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

*Jean C. J. Liu[1]

Adam J. Guastella[2]

Mark R. Dadds[1]

[1]School of Psychology, University of New South Wales

Sydney, New South Wales, Australia

[2]Brain and Mind Research Institute, University of Sydney,

Sydney, New South Wales, Australia

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*Please address correspondence to:

Jean C. J. Liu

Neuroscience and Behavioral Disorders Program

Duke-NUS Graduate Medical School

8 College Road

(S) 169857

Singapore

Email: jean.lcj@duke-nus.edu.sg

Phone: (+65) 6516 5918

Abstract

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.

KEYWORDS: Oxytocin, peptide, bond formation, romantic relationships

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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 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; Loup et al., 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, 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 can be indicated when a partner preference can be seen, when an individual selectively chooses an opposite-gendered individual 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.

Methods

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; $t(19) = 1.67$, $p = 0.11$).

Materials

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 parraben, 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 randomization codes kept by an independent third party until the end of data collection.

120 *Videoclips.* In accord with social psychological studies of romantic
121 relationship formation (e.g., White and Kight, 1984), two videoclips of fictitious
122 personas were created to introduce the "partners". Scripts for the male
123 ('Michael') and female ('Liz') personae were adapted from online dating
124 websites, with male and female scripts matched by the type and amount of
125 information introduced. To create the videoclips, 7 university-aged actors were
126 asked to read the scripts as if they were introducing themselves. The set of
127 videoclips was pilot-tested with 14 university students, with the clips chosen
128 such that they matched in viewer-rated persona attractiveness and likability, in
129 duration (approximately 1.5 mins), and in believability.
130 *Measure*. The partner preference measure involved three items assessing
131 choice of company across situations. In each situation, participants could choose
132 as company either persona they had been introduced to the day before ("old
133 partner"), or an opposite-gendered or same-gendered person they had not been
134 introduced to before ("new stranger"); participants were additionally offered a
135 choice to have no company ("alone").
136 To introduce the two "strangers" participants could choose from,
137 participants were presented with two black-and-white photographs under the
138 heading of "here are two more university students." In one photograph, 'Sarah' (a
139 female actress) was shown while in the other, 'Dan' (a male actor) was shown.
140 Stranger actors were chosen to match partner actors by age and ethnicity.
141 After the strangers were introduced, the first question involved a choice
142 about whom participants would want to find out more information about. The
143 next question led participants to believe they would work on a task with a
144 companion in a second part of the experiment; participants were then required

to choose their company (or choose to be alone). Finally, the third question led participants to believe that they could participate in a follow-up experiment on dating behaviour; participants were then asked to indicate their preferred date companion (this time, the option of having no companion was omitted).

Procedure

Day 1: Drug Administration and Introduction to Partners

At the start of the experiment, the experimenter explained that the study was to explore whether oxytocin could influence person perception. After giving their written consent, participants were administered either oxytocin or placebo in a double-blind manner.

Forty-five minutes later, participants were brought into a small room individually. As a cover story, participants were told that several university students had been filmed introducing themselves, and that participants would see two of these videoclips. Participants watched both partner videoclips in counter-balanced order, each time followed by participants answering 21 questions evaluating the partner (e.g., "I think Liz is likable")[i]; the conclusion of this segment occurred approximately 60 to 70 minutes following drug administration.

Day 2: Assessing Partner Preference

Participants returned on the second day, and were told that they would complete a questionnaire followed by a task (this task was a cover story to increase believability about the partner preference questions). To jog their memory, participants were asked a series of questions about each partner (three

[i] The evaluation and memory questionnaires were included as part of a separate study (unpublished).

free-recall and 15 true-false questions on each persona's physical appearance, attire, and what he/she had said)[i]; participants were then asked to complete the partner preference measures. On completion of these measures, participants were fully debriefed.

Data Analyses

For each level of Participant Gender and for each partner preference scenario, a chi-square analysis was run with Drug (oxytocin vs. placebo) cross-tabulated against participants' choice of company. Because Drug did not interact with the order in which participants saw the videoclips (largest χ^2 (4, N = 74) = 4.43, p = 0.35), all subsequent analyses collapsed across these variables. Finally, conclusions did not change when analyses were repeated without five participants who reported having a non-heterosexual orientation; thus, all five participants were included in the results reported.

