

# EFFECTS OF OXYTOCIN IN HUMANS: IMPACT ON THE BASIC PSYCHOLOGICAL PROCESSES OF COGNITION, EMOTIONS AND BEHAVIOR. ROLE FOR THE AUTONOMIC FUNCTIONS

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**Abstract.** Emotional intelligence enables individuals to be more effective in their personal and social life. The neural structures that support emotional and social intelligence overlap with the structures involved in autonomic functions and decision-making, i.e. ventromedial prefrontal cortex, amygdala and insular regions. Oxytocin (OT) facilitates social bonding by enhancing cognitive control from prefrontal regions to amygdala in order to regulate emotionality. It inhibits excitatory flow from the amygdala to brainstem sites mediating fear response and reduces social anxiety that results in a greater willingness to trust and bond to other people. OT has empathogenic properties and its agonists may be a useful therapy in enhancing socially motivated learning and emotional empathy in disorders such as autism and schizophrenia. This neuropeptide may promote mother–infant attachment. OT levels are associated with interactive synchrony between parent and child and appear to play an important role in promoting responsive parental caregiving. Increased values of heart rate variability (HRV) are associated with positive emotions such as cheerfulness and tranquility. Heart rate variability is a reliable indicator of the psychological background, of approach-related motivation and hence of the autonomic nervous system balance.

**Key words:** oxytocin, prosocial behavior, anxiety, heart rate variability.

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## BACKGROUND

Emotional intelligence is a type of social intelligence that determines the capacity of a person for creating sustainable and flexible social relationships. The main features of emotional intelligence are the following: the ability to be aware of one's own emotions and to express them, to be aware of others' feelings and to establish interpersonal relationships, to manage and regulate emotions, to cope with the immediate situations and solve problems of a personal and interpersonal nature and to generate positive affect in order to be sufficiently self-

motivated to achieve personal goals (Salovey, P., Mayer, J.D., 1990). Emotional intelligence enables individuals to cope with daily demands and be more effective in their personal and social life (Mayer, J., Salovey, P., 1993). Emotional intelligence marks the intersection between two fundamental components of personality: the cognitive and the emotional systems. Together with cognitive intelligence, emotional and social intelligence form important components of general intelligence. One of the major differences between the two is that the former is thought to relate primarily to higher order mental processes like reasoning,

while the latter focuses more on perceiving, immediate processing and applying emotional and social content. Cognitive intelligence is more cortically based, while emotional and social intelligence involve the limbic system for immediate behavior suited for survival and adaptation (Bar-On, R., 2001: 82-97).

The neural systems that support emotional and social intelligence overlap with the structures subserving autonomic activation and decision-making, i.e. ventromedial prefrontal cortex (VM), amygdala and insular regions. Two of the most important emotional intelligence competencies – self-regard (accurate self-awareness) and assertiveness (self-expression) are affected by brain injury in this neural circuitry. Patients with lesions to the VM prefrontal cortex manifest some autonomic disbalance and tend to exercise poor judgment in decision-making, which is displayed in the disadvantageous choices they make in their personal lives and in the ways in which they relate with others. There are a number of alterations of emotional experience, social functioning (Bechara, A., Tranel, D., Damasio, A.R., 2000: 192-214) and the ability to effectively cope with daily demands in these patients. Furthermore, lesions to the amygdala or insular cortices, especially on the right side, also compromise the same functions.

The process of judgment and decision-making depends on systems involved in: memory, which is supported by high-order association cortices as well as the dorsolateral prefrontal cortex; emotions, which are mediated by subcortical limbic structures and feelings which are supported by limbic system as well as the insula, surrounding parietal cortices and the cingulate cortex. Therefore, damage to the systems that impact emotions, feelings or memory usually compromise the ability to make advantageous decisions (Bar-On, R., Fund, S., Handley, R., 2003). The VM prefrontal cortex links these systems together. To perform well and be successful in one's professional and personal life apparently requires the ability to make emotionally and socially intelligent decisions more than just having a high IQ. One of the factors determining the emotional intelligence and the psycho-

logical state of humans is oxytocin that is the subject of our review.

## OXYTOCIN RECEPTORS IN THE BRAIN STRUCTURES AND IN THE PERIPHERY TISSUES

Oxytocin (OT) is a neuropeptide that is produced in the structures of the hypothalamus. It has many central effects mediated by the receptors in the brain and peripheral effects on the target organs.

The OT receptors are widely distributed in brain regions implicated in cognition and emotion (Hein, G., Singer, T., 2008) as well as in several central autonomic nuclei, including the dorsal motor nucleus of the vagus, nucleus ambiguus and nucleus tractus solitarius (Higa, K.T., Mori, E., Viani, F.F., Morris, M., Michelini, L.C., 2002). OT may also impact the autonomic control through its influence on neural structures such as the amygdala – a structure expressing high-density OT receptors (Tribollet, E., Dubois-Dauphin, M., Dreifuss, J.J., Barberis C., Jard, S., 1992) and orchestrating complex autonomic functions (Davis, M., Whalen, P., 2001).

The amygdala is referred to as a neural hub because of its high degree of connectivity, which is critical for the flow and integration of information between regions (Pessoa, L., 2008). It is strongly connected with other brain regions involved in emotional processing such as the orbitofrontal cortex (OFC), the supra- and subgenual parts of the anterior cingulate cortex (ACC), the brainstem and the thalamus (Pessoa, L., 2008). Several studies have shown that modulating amygdala activity can shift neural output towards other brain regions within this network. For example, Kirsch et al. (Kirsch, P., Esslinger, C., Chen, Q., Mier, D., Lis, S., Siddhanti, S., Gruppe, H., Mattay, V.S., Gallhofer, B., Meyer-Lindenberg, A., 2005) established that OT reduces amygdala-brainstem coupling that is important for fear and arousal. Van Wingen et al. (van Wingen, G., Mattern, C., Verkes, R.J., Buitelaar, J., Fernández, G., 2010) showed that OFC-amygdala coupling was reduced

after testosterone administration. The OFC is involved in reward and hedonic processing (Kringelbach, M.L., Lehtonen, A., Squire, S., Harvey, A.G., Craske, M.G., Holliday, I.E., Green, A.L., Aziz, T.Z., Hansen, P.C., Cornelissen, P.L., Stein, A., 2008).

