



## Oxytocin effects on gazing at the human face in retriever dogs

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### ABSTRACT

Oxytocin is a neurohormone involved in domestic dogs' socio-cognitive abilities which appears to be key in the display of gazing behavior as a communicative signal. However, differential effects of oxytocin have been reported in various tasks according to the dogs' breed. In the present study, we evaluated the effect of the intranasal administration of oxytocin on gazing towards the human face in Golden and Labrador Retrievers. This was assessed during a learning task in which dogs had to gaze at the human face in order to receive food that was visible but inaccessible. Results indicate that only intact dogs who received oxytocin exhibited an increase in gazing behavior, while no differences were observed for neutered dogs. This effect could be related to an interaction between oxytocin and steroid hormones in intact dogs. These findings highlight the importance of including modulating factors, such as breed and neutered status, when studying the mechanisms of oxytocin.

### 1. Introduction

Gazing at the human face is a key communicative ability in domestic dogs (e.g., Miklósi et al., 2003). Recently, the neurohormone oxytocin (OT) has been found to be involved in dogs' gazing behavior (for a review, see Kis et al., 2017a). For instance, OT levels increased after prolonged gazing between dogs and their owners (Nagasawa et al., 2015) and similar results were found after social interactions which included gazing (Hritcu et al., 2019; but see Marshall-Pescini et al., 2019; Powel et al., 2019).

Additionally, dogs gazed more at people after receiving intranasal OT instead of placebo in different situations: when an unfamiliar person approached in a threatening way (Hernádi et al., 2015), during affiliative interactions with their owners (Nagasawa et al., 2017) and in presence of inaccessible food in a communicative task (Barrera et al., 2018). In addition, they gazed more at positive human facial expressions (Somppi et al., 2017) and less at negative ones (Kis et al., 2017b).

Remarkably, some studies report differences on OT effects according to the dogs' breed. For instance, in Kovács et al. (2016), Border Collies gazed more than Siberian Huskies after receiving OT in three social tasks. However, Persson et al. (2017) reported no effect of OT administration on gazing at the human face in Golden Retrievers during an unsolvable task, but they found a modification in the frequency of

physical contact seeking. Moreover, breed differences were found when taking a genetic approach, as Border Collies differed from German Shepherds in polymorphisms of the OT receptor gene (Kis et al., 2014). These findings indicate potential differences in responsiveness to OT across and within breeds.

The aim of this study was to analyze the effects of OT administration on gazing behavior in Golden and Labrador Retriever dogs, two highly popular breeds selected for cooperative work with humans which requires frequent visual contact with people (Gácsi et al., 2009; Kovács et al., 2016). They were evaluated in a communicative task in which there was food out of their reach. First, they went through an acquisition phase in which they were reinforced for gazing to the human face to ask for the food, following an extinction phase in which this response was not reinforced anymore. Prior evidence utilizing this task indicates that Retrievers (Goldens and Labradors) gazed more than German Shepherds and Poodles during the extinction phase of this task (Jakovcevic et al., 2010). This suggests that Retrievers as a group have a high performance during this communicative task. Considering this and that these two Retriever breeds have been pooled together in other studies (e.g., Barrera et al., 2019; D'Aniello et al., 2015; MacLean et al., 2017), no differences between the two were expected in the present study. Furthermore, Barrera et al. (2018) analyzed the effect of OT administration during this task in mixed breed dogs. Results indicate

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that the ones that received OT instead of placebo gazed more during the extinction phase. Therefore, it would be interesting to replicate that study including a breed group previously found to have high gazing levels during the task, such as Retrievers. It is important to highlight that in the works of [Jakovcevic et al. \(2010\)](#) and [Barrera et al. \(2018\)](#), group differences in gazing behavior emerged only during the extinction phase. Therefore, this study aims to analyze the effects of OT administration on gaze behavior across the different phases of the communicative learning task. We expect group differences to emerge in the extinction phase. In this case, an increase in gazing during extinction would be expected for the OT group in comparison to the one receiving placebo.

This study contributes to the knowledge of how OT administration modulates socio-cognitive abilities in Retriever dogs, in particular gazing as a communicative response. In addition, it contributes to the generalization of the knowledge of the modulating effects of OT administration. This is of relevance given the important role of Retriever dogs as working dogs as well as pets.