Results

Information-Seeking

Figure 1 shows participants' choices for whom they would like more information about. Placebo participants were more likely to seek out information about a new stranger (Sarah or Dan) than were oxytocin participants, whereas oxytocin participants were more likely to seek out information about an old partner (Liz or Michael) than were placebo participants, (Figure 1 top panel) χ^2 (5, N = 74) = 6.00, p = 0.05.

However, when choices were analysed in terms of participant and stranger gender (Figure 1 bottom panel), male oxytocin participants were not more likely to prefer the female partner (Liz) than were male placebo participants (relation between drug condition and person choice: χ^2 (9, N = 37) =

193 3.72, $p = 0.45$); similarly, female oxytocin participants did not show a greater
194 interest in seeking out information about the male partner (Michael) than did the
195 placebo participants (relation between drug condition and person choice: χ^2 (9, N
196 = 37) = 7.33, $p = 0.12$).

197 [Figure 1 about here.]

198 *Choice of Company: Work Partner and Date*

199 Figure 2 shows the number of participants who chose each stranger to
200 work with on an experimental task and to date, respectively. Oxytocin had no
201 effect on participants' choice for company (to work with or date), whether the
202 data were combined across gender or analysed separately, or whether the
203 strangers were grouped by familiarity (across stranger gender) or analysed
204 separately (largest χ^2 (5, $N = 37$) = 3.49, $p = 0.18$).

205 [Figure 2 about here.]

206 Discussion

207 This experiment explored the role of oxytocin in romantic relationship
208 formation, measured by a partner preference formed towards a person
209 introduced under the influence of oxytocin. Such oxytocin effects had previously
210 been found to be robust amongst prairie voles, but had never been explored in
211 humans.

212 We found that oxytocin was able to reduce preference for a new stranger
213 and/or increase preference for a person introduced under the influence of
214 oxytocin. However, this effect does not appear to be a partner preference effect,
215 akin to that found with prairie voles: first, oxytocin only had these effects in the
216 relatively trivial context where participants chose whom they wanted to find out
217 more information about; oxytocin had no influence on participant choice in

contexts more similar to the animal partner preference tests – when participants were asked to choose one person as company (either for work or for dating). Second, even in the context where oxytocin influenced person choice (i.e., in finding out more information about someone else), this person choice was not necessarily directed towards a person of the opposite gender. This suggests that in some contexts, oxytocin merely induces a preference for the familiar person or an aversion towards a new person; this effect does not appear to be linked specifically to romantic relationship formation.

On the one hand, our observation of limited oxytocin effects may be expected, given that oxytocin effects on partner preference appear to be species-specific (Insel, 2010). It seems reasonable that oxytocin would not promote human relationship formation in exactly the same way it does prairie vole pair bonding, resulting in a partner preference after a mere short encounter under oxytocin influence.

On the other hand, it is possible that the experimental paradigm we chose was not sufficiently sensitive to detect oxytocin effects on human relationship formation. In terms of our outcome measure, we chose as translational logic to use an experimental paradigm mimicking the animal paradigm as closely as possible (namely, the partner preference test); although this strategy has been used in other areas of translational research (e.g., spatial memory; Astur et al., 1998), an alternate strategy may be to choose an outcome measure known in humans to measure romantic relationship formation. Future studies could also consider introducing the new strangers with the same modality as that used for old partners (here, videoclips), and to use continuous outcomes rather than binary choices. Finally, previous reviews suggest that oxytocin effects in humans

243 may depend on the precise context or experimental methodology used (Bartz et
244 al., 2011; Guastella and Macleod, 2012). Although our method of partner
245 introduction is commonly used in social psychological studies of romantic
246 relationship formation (video personals), we did not explicitly invoke a romantic
247 or dating context – which may be required to elicit oxytocin effects on romantic
248 relationship formation. Thus, future research could examine oxytocin effects
249 under an explicitly romantic context, such as speed-dating paradigms that have
250 been used to study romantic attraction (Finkel et al., 2007).
251 In conclusion, this study represents the first empirical test of whether
252 oxytocin promotes romantic relationship formation as it does in prairie voles –
253 through the formation of a partner preference. We found evidence that oxytocin
254 could result in a preference for a person previously introduced under the
255 influence of oxytocin; however, this was only found in one aspect of social
256 interaction (finding out more information about the person), and not in other
257 aspects more closely related to partner preferences in prairie voles (choice of
258 company to work with or for a date).
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References

Astur, R.S., Ortiz, M.L., Sutherland, R.J., 1998. A characterization of performance by men and women in a virtual Morris water task: A large and reliable sex difference. Behav Brain Res 93, 185-190.