OT receptors have been identified in cardiac tissue (Jankowski, M., Danalache, B., Wang, D., Bhat, P., Hajjar, F., et al., 2004), allowing a direct site of action for this peptide to regulate cardiac function.

Less well appreciated is the production of OT in the body, namely in the gastrointestinal tract, heart, testes, uterus, corpus luteum, placenta and amnion. OT is also present in the kidney, pancreas, thymus and in adipocytes (Kiss, A., Mikkelsen, J.D., 2005).

When human subjects receive social stimuli, this causes reactions in the heart and the gut that may themselves contribute to OT plasma levels (Yu Q, Ji R, Gao X, Fu J, Guo W, Song X, Zhao X, Burnstock, G., Shi X, He C, Xiang, Z., 2011). Visceral signals are picked up by the afferent branches of the vagus nerve and other visceral afferents and are registered as emotional signals in the brain. The motor vagus may then respond with signals to the viscera. Moreover, both OT and vasopressin hormones are released in the brain following vagal stimulation (McEwen, B.B., 2004).

Expression of OT and its receptors in the brain and in the periphery is upregulated by high levels of estrogen in combination with progesterone withdrawal (Numan, M.; Insel, T.R., 2003).

#### EFFECTS OF OXYTOCIN ON INTEGRATIVE BRAIN FUNCTIONS AND ITS ROLE FOR THE PSYCHOLOGICAL HEALTH

The fundamental ability to form attachment is indispensable for human social relationships. Attachment security is characterized as the individuals' confidence to rely on attachment figures to achieve care, safety and protection and, when alone, to have access to internalized attachment relationships. Attachment insecurity contributes to a wide spectrum of mental disorders (Maunder, R.G., Hunter, J.J., 2001).

The intranasal application of OT enhances cooperation in response to social cues (Declerck, C.H., Boone, C., Kiyonari, T., 2010), facial emotion recognition (Marsh, A.A., Yu HH, Pine, D.S., Blair, R.J., 2009), eye gaze (Gamer, M., Zurowski, B., Büchel, C., 2010), trust (Baumgartner, T., Heinrichs, M., Vonlanthen, A., Fischbacher, U., Fehr, E., 2008) and attachment, but appears to reduce some aspects of cognitive functioning, such as recall performance (Heinrichs, M., Baumgartner, T., Kirschbaum, C., Ehlert, U., 2003) and memory storage (Bruins, J., Hijman, R., Van Ree, J.M., 1992). Other studies have demonstrated that OT enhances perception and processing of positive social cues (Unkelbach, C., Guastella, A.J., Forgas, J.P., 2008) and sensitivity to biological (but not non-biological) motion (Kéri, S., Benedek, G., 2009). The middle temporal gyrus and precuneus are part of a network involved in the perception of speech and prosody and in aspects of social cognition such as mentalizing and emotion understanding (Leitman, D.I., Loughhead, J., Wolf, D.H., Ruparel, K., Kohler, C.G., Elliott, M.A., Bilker, W.B., Gur, R.E., Gur, R.C., 2008). Pessoa (Pessoa, L., 2008) suggested that the high degree of connectivity between the amygdala and other regions involved in emotional processing might contribute to the integration of emotion and cognition and the evaluation of sensory information. OT might facilitate evaluation of and responding to emotional stimuli by modulating neural connectivity. This is supported by a study of Gamer et al. (Gamer, M., Zurowski, B., Büchel, C., 2010), who showed that OT increased functional coupling between the amygdala and the superior colliculus as well as gaze changes towards the eyes of an emotional stranger in order to recognize its emotions.

The "reading the mind in the eyes" test (RMET) requires subjects to infer internal emotional state of another individual from subtle differences in the eyes and it activates the amygdala. Eye gaze monitoring is amygdala dependent (Adolphs, R., Tranel, D., Buchanan, T.W., 2005). OT increases the amount of time looking at the eyes in faces (Guastella, A.J., Mitchell, P.B., Dadds, M.R., 2008) and

this may contribute indirectly to improved performance on the RMET.

Frontal asymmetries assessed by the EEG activity of both hemispheres reflect a general tendency for approach versus withdrawal, with greater left activity reflecting greater approach motivation and greater right activity reflecting greater withdrawal motivation (Huffmeijer, R., Alink, L.R., Tops, M., Bakermans-Kranenburg, M.J., van IJzendoorn, M.H., 2012). Dorsolateral prefrontal cortex is involved in the processing of reward-related information in goal-directed behavior. Differential effects of positive and negative emotional stimuli both on left and right dorsolateral prefrontal brain activity and on working memory performance, point toward the integration of cognitive and emotional material in this brain region (Herrington, J.D., Mohanty, A., Koven, N.S., Fisher, J.E., Stewart, J.L., Banich, M.T., Webb, A.G., Miller, G.A., Heller, W., 2005). The lateral prefrontal areas influence the approach-withdrawal motivation. It was recently argued that increasing approach motivation may be one of the mechanisms through which OT achieves its prosocial effects (Kemp, A. H., Bos, P.A., Panksepp, J., Bluthe, R-M, Honk, J.V., 2011). Substantial evidence implicates OT in facilitating human bonding and trust. OT may influence the very core mechanisms of belief formation (Rubin, L.H., Carter, C.S., Drogos, L., Pournajafi-Nazarloo, H., Sweeney, J.A., Maki, P.M., 2010). Bos et al. (Bos, P.A., Panksepp, J., Bluthe, R-M, Honk, J.V., 2011) suggested that OT facilitates social bonding by enhancing cognitive control from prefrontal regions to regulate emotionality, as well as by its effects on the experience of reward during social interaction.

It has been claimed to have both promnesitic (Guastella, A.J., Mitchell, P.B., Mathews, F., 2008) and amnesitic (Heinrichs, M., Meinlschmidt, G., Wippich, W., Ehlert, U., 2004) effects. One hypothesis reconciling these contradictory findings is that OT may specifically promote learning that is socially reinforced.

