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Oxytocin

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Definition

Oxytocin (OT) is a nine amino-acid neuropeptide that is synthesized in magnocellular neurons in the paraventricular and supraoptic nuclei of the hypothalamus and stored in the posterior pituitary, from where it is released into the peripheral blood stream. In addition to being released from axonal terminals, there is also dendritic release into the extracellular space, resulting both in local action and its diffusion through the brain to reach distant targets, including the amygdala, hippocampus, striatum, suprachiasmatic nucleus, bed nucleus of stria terminalis, and brainstem (Meyer-Lindenberg et al. 2011). In addition to its hormonal actions in the uterus' contraction during birth and the let-down reflex during breastfeeding, investigations across species have shown that OT plays a key role in encoding information relevant to social interactions and is critically involved in the regulation of complex social cognition and behavior, including attachment, social recognition, social exploration, as well as anxiety and fear-related behaviors (Heinrichs et al. 2009).

Introduction

According to animal research demonstrating OT's evolutionary role in regulating social cognition and behavior, there has been rapidly growing interest in OT's role in human social interaction during the last decade and promising perspectives for the development of novel treatment approaches of mental disorders associated with social deficits (Meyer-Lindenberg et al. 2011).

Animal Studies

Numerous studies in rodents revealed OT's central role in several social behaviors. This ancient neuropeptide displays marked conservation in gene structure and expression, yet diversity in the genetic regulation of their receptors seems to underlie natural variation in social behavior both between and within species (Donaldson and Young 2008).

Behavioral Effects in Humans

The majority of studies published so far took an experimental approach and used placebo-controlled intranasal administration of OT in

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predominantly male samples. Initial studies provided evidence for social OT effects in terms of increased trust and attenuated endocrine, affective, and behavioral reactions to social stress (Heinrichs et al. 2003; Kosfeld et al. 2005). Another line of evidence revealed that OT promotes facial emotion recognition and visual attention to social cues (Shahrestani et al. 2013).

Neural Effects

Growing literature on the neural effects of OT given intranasally revealed modulatory effects in neural networks involved in social cognition and emotion processing. The most consistent finding in men is the suppression of amygdala responses to negative social stimuli. However, different effects have been demonstrated in a distributed network of brain regions involved in social and emotional processing, including sex-specific effects (Kanat et al. 2014).

Genetic Variation of the OT-Receptor

There is considerable genetic variation in the OT receptor that is presumably related to receptor affinity and thus OT-signaling in the brain. A number of association studies have revealed common variants in the OT receptor to clinical conditions associated with disturbed social cognition and behavior, such as autism spectrum disorder (ASD) (Kumsta and Heinrichs 2013). In addition, several studies have provided evidence for associations between common OXTR SNPs and general social phenotypes, such as individual differences in empathy, reward dependency, positive affect, and emotional deficits. Recent investigations demonstrate that the effects of OT administration vary depending on the OXTR genotype (Chen et al. 2015).

Therapeutic Potential

Because of OT's proposed role in attachment and social cognition, some studies explored OT's potential in the treatment of mental disorders with severe social deficits, such as ASD (Heinrichs et al. 2009; Meyer-Lindenberg et al. 2011). In sum, these studies provide initial evidence that single doses of OT promote social cognition and increase neural responding to social more than non-social stimuli (Domes et al. 2013).

Conclusion

Over the last 10 years, the evidence has accumulated of OT's crucial role in regulating human complex social cognition and behavior. Meta-analytic evidence so far revealed positive effects of exogenous administrations of OT on trust, emotion recognition, and a dampening effect on endocrine and amygdala responding to (aversive) social stimuli, as well as psychiatric symptoms related to social deficits. Individual differences, such as habitual social abilities and sex, likely modulate the effects observed so far and still have to be investigated. Finally, the therapeutic potential of interventions combining OT administration and behavior therapy has been demonstrated in pilot studies, but this also needs to be proven in large-scale randomized, controlled clinical trials.

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