Bartz, J.A., Zaki, J., Bolger, N., Ochsner, K.N., 2011. Social effects of oxytocin in humans: context and person matter. Trends Cogn Sci 15, 301-309.

Cho, M.M., DeVries, A.C., Williams, J.R., Carter, C.S., 1999. The effects of oxytocin and vasopressin on partner preferences in male and female prairie voles (Microtus ochrogaster). Behav Neurosci 113, 1071-1079.

Finkel, E.J., Eastwick, P.W., Matthews, J., 2007. Speed-dating as an invaluable tool for studying romantic attraction: A methodological primer. Pers Relationship 14, 149-166.

Getz, L.L., Carter, C.S., 1996. Prairie-vole partnerships. Am Sci 84, 56-62.

Guastella, A.J., Macleod, C., 2012. A critical review of the influence of oxytocin nasal spray on social cognition in humans: Evidence and future directions. Horm Behav 61, 410-418.

Insel, T.R., 2010. The challenge of translation in social neuroscience: a review of oxytocin, vasopressin, and affiliative behavior. Neuron 65, 768-779.

Jenkins, J.S., Ang, V.T., Hawthorn, J., Rossor, M.N., Iversen, L.L., 1984. Vasopressin, oxytocin and neurophysins in the human brain and spinal cord. Brain Res 291, 111-117.

Loup, F., Tribollet, E., Dubois-Dauphin, M., Dreifuss, J.J., 1991. Localization of high-affinity binding sites for oxytocin and vasopressin in the human brain. An autoradiographic study. Brain Res 555, 220-232.

Loup, F., Tribollet, E., Dubois-Dauphin, M., Pizzolato, G., Dreifuss, J.J., 1989. Localization of oxytocin binding sites in the human brainstem and upper spinal cord: an autoradiographic study. Brain Res 500, 223-230.

MacDonald, E., Dadds, M.R., Brennan, J.L., Williams, K., Levy, F., Cauchi, A.J., 2011. A review of safety, side-effects and subjective reactions to intranasal oxytocin in human research. Psychoneuroendocrinology 36, 1114-1126.

Marazziti, D., Baroni, S., Catena, M., Picchetti, M., Carlini, M., Giannaccini, G., Lucacchini, A., Dell'Osso, L., 2007. A relationship between social anxiety and oxytocin. Eur Psychiat 22, S281-S282.

Murphy, M.R., Seckl, J.R., Burton, S., Checkley, S.A., Lightman, S.L., 1987. Changes in oxytocin and vasopressin secretion during sexual activity in men. J Clin Endocrinol Metab 65, 738-741.

Turner, R.A., Altemus, M., Enos, T., Cooper, B., McGuinness, T., 1999. Preliminary research on plasma oxytocin in normal cycling women: Investigating emotion and interpersonal distress. Psychiatry 62, 97-113.

White, G.L., Kight, T.D., 1984. Misattribution of Arousal and Attraction - Effects of Salience of Explanations for Arousal. J Exp Soc Psychol 20, 55-64.

Williams, J.R., Carter, C.S., Insel, T., 1992a. Partner Preference Development in Female Prairie Voles Is Facilitated by Mating or the Central Infusion of Oxytocin. Ann N Y Acad Sci 652, 487-489.

Williams, J.R., Catania, K.C., Carter, C.S., 1992b. Development of partner preferences in female prairie voles (Microtus ochrogaster): the role of social and sexual experience. Horm Behav 26, 339-349.

Williams, J.R., Insel, T.R., Harbaugh, C.R., Carter, C.S., 1994. Oxytocin administered centrally facilitates formation of a partner preference in female prairie voles (Microtus ochrogaster). J Neuroendocrinology 6, 247-250.

