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Assaying the Blood of the Sacred Baboon:
Oxytocin, Arginine Vasopressin, and the Behavior of the Baboon Subspecies

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Abstract

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Anthropologists have always been interested in the mechanisms, both proximate and ultimate, that create the enormous variety of primate social and mating relationships. Even among primates, baboon societies are incredibly diverse in their sociality, from the tightly-bound mating relationships within the harems of the hamadryas baboon (*Papio hamadryas hamadryas*), to the more promiscuous, yet highly affiliative friendships of anubis baboons (*Papio hamadryas anubis*). Likewise, within these societies, there are also broad individual differences in social behavior, with some individuals having more affiliative and gregarious personalities, while others can be more aggressive and domineering in their relationships. However, it is still unknown which proximate physiological mechanisms are responsible for generating this behavioral diversity both between and within the subspecies. Converging evidence from neurobiological research has identified the neurohormones oxytocin and arginine vasopressin as essential mediators of social behavior, particularly affiliative and bonding relationships. However, our knowledge of their social functions in primates is still limited and lacks a strong comparative model that has been so successful in other non-primate species. This dissertation sought to combine these lines of inquiry by investigating how oxytocin and arginine vasopressin may influence baboon behavioral diversity. Furthermore, as studies in wild primate populations often have to rely on peripheral sources of the neurohormones (such as in the urine), this study also collected samples from different central and peripheral sources in order to better understand their independent and correlated effects on behavior. Biosamples and behavioral data were collected from captive hamadryas and anubis populations and were assayed using ELISA. Results showed that neurohormone concentrations were surprisingly identical between the baboon subspecies. Nevertheless, the neurohormones were not only found to be associated with numerous demographic variables, but more importantly also with measures of individual social temperament and personality. Furthermore, many of these associations were found in the blood concentrations, rather than the cerebrospinal fluid where they were expected. While these findings are useful contributions to the field, the question remains as to what physiological factors are moderating baboon behavioral diversity. Ultimately, these proximate mechanisms are likely to be related to the distribution of receptors in the baboon brain.

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INTRODUCTION

The ancient Egyptians knew the value of studying baboons. Baboon colonies were established in ancient Egypt, looked after by "Priests of the Living Baboon", and deceased baboons were often buried or mummified with graves bearing inscriptions of their genealogies. However, what interests me greatly, and is perhaps most relevant to the following dissertation, is the Egyptian fascination with the intense passions of the "sacred" baboon (now called the "hamadryas" baboon). Throughout Egyptian cosmology the baboon is associated with extreme violence and extreme sexual potency, particularly in the form of the baboon-god "Babi". Babi was bloodthirsty, quick to anger and violence. In fact, an Egyptian hieroglyphic for "enraged" is a male baboon with its tail raised. Babi was also a symbol of supernatural virility, with his erect phallus acting as a gate to the afterlife and was appealed to in funerary texts to allow the deceased to continue to have sex in the afterlife. Unfortunately, the current general perception of baboons has somewhat declined from "demi-god" to "cute". Nevertheless, modern primatologists, much like the ancient Egyptians, are also fascinated by the passions of the baboon, and want to know what mechanisms can produce such extremes of aggression and affiliation.

Baboons (genus *Papio*) have been of interest to primatologists since the earliest days of the field and have become an important primate species with which to explore socioecological evolution. Baboons vary widely in their social and mating structures across a range of environments, both between and among subspecies, which provides a glimpse into the dynamics between ecology, sociality, and physiology. Among the baboon subspecies, the anubis (*Papio hamadryas anubis*) and hamadryas (*Papio hamadryas hamadryas*) baboons are of particular interest. Paradoxically, they are closely related (even forming natural hybrid zones at the intersection of their ranges) yet form radically different societies. Hamadryas baboons live in multilevel societies of related males, where the strongest and most fundamental relationship is the cross-bond between a male and female harem member. In contrast, anubis baboons live in large troops with ephemeral intersexual bonds, where the strongest and most important relationships are between related females of a matriline. This subspecies comparison highlights fundamental

differences in attachment, affiliation, and aggression. What physiological mechanisms could mediate this social complexity?

Although the ancient Egyptians might have had an interesting supernatural explanation for these differences, modern research has instead mundanely concluded that hormone concentrations, and the distribution of their receptors, exert strong control over the patterning of sociality. Specifically, the neurohormones oxytocin (OT) and arginine vasopressin (AVP) have been found to be especially vital to the organization of social and mating structures across animals. Their profound impact on social life has been largely discovered through comparative research in rodents and birds which vary in bonding relationships. Although research into the behavioral importance of OT and AVP in non-human primates has advanced significantly in the last two decades, it still lacks a comparative model that has been so successful with rodents and birds. In this way, the anubis/hamadryas comparison has promise to be as useful a comparative model in neurobiology as they have been in primatology.

I can understand the ancient Egyptian's fascination with the baboon. They are capable of such ferocity and anger, yet also such tenderness and tolerance. I wanted to understand the extremes of these behaviors and their variation between individuals and subspecies. The purpose of this dissertation was to investigate the importance of baseline OT and AVP concentrations in the social lives of these non-human primates, and to determine if their social differences result from an underlying difference in the functioning of these hormonal systems. This introduction will first review the social lives of the baboon subspecies, and then briefly summarize the relevant facts of OT and AVP function, with an emphasis in non-human primates. This will prepare the reader for the hypotheses and results that I explore in the second and third chapters of this dissertation.

BABOON SOCIALITY

Baboons live complicated lives. Dr. Shirley Strum has gone so far as to say: "that the baboons I have studied live in the most complex nonhuman primate society yet described and that they reside in the most socioecological complexity documented so far for a nonhuman primate" (Strum, 2012, p. 4). While

this statement is likely contestable among primatologists, it nevertheless illustrates that even a single baboon subspecies can show an incredible diversity of social behaviors under varying ecologies. This section will contrast the social and mating systems of the two major baboon subspecies studied in this dissertation, with an emphasis on social relationships known to be mediated by OT and AVP action.

The Anubis (or Olive) Baboon (Papio hamadryas anubis)

Although the basic social and mating organization patterns of the anubis baboon society are typical of that found in other cercopithecoids, such as macaques, there is large variability in the internal relationships formed within each society. Anubis baboons live in large multimale-multifemale social groups (called "troops") of about 20-200 individuals which forage as a single unit (Jolly and Phillips-Conroy, 2003; Smuts, 1985). The mating system of anubis baboons is promiscuous (or polygynandrous), with males and females mating with multiple partners during the female's estrous period (Jolly and Phillips-Conroy, 2003).

Anubis baboons are female philopatric, with males dispersing at sexual maturity in order to migrate to new social groups. This dispersal pattern facilitates the formation of strong female-female kin bonds and matrilineal dominance hierarchies to monopolize limited resources (Barton et al., 1996; Henzi and Barrett, 2005). Indeed, initiating and maintaining affiliative intrasexual bonds is essential for female survival and reproductive success (Archie et al., 2014; Seyfarth and Cheney, 2012; Silk, 2007; Silk et al., 2010, 2006a, 2006b). Only a minority of female dyads form long, enduring social bonds, and these are preferentially with female kin, who provide not only coalitionary support but also mitigate the effect of stressors (Archie et al., 2014; Silk et al., 2006a, 2006b).

In contrast to the prominence of female-female bonds, male dispersal into new groups implies that troop males will often be unrelated, and therefore intrasexual competition for available mates through dominance hierarchies will be more intense (Berenstain and Wade, 1983; Jolly and Phillips-Conroy, 2003). However, they will often form temporary coalitions in order to monopolize estrous females. Some

have even suggested that coalition partners preferentially associate with one another in a form of reciprocal altruism (Packer, 1977), although this interpretation is disputed (Bercovitch, 1988).

Males and females also form intersexual aggressive and affiliative social relationships. During a female's estrous, males compete with one another to form brief but intense "consortships" and monopolize mating opportunities (Alberts et al., 2006). These intersexual relationships are marked by intense male mate-guarding and frequent turnovers. While dominance ranks do appear to influence consortship success, future male reproductive success is also based on prior affiliative interactions between males and females (Alberts et al., 2006; Smuts, 1985).

These affiliative, non-sexual, intersexual relationships have been called "friendships", and are marked by preferential associations and dyadic grooming relationships (Lemasson et al., 2008; Palombit, 2009; Smuts, 1985). Males and females will typically have 1-4 friends, with male friends providing anti-infanticide and anti-harassment defense(Lemasson et al., 2008; Palombit, 1999; Palombit et al., 1997), and even biparental care with male-infant food-sharing and bonding (Buchan et al., 2003; Nguyen et al., 2009). Conversely, male friends are frequently found to be preferred future consort partners (Alberts et al., 2006; Smuts, 1985).

In summary, the anubis baboon society is marked by strong intrasexual competition where female-female bonds represent the strongest and most persistent relationships. Although affiliative intersexual friendships are present and can form the basis of future consortships, there are no bonded mating relationships, with females and males mating promiscuously during periods of female estrous.

The Hamadryas (or Sacred/Desert) Baboon (Papio hamadryas hamadryas)

Hamadryas baboon society is peculiar not only among baboons, but also other Old World monkeys. Hamadryas baboons live in large multi-level societies, built out of four different social units: the troop, the band, the clan, and the one-male unit (OMU) or "harem" (Kummer, 1984; Schreier and Swedell, 2009; Swedell and Leigh, 2006; Swedell and Plummer, 2012). This OMU social structure is fundamental to their society and is highly coherent in both space and time. The OMU typically contains a

single adult male, one to nine females, their dependent offspring, and "follower" sub-adult males that stay on the periphery of the unit. It should also be noted that although the range of potential female membership is as high as nine, the majority of groups have only ~2 females (Kummer, 1968), or are simply a male-female dyad (Swedell and Plummer, 2012).

The OMU social unit also forms the basis of the monandrous polygynous mating system, with unit females mating almost exclusively with the unit leader (Henzi and Barrett, 2003, 2005; Jolly et al., 2008). This mating system is especially dependent on intense and constant mate-guarding with the "predominant motivation of hamadryas males is to assert exclusive and possessive ownership of females" (Kummer et al., 1974, p. 63). This bonded polygyny may partly result from the male-philopatric, female dispersal pattern of hamadryas baboons (Henzi and Barrett, 2005).

In contrast to the centrality of the female-female bond in anubis baboons, hamadryas females interact with one another far less frequently (Henzi and Barrett, 2005; Swedell and Plummer, 2012), with the male-female dyad instead constituting the strongest social bond, a state known as "cross-bonding" (Anderson, 1983; Kummer, 1984). In fact, several authors (Anderson, 1983; Kummer, 1984, 1968; Sigg et al., 1982) specifically refer to the dyadic social relationship of the male and female as a "pair-bond". As Anderson (1983) notes, "It seems clear that the most unusual characteristic of hamadryas baboon harem organization is this faithfulness by males to the females of their harem" (Anderson, 1983, p. 19). While anubis friendships vary in length, the hamadryas pair-bond is maintained throughout the entirety of the female's reproductive cycle, as males remain bonded to their females and refrain from attempting to obtain or consort with the females of another OMU (Anderson, 1983; Kummer, 1984). Likewise, females will frequently remain with their unit even after he suffers defeats in agonistic encounters (Anderson, 1983).

Hamadryas male reproductive success is therefore highly dependent on pair-bond formation and maintenance. Thus, male abilities are focused on maintaining OMU cohesion through intense and constant mate-guarding, while female attempts to maintain the pair-bond are centered on grooming the unit male (Jolly and Phillips-Conroy, 2003).

Intrasexual male relationships are less overtly aggressive, and instead rely on a complex series of displays and greetings to avoid conflict (Jolly and Phillips-Conroy, 2003; Swedell and Plummer, 2012). Due to male philopatry, clan males are typically male kin, and therefore may benefit from inclusive fitness. In fact, males of the same band may "respect" the ownership of females by another male, and are inhibited from attempting to take them from one another, an effect that is absent if the males are from completely different troops (Kummer et al., 1974).

Hamadryas baboons in captivity continue to form these familiar social and mating structures (Colmenares et al., 2006). In fact, captive conditions push the hamadryas social system into extreme dimensions that would not easily be observed in nature. For example, in my own observations of captive hamadryas baboons, OMU sizes could be as large as 18 females for one leader male, yet even with such skewed sex ratios, males and females appeared to maintain their fidelity to their OMU. Given the size of these harems, it is impossible for a male to effectively mate guard all females simultaneously, which would suggest that hamadryas females might be similarly motivated to maintain the cross-bond with their OMU male. Indeed, the frequent occurrence of infanticide attempts at the hamadryas colony (and its absence at the Anubis colony) may indicate that surreptitious mating between females and non-leader males is non-existent. It is highly possible that the hamadryas society, therefore, is not just a by-product of current ecological conditions, but rather has been shaped by past selective pressures to crystallize in this bonded form, even when conditions would permit promiscuous mating.

In summary, the hamadryas baboon society is primarily built from the bond between a unit leader male and the females in his OMU. In contrast to the anubis baboon where mating and social relationships are open, hamadryas baboon relationships are intensely exclusive, with both males and females contributing to maintaining the bond.

Ultimate and Proximate Mechanisms of Baboon Behavioral Diversity

It is clear that the two subspecies differ fundamentally in the relationships and skills that are essential to reproductive success. Furthermore, since both subspecies continue to produce their unique

societies even in captivity (Bramblett and Coelho, 1985; Colmenares et al., 2006; Kummer, 1984), it can be assumed that these predispositions may be under more direct genetic control. Indeed, naturally forming hamadryas/anubis hybrid troops display combinations of each subspecies' unique relationships, with some males forming OMU-like structures, while others mate promiscuously (Bergman and Beehner, 2004). The question is then raised: Why are they so different? They are closely related, yet their social lives are radically different. How is such behavioral variability developed on the evolutionary level, and how it is mediated by proximate mechanisms, such as genetics, hormones, or neurobiology?

Ultimately, the social differences between the subspecies are the result of predation, resource distribution, and infanticide. Predation favors an increase in primate group size for defense, but the increased competition for food resources pushes for group fission (Kappeler and van Schaik, 2002). The hamadryas multilevel society is likely to have resulted from increased feeding competition in a resource scarce environment. Subsequently, due to increasing predation pressures females fissioned with preferred males, as males are able to provide better predator defense in small groups (Henzi and Barrett, 2003, 2005; Swedell and Plummer, 2012). However, shifts towards smaller groups increase paternity certainty for the resident male, but decrease it for any immigrant male, making infanticide a much stronger reproductive strategy (Henzi and Barrett, 2003, 2005; Palombit, 2009, 1999). Infanticide risk would have favored greater infant and mate defense from males and may have ultimately led to the development of the more intense mate-guarding as seen in hamadryas baboons (Henzi and Barrett, 2005; Palombit, 1999). In fact, chacma baboons (*Papio hamadryas ursinus*) flexibly switch between anubis-like societies and OMU-like hamadryas structures depending on resource availability, with periods of low resource density favoring fissioning into OMUs with a male "friend", although there is no substantial development of cross-bonding in these units (Anderson, 1983; Henzi and Barrett, 2005; Swedell and Plummer, 2012). The ancestral hamadryas social system may have been similar to the chacma society, but then became "crystallized" genetically into its current form under constant conditions of resource scarcity, high predation, and high infanticide risk (Barton et al., 1996; Henzi and Barrett, 2003).

While investigations into the proximate mediation of baboon social behavior have been very productive, especially in terms of hormonal regulation (Moscovice and Ziegler, 2012; Sapolsky, 1990; Sapolsky and Ray, 1989), considerably less has been done to address the hormonal differences between hamadryas and anubis baboons. Nonetheless, the serotonin (5-HIAA), norepinephrine (MHPG), and dopamine (HVA) metabolites, were found to vary not only between subspecies, but also through the lifespan (Jolly et al., 2008; Kaplan et al., 1999). Anubis males had not only higher levels of 5-HIAA in adulthood relative to hamadryas baboons, but also as young adults around the age of dispersal. This result was interpreted as the anubis male's increased need for social skills when entering a new troop, as low 5-HIAA levels are associated with impulsivity. In contrast, the low levels of 5-HIAA in young adult hamadryas baboons was interpreted as favoring the more impulsive and aggressive behaviors needed to form an OMU. Likewise, recent genetic research comparing the two subspecies discovered that there are large differences in the dopamine receptor-mediated signaling pathway, another mechanism involved in impulsivity (Bergey et al., 2016).

Despite their recent ancestry, anubis and hamadryas baboons display vastly different social systems. The anubis baboon displays a pattern of sociality marked by both aggressive encounters (matrilines, dominance hierarchies, male coalitions), as well as remarkable degrees of affiliative and cooperative behaviors (friendships, paternal investment, male altruism), yet no long-term intersexual mating bonds. In contrast, the hamadryas baboon illustrates predominately possessive and territorial behaviors, and unusually strong and durable intersexual bonds. The following section will briefly describe the oxytocin and arginine vasopressin hormonal systems, and how they may play a large role in mediating these social differences.

