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 efficiency 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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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 mice. Further, in a mouse paradigm for social fear conditioning, OXT specifically reversed social fear – an effect which was localized within the dorsolateral septum, where social fear was associated with reduced OXT receptor binding.

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 mal-adaptations. 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.

Supported by DFG.

References

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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...
The lecture comprises the following components: biomarkers, screening, treatment, and the biological basis of alcohol dependence. Concepts and definitions: The classification of alcoholism has undergone a series of changes over the decades. In 1977, WHO organized an expert conference and presented the concept of alcohol dependence and alcohol related disabilities. This concept of alcohol dependence influenced ICD-10 and DSM III and IV criteria. Biomarkers: State and trait markers (including endophenotypes) and their clinical significance will be discussed. Screening tests: Several tests will be introduced and their significance discussed. Treatment: Medication for alcohol dependence including psychotherapy, pharmacotherapy, and the role of self-help groups in recovery will be discussed. Inhibition of neuro-stem cell differentiation by ethanol will be discussed as a biological basis of alcohol dependence.

S24: Novel Therapies for Psychiatric Disorders: From Translation to Implementation

Chair: Michael Berk, Australia
Co-Chair: Tijen Uktan, Turkey

Speaker 1: Peter Kalivas, USA

Title: Glutamate Transport: A new bench to bedside mechanism for treating drug abuse

Abstract

Glutamate transmission in cortical synapses into the basal ganglia, in particular into the nucleus accumbens, are markedly altered by addictive drugs. A primary alteration seen after withdrawal from all addictive drugs in self-administration animal models of addiction is a reduction in the elimination of glutamate that is released from these synapses. Specifically, there is a reduction in the glial glutamate transporter EAAT2. As a result of reduced EAAT2 the fidelity of cortico-accumbens transmission is corrupted such that when an animal trained to associate a cue with drug delivery is shown that cue in the absence of drug, the cue is highly motivating to seek the drug. This level of motivation is associated with a number of transient changes in the cortico-accumbens synapses that collectively indicate that the synapses are transiently potentiated (t-SP). Importantly, the same self-administration protocol for a natural reward such as sucrose pellets does not alter EAAT2, nor is cue-induced sucrose seeking associated with t-SP. After a brief description of the cortico-accumbens neuropathology that appears to contribute to relapse in animal models of addiction, we will discuss the success we and others have had in inhibiting relapse in animal models by pharmacologically restoring EAAT2. In the preclinical literature, restoration of EAAT2 can be accomplished by repeated administration of a number of compounds, including N-acetylcysteine (NAC) and ceftriaxone. However, because NAC is orally active and has a long record of clinical use for acetaminophen overdose and as a mucolytic agent in cystic fibrosis, we and others have examined NAC in clinical trials for treating addiction and other neuropsychiatric diseases that are characterized in part by symptoms of intrusive thinking. Here, I will highlight recent trials with marijuana and cocaine addicts, as well as patients co-morbid for post-traumatic stress disorder (PTSD) and substance use disorder. In these studies, NAC was at least partly effective at reducing craving, relapse and/or criteria for a

Speaker: Toshikazu Saito, Japan

Abstract

The concept of addiction will be discussed in the context of alcohol-related disabilities. In this lecture, the focus of addiction will be alcohol dependence.