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#### Review

# A general approach – avoidance hypothesis of Oxytocin: Accounting for social and non-social effects of oxytocin



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#### ABSTRACT

*Background:* We critically reexamine extant theory and empirical study of Oxytocin. We question whether OT is, in fact, a "social neuropeptide" as argued in dominant theories of OT.

*Method*: We critically review human and animal research on the social and non-social effects of Oxytocin, including behavioral, psychophysiological, neurobiological, and neuroimaging studies.

Results: We find that extant (social) theories of Oxytocin do not account for well-documented non-social effects of Oxytocin. Furthermore, we find a range of evidence that social and non-social effects of Oxytocin may be mediated by core approach – avoidance motivational processes.

Conclusions: We propose a General Approach – Avoidance Hypothesis of Oxytocin (GAAO). We argue that the GAAO may provide a parsimonious account of established social and non-social effects of Oxytocin. We thus re-conceptualize the basic function(s) and mechanism(s) of action of Oxytocin. Finally, we highlight implications of the GAAO for basic and clinical research in humans.

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Oxytocin (OT), a hypothalamic nine amino acids neuropeptide, was understood to promote pro-social positive behaviors including maternal care, trust, partner preference, and social recognition (Campbell, 2010; Lee et al., 2009; MacDonald and MacDonald, 2010). Thousands of studies conducted in animals and humans have focused on these positive social functions. Then, Shamay-Tsoory and colleagues (2009) found that a nasal administration of OT not only mediated positive social behaviors and emotions, but also negative social emotions and related behaviors, specifically gloating and envy. They hypothesized that the functional role of OT was not simply the promotion of pro-social behaviors. They posited the social salience hypothesis of OT - that OT is involved in modulating social emotions, such that it increases the perceived salience of social cues and thereby attentional processing of the cues. Moreover, they posited that OT-mediated salience up-regulates a range of both positively- and negatively valenced social emotions and corresponding behaviors as a function of the context characterizing the social interaction (Shamay-Tsoory et al., 2009). Consequently, the specific emotion or behavior - beit "pro"- (e.g., love or collaboration) or "anti"- social (e.g., envy or competing) is dependent on the specific context of the social interaction. Consistent with these paradoxical findings, De Dreu and colleagues (2010) then found that following OT administration, participants demonstrated greater in-group love and trust but greater out-group defensive aggression. These novel findings and theoretical proposition led a number of scholars to begin to question and re-conceptualize the large body of published OT research. Scholars are now asking what exactly does OT do, through what neuro-psycho-behavioral mechanism(s) does it act on human and animals behavior, and what are the basic and clinical implications of these competing theoretical accounts of OT?

Building on these developments, Bartz et al. (2011) theorized that the social effects of OT may be moderated by contextual and individual difference factors (e.g., task difficulty, attachment anxiety, genetic variations in OT receptors) (Bartz et al., 2011). For example, Taylor et al. (2000) proposed that the activation of OT is moderated by biological sex and hormones. Specifically, moderated by biological sex, OT activation impacts stress responding such that women's responding is characterized by "Tend-and-Befriend", whereas men's responding is characterized by "Fight-or-Flight (Taylor et al., 2000). Bartz et al. furthermore proposed that social effects of OT are mediated by one or more of the following mechanisms: anxiety reduction, social salience and/or affiliative motivation, though they conclude that the social salience hypothesis is the most parsimonious in light of extant findings.

Then, synthesizing long-standing and emergent findings regarding the complexity of OT action, (Kemp and Guastella, 2010; Kemp and Guastella, 2011) proposed the social-approach/withdrawal hypothesis. They theorized that the broad range of social effects of OT may be accounted for by the hypothesis that OT up-regulates social approach motivation, and down-regulates social avoidance motivation. Kemp and Guastella (2011) reviewed diverse clinical, behavioral, biological and neuroimaging data to support this novel theoretical account of OT mechanisms. Accordingly, Kemp and Guastella (2011) interpreted the findings reported by Shamay-Tsoory and colleagues (2009) in terms of social approach – avoidance. They conceptualized envy as related

to approach, since jealousy, which is similar to envy, functions to motivate approach behavior (Lazarus, 1991) and is linked to left frontal cortical activation associated with approach motivation (Carver and Harmon-Jones, 2009). They similarly conceptualized gloating as approach-related, in so far as gloating is related to happiness/pleasure (Ortony et al., 1990), and happiness/pleasure functions to motivate approach behavior and is linked to left cortical activation (Davidson et al., 1990). Kemp and Guastella (2011) also interpreted the findings of multiple studies documenting that OT is linked to greater trust, generosity, empathy and other social behaviors as mediated by social approach motivation (e.g., Domes et al., 2007a; Hurlemann et al., 2010a; Kosfeld et al., 2005; Zak et al., 2007). Furthermore, they re-interpreted a variety of extant findings as similarly reflecting OT-mediated reduction of avoidance motivation and corresponding inhibition of emotions and behaviors related to withdrawal, such as reduced anxiety and reduced aversion to angry faces (e.g., Evans et al., 2010; Guastella et al., 2009; Heinrichs et al., 2003; Petrovic et al., 2008).

#### 1. General approach – avoidance hypothesis of OT (GAAO)

In the present paper, we argue that Kemp and Guastella (2011) re-conceptualization of the mechanism of action of OT represents an important theoretical advance. We build on this work and theorize that the known social effects of OT may be accounted for by the effects of OT on the neural substrate of approach and avoidance motivation; and accordingly, the effects of OT may not be limited to social behaviors but rather extend to the broad range of adaptive and maladaptive behavior mediated by approach and avoidance motivational processes. Specifically, we posit that OT acts on the 'wanting' mesocorticolimbic circuitry of approach motivation linked to reward (Berridge et al., 2009; Treadway and Zald, 2011) as well as the cortico-amygdala circuitry of withdrawal/avoidance motivation linked to threat and fear (Elliot, 2008; Harmon-Jones, 2011). Indeed, the neural substrate of "social" approach and avoidance is not distinct from that of "non-social" approach and avoidance (Berridge et al., 2009; Treadway and Zald, 2011; Harmon-Jones, 2011). With respect to approach, the mid-brain dopamine circuit subserves social and non-social reward (Izuma et al., 2008; Lin et al., 2012; Saxe and Haushofer, 2008). Accordingly, because OT affects mid-brain dopamine, it should also be expected to influence social and non-social approach behaviors (Lin et al., 2012; Kelley and Berridge, 2002; Knutson et al., 2000; McClure et al., 2007; Rademacher et al., 2010). Similarly, with respect to avoidance/withdrawal, the cortico-amygdala fear/threat circuit subserves social and non-social avoidance/withdrawal (Anderson et al., 2003; Cain and LeDoux, 2008; Davis, 1992; Etkin and Wager, 2007; Mobbs et al., 2009; Öhman, 2005; Schiller and Delgado, 2010; Schlund and Cataldo, 2010; Seymour et al., 2007). Accordingly, because OT affects the cortico-amygdala fear/threat circuitry, it should also be expected to influence social and non-social avoidance behaviors (Petrovic et al., 2008; Condes-Lara et al., 1994; Debiec, 2005; Gozzi et al., 2010; Huber et al., 2005; Kirsch et al., 2005; Knobloch et al., 2012; Lahoud and Maroun, 2013; Lee et al., 2007; Viviani et al., 2011). Through the influence on these distinct yet inter-connected brain systems (Cain and LeDoux, 2008; Schlund and Cataldo, 2010; Kim et al., 2006; Lane et al., 1997; Schlund et al.,

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