Testing the effect of oxytocin on social grooming in bonobos

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Abstract:

Oxytocin has attracted research attention due to its role in promoting social bonding. One notable hypothesis is the biobehavioral feedback loop, which posits that some functions of the oxytocin system support the formation and maintenance of social bonds through a positive feedback loop, where oxytocin promotes social behaviours which then cause oxytocin release themselves. In the two *Pan* species, humans' closest relatives, oxytocin is known to be released following key behaviours related to social bonding, such as social grooming in chimpanzees and female-female sexual behaviour in bonobos. However, no experimental evidence has demonstrated that oxytocin promotes such socio-positive behaviours in *Pan*. To test this, we administered nebulized oxytocin or saline placebo to a group of female bonobos and subsequently observed the change in their gross behavior during free interaction. We found an overall effect of more frequent grooming in the oxytocin condition. However, on the individual level this effect remained significant for only one participant in our follow-up models, suggesting future work should explore inter-individual variation. These results provide some experimental support for the biobehavioural feedback loop hypothesis of oxytocin in bonobo social bonding and encourage more attention towards the effect of oxytocin on social behaviour in more naturalistic settings involving free interaction between participants.

Keywords: Oxytocin, bonobos, social bonding, biobehavioural feedback loop, social grooming, *Pan paniscus*

38 Introduction:

39 Oxytocin is a hormone neuropeptide conserved through mammalian evolution and plays diverse
40 roles in regulating social behaviors across species. Evidence has accumulated for an oxytocin
41 biobehavioural feedback loop in mammalian social behaviours such as maternal care [1–3], pair
42 bonding [4], and even the dog-human bond [5,6], where oxytocin both promotes and is released
43 by key behaviours related to social bonding. In great apes the presence of such a positive feedback
44 loop has also been suggested [7], though the importance of it in human and other great ape
45 species' evolution remains unclear. Currently, experimental evidence is lacking as to whether
46 oxytocin promotes socio-positive interaction in these species, a key piece of evidence that would
47 support the presence of such a positive feedback loop.

48 Among non-human great apes, the majority of studies have been conducted through
49 measurement of urinary oxytocin following key social behaviours. Crockford et al. [7] showed that
50 urinary oxytocin levels in wild chimpanzees increase following social grooming, a key socio-positive
51 behavior widely present in nonhuman primates, and proposed that a positive feedback loop
52 through oxytocin may have evolved to support social bonding in this species. Relatedly, Moscovice
53 et al. [8] found that urinary oxytocin levels in wild female bonobos increased following same-sex
54 sexual behaviour, genito-genital (GG) rubbing. Bonobos also increased proximity and coalitionary
55 support among females after GG-rubbing; though it remains unclear if oxytocin played a direct
56 role in these behavioural changes. Other studies have additionally demonstrated that urinary
57 oxytocin in chimpanzees rises after food sharing [9], reconciliation [10], border patrols [11,12], and
58 group hunting [11,13], further suggesting its importance to social bonds and coordination.

In several primate species, studies have demonstrated exogenous oxytocin can impact a wide range of social behaviours (reviewed in [14]). In macaques, several studies have demonstrated that oxytocin alters social gaze, such as increased attention to eyes [15], reduced attention to negative and fearful facial expressions [16] as well as social threats [17], and more gaze following [18]. In one of the first to test the effect of oxytocin in spontaneous social behaviour among multiple macaques, although still confined to primate chairs in a laboratory setting, Jiang and Platt [19] found evidence that oxytocin flattened the dominance hierarchy and enhanced synchrony of mutual gaze. Marmosets similarly showed an increase in attention to eyes [20] following oxytocin administration and an increase in anxiety and vigilance following administration of an oxytocin antagonist [21]. Another study found that oxytocin promoted huddling in marmosets, while an oxytocin antagonist reduced social proximity and huddling [22]. On the other hand, in capuchin monkeys oxytocin was found to reduce food sharing through increasing interindividual distance [23]; the authors interpreted these results as derived from oxytocin's anxiolytic effect, which increased social distance and thereby decreased opportunities for food sharing [23].