Wolff, K., Tsapakis, E.M., Winstock, A.R., Hartley, D., Holt, D., Forsling, M.L., Aitchison, K.J., 2006. Vasopressin and oxytocin secretion in response to the consumption of ecstasy in a clubbing population. J Psychopharmacol 20, 400-410.

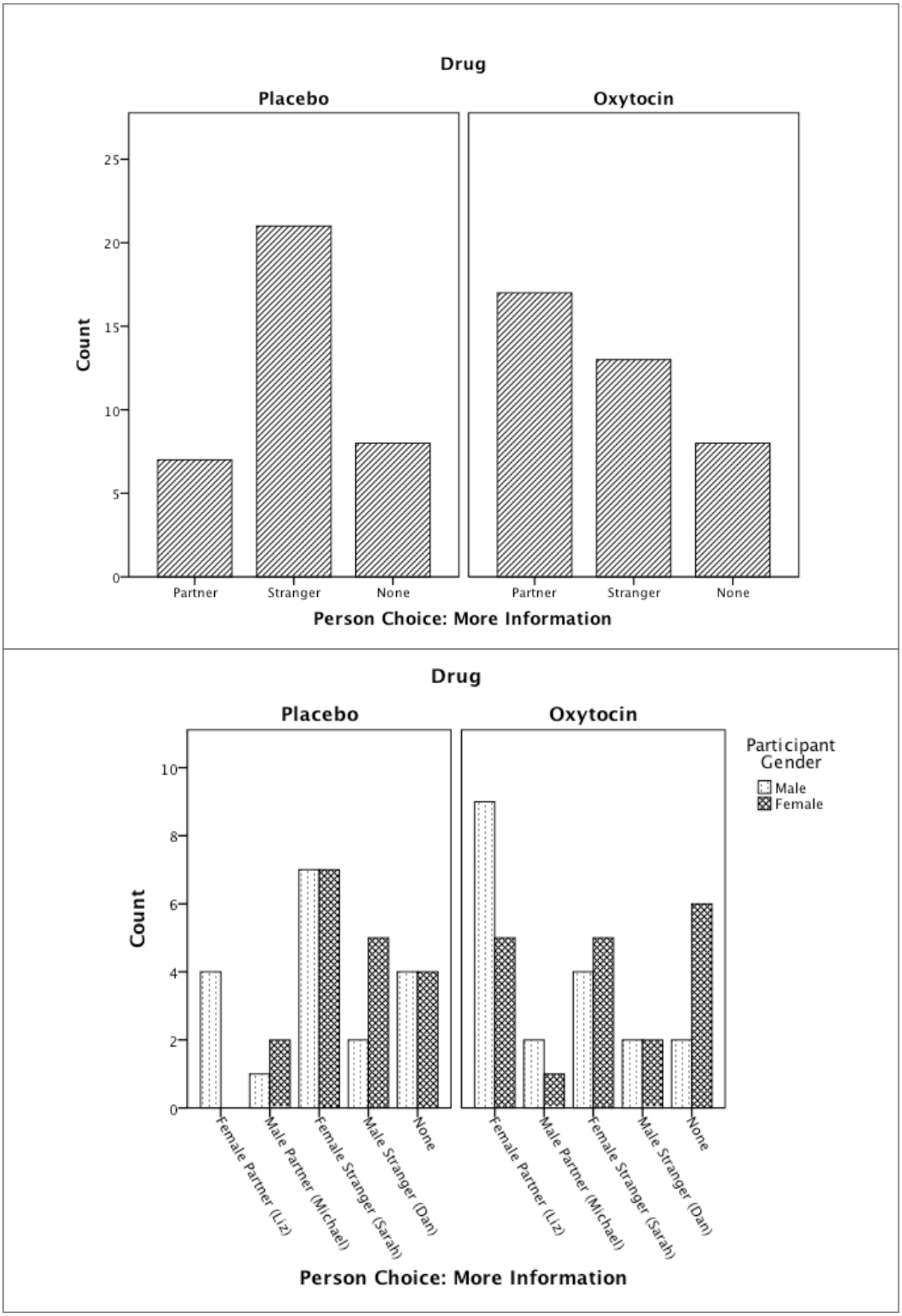

Figure 1. Oxytocin and placebo participants' choice of whom they would like to find out more information about. Bars represent the total number of participants who chose each of the following options: partners, strangers, or none. These data are presented collapsed across participant and persona gender (top panel), and as a function of participant and persona gender (bottom panel).