## 2. Ethical approval

The study complied with the current Argentine law of animal protection (Law 14.346) and was developed with the approval of the CICUAL (Institutional Commission for the Care and Use of Laboratory Animals) from the Medical Research Institute IDIM UBA-CONICET (Res. Nro. 084-18). All owners gave their consent for the participation of their dogs.

## 3. Method

### 3.1. Subjects

We assessed 38 dogs of which 20 were Golden Retrievers (5 neutered and 2 intact females, 3 neutered and 10 intact males) and 18 were Labrador Retrievers (4 neutered and 5 intact females, 5 neutered and 4 intact males). All dogs came from common type breeding lines (i.e., bred for show and pet purposes). All of them were adults (1–11 years old;  $M = 4.51$ ,  $SD = +2.75$  years) in good health, lived in houses as pets and had no particular training. Thirty dogs were assessed in their homes while 8 dogs were tested in a familiar daycare facility. Dogs had free access to water and their last meal had been between 4 and 6 h earlier. For full details of the sample see [Table 1](#).

### 3.2. Apparatus

The evaluation was carried out in a quiet room in a familiar place (i.e. home or daycare facility). A container with pieces of cooked liver was placed on a high shelf so that it was visible but out of reach. The experimenter stood beside the container. A 1 m perimeter was marked around the E. All trials were video-taped by a Sony DCR 199 SX-85 camera by an assistant who stood behind the E and ignored the dog.

### 3.3. Procedure

#### 3.3.1. Administration

The dogs received either 16 IU (international units) of intranasal OT (Syntocinon®, Novartis) ( $N = 18$ ) or saline solution as placebo ( $N = 20$ ), 40 min before the task. This time frame was selected as it is the time it takes for OT to reach the brain ([Quintana et al., 2015](#)).

Dogs had a 30 min waiting period after application in which they did not interact with people. Afterwards, an assistant took them to the testing room and then ignored them for a 10 min habituation phase. Immediately after, the testing began.

#### 3.3.2. Communicative learning task

Before starting the task, an experimenter (E), who was blind to the

**Table 1**  
Characteristics of the sample.

ID	Breed	Age (years)	Sex	Neutered State	Testing place	Treatment
1	Labrador	6	F	Neutered	Daycare	OT
2	Golden	1	M	Intact	Home	OT
3	Golden	2	M	Intact	Home	OT
4	Golden	6	F	Neutered	Home	OT
5	Labrador	2.5	M	Intact	Daycare	OT
6	Golden	1	M	Intact	Home	OT
7	Golden	8	M	Neutered	Daycare	OT
8	Labrador	4	M	Neutered	Home	OT
9	Golden	2	F	Neutered	Home	OT
10	Golden	7	M	Neutered	Home	OT
11	Golden	1	M	Intact	Home	OT
12	Golden	1	M	Intact	Home	OT
13	Labrador	5	F	Neutered	Home	OT
14	Labrador	3	M	Neutered	Home	OT
15	Labrador	2	F	Intact	Home	OT
16	Golden	6	F	Intact	Home	OT
17	Labrador	8	M	Intact	Home	OT
18	Labrador	11	M	Intact	Home	OT
19	Golden	1.8	M	Intact	Home	Saline
20	Golden	6	M	Neutered	Home	Saline
21	Golden	5	M	Intact	Home	Saline
22	Golden	2	M	Intact	Home	Saline
23	Labrador	6	M	Intact	Home	Saline
24	Golden	3	F	Neutered	Home	Saline
25	Labrador	8	F	Intact	Home	Saline
26	Labrador	6	F	Neutered	Home	Saline
27	Golden	1	M	Intact	Daycare	Saline
28	Golden	7	F	Neutered	Home	Saline
29	Labrador	3	F	Neutered	Home	Saline
30	Labrador	10	M	Neutered	Home	Saline
31	Labrador	8	M	Neutered	Daycare	Saline
32	Golden	5	F	Intact	Daycare	Saline
33	Golden	6	F	Neutered	Home	Saline
34	Labrador	7	M	Neutered	Home	Saline
35	Labrador	5	F	Intact	Home	Saline
36	Labrador	5	F	Intact	Home	Saline
37	Golden	1	M	Intact	Daycare	Saline
38	Labrador	6	F	Intact	Daycare	Saline

Note: ID (subjects' identity); F: female, M: male.

dog's treatment, interacted positively with the dog for 2 min (i.e., calling the dog and petting it if the dog allowed it). Then, E called the dog and gave it three pieces of liver immediately before starting the task, to confirm they were food motivated.