The results of three studies measuring behaviour following oxytocin administration in non-human great apes were mixed. Proctor et al. [24] administered oxytocin to eight chimpanzees individually for one trial each in both saline and oxytocin conditions then observed them in their regular social groups. Although they did not find significant effects for any behaviours measured, the authors note that it may be due to methodological issues, such as in establishing an effective dose of oxytocin for chimpanzees or influence from groupmates who did not receive oxytocin before social interaction. Hall et al. [25] similarly found no effect of oxytocin when chimpanzee

81 dyads were administered oxytocin or saline placebo and subsequently tested in a token exchange
82 task. Each participant chose one of two tokens to exchange and received rewards based on the
83 choice of both participants in distributions based on games such as the prisoner's dilemma and
84 hawk-dove. However, although this study administered oxytocin to a dyad, the authors reported
85 the same methodological concerns for the oxytocin administration procedure as well as a
86 confound between experimental condition and order. No clear patterns emerged in either the
87 placebo or oxytocin conditions, limiting interpretation of oxytocin's possible effect. On the
88 contrary to these studies reporting null results, Brooks et al. [26] found that oxytocin enhanced
89 species-typical social gaze, increasing eye contact in bonobos but not chimpanzees, indicating that
90 oxytocin can modulate gaze behaviour. While the species difference in Brooks et al. cannot be
91 attributed to differences in oxytocin administration procedure, it remains unclear whether the lack
92 of effect in Proctor et al. and Hall et al. is due to methodology of oxytocin administration or that
93 exogenous oxytocin fails to significantly affect chimpanzee social behaviour.

94 Critically, although it is central to the biobehavioural feedback loop hypothesis that both socio-
95 positive interactions cause oxytocin release and that oxytocin can lead to socio-positive
96 interactions, there is no direct evidence showing that oxytocin promotes any socio-positive
97 interaction in *Pan*. Given recent progresses in this line of research, it is worthwhile to test whether
98 oxytocin promotes key social behaviours related to social bonding in *Pan*, particularly in bonobos
99 using the updated methods of oxytocin administration. Therefore, this study administered
100 nebulized oxytocin or saline placebo to a whole group of female bonobos following the methods
101 employed in Brooks et al. [26] and subsequently observed the change in their gross interactive
102 behavior, including grooming and GG-rubbing, as well as other noninteractive behaviours during

their free interaction. As mentioned, the biobehavioural feedback loop hypothesis suggests that an oxytocin positive feedback loop has evolved to support *Pan* social bonding, and in particular we predicted that oxytocin would promote social grooming, which is known to be released through social grooming in wild chimpanzees [7]. For practical reasons, we tested bonobos instead of chimpanzees. In bonobos a similar argument about oxytocin and socio-positive behaviour was made in Moscovice et al. [8], who found that GG-rubbing led to higher urinary oxytocin in wild female bonobos. This study aimed to observe all socio-positive behaviors including play, GG rubbing, and grooming, but focused on social grooming in particular. This choice was made because our bonobos are often in close proximity and engage readily in grooming after experiments (oxytocin administration with rewards), while GG-rubbing is not often observed after these events (possibly due to low overall tension).

Methods:

Ethics statement:

All bonobo participants received regular feedings, daily enrichment, and had ad libitum access to water. No change was made to their daily care routine for the purpose of this study. Apes were never restrained at any point. We carefully considered the safety of the oxytocin administration as in previous studies. Again, we based this decision on the fact that 1) oxytocin is often administered to human children and adults, 2) oxytocin is active for only a short period of time following administration, 3) oxytocin is naturally produced in bonobos and chimpanzees following relevant behaviors [7,8] , and 4) no previous studies administering oxytocin intranasally to chimpanzees or bonobos reported any agonistic interaction [24–26]. All female bonobos were taking birth control and thus no bonobos were pregnant at any time during the course of this experiment. Ethical approval number was WRC-2020-KS014A.

Participants:

Four adult female bonobos at Kumamoto Sanctuary participated in this research. Details about participant ages and rearing histories can be found in supplementary material (Table S1). Animals were not food or water deprived at any time and were given both physical and social environmental enrichment in their daily life. The bonobos live in a dynamic grouping structure where three of the four females are together on any given day, and the fourth is with two male bonobos. These two males were not involved in this study because one male refuses to participate in any oxytocin experiments, and our aim was to test whole groups at a time with the same condition. Three of the females join the male bonobos with varying frequency, while the fourth

136 (Lenore) is always with other female bonobos. Individuals thus had a varying number of trials, with
137 Lenore having the most due to never joining the male group (24 trials), followed by Lolita (20
138 trials), followed by Louise and Ikela (14 trials each) who are most often with the males. Transfers
139 between groups typically occur in the evening and are kept consistent for at least one day and up
140 to one week. The bonobos therefore had been in the same grouping structure for the whole day
141 prior to the start of experiments.