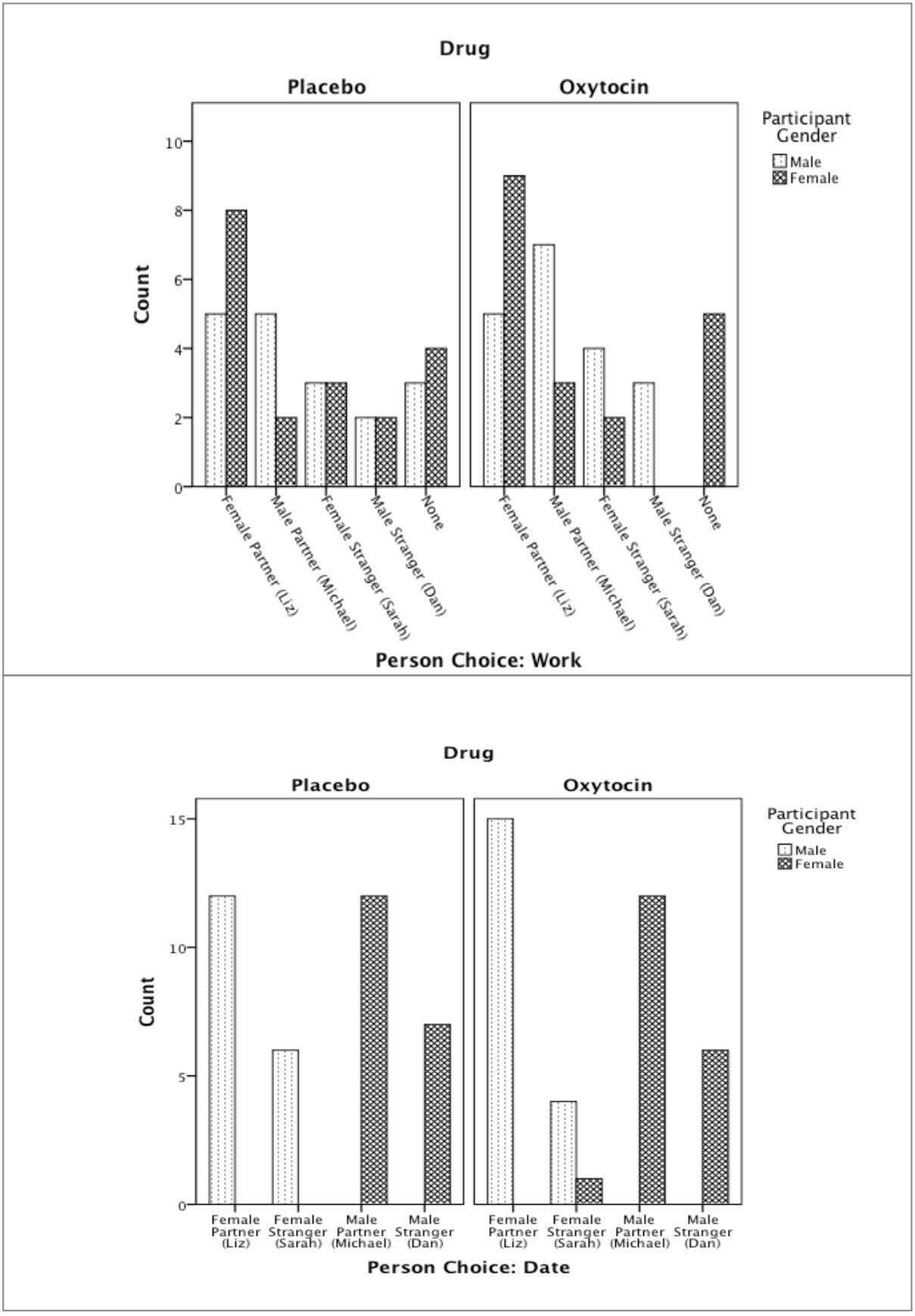

Figure 2. Oxytocin and placebo participants' choice of whom they would like to work with (top panel) or date (bottom panel). Bars represent the total number of participants who chose each of the following options: male or female partners, male or female strangers, or none (top panel only).