OT enhances inference of emotional states as well as generosity toward others (Zak, P.J., Stanton, A.A., Ahmadi, S., 2007), suggesting that OT has empathogenic properties and

could influence behavior in the context of social bonding. Furthermore studies have shown that OT reduces both social anxiety and amygdala responses to fearful faces (Kirsch, P., Esslinger, C., Chen, Q., Mier, D., Lis, S., Siddhanti, S., Gruppe, H., Mattay, V.S., Gallhofer, B., Meyer-Lindenberg, A., 2005), implying an inhibitory effect of OT on the amygdala responsivity and in turn a greater willingness to trust and bond to other people.

OT facilitates social recognition memory. This confirms that social reinforcement of learning is important. Studies reporting amnesitic effects of OT (Heinrichs, M., Meinlschmidt, G., Wippich, W., Ehlert, U., 2004) often involve highly aversive and stressful experimental contexts. It is possible that OT may facilitate amygdala activity under positive, prosocial and empathy-provoking conditions and inhibit it under more aversive and stressful conditions where stimuli are avoided (Petrovic, P., Kalisch, R., Singer, T., Dolan, R.J., 2008).

People with damaged amygdala were not compromised in cognitive empathy, but showed an impairment in emotional empathy. They seem quite capable of identifying facial emotions by cognitive strategies, but are impaired in processing and responding to the emotional consequences of this recognition (Hurlemann, R., Patin, A., Onur, O.A., Cohen, M.X., Baumgartner, T., Metzler, S., Dziobek, I., Gallinat, J., Wagner, M., Maier, W., Kendrick, K.M., 2010).

One critical question is whether OT effects on social behavior reflect its influences on specialized high-order social cognitive processes (e.g. trust, generosity, suspiciousness, mentalizing) or on underlying states and inclinations (e.g. general anxiety, affiliative motivation, global saliency of social cues). After intranasal OT administration, humans display more trust in economic game involving allocating money to a stranger (Kosfeld, M., Heinrichs, M., Zak, P.J., Fischbacher, U., Fehr, E., 2005), receive higher "mind-reading" scores in a task that involves interpreting strangers' eyes and show more in-group favoritism and ethnocentrism (De Dreu, C.K., Greer, L.L., Handgraaf, M.J., Shalvi, S., Van Kleef, G.A., Baas, M., Ten Velden, F.S., Van Dijk, E., Feith, S.W.,

2010). All these effects involve high-order psychological processes ("trust", "mentalizing", "cooperation") and hence OT selectively targets circuitry involved in sophisticated social-cognitive computations (Churchland, P.S., Winkelman, P., 2012).

The emotional empathy intensity ratings of the women were considerably higher than those of the men and only when the men received OT treatment did they become equivalent to untreated women. This fact may reflect enhanced release of OT in women as compared with men.

OTR agonist may be a useful therapy in enhancing socially motivated learning and emotional empathy in men. Hurleman (Hurlemann, R., Patin, A., Onur, O.A., Cohen, M.X., Baumgartner, T., Metzler, S., Dziobek, I., Gallinat J., Wagner, M., Maier, W., Kendrick, K.M., 2010) shows that OT treatment has rather minor effects in improving cognitive empathy. Augmenting the effectiveness of socially reinforced learning and levels of emotional empathy could, however, benefit the treatment of a number of disorders in which social emotional responsivity is aberrant, such as autism, schizophrenia (Derntl, B., Finkelmeyer, A., Toygar, T.K., Hülsmann, A., Schneider, F., Falkenberg, D.I., Habel, U., 2009) and psychopathy.

#### THE OXYTOCIN ANXIOLYTIC AND PROSOCIAL EFFECTS

Social stressors and the absence of positive social interactions have been associated with several detrimental consequences, including disrupted mood and emotion, increased reactivity of the hypothalamic-pituitary-adrenal (HPA) axis, autonomic imbalance and central nervous system dysfunction (Norman, G.J., Cacioppo, J.T., Morris, J.S., Malarkey, W.B., Berntson, G.G., Devries, A.C., 2011). Previous evidence suggests that negative social experiences may mediate the development and maintenance of affective disorders and cardiovascular diseases (Grippio, A.J., Trahanas, D.M., Zimmerman, R.R. 2nd, Porges, S.W., Carter, C.S., 2009). In humans feelings

of loneliness are associated with behavioral and cardiovascular alterations including increased ratings of hopelessness, reduced self-esteem and increased diastolic blood pressure (Steptoe, A., Owen, N., Kunz-Ebrecht, S.R., Brydon, L., 2004). The neurohormones OT, vasopressin and corticotropin-releasing hormone (CRH) play an important role in these associations (Pierrehumbert, B., Torrisi, R., Laufer, D., Halfon, O., Ansermet, F., Beck Popovic, M., 2010). Increased hypothalamic CRH, circulating cortisol, hypothalamic vasopressin and central and circulating OT levels have been observed in prairie voles after exposure to short- or long-term social stressors (Ruscio, M.G., Sweeny, T., Hazelton, J., Suppakul, P., Sue Carter, C., 2007).

Exogenous OT may have the capacity to decrease CRH during chronic stress and to down-regulate the HPA axis and HR responses in humans (Heinrichs, M., Baumgartner, T., Kirschbaum, C., Ehlert, U., 2003).

Both complex social behavior and basic emotional processing functions such as anxiety and fear extinction critically depend on the amygdala. The lateral nucleus of the amygdala receives and integrates sensory, prefrontal and limbic inputs and excites neurons in the central nucleus that evoke fear responses via their projections to brainstem regions including periaqueductal gray and reticular formation (LeDoux, J.E., 2000). In humans fearful faces potentially activate the amygdala and lesions of the amygdala impair their recognition which leads to social disinhibition (Salovey, P., Mayer, J.D., 1990).

Any social inference and especially positive inference depends on the subject's willingness to engage in social interaction and this willingness is anxiety-sensitive. Trust studies reveal the general mechanisms of anxiety down-regulation, mediated by the amygdala (Baumgartner, T., Heinrichs, M., Vonlanthen, A., Fischbacher, U., Fehr, E., 2008). Other recent works also suggest that complex mental state inferences in the mind-in-the-eye tasks depend on the general willingness to look into strangers' eyes, which in turn is anxiety-dependent (Evans, S., Shergill, S.S., Averbeck, B.B., 2010).