142

143 Administration procedure:

144 Oxytocin administration procedures followed Brooks et al. [26]. Briefly, oxytocin was dissolved in
145 saline at a concentration of 40IU/mL. The oxytocin solution or placebo control was nebulized into
146 a box using a portable nebulizer (Omron NE-U100) at a minimum rate of 0.25mL/minute, for a
147 cumulative 4 minutes while apes drank juice (thus a total of 40IU or more was nebulized during
148 the administration period). We paused counting the time while apes' noses were outside the box.
149 Participation to this administration was voluntary. Three of the bonobos could simultaneously
150 participate in oxytocin administration in their typical enclosure, while the fourth (Ikela) preferred
151 to move to another room to participate in the administration procedure. Thus, on days when Ikela
152 was in the group, we first completed the administration procedure with Ikela (accompanied by
153 other participant bonobos), and then returned her to the home enclosure with the other
154 participant bonobos; the other participant bonobos were then administered oxytocin (or saline
155 placebo control). On days when Ikela was not in the group, all participants were administered
156 oxytocin (or saline placebo) in their home enclosure. All group members received the same

condition (saline placebo or oxytocin) on any given day of experiments and finished administration procedures within 30 minutes of one another.

One trial was performed in an experimental day. The order of conditions was pseudorandomized such that the same condition (placebo and oxytocin) never occurred more than twice in consecutive trials (experimental days) and that the same number of trials were conducted for placebo and oxytocin condition for each participant and for each grouping structure. We had a minimum of 2 days between trials to avoid any possible carryover effect of oxytocin. On each experimental day, the experiment was performed between 11:00 and 12:15, and the observation window therefore started between 11:30 and 12:45. Experimental days followed the same feeding schedule; bonobos were fed breakfast around 9:00, and additional greenery is available for foraging throughout the day. Experiments took place over five calendar months across two calendar years.

Observation procedure:

Observation began 30 minutes after completion of administration procedures to the last individual, and lasted for one hour. This window was chosen based on previous studies [14], where oxytocin's effect is typically measured in the window between 30 minutes and 2 hours after completion of administration procedures. In our experiment, the last individual to complete administration procedures was always within 30 minutes of the first individual to finish, and thus all participants were observed for one hour, starting and finishing between 30 minutes and 2 hours following completion of administration procedures on any given day. We chose this window in order to

178 maximize data collection within the active window of oxytocin while ensuring consistency
179 between trials and participants, where observation windows were kept constant at 1 hour per trial
180 and all data points for all individuals were within the 30 minutes to 2 hour window employed in
181 previous studies.

182 Observation methods combined scan and event sampling. Specifically, every 2 minutes,
183 interindividual proximity was estimated for each dyad into one of four categories; in contact,
184 within arm's reach (one individual could extend their arm to touch the other), < 3 meters, and > 3
185 meters. In addition, at the same 2 minute intervals, we coded each individual's behaviour
186 (grooming - including direction and partner(s), resting, self-directed behaviour, moving, eating).
187 Finally, we recorded all occurrences of play, GG-rubbing, abnormal behaviour (in this group
188 primarily regurgitation and reingestion), and aggression towards groupmates (including displays).

189 We additionally recorded any agonistic or socio-sexual behaviour during the administration
190 procedures and during the 30 minutes before the formal observation window to check if the
191 presence of such interactions could account for our results. No agonistic behaviour was observed,
192 and GG-rubbing occurred on 4 trials during administration procedure, on 2 trials before oxytocin
193 condition and 2 trials before saline placebo condition.

194 Analysis

195 All analyses were conducted in R [29]. Behavioural scan data was analyzed with binomial GLMMs
196 (Generalized Linear Mixed Models) with package lme4 [30], where each individual at each
197 sampling point was characterized as either engaged in (1) or not engaged in (0) a given behaviour.
198 The model included a fixed effect of condition as a test effect and also fixed effects of time, the

