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SHORT COMMUNICATION

Exploring the role of intra-nasal oxytocin on the partner preference effect in humans

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Summary Previous studies with prairie voles suggest that the hormone oxytocin is crucial for bond formation — indicated when a partner preference is formed towards the target vole. In this study, we conduct the first empirical test of whether oxytocin likewise promotes partner preferences in humans. Seventy-six undergraduate students received either oxytocin or placebo before being introduced to a male and female persona (via pre-recorded videoclips). One day later, participants were assessed for a partner preference towards the personae: across three situations, participants were asked to choose as company one of the personae they had been introduced to, or an opposite- or same-gendered person they had not been introduced to before; participants were additionally offered a choice to have no company. We found evidence suggesting oxytocin increases preference for persons introduced under the influence of oxytocin; however, this was not targeted at persons of the opposite-gender, and was found in only one aspect of social interaction (finding out more information about the person, but not in choice of company to work with or for a date). Taken together, our findings suggest that oxytocin might not promote human bond formation in ways analogous to prairie voles — that is, by inducing a partner preference effect.
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When the mammalian prairie vole (*Microtus ochrogaster*) comes into extended or sexual contact with an opposite-sexed vole, it forms a pair bond, a strong relation typically associated with breeding. This bond lasts for the lifespan of the prairie vole, such that should the pair be separated (e.g., by death), the remaining vole would not find a replacement mate 80% of the time (Getz and Carter, 1996); consequentially, the prairie vole has been the key animal model for studying the neurobiology of selective, long-term bonds.

In the lab, pair bond formation is indicated by a *partner preference*: when given a choice to be in close proximity to the target vole (the 'partner') or a novel vole (the 'stranger'), the prairie vole preferentially spends time in the proximity of the partner (Williams et al., 1992b). Neurobiological studies suggest that the hormone oxytocin is crucial to this effect: for example, administering an oxytocin antagonist eliminates the partner preference following extended or sexual contact (Williams et al., 1994; Cho et al., 1999); conversely, even in the absence of extended or sexual contact, administration of an oxytocin agonist is sufficient to

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induce a partner preference for an opposite-sexed vole (Williams et al., 1992a; Cho et al., 1999).

In this paper, we explore whether oxytocin has a similar role in the formation of human romantic bonding as it does in prairie vole pair bonding. When translating from prairie voles to humans, we note caution in that oxytocin appears to have species-specific effects on bond formation depending on the precise distribution of oxytocin receptors in the brain (Insel, 2010). In humans, initial autoradiographic and radioimmunoassay postmortem analyses suggest that oxytocin receptors may not be located along the mesolimbic dopamine pathways (in particular, in the nucleus accumbens or, more generally, the ventral striatum; Jenkins et al., 1984; Loup et al., 1989, 1991); this contrasts with oxytocin receptor distribution in prairie voles, where the nucleus accumbens features strongly as a site of oxytocin action (reviewed in Insel, 2010).

Nonetheless, indirect evidence suggests that as with prairie voles, oxytocin may have a role in human romantic bonding. One line of evidence comes from activities known to increase endogenous oxytocin in humans (e.g., massage, ecstasy consumption, and sex; Murphy et al., 1987; Turner et al., 1999; Wolff et al., 2006) — these same activities are commonly associated with increased closeness and intimacy towards another party, suggesting a link between oxytocin and intimate bonding. However, these findings are correlational and preclude conclusions about causal effects; the findings are also based on increased blood plasma levels, of which relations to central oxytocin levels are unclear (e.g., Marazziti et al., 2007). Stronger evidence comes from studies involving intra-nasal oxytocin administration, which have reported oxytocin effects on a range of social cognitive processes: for example, oxytocin has been found to increase gaze to the eye region of faces, promote emotion recognition, and enhance trust behaviours (for a review, see Guastella and Macleod, 2012). Collectively, these findings suggest that oxytocin can promote sociability towards individuals encountered for the first time, which in turn can contribute to bond formation. However, it remains unclear how oxytocin may influence the expression of romantic bond formation itself, as has been studied with prairie voles.

The present study was designed to test the effects of oxytocin on human romantic bond formation. As with the animal literature (Williams et al., 1992b), we adopt the operational definition that bond formation is indicated when a partner preference can be seen, when an individual selectively chooses an opposite-gendered person as company over other alternatives. Thus, if oxytocin influences human bond formation, it will result in a consistent choice to be with a person introduced under the influence of oxytocin rather than with new strangers.

1. Methods

1.1. Participants

Undergraduate students of the University of New South Wales participated in exchange for course credit; all procedures were approved by the university's Human Research Ethics Committee (#06074). Participants were excluded if they: were pregnant; had epilepsy, severe depression, severe anxiety, or psychosis; smoked more than 15 cigarettes a day; or were addicted to illegal substances. To control for menstrual cycle variations, all female participants were asked to participate one week before their next expected menses (during the mid-luteal phase of the cycle), or anytime if they were on oral contraceptives.

Seventy-six students met the inclusion criteria and were randomly allocated to the two drug conditions in a double-blind manner: 19 men (M age = 20.53 years, SD = 2.82 years) and 19 women (M age = 20.11 years, SD = 3.03 years) received oxytocin, whereas 19 men (M age = 19.53 years, SD = 2.46 years) and 19 women (M age = 19.74 years, SD = 5.40 years) received placebo. Because one male participant from the placebo group failed to return for the second day of testing, his data were dropped from analysis.

Consistent with previous research (MacDonald et al., 2011), oxytocin and placebo participants showed no differences in which drug they thought they had received ($\chi^2(2, N = 71) = 0.85$, $p = 0.65$), nor on self-reported calmness following drug administration ($t(69) = 0.80$, $p = 0.43$). Additionally, oxytocin and placebo participants did not differ in terms of relationship status (22 single and 16 non-single participants per group), nor sexual orientation (33 heterosexual and 3 non-heterosexual participants in the placebo group, and 35 heterosexual and 2 non-heterosexual participants in the oxytocin group); largest $\chi^2(2, N = 73) = 1.05$, $p = 0.59$. Finally, female participants in both oxytocin and placebo groups did not differ by: usage of oral contraceptives (8 participants per group; $\chi^2(3, N = 38) = 0.00$, $p = 1.00$), nor of stage of menstrual cycle for participants not on oral contraception (at test, number of days since their last menstrual period: M for oxytocin group = 15.91, SD = 9.90 and M for placebo group = 22.90, SD = 9.17; $t(19) = 1.67$, $p = 0.11$).

1.2. Materials

1.2.1. Drug

Oxytocin administration involved 24 IU of synthetic oxytocin delivered intranasally in four puffs per nostril (with 3 IU per puff). The placebo nasal spray contained identical ingredients (glycerine, methyl paraben, propyl paraben, and purified water) except for the active oxytocin and the facilitating agent mannitol. Nasal sprays were developed by a commercial compounding chemist, with randomisation codes kept by an independent third party until the end of data collection.

1.2.2. Videoclips

In accord with social psychological studies of romantic relationship formation (e.g., White and Kight, 1984), two videoclips of fictitious personas were created to introduce the ''partners''. Scripts for the male ('Michael') and female ('Liz') personae were adapted from online dating websites, with male and female scripts matched by the type and amount of information introduced. To create the videoclips, 7 university-aged actors were asked to read the scripts as if they were introducing themselves. The set of videoclips was pilot-tested with 14 university students, with the clips chosen such that they matched in viewer-rated persona attractiveness and likability, in duration (approximately 1.5 min), and in believability.

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