Looking at pictures of significant others showed marked overlap with regions that show high densities of OT receptors (e.g. striatum) (Bartels, A., Zeki, S., 2004). Interestingly, intranasal OT has been shown to attenuate amygdala responses to social stimuli (emotional faces), suggesting a key role of OT in reducing the uncertainty about the predictive value of social stimuli (Domes, G., Heinrichs, M., Gläscher, J., Büchel, C., Braus, D.F., Herpertz, S.C., 2007).

OT acts on the amygdala to reduce fear and modulate aggression (Bosch, O.J., Meddle, S.L., Beiderbeck, D.I., Douglas, A.J., Neumann, I.D., 2005). It acts on the central amygdala to inhibit excitatory flow from the amygdala to brainstem sites mediating fear response (Kirsch, P., Esslinger, C., Chen Q, Mier, D., Lis, S., Siddhanti, S., Gruppe, H., Mattay, V.S., Gallhofer, B., Meyer-Lindenberg, A., 2005). Autonomic response to aversive pictures has been reported to be reduced under OT (Pitman, R.K., Orr, S.P, Lasko, N.B., 1993), compatible with the effect on amygdala activation. In autism, in which plasma OT is reduced, abnormal amygdala activation occurs during the face processing (Dalton, K.M., Nacewicz, B.M., Johnstone, T., Schaefer, H.S., Gernsbacher, M.A., Goldsmith, H.H., Alexander, A.L., Davidson, R.J., 2005). Most likely anxiolytic effects of OT reflect a complex interaction of central and peripheral mechanisms.

#### THE ROLE OF OXYTOCIN IN PARENTING AND FAMILY INTERACTIONS

OT is released during key pair-bonding events like sexual climax or childbirth. Its levels at early pregnancy and the postpartum period are related to a clearly defined set of maternal bonding behaviors. Plasma OT concentrations measured during early pregnancy and one month after delivery predict positive and adaptive maternal behaviors, such as affectionate touch, motherese vocalization and mother-to-infant gaze (Feldman, R., Weller, A., Zagoory-Sharon, O., Levine, A., 2007). They are also related to the mother's own

adult attachment capacity (Strathearn, L., Fonagy, P., Amico, J., Montague, P.R., 2009). A further study has shown that OT levels are associated with interactive synchrony between parent and child (Feldman, R., Gordon, I., Zagoory-Sharon, O., 2011). OT therefore appears to play an important role in promoting responsive parental caregiving. In addition, OT levels were also associated with bonding to one's own parents in young adults (Gordon, I., Zagoory-Sharon, O., Schneiderman, I., Leckman, J.F., Weller, A., Feldman, R., 2008).

Mothers who showed an increased OT response when interacting with their infant rated themselves as being more sensitive of moods, emotions and physical sensations, but less compulsive, schedule driven and task oriented (Kéri, S., Benedek, G., 2009). OT is only one of several neuroendocrine systems – such as vasopressin, dopamine and prolactin – which may contribute to parenting behaviors (Swain, J.E., Lorberbaum, J.P., Kose, S., Strathearn, L., 2007). Dopamine plays a role in reward signaling and reinforcement learning and OT appears to interact with the mesocorticolimbic dopamine system to reinforce maternal caregiving in response to infant cues. One model of adult attachment proposes that secure attachment is based on an integration of both affective and cognitive information processing in the brain. Optimal maternal caregiving responses may involve both sensitive attunement to infant cues, via OT-mediated mechanisms, and decision making and planning to meet the temporal needs of a family, as mediated by the nigrostriatal dopaminergic system (Strathearn, L., 2011).

New mothers who are more cognitively focused on task performance and executing plans may be less responsive to their infants' affective cues. "Orienting sensitivity" refers to one's responsiveness to sensory cues, moods and emotions. During the stages of pregnancy, childbirth and breastfeeding, new mothers gradually learn to relinquish control of their external environment, while attending more to internal sensory cues from their own body (such as during labor and delivery) and then from their new infant (such as during breastfeed-

ing). Maternal OT response during interactive mother–infant play appears to be positively associated with this important capacity.

Endogenous opioids also affect maternal attachment to infants, including maintenance of contact, grooming and responses to separation.

OT has anxiolytic and stress-reducing effects in breastfeeding mothers and this might increase mothers' sensitivity to infant signals including infant crying but also infant smiling and laughing. Taylor (Taylor, S.E., Gonzaga, G.C., Klein, L.C., Hu, P., Greendale, G.A., 2006) also suggested that OT modulates stress responses and is implicated in the seeking of affiliative contact in response to stress. Riem et al. (Riem, M.M., van IJzendoorn, M.H., Tops, M., Boksem, M.A., Rombouts, S.A., Bakermans-Kranenburg, M.J., 2012) found that OT reduces amygdala responses to infant laughter and crying, whereas it increases activation of the insula and inferior frontal gyrus (IFG), brain regions important for empathy, emotion understanding and maternal bonding. The OFC exhibits a specific neural response to infant stimuli (Kringelbach, M.L., Lehtonen, A., Squire, S., Harvey, A.G., Craske, M.G., Holliday I.E., Green, A.L., Aziz, T.Z., Hansen, P.C., Cornelissen, P.L., Stein A., 2008). Strathearn et al. (Strathearn, L., Fonagy, P., Amico, J., Montague, P.R., 2009) found that mothers with a strong increase in peripheral OT release while interacting with their infants show more activation in neural reward systems, such as the OFC and the ventral striatum, during the perception of their smiling infant than mothers with lower OT levels.

OT increases functional connectivity between the amygdala and neural reward regions, the OFC and the caudal ACC (Riem, M.M., van IJzendoorn, M.H., Tops, M., Boksem, M.A., Rombouts, S.A., Bakermans-Kranenburg, M.J., 2012). These centers are important for emotional regulation, in particular for the reduction of anxiety, by their inhibitory influence on the amygdala. Increased functional connectivity between the OFC, ACC and amygdala may promote mother–infant attachment by enhancing cognitive control over negative emotionality and

at the same time increasing the incentive salience of infant laughter (Bos, P.A., Panksepp, J., Bluthe, R-M, Honk, J.V., 2011).