199 square of time (time^2) and grouping structure (where a unique value was given for each possible
200 combination of individuals) as control effects. The model also included random effects of
201 participant and day (a factor with a unique value for each experimental day), as well as random
202 slopes of each fixed effect for each random effect. Numeric effects were z-transformed to have a
203 mean of 0 and the standard deviation of 1. Random slope structure was kept maximal, except that
204 the interaction between random slopes and intercepts was removed due to issues with
205 convergence [31]. For all GLMMs we checked model stability by comparing our models to those
206 which excluded levels of the random effects one at a time. We additionally calculated odds ratio
207 (OR) estimates and 95% confidence intervals for all significant effects. For the grooming data, we
208 analyzed rates of active grooming (giving or mutual grooming), and receiving grooming was valued
209 as 0 for not actively grooming another individual. Given considerable inter-individual variation
210 observed by visual inspection of the data, we additionally tested each individual with the same
211 model structure for significant effects (without the random effect of participant). We here used a
212 significance threshold of 0.0125 (0.05/4) to correct for multiple testing at the individual level.
213 Finally, we ran as models excluding each level of participant to check the overall model stability.

214 Proximity data was analyzed using a CLMM (cumulative link mixed model) on ordinal data
215 using the package "ordinal" [32]. Fixed and random effect structures were the same as those in
216 the behavioural scan data analysis, except for the individual participant variable was replaced by
217 dyad (a unique value for each dyad), and the addition of two random effects to represent the two
218 individuals within a dyad (randomly distributed as individual variable 1 and 2).

219 All occurrence data was analyzed with a binomial GLMM, where each individual for each
220 day was characterized as having engaged in (1) or not engaged in (0) a given behaviour. The fixed

221 and random effect structure was the same as in the scan behaviour models, except for the time

222 variables were removed due to data being summarized across a given observation day. Model

223 syntax for all model types can be found in supplemental material.

224

Results

Our model with active grooming as response revealed a significant effect of condition (oxytocin, saline placebo; β = 1.16, SE = 0.49, χ^2 = 5.47, p = 0.019, OR = 3.18 (95% CI: 1.23, 8.23); Table 1, Figure 1). In our stability check analysis excluding each participant one-by-one in the model, the effect of oxytocin on grooming was significant in all models except for that excluding Louise (excluding Ikela: β = 0.79, SE = 0.31 , χ^2 = 5.27, p = 0.022; excluding Lenore: β = 1.28, SE = 0.64, χ^2 = 8.97, p = 0.0027; excluding Lolita: β = 0.88, SE = 0.36, χ^2 = 5.06, p = 0.025; excluding Louise: β = 0.59, SE = 0.37, χ^2 = 2.34, p = 0.13). In our individual-level analysis of grooming, we found a significant effect of condition only for Louise using a significance threshold of 0.0125 (Ikela: β = 0.86, SE = 1.51, χ^2 = 0.24, p = 0.63; Lenore: β = 0.79, SE = 0.35, χ^2 = 4.61, p = 0.032; Lolita: model could not run (as Lolita never actively groomed in our dataset); Louise: β = 1.15, SE = 0.40, χ^2 = 9.09, p = 0.0026).