OXYTOCIN AND ARGININE VASOPRESSIN: A PRIMER

Oxytocin (OT) and arginine vasopressin (AVP) are essential hormones for regulating social behavior across animals. OT generally has prosocial effects, potentially through its anxiolytic functions, which, in addition to increasing the likelihood of social interaction, also facilitate partner pair-bonding

(Hammock and Young, 2006; Williams et al., 1994), parental/alloparental care (Ross et al., 2009; Ross and Young, 2009), affiliation (Campbell, 2008; Feldman, 2012), cooperation (De Dreu, 2012a, 2012b), and in-group altruism (De Dreu et al., 2011). Likewise, although AVP facilitates male prosociality, particularly in regards to male pair-bonding and paternal care(Nair and Young, 2006; Young and Wang, 2004), such behaviors are often deployed in a context of possessiveness and aggressive defense, mirroring its other roles in mediating territoriality, mate-guarding, and aggression(Gobrogge et al., 2017, 2009; Pagani et al., 2011). This section will briefly review what is known about OT and AVP, with an emphasis on its functions in non-human primates (although for more thorough reviews read Freeman and Young (2011) and Putnam et al. (2018)), in order to better draw connections between their known functions and their potential place in mediating baboon social behavior.

Evolution

OT and AVP are nine amino acid neuropeptides (nonapeptides), and form two primary lineages in vertebrates that are traced back to a genetic duplication of the arginine vasotocin (AVT) (Donaldson and Young, 2008; Goodson et al., 2012; Hoyle, 1999). OT is more closely related to the homologous nonapeptides isotocin (IT), which is found in bony fish, and mesotocin (MT), which is found in birds, reptiles, fish, amphibians, and marsupials (Goodson, 2008; Hoyle, 1999). In contrast, AVT has been maintained in most vertebrates except mammals, which have replaced it with AVP and lysine vasopressin (LVP) (Goodson, 2008; Hoyle, 1999). Despite these changes in structure, the nonapeptides have strongly conserved functions, and are primarily involved with fluid balance and reproduction. These conserved reproductive functions also display a degree of conserved sexual dimorphism, with OT more often associated with female reproduction and AVP more involved in male reproduction (Carter, 2007; De Vries and Panzica, 2006; Goodson and Bass, 2001).

Structure

In addition to the conservation of form in the OT lineage, there is also conservation of its neurobiological production and action (Goodson, 2008; Goodson and Bass, 2001; Goodson and

Thompson, 2010). Across eutherian mammals, central OT and AVP are generally produced within the supraoptic (SON) and paraventricular (PVN) hypothalamic nuclei (Goodson et al., 2012; Goodson and Thompson, 2010), although AVP is also produced within the suprachiasmatic nucleus (SCN), the bed nucleus of the stria terminalis (BNST), and the medial amygdala (MeA) (Albers, 2015; Dhakar et al., 2013; Dumais and Veenema, 2016; Ragen and Bales, 2011).

Within the SON and PVN, OT and AVP are produced by magnocellular neurons that generally project to the posterior pituitary for release into peripheral circulation; however, some of these neurohypophyseal-projecting magnocellular neurons have collateral projections to central nervous system targets, such as the nucleus accumbens (NAcc) where they act as neurotransmitters (Ross et al., 2009). Once released into circulation, OT and AVP act as hormones to affect physiological functions through the widespread distribution of their receptors in the viscera. Lastly, the magnocellular neurons of the PVN and SON also secrete AVP and OT dendritically into the extracellular space where they can act as neuromodulators (Landgraf and Neumann, 2004; Stoop, 2012).

Within the PVN, OT and AVP are also produced in populations of parvocellular neurons that have projections throughout the central nervous system, including the hippocampus, amygdala, substantia nigra, locus coeruleus, raphe nucleus, striatum, and cerebral cortex (Gimpl and Fahrenholz, 2001; Rogers et al., 2018). In addition, these parvocellular neurons also project to the median eminence, allowing for OT and AVP to influence adenohypophyseal functions (Gimpl and Fahrenholz, 2001).

In addition to sites of neuropeptide production in the central nervous system, OT and AVP are also produced throughout the body and may act in a paracrine manner (Burbach et al., 2005; Clements and Funder, 1986; Gimpl and Fahrenholz, 2001). Many of these OT- and AVP-synthesizing cells are found in the reproductive organs(e.g. ovaries, testes), the heart and pancreas (for OT) (Burbach et al., 2005), and the adrenal glands (for OT and AVP) (Burbach et al., 2005; Clements and Funder, 1986; Nicholson et al., 1984).

Central and Peripheral Secretion of Oxytocin and Arginine Vasopressin

Considering that OT and AVP are able to act as neurotransmitters, neuromodulators, and hormones across a range of targets in the CNS, PNS, and viscera, it is of importance to know what concentrations of the neuropeptides represent behaviorally in these different environments. Likewise, the cross-communication between central and peripheral compartments is possibly greater than originally expected, with not only the coordinated central/peripheral release of magnocellular axon collaterals (Ross et al., 2009), but also active transport of OT from circulation across the blood brain barrier (Lee et al., 2018; Yamamoto et al., 2019). In conjunction with the known clearance of plasma OT and AVP into urine (Leng and Sabatier, 2016), it is possible that concentrations across these sources are correlated and could potentially be used as a proxy for one another.

The most commonly studied sources of the neurohormones in primates are the cerebrospinal fluid (CSF), blood plasma, urine, and saliva. Of these sources, CSF concentrations of the neurohormones have been considered the most behaviorally informative, with peripheral concentrations considered only as a less invasive alternative to approximating CSF concentrations (Kagerbauer et al., 2019, 2013; Valstad et al., 2017). Central neuropeptide concentrations are a composite picture that results from the diffusion of extracellular OT and AVP from different brain regions into the CSF. However, it is believed that these neuropeptides might still be biologically active and that the CSF is able to "broadcast" this hormonal message throughout the CNS (Sewards and Sewards, 2003; Veening et al., 2010). In fact, OT has a long half-life in the CSF (~28 minutes) which would allow for the neuropeptides to interact with distant receptors (Veening et al., 2010).

Although some maintain that only regional extracellular fluids are a useful measure of neuropeptidergic regulation of social behavior (Landgraf and Neumann, 2004), baseline CSF concentrations of these neurohormones do correlate with personality traits and temperaments. For example, CSF OT levels are lower in humans that endured childhood abuse (Heim et al., 2009), have elevated trait anxiety (Carson et al., 2015), and greater lifetime history of aggression (Lee et al., 2009). Similarly, CSF AVP concentrations are increased in humans with a greater lifetime history of aggression

(Coccaro et al., 1998), and in more sociable rhesus macaques (Parker et al., 2018). It is also possible that species-typical temperaments are linked to the CSF concentrations of OT, with more affiliative species having higher OT in the CSF (Kramer et al., 2004; Rosenblum et al., 2002).

Despite the potential value of CSF neuropeptide concentrations in understanding their influence on social behavior, such central samples are highly invasive, and are therefore difficult to collect in some environments (e.g. from wild populations). Therefore, OT and AVP research in primates more frequently involves the collection of peripheral samples, specifically blood plasma, urine, or saliva. While many studies consider the value of these peripheral measures to be solely in their ability to infer the actions of the central neuropeptide concentrations (Kagerbauer et al., 2019, 2013; Valstad et al., 2017), others consider the potential role that peripheral OT and AVP, particularly in circulation, may play in influencing social behavior in a bottom-up fashion (Carter et al., 2020; MacLean et al., 2019).

Circulating OT and AVP have fairly short half-lives of only approximately four minutes, with both being removed from the blood either through the kidneys, the actions of enzymes (such as oxytocinase), or into the extravascular tissue (Fabian et al., 1969; Leng and Sabatier, 2016). Likewise, the neuropeptides are often found at lower concentrations in the periphery (~10pg/mL) than centrally (~20pg/mL) (Kagerbauer et al., 2013; Striepens et al., 2013), although this comparison is only true for free (i.e. unbound) OT. When protein-bound OT is considered, plasma is found to have much greater concentrations of OT (Brandtzaeg et al., 2016). While the unbound form is bioavailable for peripheral receptors, the function of the bound form of OT is still unknown (MacLean et al., 2019). Therefore, although variation exists in the assays to determine OT concentrations in plasma (Lefevre et al., 2017; MacLean et al., 2019), studies of peripheral OT generally relate behavioral variables to the concentrations of free OT.

Despite this confusion, baseline plasma concentrations of OT are frequently found to correlate with social behaviors and temperament (Andari et al., 2012; Bell et al., 2006; Michopoulos et al., 2011; Tops et al., 2007), similar to what has been found for the CSF. Circulating neuropeptides may be able to influence behavior through bottom-up processes as neuropeptide receptors are found throughout the body,

including not only in reproductive organs (uterus, ovaries, testes, mammary glands), but also in the cardiovascular system, adrenal gland, kidney, thymus, pancreas, and adipocytes (Gimpl and Fahrenholz, 2001; Guillon et al., 1998). The effects of the neuropeptides in these locations would be able to transmit anxiolytic or anxiogenic signals back to the CNS. In fact, peripheral OT has recently been found to influence central activity through the vagus nerve (Iwasaki et al., 2019).

Urinary measures of OT have also become important in connecting hormone functions to social behavior in wild, non-human primate populations (Crockford et al., 2013; Moscovice et al., 2019; Moscovice and Ziegler, 2012; Wittig et al., 2014). Urinary OT is produced by the removal of OT from circulation due to the actions of the kidneys, a process which takes approximately 30-60 minutes (Seltzer and Ziegler, 2007). This time lag means that urinary OT concentrations are best understood as a composite of changes in OT in the blood over a period of time. Furthermore, these urinary OT concentrations can vary widely due to individual differences in hydration, requiring OT values to be corrected by creatinine concentrations, which are assumed to be excreted at a constant rate (Singh et al., 2015). Despite these complications, measurements of changes in urinary OT/creatinine ratios have been informative about the management of non-human primate social relationships both in captivity (Snowdon et al., 2010) and in the wild (Rincon et al., 2020).

Although each of these sources of neuropeptides(CSF, blood, and urine) are independently associated with social behavior in some way, their relationships to one another is less well understood. As stated earlier, many studies consider peripheral neuropeptide concentrations as relevant to social behavior only insofar as they can provide a proxy for central concentrations. In this regard, the correlations between peripheral neuropeptide concentrations (particularly plasma OT) and CSF concentrations are highly contentious, with some studies reporting to find such correlations (Carson et al., 2015), while others find no evidence of a connection (Amico et al., 1990; Kagerbauer et al., 2013), and still others reporting correlations only in the context of particular events (e.g. Forced swim test) (Wotjak et al., 1998). In contrast, fewer papers (Feldman et al., 2011) have looked for correlations of urinary OT with plasma or CSF neuropeptides, although these also generally find no connection between the sources

compared. However, this lack of a relationship between urinary OT and other sources could result from the time lag associated with changes in OT in the urine.

Receptors

While it is important to understand the patterns of neuropeptide secretion, their impact on behavior is ultimately dependent on the distribution of their respective receptors (Goodson and Thompson, 2010; Young, 1999; Young et al., 2005; Young and Wang, 2004). In contrast to the relatively strong conservation of the neuropeptides' structures and their sites of production, receptor distributions are highly labile both within and between species, and during development (Champagne et al., 2001; Champagne, 2008; Dumais and Veenema, 2016; Goodson, 2008; Phelps and Young, 2003). Structurally, OT has only one receptor (OTR), and AVP has three (V1aR, V1bR, and V2R), of which V1aR is most widely expressed in the brain and strongly influences affiliative and aggressive behaviors. Due to shared ancestry and the general conservation of the two neuropeptides, it is possible for both OT and AVP to bind to each other's receptors, albeit with differing affinities (Zingg, 1996). Nevertheless, this can create an issue for interpretation, as sufficient concentrations of either neuropeptide could potentially act on behavior through the stimulation of the other receptor.

OTR and V1aR binding sites in the CNS can have causal effects on sociality and social structure, particularly in the case of pair-bonding and non-pair-bonding species (Goodson, 2008; Young, 1999). Importantly, behavioral differences between closely related species are often due to the presence or absence of these neuropeptidergic receptors in regions of the brain associated with reward and anxiety. In particular, reward structures such as the nucleus accumbens and ventral pallidum are found to be enriched in OTR and V1aR respectively in pair-bonding species compared to promiscuous species (Lim and Young, 2006; Young et al., 2005). Likewise, OT's role in anxiolysis and AVP's role in anxiogenesis, are also partly mediated by their receptor interactions within structures such as the amygdala (Huber et al., 2005). These patterns appear to somewhat hold in primates, although OTR is far sparser than in other mammals (Freeman et al., 2014; Freeman and Young, 2016). Importantly, as vision is essential to primate

social behavior, the primary locations where OTR are found are those associated with vision and attention (Freeman et al., 2014; Freeman and Young, 2016).

SOCIAL FUNCTIONS OF OXYTOCIN AND ARGININE VASOPRESSIN IN PRIMATES

Although many of the ancestral functions of OT and AVP in other mammals have been preserved in primates, there are also significant derivations to the neuropeptides' pattern of action to facilitate the unique primate life history and sociality. For example, the aforementioned shift in OTR densities from olfactory regions to visual brain structures maintains OT's role in social perception but in a modality more relevant to primate life (Freeman et al., 2014; Freeman and Young, 2016). Indeed, the OT and AVP systems that mediate maternal bonding, pair-bonding, and alloparental bonding, are further augmented and exaptated in primates as social groups create a pool of many potential partners and adversaries that must be navigated. But how is this represented in primate personality and their unique hormonal profile? This section will explore how neuropeptides function in primate social life, but with a particular emphasis on baseline OT and AVP measurements.

OT in Primates

Exogenously administered OT in primates has distinct prosocial effects towards in-group members regardless of kinship, particularly by biasing social perception of both partners and interaction outcomes towards more positive interpretations. Indeed, intranasally-administered OT biases perception towards socially-relevant stimuli, such as the regions around the eyes (Andari et al., 2010; Dal Monte et al., 2014; Ebitz et al., 2013; Gamer et al., 2010), while simultaneously enhancing the weight of positive facial expressions (Guastella et al., 2008) or decreasing the perception of negative expressions (Parr et al., 2013). In non-human primates, this is exemplified by intranasal OT's ability to decrease the anxiety (and perhaps the perception of danger) of interacting with higher-ranking partners (Ebitz et al., 2013; Jiang and Platt, 2018). These positively-biased perceptions are also accompanied by enhancing cooperative and altruistic behavior (Barraza et al., 2011; Chang et al., 2012; De Dreu, 2012a), albeit generally towards in-

group members (De Dreu et al., 2011). Furthermore, OT is able to buffer the impact of negative outcomes on relationships, by reducing betrayal aversion and maintaining trust (Baumgartner et al., 2008; Rilling et al., 2012). In these ways, acute releases of OT affect primate sociality by promoting social attention and initiative while simultaneously dampening the emotional response to negative outcomes and features.

Curley and Keverne (2005) perhaps put it best when they described OT as a "social glue" (p. 565) for primates. Acute releases of OT are not only able to bias perception, but also enhance the cohesion of individual relationships and even group-level affiliation among non-kin primates. Although conditions in the field prevent attaching cannulae to the PVN, SON, or MeA of primates, measurements of urinary OT both before and after social events can provide a window into the changing secretion of OT. For example, grooming is an essential behavior for primate relationship formation and maintenance, and has been found to elevate urinary OT (uOT) across a range of primate species (Benítez et al., 2018; Crockford et al., 2013; Rincon et al., 2020). In fact, intracerebroventricularly (i.c.v.)-administered OT increased grooming behaviors in squirrel monkeys (*Saimiri sciureus*), although some effects were also dependent on rank (Winslow and Insel, 1991). In addition to the formation and maintenance of relationships, the repair of damaged relationships through reconciliation behaviors such as grooming, also elevates uOT concentrations (Preis et al., 2018). Relationships are also strengthened through altruistic and cooperative acts like food-sharing, which is similarly found to not only increase uOT, but to an even greater extent than grooming bouts (Wittig et al., 2014).

OT secretion is also linked to group and coalition cohesion. Like grooming, genital-genital (GG) rubbing is an important part of relationship and coalition formation among bonobo females (*Pan paniscus*), and is capable of increasing uOT even more than copulation (Moscovice et al., 2019). Furthermore, similar to how OT is able to increase in-group affiliation and out-group apprehension in humans (De Dreu et al., 2011), uOT is increased prior to, and during, intergroup encounters in chimpanzees (Samuni et al., 2017).

However, this dissertation is primarily interested in how baseline concentrations of OT can be used as a marker for species-typical temperaments and individual personality. As exogenous acute rises in

OT concentrations can increase the likelihood of prosocial behaviors, it is plausible that chronic endogenous production of OT could likewise influence social behavior and temperament to be more affiliative or less aggressive. Although few studies have looked at differences in OT concentrations relative to species differences (Kramer et al., 2004; Rosenblum et al., 2002), both found that the more affiliative species tended to have higher concentrations of OT relative to less affiliative species.