OT also enhances the functional connectivity between the amygdala and the hippocampus, middle temporal gyrus and precuneus during infant laughter (Riem, M.M., van IJzendoorn, M.H., Tops, M., Boksem, M.A., Rombouts, S.A., Bakermans-Kranenburg, M.J., 2012). Amygdala-hippocampus interactions are crucial for emotional memory, an important factor in parenting (Guastella, A.J., Mitchell, P.B., Mathews, F., 2008).

Feldman et al. (Feldman, R., Gordon, I., Schneiderman, I., Weisman, O., Zagoory-Sharon, O., 2010) showed that fathers with high levels of OT displayed more stimulatory contact during play with their child. In a complementary study, Naber et al. (Naber, F., van IJzendoorn, M.H., Deschamps, P., van Engeland, H., Bakermans-Kranenburg, M.J., 2010) found that intranasally administered OT enhances paternal playful interaction.

#### OXYTOCIN AND THE AUTONOMIC FUNCTIONS. APPLICATION OF THE HEART RATE VARIABILITY METHOD

The polyvagal theory focuses on the phylogenetic shift from reptiles to mammals involving specific changes to the vagal pathways regulating the heart (Porges, S.W., 2009). Only mammals have a myelinated vagus – originating from the nucleus ambiguus – and through the process of evolution, the brainstem nuclei became integrated with the mimic muscles of the face and head that express facial emotions. The polyvagal theory proposes an automatic, subcortical mechanism – neuroception – that is capable of identifying environmental and visceral features that are safe, dangerous or life-threatening. Neuroception is triggered by feature detectors in the temporal cortex, which respond to voice prosody, facial expressions and hand movements. OT may serve to increase ones sensitivity to such cues. Neuroception may also be triggered by afferent feedback from the viscera. This visceral feedback represents a major factor for

the extent to which social engagement will take place.

There exists an important distinction between approach-motivated states that increase capacity for action versus a quiescent state associated with positive feelings of warmth and calm in which motivation to act is absent (McCall, C., Singer, T., 2012). Approach motivation would be associated with increased sympathetic activity, while quiescence would be associated with parasympathetic activity.

OT has a key role in the regulation of approach- and withdrawal-related social behaviors. It increases one's capacity for approach-related motivation but this capacity need not be a conscious process. While social behavior is associated with the motivation to approach or withdraw, this motivation may not always lead to overt, observable behavior. OT may upregulate parasympathetic and/or reduce sympathoadrenal responses through a number of mechanisms. One candidate psychophysiological marker of approach-related motivation is heart rate variability (HRV) that is the variability in consecutive heartbeats. Reduced HRV is associated with an increased risk of cardiovascular disease and sudden cardiac death (Thayer, J.F., Yamamoto, S.S., Brosschot, J.F., 2010).

Increased values of HRV are associated with positive emotions such as cheerfulness and calmness (Geisler, F.C.M., Vennwald, N., Kubiak, T., Weber, H., 2010), thus highlighting the specific role of HRV as indicator of social engagement. Reductions in HRV are displayed in unmedicated patients with depression and anxiety disorders characterized by reductions in approach and increases in withdrawal-related behaviors (Kemp, A.H., Quintana, D.S., Felmingham, K.L., Matthews, S., Jelinek, H.F., 2012) and compromised capacity to detect positive social cues and engage with others. OT and its receptors are present in cardiac tissue (Jankowski, M., Danalache, B., Wang, D., Bhat, P., Hajjar, F., et al., 2004). It alters cardiovascular reactivity via its actions on the heart itself, but also centrally – via nucleus of the solitary tract (NTS), which integrates and relays incoming peripheral visceral inputs with central influences

(Norman, G.J., Cacioppo, J.T., Morris, J.S., Malarkey, W.B., Berntson, G.G., Devries, A.C., 2011).

Exogenous OT administration to isolated prairie voles prevented several detrimental cardiac consequences of depression including altered HR and HR variability and autonomic imbalance (Grippe, A.J., Trahanas, D.M., Zimmerman, R.R. 2nd, Porges, S.W., Carter, C.S., 2009). OT increases HRV (Kemp, A.H., Quintana, D.S., Felmingham, K.L., Matthews, S., Jelinek, H.F., 2012) and high frequency (HF) – HRV (reflecting the parasympathetic activity) while participants are engaged in a variety of non-stressful activities. That leads to increased flexibility and adaptiveness to the environment. Attentional demand decreases HRV (Marsh, A.A., Yu H.H., Pine, D.S., Blair, R.J., 2009) and OT may either attenuate or reverse these effects.

Oxytocin affects psychological health through interactions with the brain structures involved in cognitive functions, emotional processing and behavioral disposition. The integrative brain centers are connected with the subcortical autonomic centers – the amygdala and the brainstem nuclei of the cranial nerves, which, in turn, control the physiological processes of the organs. The higher and lower brain structures interact with various endocrine factors and determine the somatic state. This sophisticated system could be easily evaluated by means of the heart rate variability method. HRV is an indicator of the psychological state and of the psychosomatic effects on organs mediated via the autonomic nerve system.

(Marsh, A.A., Yu H.H., Pine, D.S., Blair, R.J. 2009)

## REFERENCES

- Salovey, P., Mayer, J.D. (1990) Emotional intelligence. *Imagination, cognition and personality*, 9, 185-211.
- Mayer, J., Salovey, P. (1993). The intelligence of emotional intelligence. *Intelligence* 17, 433-442.
- Bar-On, R. (2001). Emotional intelligence and self-actualization. In: Ciarrochi J, Forgas JP, Mayer JD, editors. *Emotional intelligence in everyday life: As-*