The task was the same as in [Jakovcevic et al. \(2010\)](#) and [Barrera et al. \(2018\)](#). The procedure consisted of three phases:

**Acquisition.** Three 2 min trials in which gazing was reinforced. These trials started with E standing beside the food container, calling the dog by its name and giving it a piece of liver. Afterwards, the dog received a piece of food each time it gazed at the E's face.

**Extinction.** Then, there were three 2 min extinction trials in which gazing behavior was no longer reinforced.

**Reacquisition.** Finally, the dog received one trial which was identical to the acquisition trials. This phase discarded potential satiety or fatigue effects.

During all trials, the E remained in the same position gazing at the dog's face. The interval between trials and phases was of 2 min, during that time E stood in a corner of the room facing backwards.

The dependent variable in all trials was the cumulative gaze duration (s) toward the E's face.

## 4. Data analysis

An E analyzed 100 % of the video-taped material. Additionally, in order to assess interobserver reliability, a second observer blind to the dog's treatment (OT- Saline) analyzed 40 % of the material. We calculated Spearman's coefficients of correlation for all trials and they showed high reliability ( $r_s > .87$ ,  $p_s < .001$ ,  $N = 16$ ).

Data were analyzed using generalized linear mixed models (GLMM) fitted with the Mixed Models option from IBM SPSS software (version 24). The distribution of Gaze (s) was set to normal and related to the fixed factors through the identity link function. Models were built using the Backward method, based on the gradual elimination of variables to find a reduced model that best explains the data. The models were compared using Akaike and Bayesian information criteria.

The initial model included Treatment (OT, Saline), Breed (Golden, Labrador), Sex (Female, Male), Neutered Status (Neutered, Intact), Testing place (House, Daycare), and Phase (Acquisition, Extinction, Reacquisition), as fixed effects, and Age (years) as a covariate in the fixed effects' structure. This model also included six two-way interactions that resulted from crossing the Treatment with all the factors (Breed, Sex, Neutered Status, Age, Testing Place and Phase). However, Breed and its interaction failed to reach significance. Thus, this factor was not included in the best model reported below.

The final model included Treatment, Sex, Neutered status, Age, Testing place, and Phase as fixed factors; it also included five two-way interactions resulting from pair-crossing Treatment with the rest of the factors.

The Satterthwaite approximation was specified as the method to estimate the degrees of freedom due to different cluster sizes in the between and within-participants factors (e.g., Li and Redden, 2015). The random effects structure included intercepts to account for variability across subject's ID and across Trials. In case of significance, the estimated coefficients, standard errors (SE), and confidence intervals (CI) (95 %) are reported as an indication of the degree of change in the outcome. Additional comparisons were conducted using paired contrasts (sequential adjusted Bonferroni) when required.

## 5. Results

The descriptive results indicated that during the Acquisition Phase, dogs gazed  $11.57 \pm 8.38$  s after OT Treatment and  $9.09 \pm 5.53$  s after Saline Treatment. During the Extinction Phase, dogs gazed  $55.56 \pm 28.50$  s after OT Treatment and  $46.49 \pm 3.00$  s after Saline Treatment. Finally, in the Reacquisition phase, dogs gazed  $11.84 \pm 8.20$  s after OT Treatment and  $10.85 \pm 6.64$  s after Saline Treatment.

Analyses showed that Phase affected Gaze ( $F(2, 4) = 64.66, p = .001$ ), so that the average Gaze duration in the Extinction Phase increased by  $43.99$  s ( $SE = 4.38, CI_{.95} = 33.64, 54.35$ ) compared to the Acquisition Phase, and by  $36.14$  s ( $SE = 6.11, CI_{.95} = 21.53, 50.75$ ) compared to the Reacquisition Phase. No difference was observed between the Acquisition and Reacquisition Phases ( $b = -1.25, SE = 6.11, CI_{.95} = -15.86, 13.36$ ).

Moreover, Testing place affected Gaze ( $F(1, 28) = 5.14, p = .031$ ). Dogs tested in their Home gazed more than dogs evaluated in the Daycare facility ( $b = 11.55, SE = 5.09, CI_{.95} = 1.12, 21.97$ ).