Baseline concentrations of OT have been found to be related to individual differences in affiliative disposition. In fact, mirroring the influence of OT in the pair-bonding vole species (e.g. *Microtus ochrogaster*) where OT mediates much of the pair-bonding, parental, and alloparental behaviors, monogamous and cooperatively breeding primates such as marmosets (*Callithrix jacchus*) and cotton-top tamarins (*Saguinus oedipus*) have baseline uOT levels that are correlated with the strength of dyadic relationships, alloparental care, and frequency of affiliative behavior (Finkenwirth et al., 2016, 2015; Snowdon et al., 2010). Even among non-monogamous primates, baseline OT is related to affiliative behaviors specifically, and personality more generally. For example, within chacma baboons there is a positive relationship between the female's investment in a consortship relationship and their baseline uOT levels (Moscovice and Ziegler, 2012). Among rhesus macaques (*Macaca Mulatta*), nursery-reared monkeys are significantly less affiliative and more aggressive compared to mother-reared rhesus monkeys, and these individual differences in temperament correspond to a similar significant reduction in baseline CSF OT levels of the nursery-reared monkeys relative to the mother-reared ones (Winslow et al., 2003). Conversely, rhesus macaque mothers that displayed greater maternal warmth (as defined as increased time nursing, cradling, and grooming the infant) were found to have significantly higher concentrations of baseline plasma OT (Maestripieri et al., 2009).

Even within humans, baseline OT is found to correlate with individual differences in personality and temperament. In particular, baseline CSF OT is found to be negatively correlated with a lifetime history of aggression (Lee et al., 2009) and anxiety (Carson et al., 2015). Likewise, measurements of OT in peripheral samples also find that baseline OT concentrations are positively correlated with measures of affiliative behaviors in parents (Feldman et al., 2012, 2011, 2010), and negatively correlated with feelings

of distrust (McQuaid et al., 2016). In fact, Feldman (2010) went so far as to say that "baseline levels of OT represent a relatively stable trait of the individual that reflect his or her habitual mode of social relatedness and parenting style. This baseline component may tap a different aspect of the OT system as compared to the more pulsatile release of OT that occurs during specific physiological processes, such as breast-feeding or sexual intercourse." (p. 1139).

AVP in Primates

Compared to OT, less research has been done on the influence of AVP in primate social life, and consequently, broad generalizations on its functions are more difficult to generate. For example, although AVP does appear to affect social perception, its effects are highly dependent on additional variables such as the situational context, sex of the participants, and personality (Price et al., 2017; Shalev et al., 2011; Taylor et al., 2017). Furthermore, although AVP is an important element in facilitating male pair-bonding and paternal behavior (Winslow et al., 1993), it is also a central proximate mechanism for the regulation of aggressive, particularly possessive and territorial, behaviors (Gobrogge et al., 2009). As such, research into AVP in primates has likewise found its influences in prosocial behaviors such as pair-bonding (Jarcho et al., 2011), as well anti-social behaviors aggression (Coccaro et al., 1998).

AVP is often associated with anxiety and aggression, and this observation is borne out in primates. In humans, baseline CSF AVP has a positive correlation with lifetime history of aggression (Coccaro et al., 1998), in much the opposite pattern observed for OT (Lee et al., 2009). Likewise, intranasal AVP appears to bias social perceptions to more emotional interpretations, with AVP enhancing the memory of emotional faces relative to neutral faces, regardless of valence (Guastella et al., 2010), and causing neutral faces to be interpreted as more threatening (Thompson et al., 2004). In males playing the Prisoner’s Dilemma economic game, subjects treated with AVP were much more likely to defect in retaliation for a partner defection, although paradoxically AVP also increased cooperation following their own defection or when a partner cooperated as Player 1 (Rilling et al., 2012). This illustrates a tendency of increased AVP to push social interpretation and social action to extreme ends rather than tolerate

ambiguity. Interestingly, the results of this same study with female participants yielded very different results, with AVP increasing cooperation following partner defection (Rilling et al., 2014). Similarly, intranasal AVP in marmosets was found to decrease food-sharing with offspring, and increased aggressive vocalizations, but only in males (Taylor et al., 2017).

In contrast, AVP is also represented in several prosocial functions as well. Among monogamous titi monkeys (*Callicebus cupreus*) intranasal AVP was found to increase the male's interest in the female partner, rather than an unknown female (Jarcho et al., 2011). In addition, AVP injected into the anterior cingulate was found to be as effective as OT, if not more so, in reducing aversion to dominant individuals in rhesus macaques (Jiang and Platt, 2018). Furthermore, male rhesus macaque baseline CSF AVP values have been found to be positively correlated with a composite measure of sociality, and in particular with time spent grooming (Parker et al., 2018). These measures were also found to be individually stable across multiple timepoints of collection, suggesting that CSF AVP may engender trait-like qualities.

DISSERTATION OBJECTIVES

This dissertation had three objectives:

1. To add new insight into baboon comparative ethology.
2. To add a comparative non-human model to our understanding of neuropeptide social functions.
3. To compare neuropeptides concentrations between central and peripheral sources to see their individual and correlated contributions to social behavior.

This dissertation attempted to address these objectives through behavioral observation of captive anubis and hamadryas populations, and through the collection of hormone biosamples from the CSF, blood, and urine. The following two chapters will detail the investigation into two specific research questions. The first chapter studies the most basic question of this dissertation: Do hamadryas and anubis baboons differ in their baseline concentrations of OT or AVP? This chapter additionally addresses several

important demographic factors in OT and AVP function, specifically the influence of variables such as age, sex, and reproductive status. Lastly, this chapter will also discuss the correlations between the baseline concentrations of each neuropeptide. The second chapter will more specifically address the connection between neuropeptide concentrations and individual temperament and social behavior. Although subspecies membership is a variable to consider in this chapter, the primary objective is to look within each subspecies and to see how OT and AVP are related to individual differences in sociality.

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Chapter 2: Between-Species Comparison

ABSTRACT

Primates societies are highly varied, ranging from solitary life, to large and gregarious troops with diverse mating and social relationships. However, it is still not completely understood if substantial differences in social life are reflected in corresponding differences in baseline hormone levels. This study investigated whether the marked differences social differences between the closely related anubis (*Papio hamadryas anubis*) and hamadryas (*Papio hamadryas hamadryas*) baboons could be similarly detected as differences in the basal levels of oxytocin and arginine vasopressin found in the cerebrospinal fluid, blood plasma, and urine. Biosamples were collected from 84 baboons (38 hamadryas and 46 anubis) and were assayed using ELISA. Results were then analyzed using a Bayesian multilevel model in order to determine the relationship of the hormone concentrations to subspecies and demographic factors. Despite their great social and mating system disparities, no differences were found between the two subspecies for any of the biosample sources. However, effects of sex, age, and reproductive state were found. Oxytocin was higher in females across all hormone sources, although weakest in blood plasma. Oxytocin also decreased with age in the CSF but increased in urine. In addition, although lactating females did not differ in basal levels from cycling females, pregnant females had strongly elevated oxytocin values in the plasma and urine, and this relationship was related to the estimated gestational day of the pregnancy. Lastly, the hormone sources were found to be unrelated to one another as residual correlations were very weak. Therefore, basal hormones values of oxytocin and arginine vasopressin are more affected by within-species demographic variables than between-species social differences.

INTRODUCTION

Primates form a diverse range of societies, including not only large multimale-multifemale groups, but also solitary, monogamous, polyandrous, and polygynous groups, with great social variety within each type of society (Kappeler and van Schaik, 2002). The two primate subspecies we compared, the anubis (or olive) baboon (*Papio hamadryas anubis*) and the hamadryas baboon (*Papio hamadryas*

hamadryas), which, despite being closely related, differ greatly in their societies and relationships. While the anubis baboon lives in large multimale-multifemale societies with male emigration, female philopatry, and strong matrilineal relationships (Barton et al., 1996; Henzi and Barrett, 2003, 2005), the hamadryas baboon lives in large and complex multilevel societies, with male philopatry, female emigration, and strong male-female relationships (Anderson, 1983; Kummer, 1984; Swedell, 2006). Most importantly, while the anubis mating system is polygynandrous (or "promiscuous"), with no long-term bonded sexual relationships between males and females (Bergman et al., 2008; Jolly and Phillips-Conroy, 2003), within the polygnous harem hamadryas society the "cross-bond" between a male and a female is the strongest relationship (Anderson, 1983; Kummer, 1984). Although anubis males and females will selectively form non-sexual relationships ("Friendships") with a few preferred opposite sex partners (Lemasson et al., 2008; Smuts, 1985), mating relationships are more determined by female estrous state and male-male competition (Packer, 1979). In contrast, hamadryas baboon cross-bonds are characterized by temporal and spatial stability, as females avoid other adult males, and males remain with their harem females regardless of reproductive state (Sigg and Falett, 1985). However, hamadryas males possessively and aggressively maintain the integrity of their harem and its cross-bonds through intense mate-herding and violence.

When considering such contrasting societies, especially among closely related species, one question of great interest to biologists is which proximate mechanisms are responsible for this diversity. Of the potential proximate mechanisms, neurobiological and endocine factors have been a promising focus of research (Curley and Keverne, 2005; Donaldson and Young, 2008). In particular, the neurohormones oxytocin (OT), arginine vasopressin (AVP), and their homologues influence a variety of sociosexual and mating behaviors, as well as species-typical social grouping patterns (Anacker and Beery, 2013; Goodson and Thompson, 2010; Walum and Young, 2018).

OT is an anxiolytic neurohormone that increases the likelihood of social interaction by enhancing prosocial behaviors such as partner pair-bonding (Johnson et al., 2016; Keebaugh et al., 2015), parental/alloparental care (Keebaugh and Young, 2011; Olazábal and Young, 2006; Rilling and Young, 2014), altruism (Burkett et al., 2016),and affiliation (Crockford et al., 2013; Feldman, 2012; Preis et al.,

2018). In contrast, while the anxiogenic AVP does have prosocial effects, particularly in males, such as male pair-bonding and paternal care,(Barrett et al., 2013; Donaldson et al., 2010) these are often in the context of possessiveness, such as territoriality (Yohn et al., 2017), aggression (Ferris and Delville, 1994), and mate-guarding (Gobrogge et al., 2009; Yokoi et al., 2015). Although much of this work has been conducted in non-primate species or humans, even among non-human primates these neurohormones are often infuential in contexts of bonding, relationship formation and maintainence, and sociability (Cavanaugh et al., 2014; Parker et al., 2018; Putnam et al., 2018; Wittig et al., 2014). It is therefore possible that the differential activity of these neurohormones may underlie observed variation in primate social and mating organizations.

However, most of the social and mating effects of the neurohormones are primarily dependent on the distribution of the OT (OTR) and AVP 1a receptors (V1aR) in the brain, and therefore similar neurohormone concentrations can produce different behavioral outcomes (Insel et al., 1994; Insel and Shapiro, 1992; Lim et al., 2004). For example, AVP that is administered centrally to pair-bonding prairie voles results in aggressive mate-guarding behavior; however, this behavior is not elicited under the same conditions in the promiscuous male montane vole (Young et al., 1997). It is conceivable, then, that differences in the neurobiological distribution of OTR and V1aR is responsible for non-human primate social diversity, and indeed studies mapping primate receptor distributions and fiber patterns have found differences among species that may be related to differing social lives (Freeman et al., 2014a, 2014b; Freeman and Young, 2016; Rogers et al., 2018).

Nevertheless, baseline OT and AVP concentrations often correlate with measures of temperament and social behaviors. For example, compared to mother-reared rhesus macaques, nursery-reared macaques are significantly less affiliative and more aggressive, and these individual differences in temperament correspond to a similar significant reduction in basal cerebrospinal fluid (CSF) OT levels of the nursery-reared monkeys relative to the mother-reared ones (Winslow et al., 2003). Most importantly, such differences in personality and basal OT levels were found to persist over time within individuals, suggesting a degree of inter-individual stability in OT profiles. Likewise, the few papers that have

compared species' baseline OT and AVP concentrations have reported differences that align with predicted effects of OT and AVP. Specifically, the comparatively more affiliative bonnet macaques had higher levels of OT in their cerebrospinal fluid (CSF) than the less affiliative pigtail macaques (Rosenblum et al., 2002), and pair-bonding prairie voles were found to have higher plasma OT than the polygynous Sprague-Dawley rat (Kramer et al., 2004). These findings suggest that basal neurohormone concentrations can potentially mediate species-specific sociality and temperament.

Lastly, the correlations between social behavior and neurohormone concentrations are often dependent on source of the collection, specifically central (i.e. CSF) or peripheral (i.e. blood, urine, saliva). The relative significance of OT and AVP concentrations in the central vs. peripheral sources has been a concern for some time with central sources having been traditionally seen as more indicative of the neurohormones' behavioral functions. (Amico et al., 1990; Crockford et al., 2014; Wotjak et al., 1998). Nonetheless, peripheral sources of these hormones have been found to consistently correlate with behavioral variables (Crockford et al., 2014). In addition, some studies investigating OT and AVP from two or more sources have found no correlation between central and peripheral levels (Amico et al., 1990; Freeman et al., 2016; Kagerbauer et al., 2013), while others claim to have found such correlations (Carson et al., 2015). This question is particularly important in the case of primates as central collection is often impossible, while peripheral sources, particularly urine, are the least invasive and most readily accessible source to any field or laboratory primatologist (Moscovice and Ziegler, 2012; Preis et al., 2018; Snowdon et al., 2010). Therefore, it would be useful to be able to compare the relative utility of these sources within an individual in order to better understand their relationship to one another and to species-typical behaviors.

The social differences between these two subspecies appear to involve behaviors commonly associated with OT and AVP function. Therefore it seems probable that they should also differ in their neuroendocrine physiology, and that these differences should be detectable using measures of the concentrations of these hormones. Specifically, we hypothesized that due to the importance of the cross-bond between males and harem females, and the intense continuous mate-guarding by harem leaders, that

hamadryas baboons would have higher levels of OT and AVP in the CSF. We further hypothesized that species differences would not be present in the peripheral sources of the hormones. Several other demographic variables, such as sex, age, and reproductive state, were also included in order to control for any potential confounds in determining the species differences.

METHODS

a) Study Location and Dates of Collection

Biosamples were collected from 84 baboons (see **Table 1**). All baboons were either pure hamadryas or pure anubis, with no hybrids. Samples from 38 hamadryas baboons (30 female, 8 male) were collected at the Mannheimer Foundation from October 2013 to March 2014. Samples from 46 anubis baboons (27 female, 19 male) were collected at Baboon Research Resource at the University of Oklahoma's Health Science Center (UOHSC) from May to October 2014. Both institutions have large colonies, with most baboons living in mixed-sex and mixed-age corrals. Institutional Animal Care and Use Committee (IACUC) approvals were obtained from both the Mannheimer Foundation (protocol #2013-05) and UOHSC (protocol #14-024) before any data collection began. As many of the species-typical behaviors become prominent at adulthood, nearly all subjects were full adults or subadults as determined by established age divisions for baboons (Jolly and Phillips-Conroy, 2003; Swedell, 2006).

b) Subject Selection

All socially housed males were sampled. Additionally, anubis males that were part of an associated study were also sampled. While this increased the sample size of males, many of these males were not currently living in large social groups, although later results show that these males were not systematically different from socially housed males.

Pregnant females were generally avoided if possible. Hamadryas females were separated by harem membership, in order to avoid any systematic confounds caused by harem. Harem membership was determined by: 1. Which male the female grooms and sits in close contact with (within 10cm), 2. The male that the female follows in group travels, and 3. Which male the female runs to for aid in agonistic

encounters. Female anubis were selected in a similar manner as the hamadryas females. Since anubis females do not form harems, females were separated based on their matrilineal membership in order to avoid over-sampling from the same matriline. Two females that were chosen outside of this scheme were the result of opportunistic collection.

Subjects were additionally divided by age in order to avoid overrepresentation of a particular age. Ages ranged from 5 to 25 years old.

c) Collection Procedures

Of the 84 subjects, 2.0 mL of CSF was collected from 75, 5.0 mL blood plasma from 81, and 10mL urine from 77. Due to difficulties in collection, especially for the CSF, not all subjects had samples from all sources collected, although these subjects are a small minority of the full collection. All biosamples were divided into 1.0mL aliquots before freezing.

All biological samples were collected either by veterinarians or veterinary technicians. Collections were conducted during biannual physicals which had the advantages of sampling each subject within a corral simultaneously and decreasing the stress of capture and collection for each subject. All collections were performed before 12:00pm, decreasing any potential confounds associated with hormonal changes due to circadian rhythms (Perlow et al., 1982). All subjects were anesthetized with 10mg/kg of ketamine, injected intramuscularly.

While under anesthesia, hamadryas females were also given an abdominal ultrasound to estimate the gestational day of their pregnancy. Gestational day was determined by measuring the biparietal diameter of the fetus and comparing this to known growth rates (Fortman et al., 2001).

CSF was collected directly from the cisterna magna, as this region is considered representative of the action of the neurohormones on the brain. Due to the fast degradation of these neurohormones, these aliquots were immediately placed into either a -80°C freezer, or into a cooler with dry ice, and then transferred to a -80°C freezer.

10.0mL of blood was collected from the femoral vein, and immediately placed on ice. This blood was then placed in a refrigerated centrifuge at 4°C and spun at 3000rpm for 15 minutes. The 10.0mL of blood produced approximately 5.0mL of plasma.