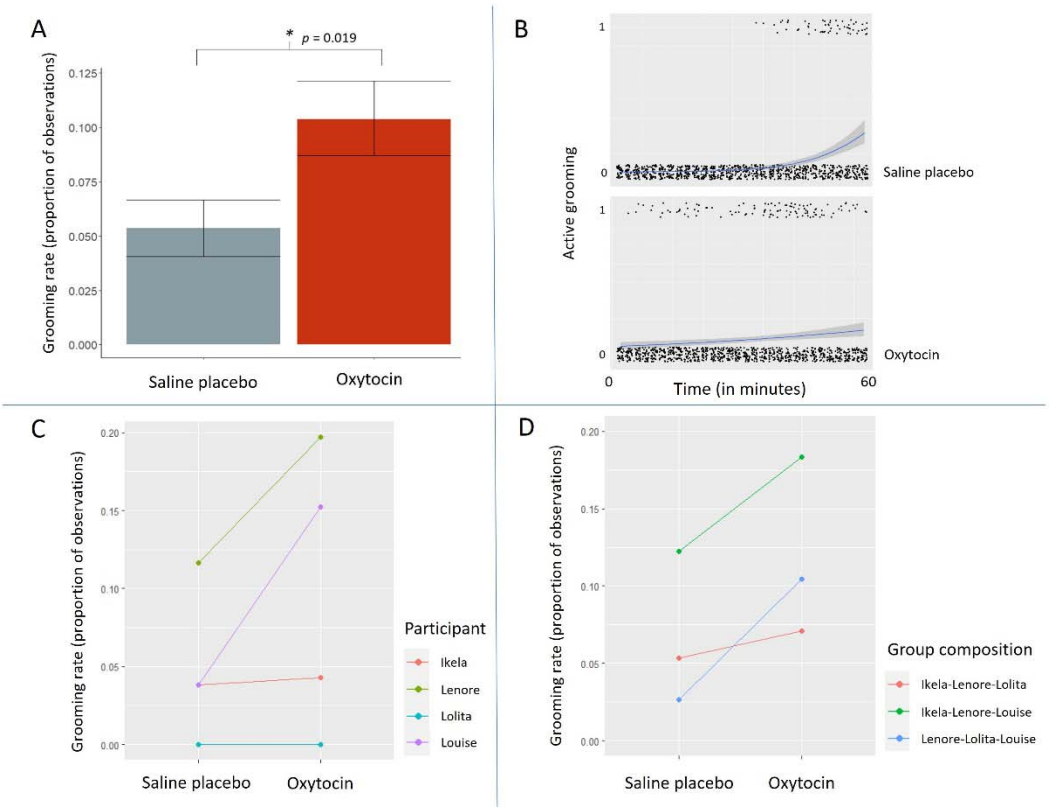

Figure 1: Rates of active (giving) grooming in the oxytocin and saline placebo conditions over the observation window. A) Absolute rates of grooming across all trials and participants B) Time course of grooming by condition, 1 represents giving grooming and 0 represents not giving grooming C) Grooming rates by participant and condition D) Grooming rates by group structure by condition.

Table 1; Details of grooming and self-directed behaviour models with significant terms in bold.

Response	Term	Estimate ± SE	χ^2	*df*	*p*
Active grooming	(Intercept)	-15.57±6.29			
	Test predictors:				
	Condition	**1.156±0.49**	**5.47**	**1**	**0.019***
	Control predictors:				
	Group		*4.73*	*2*	*0.094.*
	Ikela-Lenore-Louise	*12.61±6.29*			
	Lenore-Lolita-Louise	*8.14±6.70*			
	Time (time + time^2)	**1.59±0.44**	**9.15**	**1**	**0.0025***

Self-directed behaviour	(Intercept)	-2.81±0.60			
	Test predictors:				
	Condition	**-0.33±0.14**	**5.16**	**1**	**0.018***
	Control predictors:				
	Group		3.09	2	0.21
	Ikela/Lenore/Louise	-0.094±0.53			
	Lenore/Lolita/Louise	0.75±0.53			
	Time	**-0.31±0.13**	**4.42**	**1**	**0.035***

There was also a significant reduction in self-directed behaviour in the oxytocin compared to placebo condition (β = -0.33, SE = 0.14, χ^2 = 5.16, p = 0.018, OR = 0.72 (95% CI: 0.54, 0.94); Table 1). In our stability check analysis excluding each participant one-by-one in the model, the effect of oxytocin on self-directed behaviour was significant in the model excluding Lenore and the model excluding Lolita (excluding Ikela: β = -0.26, SE = 0.13, χ^2 = 3.52, p = 0.061; excluding Lenore: β = -0.41, SE = 0.14, χ^2 = 8.89, p = 0.0029; excluding Lolita: β = -0.51, SE = 0.16, χ^2 = 9.81, p = 0.0017; excluding Louise: β = -0.34, SE = 0.17, χ^2 = 3.65, p = 0.056). In our individual-level analysis, we found a significant effect only for Ikela using a significance threshold of 0.0125 (Ikela: β = -0.71, SE = 0.21, χ^2 = 12.19, p = 0.00048; Lenore: β = -0.15, SE = 0.28, χ^2 = 0.27, p = 0.60; Lolita: β = -0.59, SE = 0.24, χ^2 = 5.58, p = 0.018; Louise: β = -0.58, SE = 0.41, χ^2 = 2.48, p = 0.11).

There were no significant differences in interindividual proximity (β = -0.15, χ^2 = 0.32, p = 0.57), frequency of the abnormal behaviour regurgitation and reingestion (β = -1.05, SE = 0.66, χ^2 = 2.65, p = 0.10), or rate of rest (β =-0.10, SE = 0.18, χ^2 = 0.34, p =0.56) between the oxytocin and placebo condition. Bonobos engaged in GG-rubbing only once (oxytocin condition) and displayed no

aggression toward groupmates or any bouts of play during the observation period. See supplementary material Table S2 for full details of all models.