In addition, the model yielded a significant Treatment x Neutered Status interaction ( $F(1, 28) = 4.82, p = .037$ ). Paired contrasts revealed that, OT Treatment increased Gaze duration as compared to Saline only in Intact dogs ( $b = 15.42, SE = 6.44, CI_{.95} = 2.26, 28.59$ ) (see Fig. 1). Note though, that CIs are wide, so we cannot exclude that the effect may be larger or smaller than reported. Neutered dogs, on the other hand, showed no differences in Gaze as a function of Treatment ( $b = -2.60, SE = 6.55, CI_{.95} = -15.98, 10.78$ ). The rest of the fixed factors and interactions yielded no significant effects ( $ps > .05$ ).

## 6. Discussion

Results indicate that Golden and Labrador Retrievers gazed more during the extinction phase of the communicative learning task, than during the acquisition and reacquisition phases. This increase replicates the findings of previous studies (e.g. Bentosela et al., 2008; Jakovcevic et al., 2010). The persistence of dogs during the extinction phase could

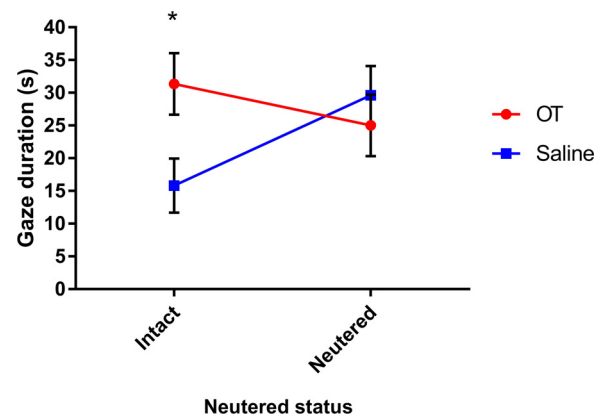


Fig. 1. Mean of Gaze duration (s) depending on the Neutered status (Intact or Neutered) for each treatment (OT and Saline). Bars show SEM. \*  $p < .05$ .

be attributed to the previous reinforcement of gazing behavior during acquisition. Moreover, it is probably related to the characteristics of the task itself. During the extinction phase dogs are free to gaze to the person for longer times, while in the other phases total gazing time is diminished because they tend to follow with their eyes the arm movement towards the food recipient each time they are reinforced.

An important aspect to consider is that Golden and Labradors were combined into a single sample in this study. This is in line with previous research combining these two breeds (e.g. Barrera et al., 2019; D'Aniello et al., 2015; Jakovcevic et al., 2010; MacLean et al., 2017). Moreover, it is supported by the lack of significant differences between both breeds in our study, which allowed the results to be pooled together. However, other works found differences between the two. For instance, Labradors had a higher score in curiosity/fearlessness compared to Golden (Svartberg, 2006), and Golden exhibited more indicators of distress than Labradors during the Strange Situation Test (Fallani et al., 2007). These differences across studies may be related to the particular characteristics of the tasks featured in them.

Besides differences between breeds, some authors have found differences in the behavior of dogs within breeding lines. For example, Sundman et al. (2017) found that field type (i.e., bred for hunting) Labradors exhibited greater eye and physical contact with the owner during a problem-solving test, compared to common type ones (i.e., bred for pet and show purposes). This aspect could not be analyzed in the present study, however, as all dogs were of the common type breeding lines.

We found a testing place effect, as dogs evaluated in their homes gazed longer compared to dogs assessed in the daycare facility. Dogs may have felt more comfortable in their own homes where the owner was close by in another room and there were fewer possible distractions. In contrast, although daycare dogs were used to being in the facility, they may have felt less at ease outside of their home without their owner present, and may have been more distracted by factors such as the noises or smells of the other dogs housed in the facility.

However, it is noteworthy that no effect was found on the interaction between treatment and testing place, which suggests that OT acted similarly in both conditions. This result is consistent with Barrera et al. (2018) in which both shelter and pet dogs increased their gazing at the human face during the extinction phase after receiving OT. In this sense, although it is for a short period of time, dogs that are housed in daycare facilities have a lower frequency of interactions with people than dogs in their homes. Therefore, dogs that live in different conditions appear to be similarly affected by OT administration.