10.0mL of urine was collected via catheterization and was immediately placed on ice before being frozen in a -80°C freezer.

Minor blood contamination, as determined visually, in the CSF sample occurred in a few individuals (16 of 84, ~19% of subjects). In addition, some plasma samples (12 of 84, 7% of subjects) were found to have lysed during centrifugation. Therefore "CSF impurity" and "Plasma Impurity" were included as parameters in the model to ensure that these individuals were not significantly different from the mean.

d) Hormone Analysis

All hormones were assayed using enzyme-linked immunosorbent assay (ELISA) after Solid-Phase Extraction (SPE) at the lab of Dr. Toni E. Ziegler at the Wisconsin National Primate Research Center using protocols established in (Moscovice and Ziegler, 2012). SPE is a process that purifies hormone samples by removing potentially interfering matrix components, resulting in a more concentrated sample that increases detection by the ELISA. CSF, plasma, and urine were first thawed, vortexed, and centrifuged at 2000 RPM for 10 minutes. The SPE cartridges were then conditioned using 1.0mL of 100% methanol and 1.0mL of double distilled water. 1.0mL of the sample would then be placed in the cartridge and then washed using a 1.0mL aqueous solution of 10% acetonitrile (ACN) and 0.1% trifluoroacetic acid (TFA). The sample was then eluted using an aqueous solution of 80% ACN, and allowed to dry. The solid sample was then resuspended into 300.0µL, vortexed, and then stored at 2°C - 8°C until being prepared for ELISA. All samples were suspended in 250.0µL of assay buffer and placed in the microtiter plate according to the ELISA kit instructions (Enzo Life Sciences). All samples were done in duplicate and compared to known standards.

e) Data Analysis

This study involved a multilevel data structure with four different hormone measures collected in the same subjects within varying social units and corrals. Some data were missing because certain biosamples could not be collected or lacked sufficient volume for the ELISA. Such data structures are best analyzed using multilevel models, with imputation of missing data rather than the removal of incomplete cases (which makes the assumption of data missing completely at random) (McElreath, 2016; Nakagawa and Hauber, 2011). We implemented these analyses within a Bayesian framework, which propagates the uncertainty inherent in missing data imputation into final parameter estimates, using the brms package v. 2.8.9 (Bürkner, 2018, 2017) in R 3.9.3. (R Core Team, 2019).

Specifically, we used multi-response models, which model CSF OT, plasma OT, urinary OT (controlling for creatinine), and CSF AVP as correlated outcomes, and included corral ID as a random intercept. All hormone levels were log transformed and centered. As urinary concentration is susceptible to individual variability in hydration, the measures of urinary OT were corrected using creatinine levels, which are assumed to be excreted at a constant rate (Singh et al., 2015). Therefore, urinary OT values were first converted to a ratio of OT pg/mg creatinine.

Subspecies was the main predictor of interest and we further included sex, age, log weight, lactation, gestational day of pregnancy, date of collection, and corral size as controls (males were coded as "not lactating" for the lactation predictor and "0" for gestational day). In addition, subspecies, sex, and age were included as a three-way interaction, as it is possible that male and females will differ within each subspecies (Yokoi et al., 2020), and previous research has shown differing age effects on hormone levels between hamadryas and anubis baboons (Jolly et al., 2008). All predictor variables were standardized, and the effect of "date of collection" was modeled using a penalized regression spline function to allow for nonlinearity. The full model is:

Log Hormone

$$= \beta_0 + \gamma Corral\ ID + \beta_1 Weight + \beta_2 Corral\ Size + \beta_3 Gestational\ Day + \beta_4 Lactating$$
$$+ \beta_5 Subspecies + \beta_6 Sex + \beta_7 Age + \beta_8 Subspecies{:}Sex + \beta_9 Subspecies{:}Age + \beta_{10} Sex{:}Age$$
$$+ \beta_{11} Subspecies{:}Sex{:}Age + \beta_{12} Sample\ Impurities + \sum_{k=1}^{K} w_k \beta_{k,13} Date\ of\ Collection$$

Importantly, using multi-response models allowed us to estimate the residual correlations among the different hormone levels after parsing out all other sources of variation, and allowed parameter estimates to be pooled across outcomes resulting in more precise and conservative estimates (McElreath, 2016). All models used slightly regularizing priors (fixed effects: β_0~Normal(0,2), β_{1-13}~Normal(0,1); random effects: γ~ Cauchy(0,1); residual correlations: LKJcorr(2)) to impose further conservatism on parameter estimates. Models were run for 8,000 iterations per chain of three chains and converged well as indicated by visual inspection of trace plots, effective sample sizes (all > 4000) and convergence diagnostics (all Rhat =1). Further details on model fitting can be gleaned from the accompanying R code.

Bayesian analyses produce a posterior distribution for each estimated parameter and these distributions can be summarized in several ways. Here we report the mean, 95% credible intervals, and the proportion of the posterior distribution that supports a given association (PP > 0 or PP < 0). For instance, when evaluating the hypothesized species difference of higher OT in *P.h. anubis*, PP > 0 provides a direct measure of support for that hypothesis. Furthermore, we plot the entire posterior distribution for the main parameters of interest.

RESULTS

a) Population Level Effects

A full table of all population level effects and their associated coefficients can be found in **Table 2**.

No subspecies difference in either OT or AVP was found in any of the hormone sources (CSF OT: PP anubis > hamadryas = 0.34; plasma OT: PP anubis > hamadryas = 0.64; urinary OT: PP anubis > hamadryas = 0.69; CSF AVP: PP anubis > hamadryas = 0.52; see **Figure 1**).

Sex impacted OT and AVP basal levels to varying degrees. CSF and urinary OT showed the strongest effects for sex (CSF OT: PP female > male = 0.91; urinary OT: PP female > male = 0.91; see **Figure 2**) while plasma OT showed weaker effects (PP female > male = 0.32), with female hormone values being higher than males. In contrast, males tended to have higher CSF AVP, though this effect was very weak and highly uncertain (PP male > female = 0.68). Lastly, no strong subspecies/sex interactions were found across any sources (subspecies/sex - CSF OT: PP $\beta < 0 = 0.45$; plasma OT: PP $\beta < 0 = 0.57$; urinary OT: PP $\beta < 0 = 0.65$; CSF AVP: PP $\beta < 0 = 0.76$), demonstrating that the pattern of sex effects on basal hormone levels was similar between the subspecies.

There were also strong effects for age on basal OT levels (**Figure 3**). Specifically, CSF OT (PP $\beta < 0 = 0.97$) and plasma OT (PP $\beta < 0 = 0.9$) declined with age, while urinary OT increased (PP $\beta > 0 = 1$). No strong effects for age were detected with CSF AVP (PP $\beta > 0 = 0.65$). In addition, there were some weak effects for the interaction between sex and age with CSF OT and urinary OT (CSF OT: PP $\beta > 0 = 0.83$; urinary OT: PP $\beta < 0 = 0.86$). These interactions suggest that females are partly driving the effects for age in basal hormone levels. In contrast, there was no strong support for the three-way interaction between subspecies, sex, and age.

Lastly, in regards to female reproductive state (**Figure 4**), lactation had no strong effects on basal hormone levels (CSF OT: PP $\beta > 0 = 0.79$; plasma OT: PP $\beta < 0 = 0.73$; urinary OT: PP $\beta > 0 = 0.59$; CSF AVP: PP $\beta < 0 = 0.83$). In contrast, there were very strong effects for pregnancy on increasing peripheral OT levels (**Figure 4**). More specifically, urinary and plasma OT levels increase with increasing gestational day (urinary OT: PP $\beta > 0 = 1$; plasma OT: PP $\beta > 0 = 0.97$; see **Figure 5**). Curiously, there was a weak decrease in CSF OT with gestational day (PP $\beta < 0 = 0.85$). There was no effect for gestational day on CSF AVP (PP $\beta < 0 = 0.51$).

b) Residual Correlations

A full table of all residual correlations and their coefficients can be found in **Table 3**. After accounting for the effects of each of the predictor variables and random effects on OT and AVP level variation, very small and uncertain (all PP's < 0.9) correlations were found between some of the sources of hormones (**Figure 6**). CSF AVP and urinary OT had the strongest correlation, which was only -0.26, and which was still very uncertain ($r = -0.26$, PP $r < 0 = 0.88$). CSF OT had a similarly weak and uncertain positive correlation with CSF AVP ($r = 0.17$, PP $r > 0 = 0.85$). There is also a very weak negative correlation between CSF OT and urinary OT ($r = -0.12$, PP $r < 0 = 0.80$). All other correlations were negligible and highly uncertain; for instance there was virtually no correlation between CSF and plasma OT ($r=-0.05$, 95% CI = -0.21, 0.30, PP $r > 0 = 0.64$).

DISCUSSION

a) Subspecies Differences

We found no substantial differences between hamadryas and anubis baboons in OT or AVP in any of the central or peripheral sources. This finding was surprising, as the two subspecies form disparate societies and show marked differences in social behavior (Henzi and Barrett, 2003, 2005), even in captivity (Colmenares, 1992), and especially in social behaviors strongly linked to OT and AVP mediation.

A subspecies difference was expected due to prior studies that found associations between species-typical sociality and basal hormone levels (Kramer et al., 2004; Rosenblum et al., 2002). However, there may be some explanations for these contrasting conclusions. For example, (Kramer et al., 2004) compared plasma OT values between prairie voles and Sprague-Dawley rats, two species whose distant phylogenetic relationship obscures the potential meaning of the basal levels of the neuropeptide. With such a distant relationship, it is harder to assume that basal levels are even comparable, as they could represent different functions for their own physiologies and behaviors.

The more similar study (Rosenblum et al., 2002), that compared CSF OT in the closely related pigtail and bonnet macaques, also has several methodological differences. Specifically, Rosenblum et al. had only 26 subjects compared to this study's 84. Furthermore, there were uneven distributions of male and female subjects, where the "aggressive" pigtail macaque sample, which was found to have lower CSF OT, was composed of 9 males and 3 females (75% male), while the "less aggressive" bonnet macaque sample was composed of 5 males and 9 females (36% male). Given the findings from our study that females have higher CSF OT than males, the higher proportion of males in the pigtail sample could account for the observed species differences. In fact, when age and sex were considered as covariates in the original paper, the species difference nearly disappeared.

Another explanation for the lack of a subspecies differences is perhaps that baseline OT and AVP are less important in regulating species-typical social behaviors, than the acute effects of the neurohormones. The functions and effects of OT and AVP have often been studied in primates in relationship to acute events, such as grooming and food sharing with bonded partners in chimpanzees (Crockford et al., 2013; Wittig et al., 2014), affiliative behavior in pair-bonded tamarins (Snowdon et al., 2010), and through experimental introduction of exogenous OT and observing its resulting effects on social behavior (Saito and Nakamura, 2011; Smith et al., 2010). As mentioned earlier, such studies have frequently found associations between these acute changes in neurohormones and social behavior. However, it is possible that OT or AVP reactivity to social stimuli may differ between the baboon subspecies, and that this accounts for the observed social differences.

Perhaps such neurohormone baseline level variations could be more due to individual differences in temperament, rather than larger species-typical social patterns. For example, basal CSF AVP was positively (Coccaro et al., 1998), but basal CSF OT negatively (Lee et al., 2009), correlated with a lifetime history of aggression. Likewise in female chacma baboons (*Papio hamadryas ursinus*), urinary OT was correlated with maintaining proximity during sexual consortships (Moscovice and Ziegler, 2012). Therefore, among more closely related species, basal hormones may be more related to individual differences in temperament and behavioral strategy. Equally likely, and as will be discussed later, the differences between subspecies could lie in receptor distributions.

b) Sex and Reproductive State Differences

Despite the lack of a subspecies difference, we found strong effects for sex for CSF OT, urinary OT, and to a lesser extent, plasma OT. While it has been well-established that OT and AVP have differing effects in the sexes (Caldwell, 2018; Yokoi et al., 2020), the relationship between basal levels of OT/AVP and sex has been more elusive. Most frequently, basal levels of OT do not differ significantly by sex (Amico et al., 1981; Gordon et al., 2008; Kagerbauer et al., 2019, 2013; Lee et al., 2009; Snowdon et al., 2010; Taylor et al., 2010), although some studies have identified greater female basal OT than males (Kramer et al., 2004), or greater male basal OT than females (Weisman et al., 2012). However, the majority of studies that find no sex differences are looking at basal plasma OT levels which were likewise found to be moderately weak in the current study. Furthermore, the majority of studies were performed in humans or in the monogamous tamarin, both species with low sexual dimorphism. Therefore, the substantially higher CSF OT basal values in females for this study could represent a novel pattern more prevalent in non-monogamous primates that display large sexual dimorphisms. However, a recent meta-analysis also found evidence for increased OT concentrations in human females (Engel et al., 2019).

This sex difference is likely the result of variation in OT production in the brains of males and females. Specifically, estrogen influences the production of OT (Amico et al., 1981), thereby affecting females more than males. In fact, female peripheral OT basal levels vary throughout the menstrual cycle

(Aulinas et al., 2019) and reproductive state (Aulinas et al., 2019; Parker et al., 2010), where periods with less estrogen (non-pregnant females & the early-to-mid follicular phase of the menstrual cycle) were found to have less OT than in more estrogen-rich periods, although importantly no effect was found in the CSF (Amico et al., 1990; Aulinas et al., 2019; Parker et al., 2010).

Along with these findings, the current study also found few differences in basal CSF OT levels between cycling, pregnant, and lactating females, but larger effects for peripheral OT measures. This finding is well-supported by virtually all similar research on this topic. In particular, it has been found that although pregnancy and lactation do not affect basal CSF OT levels (Altemus et al., 2004; Amico et al., 1990; Parker et al., 2010; Takagi et al., 1985; Takeda et al., 1985), they do increase peripheral values (Amico et al., 1990; Maestripieri et al., 2009; Morris et al., 1980; Takagi et al., 1985; Takeda et al., 1985). Likewise, other research (Amico et al., 1990; Parker et al., 2010) has found that the state of lactation alone does not necessarily produce higher basal levels, but rather plasma levels of OT react acutely to suckling.

In contrast, pregnancy was found to have strong effects on both peripheral sources. It was found that gestational day was strongly and positively related to urinary and plasma OT values. In contrast, there was a moderate effect for decreased CSF OT, which has not been previously reported in the literature. Although this could potentially be related to the small number of pregnant females collected, it could also relate to the behavioral state of pregnant females. It has been noted among hamadryas females that their sociality and proximity maintenance with the unit male changes with reproductive status, with pregnant females spending less time grooming with the unit male, and more time interacting with non-leader males that follow the unit (Swedell, 2006).

c) Age Effects

There were also strong relationships between age and basal levels of OT. In the current study, OT decreased across age strongly in the CSF, and only slightly more weakly in the plasma. Conversely, urinary OT increases strongly throughout age. Although this latter finding could theoretically result from

decreasing creatinine through life, creatinine did not appear to decrease over the different ages. Interestingly, these age effects were stronger in females, while males, on average, do not change with age. Nevertheless, these results agree with other studies that have found virtually identical levels of CSF OT and AVP in young and old men (Forsling et al., 1998), decreasing plasma OT with age in mice (Elabd et al., 2014) and human females (Aulinas et al., 2019), and near constant or slightly decreased CSF OT in non-lactating female rhesus macaques (Parker et al., 2010). A meta-analysis by Engel et al. (2019) found that OT increased with age, although this conclusion could be possible if the effects of age were not controlled for source, as the age effects were strongest in the urine.

d) Hormone Source Comparison

One of the primary objectives of this study was to compare central and peripheral levels of OT and AVP, and their relationships to each other. Many studies (Amico et al., 1990; Freeman et al., 2016; Kagerbauer et al., 2013) find no relationship between central and peripheral levels of the neurohormones, while others (Carson et al., 2015) find connections between sources. This may partly result from the context of collection, as sources appear to be correlated under certain conditions (e.g. stress tests) (Wotjak et al., 1998), while basal levels are more often uncorrelated (Valstad et al., 2017). Early work considered the central and peripheral levels of OT to constitute two separate systems (Amico et al., 1990), while later research has shown that neurohypophysial projecting paraventricular magnocellular OT producing neurons also have collaterals that project back into the brain, and can coordinate central/peripheral release (Ross et al., 2009). Inversely, recent work has shown both that radiolabeled OT injected peripherally is able to cross the blood-brain barrier (Lee et al., 2018), and that this peripheral OT is actively transported into the central nervous system (Yamamoto et al., 2019). Lastly, there are numerous OT receptors throughout the body (Jurek and Neumann, 2018), which provides another way for peripheral OT to influence the brain.

Despite the several findings of no correlation between sources, peripheral sources are nonetheless consistently associated with social behavior (Crockford et al., 2014). Therefore, it is important to add

more illumination to these potential relationships between sources. This study found no strong correlations between any source. The “strongest” correlation found was between CSF AVP and urinary OT, and this correlation only reached a value of -0.26.