- scientific inquiry. Philadelphia: PsychologyPress; 2001. p. 82-97.
- Bechara, A., Tranel, D., Damasio, A.R. (2000). Poor judgment in spite of high intellect: neurological evidence for emotional intelligence. In:
- Bar On R, Parker JDA, editors. The handbook of emotional intelligence. San Francisco: Jossey-Bass; 2000. p. 192-214.
- Bar-On, R., Fund, S., Handley, R. (2003). The impact of emotional intelligence on performance. In: Druskat V, Sala F, Mount G, editors. Emotional intelligence and performance at work. San Francisco: Jossey-Bass.
- Hein, G., Singer, T. (2008). I know how you feel but not always: the empathic brain and its modulation. *Curr Opin Neurobiol* 18:153–158.
- Higa, K.T., Mori, E., Viani, F.F., Morris, M., Michelini, L.C. Baroreflex control of heart rate by oxytocin in the solitary-vagal complex. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* 2002; 282:R537–R545.
- Tribollet, E., Dubois-Dauphin, M., Dreifuss, J.J., Barberis, C., Jard, S. (1992). Oxytocin receptors in the central nervous system. Distribution, development, and species differences. *Ann N Y Acad Sci* 652: 29–38.
- Davis, M., Whalen, P. (2001). The amygdala: vigilance and emotion. *Mol Psychiatry* Pessoa, L. (2008). On the relationship between emotion and cognition. *Nat Rev Neurosci.* 2008 Feb;9(2):148-58.
- Kirsch, P., Esslinger, C., Chen, Q., Mier, D., Lis, S., Sidhanti, S., Gruppe, H., Mattay, V.S., Gallhofer, B., Meyer-Lindenberg, A. (2005). Oxytocin modulates neural circuitry for social cognition and fear in humans. *J Neurosci.* 2005 Dec 7;25(49):11489-93.
- van Wingen, G., Mattern, C., Verkes, R.J., Buitelaar, J., Fernández, G. (2010). Testosterone reduces amygdala-orbitofrontal cortex coupling. *Psychoneuroendocrinology.* 2010 Jan;35(1):105-13.
- Kringelbach, M.L., Lehtonen, A., Squire, S., Harvey, A.G., Craske, M.G., Holliday, I.E., Green, A.L., Aziz, T.Z., Hansen, P.C., Cornelissen, P.L., Stein, A. (2008). A specific and rapid neural signature for parental instinct. *PLoS One.* 2008 Feb 27;3(2):e1664.
- Jankowski, M., Danalache, B., Wang, D., Bhat, P., Hajjar, F., et al. (2004). Oxytocin in cardiac ontogeny. *Proc Natl Acad Sci USA* 101: 13074–13079.
- Kiss, A., Mikkelson, J.D. (2005). Oxytocin—anatomy and functional assignments: a minireview. *Endocr Regul.* 2005 Sep;39(3):97-105. Review.
- Yu Q, Ji R, Gao X, Fu J, Guo W, Song X, Zhao X, Burnstock G., Shi X, He C, Xiang, Z. (2011). Oxytocin is expressed by both intrinsic sensory and secretomotor neurons in the enteric nervous system of guinea pig. *Cell Tissue Res.* 2011 May;344(2):227-37.
- McEwen, B.B. (2004). Brain-fluid barriers: relevance for theoretical controversies regarding vasopressin and oxytocin memory research. *Adv Pharmacol.* 2004; 50592:531. 655–708.
- Numan, M., Insel, T.R. (2003). The neurobiology of parental behavior. New York: Springer.
- Maunder, R.G., Hunter, J.J. (2001). Attachment and psychosomatic medicine: developmental contributions to stress and disease *Psychosom Med.* 2001 Jul-Aug;63(4):556-67. Review.
- Declerck, C.H., Boone, C., Kiyonari, T. (2010). Oxytocin and cooperation under conditions of uncertainty: the modulating role of incentives and social information *Horm Behav.* 2010 Mar;57(3):368-74.
- Marsh, A.A., Yu HH, Pine, D.S., Blair, R.J. Oxytocin improves specific recognition of positive facial expressions. *Psychopharmacology (Berl).* 2010 Apr; 2009(3):225-3
- Gamer, M., Zurowski, B., Büchel, C. (2010). Different amygdala subregions mediate valence-related and attentional effects of oxytocin in humans. *Proc Natl Acad Sci U S A.* 2010 May 18;107(20):9400-5
- Baumgartner, T., Heinrichs, M., Vonlanthen, A., Fischbacher, U., Fehr, E. Oxytocin shapes the neural circuitry of trust and trust adaptation in humans. *Neuron.* 2008 May 22;58(4):639-50.
- Heinrichs, M., Baumgartner, T., Kirschbaum, C., Ehlert, U. (2003). Social support and oxytocin interact to suppress cortisol and subjective responses to psychosocial stress. *Biol Psychiatry.* 2003 Dec 15;54(12):1389-98.
- Bruins, J., Hijman, R., Van Ree, J.M. (1992). Effect of a single dose of des-glycinamide-[Arg8]vasopressin or oxytocin on cognitive processes in young healthy subjects. *Peptides.* 1992 May-Jun;13(3):461-8.
- Unkelbach, C., Guastella, A.J., Forgas, J.P. (2008). Oxytocin selectively facilitates recognition of positive sex and relationship words. *Psychol Sci.* 2008 Nov;19(11):1092-4.
- Kéri, S., Benedek, G. (2009). Oxytocin enhances the perception of biological motion in humans. *Cogn Affect Behav Neurosci.* 2009 Sep;9(3):237-41
- Leitman, D.I., Loughhead, J, Wolf, D.H., Ruparel, K., Kohler, C.G., Elliott, M.A., Bilker, W.B., Gur, R.E., Gur, R.C. (2008). Abnormal superior temporal connectivity during fear perception in schizophrenia. *Schizophr Bull.* 2008 Jul;34(4):673-8.
- Adolphs, R., Tranel, D., Buchanan, T.W. (2005). Amygdala damage impairs emotional memory for gist but not details of complex stimuli. *Nat Neurosci.* 2005 Apr;8(4):512-8. Epub 2005 Feb 27.
- Guastella, A.J., Mitchell, P.B., Dadds, M.R. (2008). Oxytocin increases gaze to the eye region of human faces. *Biol Psychiatry.* 2008 Jan 1;63(1):3-5.
- Huffmeijer, R, Alink, LR, Tops, M, Bakermans-Kranenburg, MJ, van IJzendoorn, MH. (2012). Asymmetric frontal brain activity and parental rejection predict altruistic behavior: moderation of oxytocin effects. *Cogn Affect Behav Neurosci.* 2012 Jun;12(2):382-92.
- Herrington, J.D., Mohanty, A., Koven, N.S., Fisher, J.E., Stewart, J.L., Banich, M.T., Webb, A.G., Miller, G.A., Heller, W. (2005). Emotion modulated performance and activity in left dorsolateral prefrontal cortex. *Emotion.* 2005 Jun;5(2):200-7.