Surprisingly, an increase in gazing behavior was observed in intact dogs which received OT compared to those that received saline solution, while no differences were found in neutered dogs. Therefore, OT administration appears to have a greater impact on subjects with

unaltered levels of reproductive hormones. This may be due to an interaction between OT and the dogs' gonadal hormones, as gonadal steroids regulate OT brain receptors (for a review, see Gimpl and Fahrenholz, 2001) and a decrease of these receptors has been reported in neutered rats (Tribollet et al., 1990). In addition, there could be an interaction between breed and the neutered status, as female gonadectomized Golden and Labrador Retrievers were less responsive to following human pointing than intact dogs (Scandurra et al., 2019). However, given that no relation between OT and dogs' neutered status has been found in previous studies (Cimarelli et al., 2017; Kis et al., 2015; Oliva et al., 2019), these results must be interpreted with caution and further research is needed to clarify this matter.

These findings contrast with those obtained by Barrera et al. (2018), who found an increase in gazing behavior after OT treatment during the extinction phase in mixed breed dogs. However, in the present study, we did not observe a general effect of OT administration in Retriever dogs, but only in intact ones. Unfortunately, Barrera et al. (2018) did not report the dogs' neutered status in their study, so it is not possible to analyze its effect on the dogs' behavior.

The particular effects of OT administration observed in the present study may be due to characteristics of the breeds included (i.e., Retrievers). This is in line with studies that suggest there are differences in the OT system across breeds (i.e., Kis et al., 2014; Kovács et al., 2016). In particular, Kovács et al. (2016) proposed that breeds could have different baseline OT levels. Consequently, Retrievers may have increased basal OT levels and thus intranasal OT administration could have reached a ceiling effect in these breeds. For instance, Retrievers gazed more than other breeds in this task on a previous study with no OT administration (Jakovcevic et al., 2010). Thus, they may have higher baseline levels of gazing and it may be difficult to observe facilitating effects of OT administration in this breed.

Finally, it is needed to proceed with caution when interpreting the effects of OT on dogs' social behavior, as results on the matter have been mixed (for a review see Kis et al., 2017a, but see Powell et al., 2019; Marshall-Pescini et al., 2019; Thielke and Udell, 2017). Discrepancies in the methodology of the studies may be behind their differences, as the use of different protocols hinders the generalization of the results. One strength of the current study is that it is a replica of Barrera et al. (2018), but focuses on Golden and Labrador Retrievers.

## 7. Conclusion

In conclusion, intranasal OT administration affected gazing behavior in intact but not in neutered Retriever dogs during an inaccessible food task. It is possible for this to be due to the interaction of OT with specific characteristics of Retrievers and the dogs' neutered status. Future studies should delve in the importance of these factors in order to deepen the understanding of OT mechanisms and how it modulates dog social cognition.

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## CRediT authorship contribution statement

**M.V. Dzik:** Conceptualization, Methodology, Formal analysis, Investigation, Writing - review & editing. **C.M. Cavalli:** Conceptualization, Methodology, Investigation, Writing - review & editing. **G. Barrera:** Conceptualization, Methodology, Investigation, Writing - review & editing. **M. Bentosela:** Conceptualization, Methodology, Investigation, Formal analysis, Writing - review & editing, Supervision.

## Declaration of Competing Interest

The authors declare that they have no conflict of interests.