Nevertheless, stronger and more predictive correlations between central and peripheral hormones may still exist, but can only be detected by an approach that accounts for both the time-lag between central secretion into the periphery, and for the social activity preceding collection. For example, following intranasal OT inhalation, urinary OT levels peak 30 minutes later, and therefore more likely represents a summation of all recent acute changes in OT (Franke et al., 2019). Moreover, the behavoiral contexts which elicit coordinated central/peripheral OT and AVP release are still not completely understood, and this factor would as well potentially mask any attempt to elucidate the connections between these hormone sources.

CONCLUSION

Although the negative findings for subspecies in the current study may appear initially surprising, especially considering the great differences in species-typical behaviors between the subspecies, these results may reveal important facts about the connections between basal hormone levels and behavior. For example, as noted earlier, it is possible that the variation in basal hormone values are more representative of intraspecific temperament differences, rather than interspecific sociality differences. Even among the differing baboon societies, individuals still differ in their tendencies towards affiliative and aggressive social behaviors, and it is these individual differences that are most diagnostic of basal hormone values. This possibility will be investigated in an upcoming paper (Coppeto, in prep) which will pair the above hormone data with behavioral data collected from these same individuals.

Additionally, as has been noted in some of the earliest research on OT and AVP (Insel et al., 1994; Insel and Shapiro, 1992), non-monogamous montane voles do not respond to OT or AVP in the same way as the pair-bonding prairie voles, and that this difference is due to their differences in brain

receptors. Therefore, it is highly likely that differences in species typical behaviors are not the result of differences in basal levels of hormones, but rather the distributions of OT and AVP receptors in the brain. Again, these potential differences are investigated in an upcoming paper (Coppeto, in prep) which examines differences in OT and AVP receptor distributions between anubis and hamadryas baboons.

FIGURES & TABLES

Figure 2.1: *Subspecies Parameter*

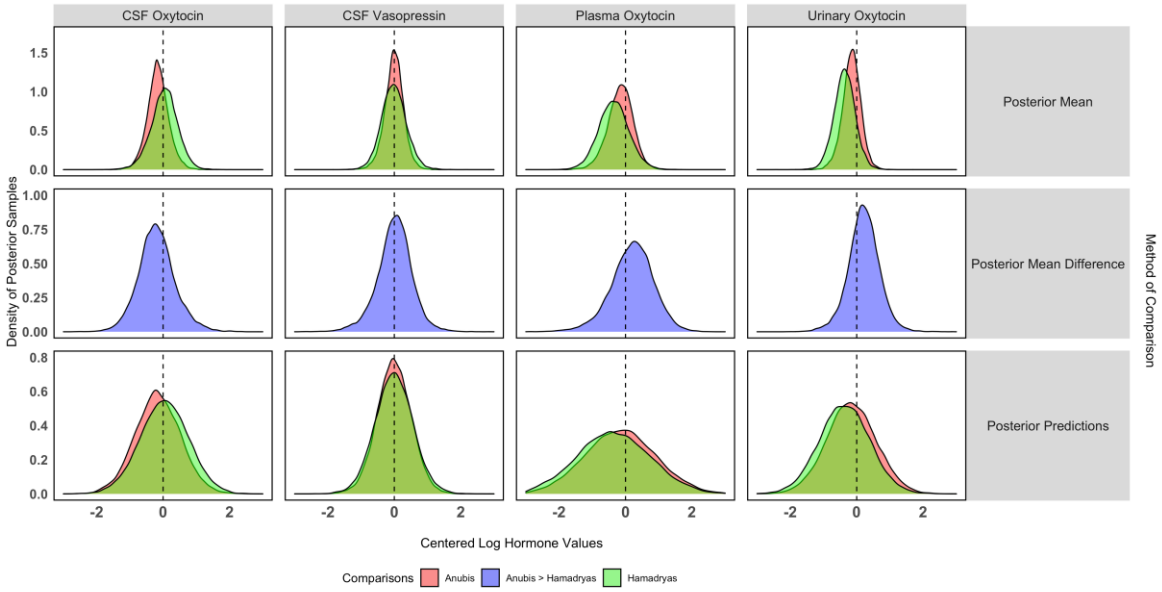

Figure 1 Comparison between subspecies for each different biosource. The first row represents the estimation of the subspecies beta value, while the second row is the difference between these estimates. The final row represents simulated data of how estimates and variability are likely present in a real population.

Figure 2.2: *Sex Parameter*

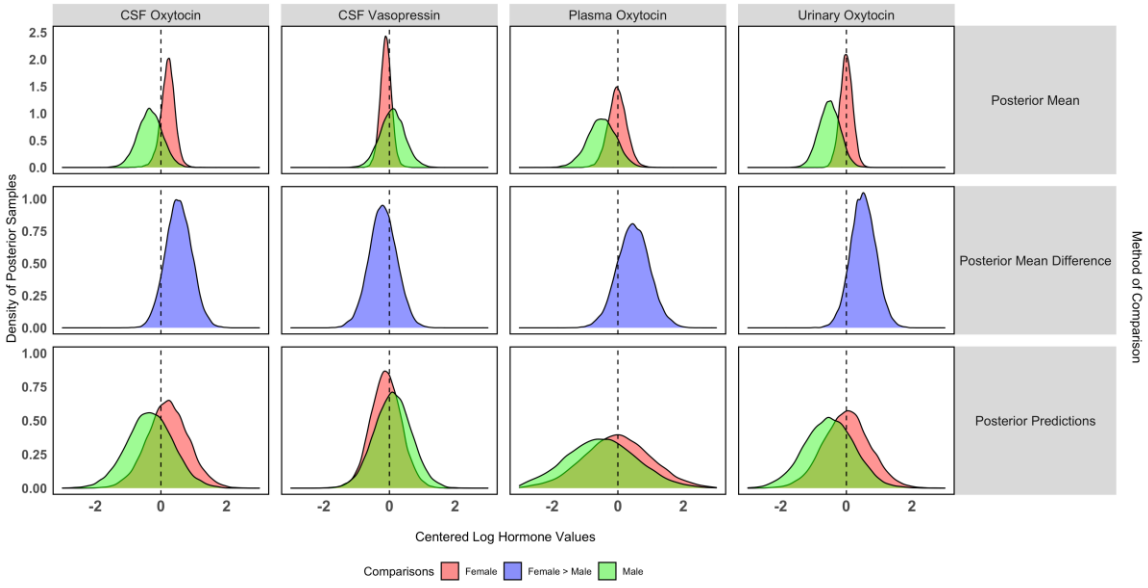

Figure 2 Comparison between sex for each different biosource. The first row represents the estimation of the sex beta value, while the second row is the difference between these estimates. The final row represents simulated data of how estimates and variability are likely present in a real population.

Figure 2.3: ***Age Parameter***

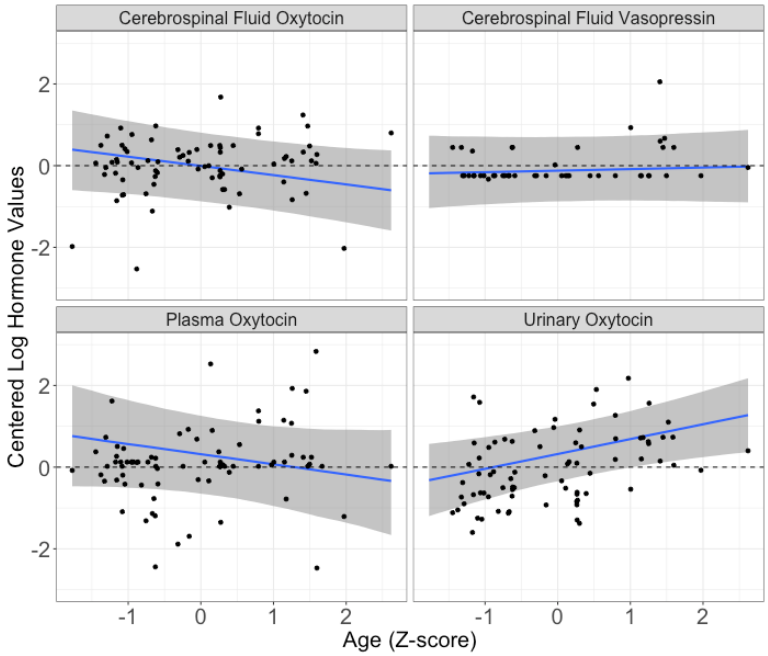

Figure 3 Relationship between hormone values and age paramter. Blue line represents posterior mean while grey regions are the 95% credible intervals. Points represent actual data points.

Figure 2.4: *Reproductive State Parameter*

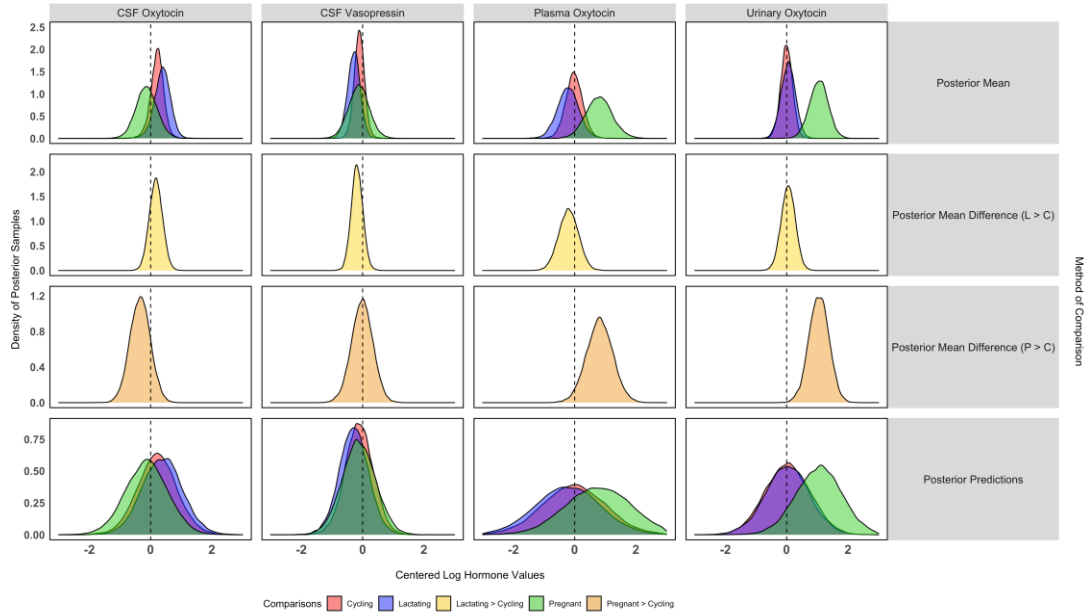

Figure 4 Comparison between reproductive states for each different biosource. The pregnant female distribution is composed of posterior samples at the latest gestational day in the original data. The first row represents the estimation of the reproductive state beta value, while the second and third rows are the differences between the cycling and lactating females, and cycling and pregnant females, respectively for these estimates. The final row represents simulated data of how estimates and variability are likely present in a real population.

Figure 2.5: ***Gestational Days***

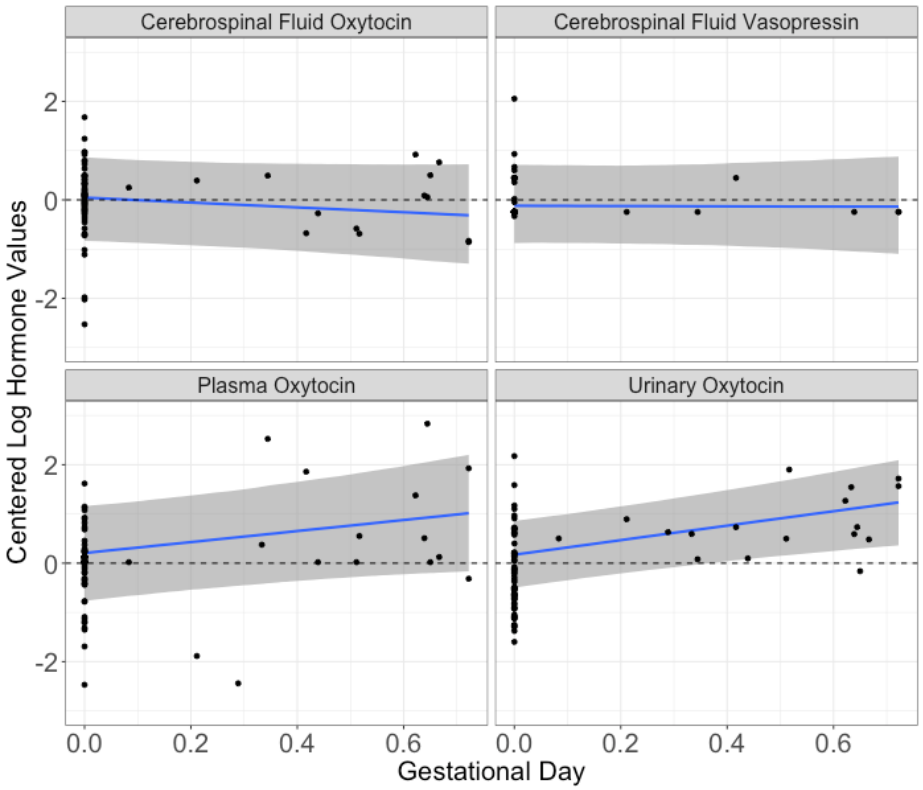

Figure 5 Relationship between hormone values and gestational day (as a proportion of the typical baboon gestation length of 180 days). Males and non-pregnant females are scored as 0. Blue line represents posterior mean while grey regions are the 95% credible intervals. Points represent actual data points.

Figure 2.6: *Residual Correlations*

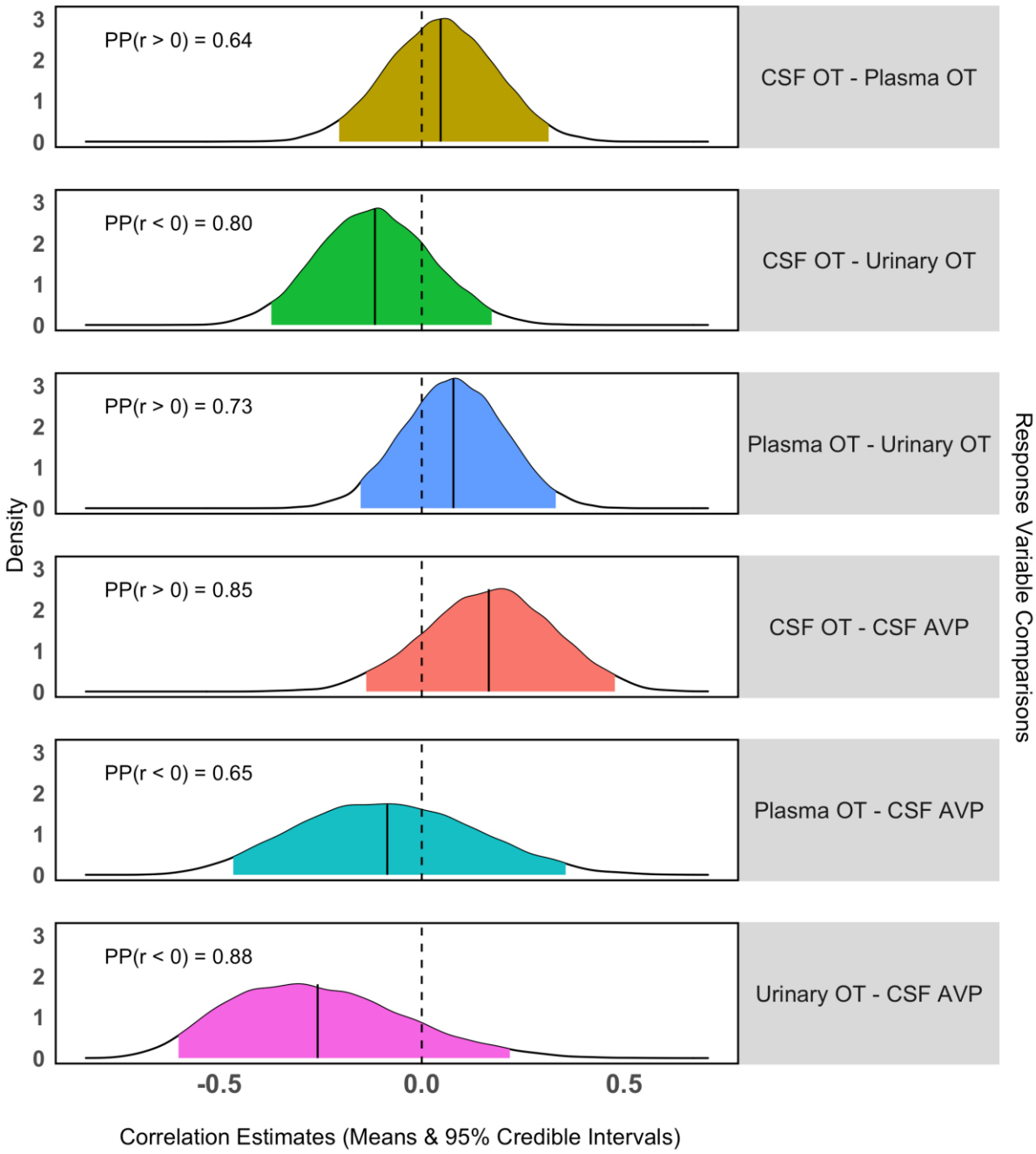

Figure 6 Plot of residual correlation coefficients, and the respective posterior probabilities. Shaded regions represent 95% credible intervals.

