specifically reversed social fear – an effect which was localized within the dorsolateral septum, where social fear was associated with reduced OXT receptor binding³.

In contrast to its acute effects, chronic central OXT infusion over 14 days using osmotic minipumps dose-dependently increased anxiety of male mice and reduced OXT receptor binding in the basolateral amygdala, nucleus raphe and dorsolateral

septum. At lower dose, continuous chronic infusion of OXT was able to prevent a variety of chronic stress-induced maladaptations. We are currently studying the consequences of chronic OXT on OXT receptor-coupled intracellular signaling pathways in males and females.

Although the acute effects point towards the therapeutic use of OXT for anxiety-related disorders including social phobia more detailed behavioral and molecular studies are needed to reveal chronic effects.

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References

1. Lukas M et al. (2011) *Neuropsychopharmacology* 36:2159–68
2. Toth I, et al. (2012) *Neuropsychopharmacology* 37:1433–43
3. Zoicas I et al. (2014) *Neuropsychopharmacology*. doi: 10.1038/npp.2014.156

Speaker 3: Youl-Ri Kim, Republic of Korea

Title: Oxytocin as a multidimensional pharmacotherapy in psychiatric disorders

Abstract

The core pathology of anorexia nervosa (AN) is associated with anomalies in systems related to fear and defense of appetite behavior. Anomalies in social and emotional development have been linked to oxytocin systems. In this session we will (1) review comprehensively the literatures about the possible link between oxytocin and AN, (2) present our findings of genetic and epigenetic variants of the OXTR gene, and of the impact of oxytocin on social processing and appetite in people with AN, and (3) talk about the potential of oxytocin as for AN a treatment via a reduction in the fear circuit.

Speaker 4: Junghee Lee, USA

Title: Oxytocin facilitation of social cognition skills training.

Abstract

Oxytocin (OT) can enhance the salience of social information. We evaluated whether this property of OT would enhance learning during social cognitive skills training exercises in individuals with schizophrenia. Subjects were 27 male schizophrenia outpatients who met DSM-IV-TR criteria for schizophrenia and were taking antipsychotic medications. We also evaluated potential indicators of OT effects in brain.

Methods: Subjects participated in a 6-week (12-session) course of Social Cognitive Skills Training (SCST) that focused on 3 areas: 1. Facial Affect Recognition; 2. Recognizing non-verbal gestures and vocal cues; 3. Empathy. Subjects were randomly assigned to receive either intranasal OT (40 IU) or placebo 30 minutes prior to each session. Hence, each session included both patients taking OT and placebo. We evaluated scores on social cognition measures; clinical symptoms; and neurocognition (MATRICS Consensus Cognitive Battery (MCCB)). Participants only received OT immediately prior to each training session; they did not receive OT between sessions or on the day of assessments. In a separate study we evaluated two potential biomarkers indicating OT's target engagement in brain: pupillary response to a facial identification task and EEG mu suppression during a biological motion task. For these studies patients received single intranasal doses of OT or placebo in randomized order one week apart.

Results: 13 patients were randomized to receive OT and 14 to placebo, and there were no significant demographic differences between the groups. On the social cognitive tests, subjects receiving OT demonstrated significantly greater improvements