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## References

- Barrera, G., Dzik, V., Cavalli, C., Bentosela, M., 2018. Effect of intranasal oxytocin administration on human-directed social behaviors in shelter and pet dogs. *Front. Psychol.* 9, 2227. <https://doi.org/10.3389/fpsyg.2018.02227>.
- Barrera, G., Alterisio, A., Scandurra, A., Bentosela, M., D'Aniello, B., 2019. Training improves inhibitory control in water rescue dogs. *Anim. Cogn.* 22 (1), 127–131. <https://doi.org/10.1007/s10071-018-1224-9>.
- Bentosela, M., Barrera, G., Jakovcevic, A., Elgier, A.M., Mustaca, A.E., 2008. Effect of reinforcement, reinforcer omission and extinction on a communicative response in domestic dogs (*Canis familiaris*). *Behav. Processes* 78 (3), 464–469. <https://doi.org/10.1016/j.beproc.2008.03.004>.
- Cimarelli, G., Virányi, Z., Turcsán, B., Rónai, Z., Sasvári-Székely, M., Bánlaki, Z., 2017. Social behavior of pet dogs is associated with peripheral OXTR methylation. *Front. Psychol.* 8, 549. <https://doi.org/10.3389/fpsyg.2017.00549>.
- D'Aniello, B., Scandurra, A., Prato-Previde, E., Valsecchi, P., 2015. Gazing toward humans: a study on water rescue dogs using the impossible task paradigm. *Behav. Processes* 110, 68–73. <https://doi.org/10.1016/j.beproc.2014.09.022>.
- Fallani, G., Prato Previde, E., Valsecchi, P., 2007. Behavioral and physiological responses of guide dogs to a situation of emotional distress. *Physiol. Behav.* 90 (4), 648–655. <https://doi.org/10.1016/j.physbeh.2006.12.001>.
- Gácsi, M., McGreevy, P., Kara, E., Miklósi, Á., 2009. Effects of selection for cooperation and attention in dogs. *Behav. Brain Funct.* 5 (1), 31. <https://doi.org/10.1186/1744-9081-5-31>.
- Gimpl, G., Fahrenholz, F., 2001. The oxytocin receptor system: structure, function, and regulation. *Physiol. Rev.* 81 (2), 629–683. <https://doi.org/10.1152/physrev.2001.81.2.629>.
- Hernádi, A., Kis, A., Kanizsár, O., Tóth, K., Miklósi, B., Topál, J., 2015. Intranasally administered oxytocin affects how dogs (*Canis familiaris*) react to the threatening approach of their owner and an unfamiliar experimenter. *Behav. Processes* 119, 1–5. <https://doi.org/10.1016/j.beproc.2015.07.001>.
- Hritcu, L.D., Horhoge, C., Ciobica, A., Spataru, M.C., Spataru, C., Kis, A., 2019. Conceptual replication of canine serum oxytocin increase following a positive dog-human interaction. *Revista de Chimie* 70 (5), 1579–1581 Huang et al., 2014.
- Jakovcevic, A., Elgier, A.M., Mustaca, A.E., Bentosela, M., 2010. Breed differences in dogs (*Canis familiaris*) gaze to the human face. *Behav. Processes* 84 (2), 602–607. <https://doi.org/10.1016/j.beproc.2010.04.003>.
- Kis, A., Bence, M., Lakatos, G., Pergel, E., Turcsán, B., Pluijmakers, J., et al., 2014. Oxytocin receptor gene polymorphisms are associated with human directed social behavior in dogs (*Canis familiaris*). *PLoS One* 9 (1), e83993. <https://doi.org/10.1371/journal.pone.0083993>.
- Kis, A., Hernádi, A., Kanizsár, O., Gácsi, M., Topál, J., 2015. Oxytocin induces positive expectations about ambivalent stimuli (cognitive bias) in dogs. *Horm. Behav.* 69, 1–7. <https://doi.org/10.1016/j.yhbeh.2014.12.004>.
- Kis, A., Ciobica, A., Topál, J., 2017a. The effect of oxytocin on human-directed social behaviour in dogs (*Canis familiaris*). *Horm. Behav.* 94, 40–52. <https://doi.org/10.1016/j.yhbeh.2017.06.001>.
- Kis, A., Hernádi, A., Miklósi, B., Kanizsár, O., Topál, J., 2017b. The way dogs (*Canis familiaris*) look at human emotional faces is modulated by oxytocin. An eye-tracking study. *Front. Behav. Neurosci.* 11. <https://doi.org/10.3389/fnbeh.2017.00210>.
- Kovács, K., Kis, A., Pogány, Á., Koller, D., Topál, J., 2016. Differential effects of oxytocin on social sensitivity in two distinct breeds of dogs (*Canis familiaris*). *Psychoneuroendocrinology* 74, 212–220. <https://doi.org/10.1016/j.psyneuen.2016.09.010>.
- Li, P., Redden, D.T., 2015. Comparing denominator degrees of freedom approximations for the generalized linear mixed model in analyzing binary outcome in small sample cluster-randomized trials. *BMC Med. Res. Methodol.* 15 (1). <https://doi.org/10.1186/s12874-015-0026-x>.
- MacLean, E.L., Gesquiere, L.R., Gruen, M.E., Sherman, B.L., Martin, W.L., Carter, C.S., 2017. Endogenous oxytocin, vasopressin, and aggression in domestic dogs. *Front. Psychol.* 8, 1613. <https://doi.org/10.3389/fpsyg.2017.01613>.
- Marshall-Pescini, S., Schaebs, F.S., Gaugg, A., Meinert, A., Deschner, T., Range, F., 2019. The role of oxytocin in the dog–owner relationship. *Animals* 9 (10), 792. <https://doi.org/10.3390/ani9100792>.
- Miklósi, Á., Kubinyi, E., Topál, J., Gácsi, M., Virányi, Z., Csányi, V., 2003. A simple reason for a big difference. *Curr. Biol.* 13 (9), 763–766. [https://doi.org/10.1016/s0960-9822\(03\)00263-x](https://doi.org/10.1016/s0960-9822(03)00263-x).
- Nagasawa, M., Mitsui, S., En, S., Ohtani, N., Ohta, M., Sakuma, Y., et al., 2015. Oxytocin-gaze positive loop and the coevolution of human-dog bonds. *Science* 348 (6232), 333–336. <https://doi.org/10.1126/science.1261022>.
- Nagasawa, M., Ogawa, M., Mogi, K., Kikusui, T., 2017. Intranasal oxytocin treatment increases eye-gaze behavior toward the owner in ancient Japanese dog breeds. *Front. Psychol.* 8. <https://doi.org/10.3389/fpsyg.2017.01624>.