Table 2.1: *Subject Demographics and Biosample Distribution*

			Age (in years)		Number of Hormone Samples			
Subspecies	Sex	Number of Subjects	Median	Range	CSF OT	Plasma OT	Urinary OT	CSF AVP
Hamadryas	Male	8	12.6	12.6-18.7	8	8	7	2
Hamadryas	Female	30	12.8	5.4-24.5	23	27	27	13
Anubis	Male	19	7.4	2.3-17.6	18	19	18	11
Anubis	Female	27	11.1	4.3-21.2	26	27	25	19

Table 1 Breakdown of subjects involved in this study.

Table 2.2: *Fixed Effect Parameters*

	Table of Beta Coefficient Values				
Parameter	Mean	SD	Lower 95% CI	Upper 95% CI	PP
Cerebrospinal Fluid Oxytoxin					
log Weight	0.06	0.13	-0.19	0.31	0.69
Corral Size	-0.04	0.14	-0.29	0.25	0.63
Subspecies (Hamadryas)	0.19	0.56	-1.02	1.27	0.66
Sex (Male)	-0.54	0.40	-1.32	0.24	0.91
Sex (Male):Age Interaction	0.30	0.31	-0.32	0.92	0.83
Subspecies (Hamadryas):Age Interaction	0.11	0.17	-0.23	0.43	0.75
Subspecies (Hamadryas):Sex (Male) Interaction	0.06	0.52	-0.97	1.09	0.55
Subspecies (Hamadryas):Sex (Male):Age Interaction	0.19	0.55	-0.89	1.27	0.63
Age	-0.23	0.12	-0.46	0.02	0.97
Lactating	0.17	0.22	-0.25	0.60	0.79
Gestational Day	-0.47	0.46	-1.38	0.43	0.85
CSF Impurity	-0.08	0.20	-0.47	0.32	0.66
Plasma Oxytoxin					
log Weight	0.14	0.19	-0.23	0.52	0.77
Corral Size	-0.09	0.17	-0.44	0.22	0.70
Subspecies (Hamadryas)	-0.20	0.65	-1.39	1.20	0.64
Sex (Male)	-0.47	0.49	-1.45	0.50	0.83
Sex (Male):Age Interaction	0.22	0.36	-0.50	0.92	0.73
Subspecies (Hamadryas):Age Interaction	0.52	0.27	-0.01	1.04	0.97
Subspecies (Hamadryas):Sex (Male) Interaction	-0.12	0.84	-1.71	1.61	0.57
Subspecies (Hamadryas):Sex (Male):Age Interaction	0.01	0.72	-1.37	1.41	0.50
Age	-0.25	0.20	-0.63	0.13	0.90
Lactating	-0.20	0.32	-0.83	0.42	0.73
Gestational Day	1.13	0.59	-0.04	2.30	0.97
Plasma Impurity	0.29	0.42	-0.52	1.12	0.76
Urinary Oxytoxin					
log Weight	0.11	0.15	-0.19	0.40	0.76
Corral Size	-0.14	0.11	-0.36	0.09	0.89
Subspecies (Hamadryas)	-0.21	0.47	-1.14	0.76	0.69
Sex (Male)	-0.51	0.38	-1.27	0.24	0.91
Sex (Male):Age Interaction	-0.29	0.27	-0.83	0.25	0.86
Subspecies (Hamadryas):Age Interaction	-0.10	0.19	-0.48	0.27	0.71
Subspecies (Hamadryas):Sex (Male) Interaction	-0.26	0.78	-1.71	1.39	0.65
Subspecies (Hamadryas):Sex (Male):Age Interaction	-0.07	0.97	-1.95	1.83	0.53
Age	0.36	0.14	0.09	0.64	1.00
Lactating	0.05	0.23	-0.40	0.50	0.59
Gestational Day	1.46	0.45	0.55	2.32	1.00
Cerebrospinal Arginine Vasopressin					
log Weight	-0.06	0.13	-0.31	0.20	0.67
Corral Size	0.06	0.11	-0.14	0.29	0.72
Subspecies (Hamadryas)	0.00	0.53	-1.03	1.15	0.52
Sex (Male)	0.20	0.42	-0.62	1.03	0.68
Sex (Male):Age Interaction	-0.16	0.31	-0.78	0.44	0.69
Subspecies (Hamadryas):Age Interaction	0.07	0.16	-0.24	0.37	0.67
Subspecies (Hamadryas):Sex (Male) Interaction	-0.44	0.63	-1.66	0.83	0.76
Subspecies (Hamadryas):Sex (Male):Age Interaction	0.22	0.52	-0.80	1.24	0.66
Age	0.04	0.10	-0.16	0.24	0.65
Lactating	-0.18	0.19	-0.55	0.20	0.83
Gestational Day	-0.02	0.48	-0.98	0.91	0.51
CSF Impurity	0.17	0.19	-0.20	0.53	0.81

Table 2 Complete list of all means, standard deviations, 95% credible intervals, and proportions of the posterior for each hormone response variable's fixed effects.

Table 2.3: *Residual Correlations*

Comparison	Table of Residual Correlation Values				
	Mean	SD	Lower 95% CI	Upper 95% CI	PP
CSF OT - Plasma OT	0.05	0.13	-0.21	0.30	0.64
CSF OT - Urinary OT	-0.12	0.14	-0.38	0.16	0.80
Plasma OT - Urinary OT	0.08	0.12	-0.16	0.32	0.73
CSF OT - CSF AVP	0.17	0.16	-0.15	0.46	0.85
Plasma OT - CSF AVP	-0.09	0.21	-0.48	0.34	0.65
Urinary OT - CSF AVP	-0.26	0.21	-0.61	0.19	0.88

Table 3 Complete list of all means, standard deviations, 95% credible intervals, and proportions of the posterior for each residual correlation.

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Chapter 3: Between-Individual Comparisons

ABSTRACT

Forming and maintaining social relationships is important for achieving reproductive success in many primate societies. However, individual primates vary greatly in their social strategies, with some more frequently engaging in affiliative interactions, while others pursue more aggressive strategies. This study investigated whether individual differences in social behavior were associated with baseline levels of arginine vasopressin (AVP) in cerebrospinal fluid (CSF), and oxytocin (OT) in CSF, plasma, and urine. We predicted that OT would correlate most strongly with affiliative behaviors, and AVP with aggressive behaviors. Biosamples and behavioral observations were collected from 70 captive baboons of two subspecies (Papio hamadryas anubis & Papio hamadryas hamadryas), and all hormones were assayed using ELISA. We used a Bayesian multivariate multilevel model to detect stable individual differences (i.e. "personality") in nine behaviors as and test for associations with hormone levels. Plasma OT was positively associated with initiation of close proximity and grooming. In contrast, CSF AVP was negatively associated with time spent in close proximity. In addition, both urinary and plasma OT were associated with submissive behaviors, albeit in opposite directions. Therefore, although OT and AVP did correlate with some social behaviors, the exact role that baseline hormone concentrations play in social strategies needs to be better understood.

INTRODUCTION

Longitudinal studies of primates have shown that the formation and maintenance of relationships can affect survivorship, and that reproductive success is dependent on the correct deployment of affiliative and agonistic behaviors (Alberts, 2019; Silk, 2007). Primatologists have attempted to understand the proximate mechanisms underlying primate social behavior through a variety of techniques, with behavioral endocrinology as a central tool of this investigation (Higham, 2016). This research has demonstrated that primate social behavior is substantially influenced by hormone concentrations, both

through their acute actions on facilitating behavior, and for their influence on shaping the general temperament or personality of individuals.

The neurohormones oxytocin (OT) and arginine vasopressin (AVP) in particular have been found to have key roles in modulating social behavior (Caldwell, 2017; Johnson and Young, 2015). In general, OT is an anxiolytic hormone that increases the likelihood of social interactions (Kemp and Guastella, 2010; Shamay-Tsoory and Abu-Akel, 2016). In this capacity, OT has roles not only in partner and parental bonding, but also with behaviors that manage social relationships, such as affiliation, and cooperation (Crockford et al., 2014; De Dreu, 2012; Maroun and Wagner, 2016). In contrast to the affiliation-enhancing effects of OT, AVP is generally anxiogenic, and can enhance several aggressive behaviors, such as territoriality and mate-guarding (Carter, 2017; Goodson and Bass, 2001). Although AVP can facilitate male prosociality, particularly male pair-bonding and paternal care (Jarcho et al., 2011; Nair and Young, 2006; Taylor and French, 2015), such behaviors are often deployed in a context of possessiveness and aggressive defense (Delville et al., 1996; Ferris and Delville, 1994). Despite these findings, less is known about the full range of behaviors mediated by these neurohormones in non-human primates (Putnam et al., 2018), which may partly result due to the difficulty in hormone sample collection, particularly in wild settings.

Nevertheless, the functions of OT in non-human primates are similar to what has been observed in non-primate animals. For example, among monogamous and cooperatively breeding primates such as common marmosets (*Callithrix jacchus*) and cotton-top tamarins (*Saguinus oedipus*), basal urinary OT levels are correlated with the strength of dyadic relationships, alloparental care, and frequency of affiliative behavior (Finkenwirth et al., 2016, 2015; Snowdon et al., 2010). Even among non-monogamous primates, OT is associated with affiliative behaviors and social relationships (Berg et al., 2019; Rincon et al., 2020), and may partly operate by decreasing social anxiety and enhancing perception of social cues (Jiang and Platt, 2018). For example, intranasally-administered OT in rhesus macaques (*Macaca mulatta*) not only decreases vigilance to potential social threats and increases prosocial decision-making, but also increases attention to the recipient monkey's face and eyes (Ebitz et al., 2013).

Similarly, less affiliative and more aggressive rhesus macaques had significantly decreased baseline cerebrospinal fluid (CSF) levels of OT, a pattern which persisted across time (Winslow et al., 2003). Lastly, among chacma baboon (*Papio hamadryas ursinus*) females, there is a positive relationship between the female's maintenance of close proximity to a consorting male and their baseline urinary OT levels, suggesting a correspondence between OT and female investment in this social relationship (Moscovice and Ziegler, 2012).

However, these correlations between OT and social behavior may also result from affiliative behaviors stimulating the endogenous release of the neuropeptide. For example, urinary OT levels are elevated in chimpanzees (*Pan troglodytes*) following cooperative and affiliative behaviors such as grooming with preferred partners, food sharing, and intergroup encounters, and in female bonobos (*Pan paniscus*) following same-sex sex bouts (Crockford et al., 2013; Moscovice et al., 2019; Samuni et al., 2017; Wittig et al., 2014).

Compared to OT, less research has been done on the relationship between basal AVP values and non-human primate social behavior and personality. Among non-primate species, exogenous AVP has been found to greatly increase aggressive interactions, and can enhance not only indicators of dominance, but also physical violence (Ferris, 1992; Ferris and Delville, 1994). However, while basal CSF AVP levels in humans can be positively correlated with a life history of aggression (Coccaro et al., 1998), the connection between aggression and AVP in non-human primates is less clear. Among rhesus macaques, baseline CSF AVP was not associated with aggression (Winslow et al., 2003), and intranasal AVP had slightly stronger effects than intranasal OT in decreasing the length of time engaging in dominance behaviors between two partners (Jiang and Platt, 2018). Similarly, intracerebroventricularly administered AVP into male squirrel monkeys (*Saimiri sciureus*) did not increase aggressive behavior, and perhaps even decreased it (Winslow and Insel, 1991).

Similar to OT, AVP can also influence prosocial behaviors and relationships among non-human primates. Specifically, as in non-primate species, AVP can promote male partner preference, as intranasally administered AVP to monogamous titi monkeys (*Callicebus cupreus*) increased the male's

interest in the female partner compared to an unknown female (Jarcho et al., 2011). Among non-monogamous species, such as male rhesus macaques, baseline CSF AVP values were directly related to a composite measure of sociality, with highly social individuals having higher AVP concentrations, and vice versa; furthermore these measures were also found to be individually stable across multiple timepoints of collection (Parker et al., 2018).

Despite the correlations between these neurohormones and social behavior, debate continues as to the informational value, and connections between, the sources of collection: specifically, central (e.g. cerebrospinal fluid) and peripheral (e.g. blood plasma, urine) sources. Central values of the neurohormones are frequently considered to be most indicative of their behavioral influence (Kagerbauer et al., 2013). Unfortunately, central collection is difficult in non-human primates, particularly in wild populations where ethical considerations preclude invasive sampling. Nevertheless, peripheral sources of the neurohormones, especially urine, have been found to consistently correlate with measures of social behavior in non-human primates (Benítez et al., 2018; Crockford et al., 2014), although these peripheral measures and central levels are frequently not correlated to one another. It would therefore be useful to compare baseline central and peripheral sources of the neurohormones to an individual's social behavior to elucidate any connections that might exist between the sources and behavior.

In order to better understand the manner in which OT and AVP influence non-human primate social behaviors, this study compared behavioral data from two baboon subspecies with hormone samples collected from both central and peripheral sources.We use a modern statistical framework that models the effects of hormones and other factors like age, sex, and subspecies on behavior while also detecting stable individual differences in behavior, i.e. personality. Baboons (genus *Papio*) are useful primates for studying the relationship between hormones and behavior. Although similar to other primates that live in large and complex social groups, many baboon populations have been studied for several decades, leading to a better understanding of how an individual's temperament and sociality can influence eventual reproductive fitness (Alberts and Altmann, 2012; Silk, 2007; Silk et al., 2010). For example, females with enduring social bonds and strong social integration reproduce more successfully than competitors

(Alberts, 2019; Archie et al., 2014). Likewise, despite the importance of intrasexual competition in male mating opportunities among savannah baboons, affiliative behavior is also essential in both successful male emigration and intersexual relationships (Smuts, 1985). It is specifically hypothesized that individuals with more affiliative personalities, as shown for example through higher rates of grooming or close contact maintenance, will present higher basal OT levels. Likewise, individuals that engage in more aggressive or dominance-related activities should be found to have higher baseline AVP levels.

METHODS

a) Study Location and Dates of Collection

Biosamples and behavioral data were collected from 70 baboons (Table 1). All baboons were either pure hamadryas or pure anubis, with no hybrids. Biosamples and behavioral observations from 36 hamadryas baboons (28 female, 8 male) were collected at the Mannheimer Foundation from October 2013 to May 2014. Biosamples and behavioral data from 34 anubis baboons (26 female, 8 male) were collected at Baboon Research Resource at the University of Oklahoma's Health Science Center from May to October 2014. Both institutions have large colonies, with the majority of baboons living in mixed-sex and mixed-age corrals. Institutional Animal Care and Use Committee (IACUC) approvals were obtained from both the Mannheimer Foundation (protocol #2013-05) and UOHSC (protocol #14-024) before any data collection began. As many of the species-typical behaviors become prominent at adulthood, nearly all subjects were full adults or subadults as determined by established age divisions for baboons (Jolly and Phillips-Conroy, 2003; Swedell, 2006).

b) Subject Selection & Hormone Collection Procedures

Subject selection, biosamples collection, and biosample analysis is as previously described in Coppeto et al. (in prep.). Of the 70 subjects, 2.0 mL of CSF was collected from 62, 5.0 mL blood plasma from 69, and 10mL urine from 67. Due to difficulties in collection, especially for the CSF, not all subjects had samples from all sources collected, although these subjects are a small minority of the full collection. Every subject was sampled once from each source (CSF, blood, urine) during biannual physicals, which

had the advantages of sampling each subject within a corral, and also decreasing the stress of capture and collection for each subject. As such, we cannot assess the stability of individual differences in hormone levels over time, nor can we relate hormone levels to specific behavioral events. Hence, we test whether the single hormone samples are associated with stable individual differences in behavior, and with each other.

c) *Behavioral Data Collection*

(i) *Ethogram & Observation*

A composite ethogram was created that included elements from a variety of different published ethograms (Smuts, 1985; Swedell and Leigh, 2006) and from an ethogram used for primate observation at the Yerkes National Primate Research Center (see ethogram in appendix). Each observation was conducted as 20 minute continuous focal samples, and a total of approximately 13 focals were collected per individual, although some individuals had fewer focals collected (range = 6-14 focals). Each individual and behavior had a unique four character code which were combined in the form of "Actor/Behavior/Recipient" for a total of a twelve character string. Code was written in R 3.9.3.(R Core Team, 2019) that organized all focal data and checked for misspellings or errors. The code then recorded the frequencies and durations of behaviors and their partners.

(ii) *Selection of Behaviors for Analysis*

For the purpose of the current analysis we focused on the most common behaviors related to proximity, affiliation, and aggression (Table 2).

d) *Data Analysis*

This study involved a multilevel data structure with nine different behavioral response measures, four hormone variables, and five control variables, with subjects nested within corrals. Some hormone data were missing because certain biosamples could not be collected or lacked sufficient volume for the ELISA. Such data structures are best analyzed using multilevel models, with imputation of missing data rather than the removal of incomplete cases (which makes the assumption of data missing completely at random) (McElreath, 2016; Nakagawa and Hauber, 2011). We implemented these analyses within a

Bayesian framework, which propagates the uncertainty inherent in missing data imputation into final parameter estimates, using the brms package v. 2.8.9 (Bürkner, 2018, 2017) in R 3.9.3. (R Core Team, 2019).