Discussion:

We found that on the whole grooming rates of captive female bonobos were higher in the oxytocin compared to saline placebo condition, though when conducting individual-level analyses this was only significant after correcting for multiple testing in one participant (Louise). Still, in combination with the previous studies showing oxytocin is released in bonobos and chimpanzees following socio-positive interaction [7,8], our results provide some support for the biobehavioural feedback loop hypothesis of oxytocin in social bonding for bonobos. The bonobos also engaged in self-directed behaviour less in the oxytocin compared to placebo condition (though again this was significant on an individual level in just one participant - Ikela), which is likely related to its anxiolytic effect, though it should be noted we did not distinguish between kinds of self-directed behaviours such as self-scratching or self-grooming which may have different relations to stress. The proportion of rest and frequency of regurgitation and reingestion did not differ between conditions, while GG-rubbing, play, and aggression were rarely or never observed during our 1-hour observation window, likely due to low overall tension, precluding formal analysis.

Despite our overall model showing an increase in grooming in the oxytocin condition, our individual-level analyses revealed only one individual, Louise, a 48-year-old female bonobo relatively dominant to other groupmates. Lenore, a 38-year-old, also groomed groupmates more in the oxytocin compared to the saline condition, but was not significant after correcting for multiple testing. Ikela, a 29-year-old, groomed slightly more, but this effect was also not significant. Lolita was never observed actively grooming throughout our experiment, and thus her rate of grooming was completely unchanged by oxytocin. Future studies are needed to examine what factors drive these potential individual differences. It is also important to note that given social

287 grooming necessarily requires a grooming partner, and given our experimental design
288 administering the same condition to all group members simultaneously, oxytocin's effect on the
289 group may not be entirely reducible to the individual level. Oxytocin may as a whole promote a
290 group dynamic more conducive to grooming, which is measurable in the behaviour of certain key
291 individuals. This hypothesis can be directly tested by administering oxytocin compared to saline
292 placebo only to Louise, and always saline placebo to others, and examining if the same effect is
293 found.

294 Although we present the first observation that oxytocin can promote socio-positive
295 interactions in female bonobos, there are several important limitations in this study. Due to
296 limited possibility of testing, enclosures suitable for detailed observation, and some apes'
297 willingness to join experiments, the sample was limited to just four adult female bonobos. This
298 limits firm conclusions about a biobehavioural feedback loop, as Crockford et al. [7] measured
299 urinary oxytocin after grooming only in chimpanzees, while Moscovice et al. [8] focused on sexual
300 interactions rather than grooming in bonobos. While these previous studies characterized the
301 changes similarly as socio-positive behaviours strengthening bond formation, conclusive proof of a
302 biobehavioural feedback loop in one or both species would require evidence of increased urinary
303 oxytocin following grooming in bonobos, administration of oxytocin promoting GG-rubbing in
304 bonobos, or administration of oxytocin promoting grooming among bond partners in chimpanzees.
305 It remains possible that exogenous oxytocin promotes grooming in bonobos but not chimpanzees,
306 or that oxytocin is released following grooming in chimpanzees but not bonobos. Of relevance,
307 Proctor et al. [24] did not find any behavioural change after administration of oxytocin on captive
308 chimpanzees, though they focused on oxytocin administration and observation to only one

individual at a time, instead of the group level as in the current study, limiting our ability to directly compare the results. In addition, previous work has indicated sex-specific effects of oxytocin [33–35], and thus it remains unclear whether our results can be generalized to different sex pairs, though it should be noted that Crockford et al. [7] did not find significant differences between female-female, female-male, and male-male dyads in urinary oxytocin level following grooming in wild chimpanzees. We also could not investigate the possible effect of different genetic background contributing to differences in the amount of change between conditions across individuals, which should be directly explored in the future. Finally, the small number of participants did not enable us to test the effect of existing social bond strength and relatedness among groupmates, which may interact with the observed increase in grooming.

In conclusion, although limited, our finding offers some experimental evidence that oxytocin can promote socio-positive interaction in bonobos. The oxytocin system may have been coopted through evolution to the formation and maintenance of social bonds though a positive feedback loop. Moreover, we suggest that oxytocin administration can be an effective tool in great ape research involving free interactions among groupmates. Future work should further test potential differences in oxytocin's effect between species, should examine inter-individual variation with respect to social closeness and centrality, and should study how social contexts such as feeding tension interact with this effect. We demonstrate that exogenous oxytocin can affect great ape behaviour in naturalistic, spontaneous social interactions and provide experimental support for the biobehavioural feedback loop hypothesis of oxytocin in the evolution of bonobo social bonding.

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