- Oliva, J.L., Mengoli, M., Mendonça, T., Cozzi, A., Pageat, P., Chabaud, C., et al., 2019. Working smarter not harder: oxytocin increases domestic dogs' (*Canis familiaris*) accuracy, but not attempts, on an object choice task. *Front. Psychol.* 10. <https://doi.org/10.3389/fpsyg.2019.02141>.
- Persson, M.E., Trottier, A.J., Bélteky, J., Roth, L.S., Jensen, P., 2017. Intranasal oxytocin and a polymorphism in the oxytocin receptor gene are associated with human-directed social behavior in golden retriever dogs. *Horm. Behav.* 95, 85–93. <https://doi.org/10.1016/j.yhbeh.2017.07.016>.
- Powell, L., Edwards, K.M., Bauman, A., Guastella, A.J., Drayton, B., Stamatakis, E., McGreevy, P., 2019. Canine endogenous oxytocin responses to dog-walking and affiliative human–Dog interactions. *Animals* 9 (2), 51. <https://doi.org/10.3390/ani9020051>.
- Quintana, D.S., Alvares, G.A., Hickie, I.B., Guastella, A.J., 2015. Do delivery routes of intranasally administered oxytocin account for observed effects on social cognition and behavior? A two-level model. *Neurosci. Biobehav. Rev.* 49, 182–192. <https://doi.org/10.1016/j.neubiorev.2014.12.011>.
- Scandurra, A., Alterisio, A., Di Cosmo, A., D'Ambrosio, A., D'Aniello, B., 2019. Ovariectomy impairs socio-cognitive functions in dogs. *Animals* 9 (2), 58. <https://doi.org/10.3390/ani9020058>.
- Somppi, S., Törnqvist, H., Topál, J., Koskela, A., Hänninen, L., Krause, C.M., Vainio, O., 2017. Nasal oxytocin treatment biases dogs' visual attention and emotional response toward positive human facial expressions. *Front. Psychol.* 8, 1854. <https://doi.org/10.3389/fpsyg.2017.01854>.
- Sundman, A.-S., Persson, M.E., Grozelier, A., Halldén, L.-L., Jensen, P., Roth, L.S.V., 2017. Understanding of human referential gestures is not correlated to human-directed social behaviour in Labrador retrievers and German shepherd dogs. *Appl. Anim. Behav. Sci.* 201, 46–53. <https://doi.org/10.1016/j.applanim.2017.12.017>.
- Svartberg, K., 2006. Breed-typical behaviour in dogs—historical remnants or recent constructs? *Appl. Anim. Behav. Sci.* 96 (3–4), 293–313. <https://doi.org/10.1016/j.applanim.2005.06.014>.
- Thielke, L.E., Udell, M.A., 2017. The role of oxytocin in relationships between dogs and humans and potential applications for the treatment of separation anxiety in dogs. *Biol. Rev.* 92 (1), 378–388. <https://doi.org/10.1111/brv.12235>.
- Tribollet, E., Audigier, S., Dubois-Dauphin, M., Dreifuss, J.J., 1990. Gonadal steroids regulate oxytocin receptors but not vasopressin receptors in the brain of male and female rats. An autoradiographical study. *Brain Res.* 511 (1), 129–140. [https://doi.org/10.1016/0006-8993\(90\)90232-z](https://doi.org/10.1016/0006-8993(90)90232-z).