The hormone values were the main predictor variables of interest. All hormone data were log transformed and centered. As urinary concentration is susceptible to individual variability in hydration, the measures of urinary OT were corrected using levels of creatinine, which is assumed to be excreted at a constant rate (Singh et al., 2015). Therefore, urinary OT values were first converted to a ratio of OT pg/mg creatinine. Missing hormone data were imputed using additional sub-models that included the other hormone measures and the five control variables as predictors.

The control variables included subspecies, sex, age, timing of observation, and gestational day at time of hormone collection (males and non-pregnant females were coded as "0" for gestational day). All continuous control variables were standardized.

The model also included three random effects: corral membership, subject ID, and observation ID. Subject ID and observation ID further allowed for the calculation of correlations between the response variables both among and within individuals. Earlier model comparisons also suggested that the behavioral patterns between anubis and hamadryas baboons were different enough that the subject ID and observation ID random effects were additionally calculated with subspecies as a modifier, i.e. the correlation structures among different behaviors were allowed to differ between the subspecies.

The full model is:

$$\begin{aligned} Behavior\ Measure\ = \beta_0 + \gamma_1 Corral\ ID + \gamma_2 Subject\ ID + \gamma_3 Observation\ ID + \\ \beta_1 CSF\ OT + \beta_2 CSF\ AVP + \beta_3 Plasma\ OT + \beta_4 Urinary\ OT + \\ \beta_5 Subspecies + \beta_6 Sex + \beta_7 Age + \beta_8 Time\ of\ Day\ of\ Observation + \\ \beta_9 Gestational\ Day\ at\ Hormone\ Collection \end{aligned}$$

Importantly, using multivariate models allowed parameter estimates to be pooled across outcomes resulting in more precise and conservative estimates (McElreath, 2016). All models used slightly regularizing priors (fixed effects: β_{0-9}~Normal(0,1); random effects: γ_{1-3}~ Cauchy(0,1)) to impose further conservatism on parameter estimates. Furthermore, based on observations of the structure of the

raw data, all event behaviors were modeled using a poisson distribution, while duration behaviors were modeled using a gamma distribution. Models were run for 4,000 iterations per chain of eight chains and converged well as indicated by visual inspection of trace plots and convergence diagnostics (all Rhat =1). Further details on model fitting can be gleaned from the accompanying R code.

Bayesian analyses produce a posterior distribution for each estimated parameter and these distributions can be summarized in several ways. Here we report the mean, 95% credible intervals, and the proportion of the posterior distribution (PP) that supports a given association. For instance, when evaluating the hypothesized higher OT in affiliative behavior, PP > 0 provides a direct measure of support for that hypothesis. Furthermore, we plot the entire posterior distribution for the main parameters of interest. While we report all posteriors to facilitate readers making their own inference, we consider associations with PP > 0.85 worth highlighting in the text.

RESULTS

Fixed Effect Results:

All fixed effect coefficient estimates, standard deviations, 95% credible intervals, and proportions of the posterior are summarized in Table 3 and Figure 1(hormone parameters) and Table 4 and Figure 2(control parameters). In addition, the marginal effects for a selection of findings with proportions of the posterior greater than 0.85 are summarized in Figure 3.

Hormone Parameters

Approach and Proximity

Neither Approach (moving within 1 meter of another) nor Proximity (time spent within 1 meter of another) behaviors were strongly associated with hormone levels. Nevertheless, CSF OT was positively associated with Approach and Proximity (Approach: B = 0.11, $PP_{B>0}$ = 0.85; Proximity: $PP_{B>0}$

= 0.87). This weak association suggests that individuals with higher CSF OT approached others more frequently and spent more time in proximity.

Close Approach and Close Proximity

Close Approach (moving to within 10cm of another individual) was strongly and positively associated with plasma OT (B = 0.06, $PP_{B>0}$ = 0.95). This indicates that individuals with higher baseline plasma OT more frequently initiated close proximity with a partner. In contrast, and somewhat surprisingly, CSF AVP was equally strongly, yet negatively associated with close proximity (B = -0.35, $PP_{B<0}$ = 0.97). In other words, individuals with higher CSF AVP baseline values spent less time in close contact with others.

Groom Initiation and Grooming Durations

Plasma OT was strongly and positively associated with initiating grooming (B = 0.77, $PP_{B>0}$ = 1.00). Specifically, individuals with higher baseline levels of plasma OT initiate grooming bouts more frequently. CSF AVP was positively associated with grooming bout durations (B = 0.21, $PP_{B>0}$ = 0.86); suggesting that individuals that have higher baseline levels of CSF AVP also have longer grooming bouts.

Aggression and Submission

None of the hormone measures were strongly associated with dominance/aggressive behaviors, although urinary OT did have a weak negative association with dominance behaviors (B = -0.48, $PP_{B<0}$ = 0.86). In contrast, there were stronger relationships between hormones and submissive behaviors. In particular, urinary OT has a very strong and well-supported positive association with submissive behaviors (B = 0.78, $PP_{B>0}$ = 0.99). Therefore, individuals with higher baseline urinary OT frequently perform submissive gestures. Surprisingly, plasma OT showed an equally strong but negative relationship with submissive behaviors (B = -0.44, $PP_{B<0}$ = 0.95), such that individuals with low plasma OT most frequently perform submissive behaviors.

Self-Directed

There were no relationships between baseline hormone measures and self-directed actions.

Control Parameters

Among control parameters, there were several findings that were expected from these primate populations. In particular, Aggressive and Submissive behaviors were sexually dimorphic, with males performing more aggressive behaviors (B = 1.38, $PP_{B>0}$ = 1) and females performing more submissive behaviors (B = -2.40, $PP_{B<0}$ = 0.97). In addition, younger individuals were far more likely to perform submissive behaviors and less likely to perform aggressive behaviors (Aggression:B = 0.30, $PP_{B>0}$ = 0.92; Submission: B = -0.90, $PP_{B<0}$ = 1).

There were also some significant differences in behavior between the subspecies, particularly in relation to affiliative behaviors. In contrast to the anubis baboons, hamadryas baboons form one-male units (OMU; or "harems"), where several females exclusively associate with a single male, and often remain only a few meters from him. In line with the centrality of the male harem leader, there was increased proximity initiation in hamadryas baboons (B = 0.26, $PP_{B>0}$ = 0.89), as OMU members would frequently cluster around each other and the OMU leader throughout the day. Likewise, females would often compete for close proximity and grooming with the OMU leader, which would also account for the associations between hamadryas baboons and time spent in close proximity(B = 0.85, $PP_{B>0}$ = 0.99), and more frequent grooming initiations(B = 0.85, $PP_{B>0}$ = 0.98).

DISCUSSION

OT and Affiliation

The results of this study show a connection between individual social temperament and baseline hormone levels. In particular, as predicted, higher baseline OT values were most strongly associated with highly affiliative individuals. Specifically, individuals that most frequently initiated sitting close (within 10cm), or who most frequently initiated allogrooming bouts, were found to have elevated baseline plasma levels of OT. Both behaviors are intimate interactions that can be viewed as a deliberate choice by the initiator to socialize. This is especially important in allogrooming which, besides its basic function in primate hygiene, has important social functions in increasing tolerance between partners, sexual access, and bond establishment and maintenance (Grueter et al., 2013). Indeed, research has already established a strong connection between primate grooming behavior and both subsequent increases of OT secretion as detected in urine (Crockford et al., 2013; Rincon et al., 2020), and baseline measures of OT (Berg et al., 2019; Maestripieri et al., 2009; Winslow et al., 2003). Most importantly, these interactions can potentially leave the initiator vulnerable to aggression should the recipient reject the gesture. This fundamental risk of socializing means that anxiety about the outcome of the interaction must be overcome in order to initiate these intimate and highly physical behaviors.

This intimacy and deliberate selection of partners is perhaps why associations between one meter proximity initiation and OT were very weak to negligible: Such approaches may often be incidental, with the intended target of the approach being surrounded by other individuals. Indeed, other studies have found that such selective choices in partners are often a crucial aspect of the association between OT and proximity maintenance (Moscovice et al., 2019; Moscovice and Ziegler, 2012). Likewise, it is probable that entering within a one meter proximity to another individual is less stressful than coming into physical contact with them; therefore an approach to one meter would have a lower barrier to initiate.

However, most of these affiliative behavior/OT associations were found in the periphery, specifically the plasma, rather than in the CSF, contrary to our expectations. The CSF values of neurohormones, and OT/AVP in particular, have often been viewed as being more representative of the

aggregate activity of the neurohormones in the brain, and therefore of social behavior (Kagerbauer et al., 2013), while peripheral concentrations of OT are representative of different physiological processes and only indirectly provide a view on social behavior, if at all. Indeed, in support of this view, there are numerous examples of CSF OT associations with individual behavioral traits, such as affiliation (Winslow et al., 2003), anxiety (Carson et al., 2015), or lifetime history of aggression (Lee et al., 2009). Nevertheless, peripheral measures of OT, particularly urine in non-human primates (Crockford et al., 2013; Finkenwirth et al., 2016; Snowdon et al., 2010), have been frequently found to correlate with social behavior in a significantly informative way (Crockford et al., 2014).

In the current study, baseline CSF and urinary OT values were only weakly associated with measures of affiliative behavior. It is especially surprising that no correlations were found between baseline urinary OT and affiliative behavior, given the previous findings of these positive associations in marmosets and tamarins (Finkenwirth et al., 2016, 2015; Snowdon et al., 2010). Indeed, urinary OT levels represent filtration of the circulating OT by the kidneys, with a time delay of approximately thirty minutes to two hours (Seltzer and Ziegler, 2007). Therefore, it would be expected that baseline urinary and plasma OT should be associated similarly with individual social temperament, as the time delay should have less impact than in a measurement of the acute actions of OT. Nevertheless, other studies (Feldman et al., 2011) have also failed to find an association between baseline urinary OT and affiliative behavior. In fact, urinary OT was not only most strongly associated with anxiety or stress, but was also unrelated to baseline plasma OT values. It is possible that urinary OT best represents acute behavioral states, such as grooming, rather than circulating OT.

Instead, baseline plasma OT was most strongly associated with measures of affiliation, and especially for intimate social behaviors. The importance of baseline plasma OT measures for indications of a prosocial behavioral temperament is well-represented in the human and non-human primate research. Specifically, baseline plasma OT can be a stable individual trait (Feldman et al., 2010), and its baseline values are positively associated with the frequency of affiliative behaviors, particularly social touch, close contact, and affection (Berg et al., 2019; Feldman et al., 2012, 2011, 2010; Maestripieri et al., 2009).

However, it is not certain how the increased baseline plasma OT levels are affecting individual-specific social temperament. Baseline plasma OT is often found to be positively associated with feelings of trust, and inversely with measures of anxiety and cortisol (Carson et al., 2015; McQuaid et al., 2016; Scantamburlo et al., 2007; but see also Tops et al., 2007; Weisman et al., 2012 for an opposite association). In fact, Legros et al., (1988) found that exogenous OT delivered into the adrenal glands (where OT receptors are present (Gimpl and Fahrenholz, 2001)) prevented an increase in cortisol from exogenous ACTH. Depending on the theoretical interpretation, higher baseline OT in these results can be seen as decreasing the baseline anxiety of the individual, and thereby permitting more frequent potential social approach behaviors (Bartz et al., 2011; Kemp and Guastella, 2010; Shamay-Tsoory and Abu-Akel, 2016). Indeed, in non-human primates in particular, intranasally administered OT is found to relax perceptions of dominance hierarchies, and reduce normally aroused and vigilant states when presented with a dominant conspecific (Dal Monte et al., 2014; Jiang and Platt, 2018). Furthermore, as in humans(Eckstein et al., 2019; Guastella et al., 2008), intranasal OT increases gaze to the eye regions of partners in rhesus macaques (Dal Monte et al., 2014; Ebitz et al., 2013), an act which is otherwise provocative under normal circumstances. Therefore, higher baseline plasma OT may contribute to this prosocial disposition through its interactions with peripheral OT receptors, and especially those located in the adrenal glands, and therefore affect behavior in a bottom-up manner.

OT and Submissive Behaviors

OT had virtually no associations with aggressive or dominant behaviors, except for a weak positive effect for urinary OT. Although some literature suggests that dominance rank is positively associated with circulating levels of serum OT (Michopoulos et al., 2011), the current study correlated behaviors involving aggression and dominance with OT, rather than just rank alone.

However, submissive behaviors were strongly associated both with plasma OT and urinary OT, although with opposite effects. Specifically, individuals that performed more submissive behaviors had not only lower baseline plasma OT but also higher baseline urinary OT. The low values of plasma OT

may again be related to its anxiolytic effects. As noted earlier, baseline plasma OT is frequently found to be low in depressed and anxious individuals (Carson et al., 2015; Gordon et al., 2008; McQuaid et al., 2016; Scantamburlo et al., 2007). Likewise, plasma OT is also found to be higher in individuals with good attachment histories to families and friends (Feldman et al., 2011; Gordon et al., 2008). These two lines of evidence suggest perhaps that individuals that more frequently perform submissive behaviors have higher levels of stress and might also lack a kin or non-kin network to buffer the received antagonism.

Likewise, the positive association between urinary OT and submission is possibly related to the findings of Feldman et al. (2011), which noted that baseline urinary OT was positively related to relationship anxiety and stress. In addition, urinary OT is also found to be directly and positively associated with the presence of psychopathic traits (Mitchell et al., 2013). It is therefore possible that baseline urinary OT, as opposed to acute changes in urinary OT, is more informative about the level of stress in an individual.

AVP and Social Behavior

In contrast to our predictions, CSF AVP did not associate with measures of dominance and aggression. Given the importance of AVP in aggressive behaviors (Caldwell et al., 2008; Coccaro et al., 1998; Ferris, 1992; Ferris et al., 1997), it was believed that individuals that engaged most frequently in aggressive behaviors would likewise have an increased baseline of CSF AVP. Instead, AVP was strongly and negatively associated with some measures of affiliation: specifically, individuals that spend more time in close proximity have lower baseline CSF AVP values. This finding could be explained by the anxiogenic effects of AVP. As baseline plasma OT is able to lower the anxiety associated with social interaction, and thereby promote more approach behaviors, baseline CSF AVP in contrast may heighten such trait anxiety, and therefore limit the individual's tolerance for long social interactions.

However, this contradicts recent findings by Parker et al. (2018), who found that CSF AVP was a strong positive predictor of sociality and time spent grooming in rhesus macaques. It is interesting that the

current study also found a very weak positive relationship between grooming duration length and AVP, such that individuals that groomed for longer durations likewise had higher baseline levels of CSF AVP. However, this weakness in the effect could be related to differences in experimental design as Parker et al. (2018) specifically chose subjects at the extremes of sociability out of a larger pool in order to get a strong behavior/hormone signal. The current study looked at all individuals with varying degrees of sociality, and therefore perhaps this diluted the stronger positive relationship between grooming durations and AVP.

Neurohormones and Self-Directed Behaviors

In addition, it was surprising that there were no relationships found for self-directed behaviors and hormone values. Constantly engaging in self-directed behaviors is often an indication of anxiety or stress in non-human primates (Brent et al., 2002; Castles et al., 1999; Ellis et al., 2011), behaviors which OT and AVP are intricately linked to. However, other studies (Ellis et al., 2011) have also failed to find a connection between self-directed behaviors and faecal gluco-corticoids in anubis baboons, suggesting that the baseline hormonal connection to self-directed behaviors is more complicated than previously assumed.

Conclusion: Baseline vs. Acute Release and Neurohormone Function

Experiments involving the administration of exogenous OT and AVP via intracerebroventricular injection, intranasal absorption, or other techniques, have done much to clarify the influence of these neurohormones on modulating immediate social behavior (Andari et al., 2010; Rilling et al., 2012; Williams et al., 1994). However, it is also important to consider the role of baseline neurohormones in the larger scheme of OT and AVP social functions. Indeed, baseline concentrations of different hormones and neurohormones are frequently found to correlate with the general temperament and personality of individuals (Anestis, 2011); for example, baseline CSF levels of the serotonin metabolite 5-HIAA have been repeatedly found to be inversely related to impulsive and aggressive temperaments in non-human

primates(Westergaard et al., 2003, 1999). However, our understanding of how baseline OT and AVP mold individual human and non-human primate personalities and social temperament is still less developed than our understanding of acute changes in the neurohormones. The current study suggests that baseline OT (particularly within circulation) is likely an important component in modulating individual sociability, possibly through its effects in decreasing baseline anxiety. Future studies can investigate this possibility through simultaneous comparison of not only OT with behavior, but also other hormones such as testosterone or cortisol, whose baseline contributions to behavior are better understood. Likewise, the role of baseline CSF AVP in personality requires further study, as its associations in this study and others(Parker et al., 2018) suggest both prosocial(e.g. Increased time grooming) and antisocial(e.g. Decreased time in close proximity) functions. Most importantly, this study suggests that more research must be placed on understanding the potential bottom-up links between circulating neurohormones and their influences on central activity. Although many papers have speculated on the importance of OT on influencing adrenal or vagal activities, less research has been conducted on proving these connections. The results of this study suggest that circulating neurohormones are influencing behavior through their peripheral receptors, and that this mechanism needs to be understood.