- Kemp, A. H., Bos, P.A., Panksepp, J., Bluthe, R-M, Honk, J.V. (2011). Acute effects of steroid hormones and neuropeptides on human social emotional behavior: a review of single administration studies. *Front Neuroendocrinol*, 2011 Jan.
- Bos, P.A., Panksepp, J., Bluthe, R-M., Honk, J.V. (2011). Acute effects of steroid hormones and neuropeptides on human social-emotional behavior: a review of single administration studies. *Front Neuroendocrinol*, 2011 Jan.
- Rubin, L.H., Carter, C.S., Drogos, L., Pournajafi-Nazarloo, H., Sweeney, J.A., Maki, P.M. (2010). Peripheral oxytocin is associated with reduced symptom severity in schizophrenia *Schizophr Res*. 2010 Dec;124(1-3):13-21.
- Guastella, A.J., Mitchell, P.B., Mathews, F. (2008). Oxytocin enhances the encoding of positive social memories in humans. *Biol Psychiatry*. 2008 Aug 1;64(3):256-8.
- Heinrichs, M., Meinlschmidt, G., Wippich, W., Ehlert, U., Hellhammer, D.H. (2004). Selective amnesic effects of oxytocin on human memory. *Physiol Behav*. 2004 Oct 30;83(1):31-8.
- Zak, P.J., Stanton, A.A., Ahmadi, S. (2007). Oxytocin increases generosity in humans. *PLoS One*. 2007 Nov 7;2(11):e1128.
- Hurlemann, R., Patin, A., Onur, O.A., Cohen, M.X., Baumgartner, T., Metzler, S., Dziobek, I., Gallinat, J., Wagner, M., Maier, W., Kendrick, K.M. (2010). Oxytocin enhances amygdala-dependent, socially reinforced learning and emotional empathy in humans. *J Neurosci*. 2010 Apr 7;30(14):4999-5007.
- Petrovic, P., Kalisch, R., Singer, T., Dolan, R.J. (2008). Oxytocin attenuates affective evaluations of conditioned faces and amygdala activity. *J Neurosci*. 2008 Jun 25;28(26):6607-15.
- Kosfeld, M., Heinrichs, M., Zak, P.J., Fischbacher, U., Fehr, E. (2005). Oxytocin increases trust in humans. *Nature*. 2005 Jun 2;435(7042):673-6.
- De Dreu, C.K., Greer, L.L., Handgraaf, M.J., Shalvi, S., Van Kleef, G.A., Baas, M., Ten Velden, F.S., Van Dijk, E., Feith, S.W. (2010). The neuropeptide oxytocin regulates parochial altruism in intergroup conflict among humans. *Science*. 2010 Jun 11;328(5984):1408-11.
- Churchland, P.S., Winkielman, P. (2012). Modulating social behavior with oxytocin: how does it work? What does it mean? *Horm Behav*. 2012 Mar;61(3):392-9.
- Norman, G.J., Cacioppo, J.T., Morris, J.S., Malarkey, W.B., Berntson, G.G., Devries, A.C. (2011). Oxytocin increases autonomic cardiac control: moderation by loneliness. *Biol Psychol*. 2011 Mar;86(3):174-8
- Grippe, A.J., Trahanas, D.M., Zimmerman, R.R. 2nd, Porges, S.W., Carter, C.S. (2009). Oxytocin protects against negative behavioral and autonomic consequences of long-term social isolation. *Psychoneuroendocrinology*. 2009 Nov;34(10):1542-53
- Stepoe, A., Owen, N., Kunz-Ebrecht, S.R., Brydon, L. (2004). Loneliness and neuroendocrine, cardiovascular, and inflammatory stress responses in middle-aged men and women. *Psychoneuroendocrinology*. 2004 Jun;29(5):593-611.
- Pierrehumbert, B., Torrissi, R., Lauffer, D., Halfon, O., Ansermet, F. Beck Popovic, M. (2010). Oxytocin response to an experimental psychosocial challenge in adults exposed to traumatic experiences during childhood or adolescence. *Neuroscience*. 2010 Mar 10;166(1):168-77.
- Ruscio, M.G., Sweeny, T., Hazelton, J., Suppatkul, P., Sue Carter, C. (2007). Social environment regulates corticotropin releasing factor, corticosterone and vasopressin in juvenile prairie voles. *Horm Behav*. 2007 Jan;51(1):54-61.
- LeDoux, J.E. (2000). Emotion circuits in the brain. *Annu Rev Neurosci*. 2000;23:155-84. Review.
- Evans, S., Shergill, S.S., Averbeck, B.B. (2010). Oxytocin decreases aversion to angry faces in an associative learning task. *Neuropsychopharmacology*. 2010 Dec;35(13):2502-9.
- Bartels, A., Zeki, S. (2004). The neural correlates of maternal and romantic love. *Neuroimage*. 2004 Mar;21(3):1155-66.
- Domes, G., Heinrichs, M., Gläscher, J., Büchel, C., Braus, D.F., Herpertz, S.C. (2007). Oxytocin attenuates amygdala responses to emotional faces regardless of valence. *Biol Psychiatry*. 2007 Nov 15;62(10):1187-90.
- Bosch, O.J., Meddle, S.L., Beiderbeck, D.I., Douglas, A.J., Neumann, I.D. (2005). Brain oxytocin correlates with maternal aggression: link to anxiety. *J Neurosci*. 2005 Jul 20;25(29):6807-15.
- Pitman, R.K., Orr, S.P., Lasko, N.B. (1993). Effects of intranasal vasopressin and oxytocin on physiologic responding during personal combat imagery in Vietnam veterans with posttraumatic stress disorder. *Psychiatry Res*. 1993 Aug;48(2):107-17.
- Dalton, K.M., Nacewicz, B.M., Johnstone, T., Schaefer, H.S., Gernsbacher, M.A., Goldsmith, H.H., Alexander, A.L., Davidson, R.J. (2005).
- Gaze fixation and the neural circuitry of face processing in autism. *Nat Neurosci*. 2005 Apr;8(4):519-26.
- Feldman, R., Weller, A., Zagoory-Sharon, O., Levine, A. (2007). Evidence for a neuroendocrinological foundation of human affiliation: plasma oxytocin levels across pregnancy and the postpartum period predict mother-infant bonding. *Psychol Sci*. 2007 Nov;18(11):965-70.
- Strathearn, L., Fonagy, P., Amico, J., Montague PR. (2009). Adult attachment predicts maternal brain and oxytocin response to infant cues. *Neuropsychopharmacology*. 2009 Dec;34(13):2655-66.
- Feldman, R., Gordon, I., Zagoory-Sharon, O. (2011). Maternal and paternal plasma, salivary, and urinary oxytocin and parent-infant synchrony: considering stress and affiliation components of human bonding. *Dev Sci*. 2011 Jul;14(4):752-61.
- Gordon, I., Zagoory-Sharon, O., Schneiderman, I., Leckman, J.F., Weller, A., Feldman, R. (2008). Oxytocin and cortisol in romantically unattached young adults: associations with bonding and

- psychological distress. *Psychophysiology*. 2008 May;45(3):349-52
- Swain, J.E., Lorberbaum, J.P., Kose, S., Strathearn, L. (2007). Brain basis of early parent-infant interactions: psychology, physiology, and in vivo functional neuroimaging studies. *J Child Psychol Psychiatry*. 2007 Mar-Apr;48(3-4):262-87.
- Strathearn, L. (2011). Maternal neglect: oxytocin, dopamine and the neurobiology of attachment. *J Neuroendocrinol*. 2011 Nov;23(11):1054-65.
- Taylor, S.E., Gonzaga, G.C., Klein, L.C., Hu P, Green-dale, G.A., Seeman, T.E. (2006). Relation of oxytocin to psychological stress responses and hypothalamic-pituitary-adrenocortical axis activity in older women. *Psychosom Med*. 2006 Mar-Apr;68(2):238-45.
- Riem, M.M., van IJzendoorn, M.H., Tops, M., Boksem, M.A., Rombouts, S.A., Bakermans-Kranenburg, M.J. (2012). No laughing matter: intranasal oxytocin administration changes functional brain connectivity during exposure to infant laughter. *Neuropsychopharmacology*. 2012 Apr;37(5):1257-66.
- Feldman, R., Gordon, I., Schneiderman, I., Weisman, O., Zagoory-Sharon, O. (2010). Natural variations in maternal and paternal care are associated with systematic changes in oxytocin following parent-infant contact. *Psychoneuroendocrinology*. 2010 Sep;35(8):1133-41.
- Naber, F., van IJzendoorn, M.H., Deschamps, P., van Engeland, H., Bakermans-Kranenburg, M.J. (2010). Intranasal oxytocin increases fathers' observed responsiveness during play with their children: a double-blind within-subject experiment. *Psychoneuroendocrinology*. 2010 Nov;35(10):1583-6.
- Porges, S.W. (2009). The polyvagal theory: new insights into adaptive reactions of the autonomic nervous system. *Cleve Clin J Med* 76 Suppl 2: S86-S90.
- McCall, C., Singer, T. (2012). The animal and human neuroendocrinology of social cognition, motivation and behavior. *Nature Publishing Group* 15: 681-688.
- Thayer, J.F., Yamamoto, S.S., Brosschot, J.F. (2010). The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors. *Int J Cardiol* 141: 122-131.
- Geisler, F.C.M., Vennwald, N., Kubiak, T., Weber, H. (2010). The impact of heart rate variability on subjective well-being is mediated by emotion regulation. *Personality and Individual Differences* 49: 723-728.
- Kemp, A.H., Quintana, D.S., Felmingham, K.L., Matthews, S., Jelinek, H.F. (2012). Depression, comorbid anxiety disorders, and heart rate variability in physically healthy, unmedicated patients. *PLoS ONE*.
- Derntl, B., Finkelmeyer, A., Toygar, T.K., Hülsmann, A., Schneider, F., Falkenberg, D.I., Habel, U. (2009). Generalized deficit in all core components of empathy in schizophrenia. *Schizophr Res*. 2009 Mar;108(1-3):197-206.

## ЕФЕКТИ НА ОКСИТОЦИНА ВЪРХУ КОГНИТИВНИТЕ ПРОЦЕСИ, ЕМОЦИИТЕ, ПОВЕДЕНИЕТО И ВЪРХУ ВЕГЕТАТИВНИТЕ ФУНКЦИИ ПРИ ХОРА

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**Резюме.** Емоционалната интелигентност е от значение за функционирането на личностно и социално ниво. Нервните структури, които определят емоционалната и социална интелигентност, участват също в регулацията на вегетативните функции и в някои когнитивни процеси като вземането на решения. Това са вентромедиалната префронтална кора, амигдалата и инсуларната кора. Окситоцинът улеснява създаването на социални връзки, като усилва контрола от префронталната кора върху амигдалата. По този начин се потенцира когнитивният контрол върху емоционалните реакции. Окситоцинът подтиква и възбудните влияния от амигдалата към мозъчния ствол, като намалява реакциите на страх, тревожността в социална среда и усилва доверието към другите хора. Свързан е с проявите на емпатия и социално мотивираното обучение, поради което може да подпомогне лечението на заболявания като аутизъм и шизофрения. Участва в създаването на емоционалната връзка между майката и бебето и на отговорното родителско поведение. Повишените стойности на вариабилността на сърдечната честота са свързани с наличието на позитивни емоции като щастие и спокойствие. Вариабилността на сърдечната честота е надежден показател за базалното психоемоционално състояние, за просоциалната нагласа и за вегетативния баланс.

**Ключови думи:** окситоцин, просоциално поведение, тревожност, вариабилност на сърдечната честота.

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