FIGURES & TABLES

Table 3.1: *Subject Demographics and Biosample Distribution*

				Age (in years)		Number of Hormone Samples			
Subspecies	Sex	Number of Subjects	Hours of Observation	Median	Range	CSF OT	Plasma OT	Urinary OT	CSF AVP
Hamadryas	Male	8	35	12.6	12.6-18.7	8	8	7	2
Hamadryas	Female	28	121.7	12.6	5.4-24.5	21	27	27	11
Anubis	Male	8	25	8.1	4.6-13.2	8	8	8	5
Anubis	Female	26	70	11	4.3-21.2	25	26	25	18

Table 1 Breakdown of the subjects used in this study. "Hours of Observation" represents the sum of 20 minute focals for all subjects within that category.

Table 3.2*: Behavior Response Variables*

Behavior	Type	Description
Approach	*Event*	Focal subject enters within 1 meter of another adult.
Close Approach	*Event*	Focal subject enters within 10 cm of another adult.
Groom Initiation	*Event*	Focal subject initiated grooming with another adult.
Proximity	*Duration*	Total amount of time within the 20 minute focal when the focal subject was within 1 meter of at least 1 other adult, but not within 10 cm of any adult.
Close Proximity	*Duration*	Total amount of time within the 20 minute focal when the focal subject was within 10cm of at least 1 other adult, but not grooming.
Grooming Duration	*Duration*	Total amount of time within the 20 minute focal when the focal subject was grooming with another adult.
Aggression/Dominance	*Event*	Composite measure including counts of focal subject's threats and attacks toward other adults. Also includes acts of dominance towards other adults (e.g. Mounting, displacements), and acts of submission by other adults directed towards the focal subject (e.g. Submissive vocalizations).
Submission	*Event*	Composite measure including counts of focal subject's receipt of threats and attacks from other adults. Also includes acts of submission towards other adults (e.g. Submissive vocalizations), and acts of dominance by other adults directed towards the focal subject (e.g. Mounting, displacements).
Self-Directed	*Event*	Focal subject scratches self or autogrooms

Table 2 Definitions for the behavioral response variables used in this study.

Table 3.3: *Hormone Parameters*

	Table of Beta Coefficient Values				
Source	Mean	SD	Lower 95% CI	Upper 95% CI	PP
Approach					
CSF OT	0.105	0.103	-0.100	0.308	0.846
CSF AVP	-0.001	0.117	-0.234	0.224	0.501
Plasma OT	0.092	0.100	-0.105	0.291	0.822
Urinary OT	0.036	0.162	-0.288	0.348	0.597
Close Approach					
CSF OT	0.063	0.137	-0.204	0.331	0.677
CSF AVP	-0.127	0.155	-0.439	0.172	0.795
Plasma OT	0.208	0.130	-0.040	0.468	0.948
Urinary OT	-0.179	0.207	-0.597	0.220	0.807
Groom Initiation					
CSF OT	-0.162	0.279	-0.705	0.385	0.719
CSF AVP	0.258	0.290	-0.303	0.837	0.816
Plasma OT	0.772	0.271	0.257	1.321	0.999
Urinary OT	0.109	0.395	-0.648	0.908	0.606
Proximity					
CSF OT	0.112	0.099	-0.083	0.305	0.870
CSF AVP	0.056	0.100	-0.140	0.254	0.714
Plasma OT	0.039	0.094	-0.149	0.223	0.661
Urinary OT	0.108	0.151	-0.190	0.404	0.762
Close Proximity					
CSF OT	0.107	0.177	-0.245	0.452	0.729
CSF AVP	-0.347	0.179	-0.694	0.005	0.973
Plasma OT	-0.076	0.160	-0.388	0.236	0.682
Urinary OT	0.025	0.249	-0.467	0.503	0.540
Grooming Duration					
CSF OT	-0.046	0.195	-0.433	0.331	0.589
CSF AVP	0.209	0.192	-0.170	0.589	0.860
Plasma OT	0.023	0.179	-0.327	0.363	0.553
Urinary OT	0.146	0.282	-0.406	0.704	0.697
Aggression					
CSF OT	-0.166	0.326	-0.795	0.477	0.701
CSF AVP	-0.102	0.325	-0.742	0.536	0.626
Plasma OT	0.059	0.330	-0.588	0.710	0.572
Urinary OT	-0.483	0.450	-1.349	0.425	0.861
Submission					
CSF OT	0.202	0.266	-0.329	0.719	0.778
CSF AVP	0.092	0.267	-0.430	0.612	0.634
Plasma OT	-0.436	0.261	-0.949	0.081	0.953
Urinary OT	0.776	0.319	0.126	1.391	0.989
Self-Directed					
CSF OT	-0.042	0.178	-0.388	0.305	0.597
CSF AVP	0.073	0.185	-0.291	0.443	0.653
Plasma OT	0.042	0.163	-0.279	0.360	0.605
Urinary OT	-0.010	0.247	-0.488	0.483	0.518

Table 3 Complete list of all means, standard deviations, 95% credible intervals, and proportions of the posterior for each response variable's hormone fixed effects.

Table 3.4: *Control Parameters*

	Table of Beta Coefficient Values				
Variable	Mean	SD	Lower 95% CI	Upper 95% CI	PP
Approach					
Sex (Male)	-0.019	0.127	-0.262	0.232	0.564
Subspecies (Hamadryas)	0.258	0.234	-0.241	0.703	0.888
Time of Day (Morning)	0.109	0.059	-0.008	0.224	0.966
Age	-0.064	0.099	-0.257	0.134	0.748
Gestational Day	0.094	0.250	-0.376	0.614	0.639
Close Approach					
Sex (Male)	0.062	0.156	-0.240	0.374	0.648
Subspecies (Hamadryas)	0.212	0.322	-0.445	0.850	0.773
Time of Day (Morning)	0.083	0.081	-0.075	0.244	0.846
Age	0.016	0.129	-0.235	0.268	0.554
Gestational Day	0.172	0.318	-0.446	0.811	0.706
Groom Initiation					
Sex (Male)	-0.355	0.307	-0.951	0.255	0.878
Subspecies (Hamadryas)	0.848	0.426	0.003	1.687	0.975
Time of Day (Morning)	-0.406	0.164	-0.730	-0.089	0.994
Age	-0.426	0.257	-0.937	0.067	0.954
Gestational Day	0.148	0.514	-0.859	1.156	0.619
Proximity					
Sex (Male)	0.024	0.111	-0.196	0.244	0.586
Subspecies (Hamadryas)	0.012	0.161	-0.299	0.322	0.532
Time of Day (Morning)	-0.024	0.074	-0.169	0.121	0.633
Age	0.021	0.096	-0.167	0.208	0.589
Gestational Day	-0.067	0.241	-0.537	0.402	0.609
Close Proximity					
Sex (Male)	0.517	0.192	0.139	0.895	0.996
Subspecies (Hamadryas)	0.853	0.311	0.187	1.415	0.988
Time of Day (Morning)	0.036	0.088	-0.137	0.208	0.658
Age	0.179	0.163	-0.138	0.496	0.862
Gestational Day	-0.204	0.396	-0.974	0.584	0.697
Grooming Duration					
Sex (Male)	0.342	0.194	-0.037	0.722	0.960
Subspecies (Hamadryas)	-0.289	0.266	-0.813	0.235	0.875
Time of Day (Morning)	-0.136	0.131	-0.392	0.118	0.849
Age	-0.048	0.186	-0.410	0.314	0.603
Gestational Day	0.095	0.406	-0.696	0.889	0.594
Aggression					
Sex (Male)	1.376	0.410	0.589	2.194	1.000
Subspecies (Hamadryas)	0.027	0.423	-0.801	0.874	0.524
Time of Day (Morning)	0.164	0.158	-0.144	0.474	0.849
Age	0.303	0.315	-0.317	0.919	0.833
Gestational Day	-1.028	0.697	-2.380	0.327	0.930
Submission					
Sex (Male)	-2.359	0.329	-3.014	-1.725	1.000
Subspecies (Hamadryas)	-0.803	0.387	-1.516	0.008	0.974
Time of Day (Morning)	-0.064	0.132	-0.325	0.192	0.688
Age	-0.902	0.230	-1.363	-0.453	1.000
Gestational Day	-0.244	0.623	-1.477	0.972	0.654
Self-Directed					
Sex (Male)	-0.327	0.192	-0.712	0.048	0.956
Subspecies (Hamadryas)	-0.592	0.470	-1.487	0.408	0.902
Time of Day (Morning)	0.160	0.084	-0.006	0.325	0.971
Age	-0.252	0.158	-0.561	0.060	0.944
Gestational Day	0.510	0.410	-0.289	1.320	0.894

Table 4 Complete list of all means, standard deviations, 95% credible intervals, and proportions of the posterior for each response variable's control fixed effects.

Figure 3.1: *Hormone Parameters*

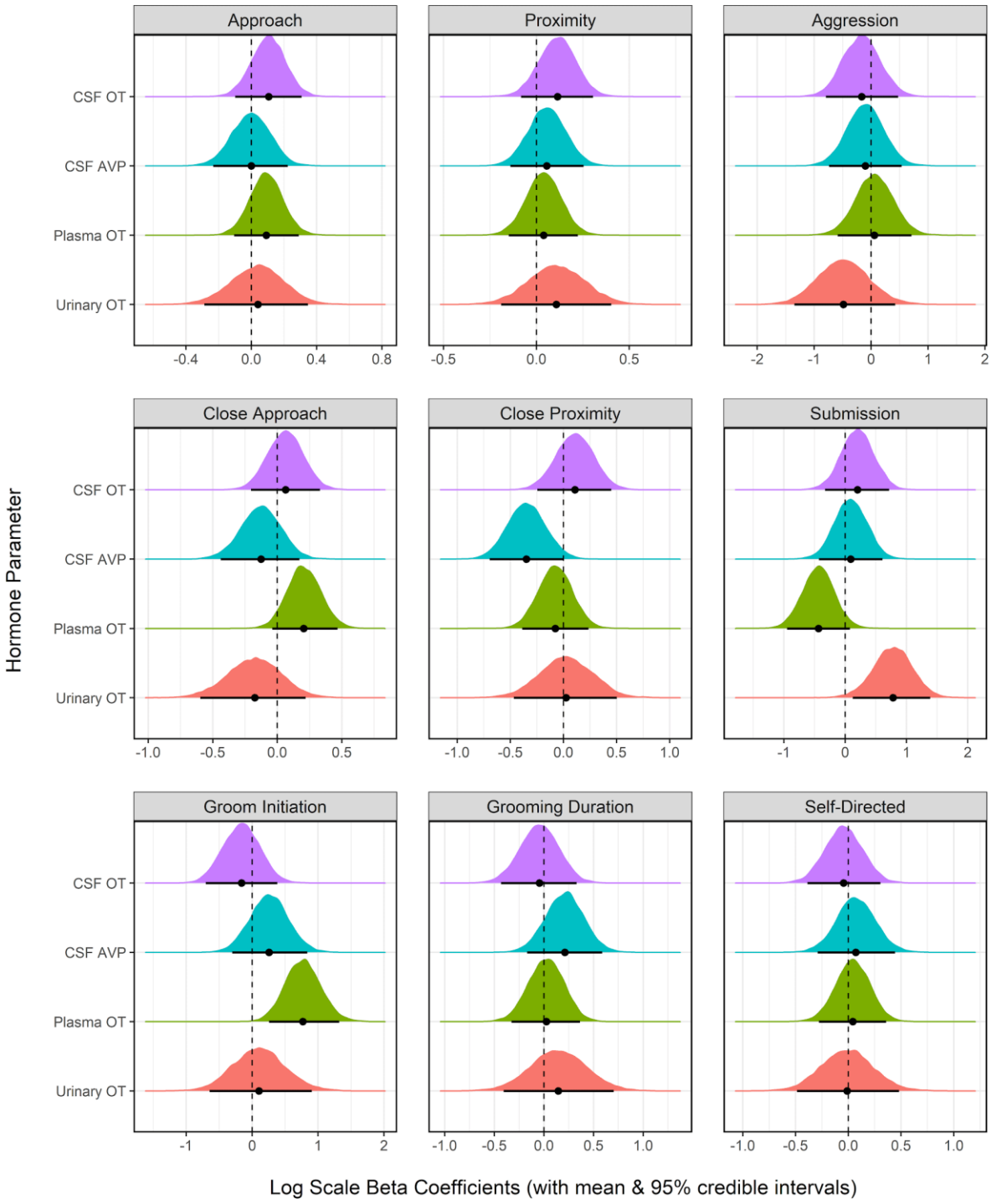

Figure 1 Distributions of posterior samples for coefficient estimates for each response variable's hormone parameters. Black lines at the bottom of the distribution represent the mean of the coefficient estimate and the 95% credible intervals.

Figure 3.2: *Control Parameters*

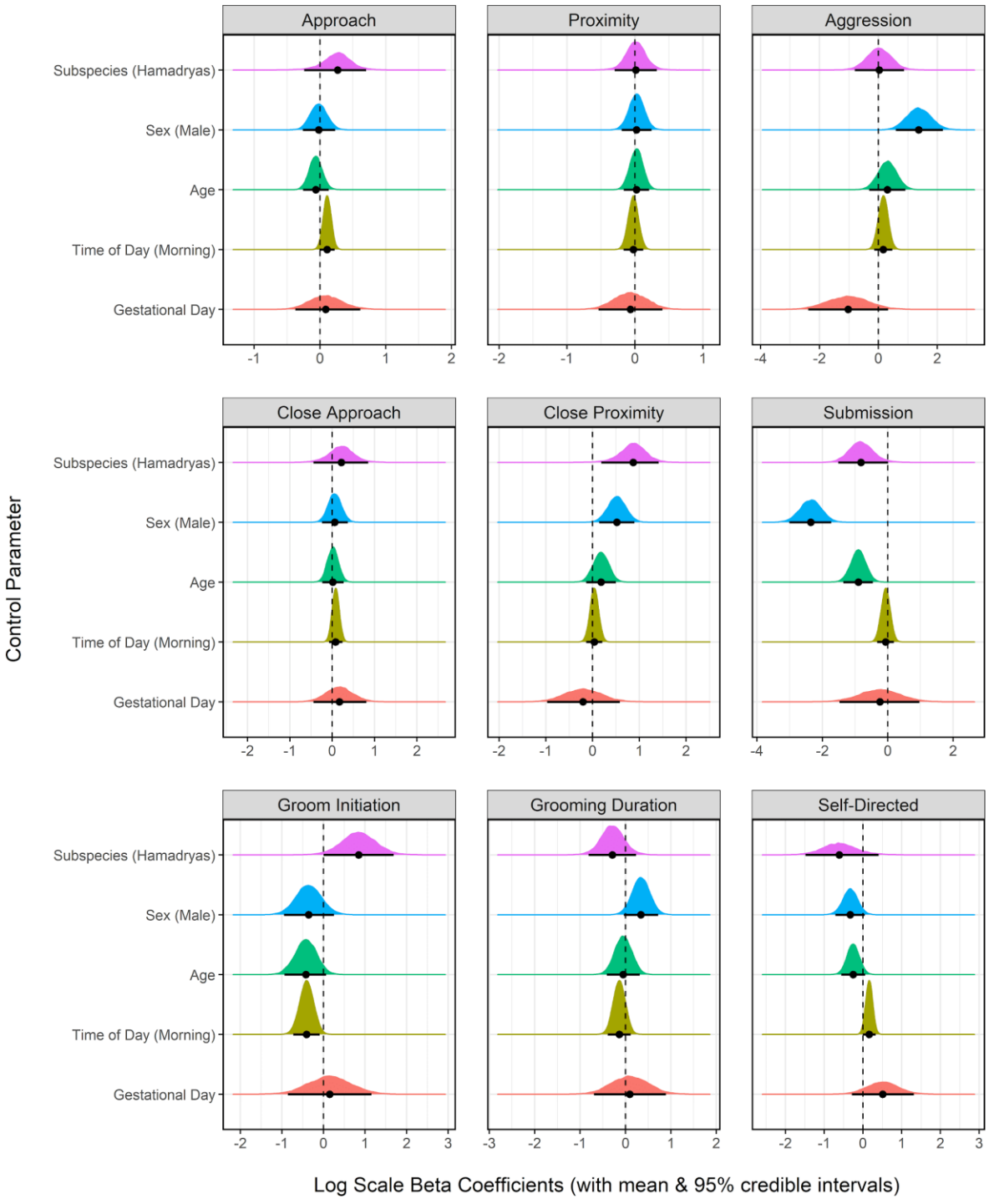

Figure 2 Distributions of posterior samples for coefficient estimates for each response variable's control parameters. Black lines at the bottom of the distribution represent the mean of the coefficient estimate and the 95% credible intervals.

Figure 3.3: *Marginal Effects of Strong and Weak Fixed Effects*

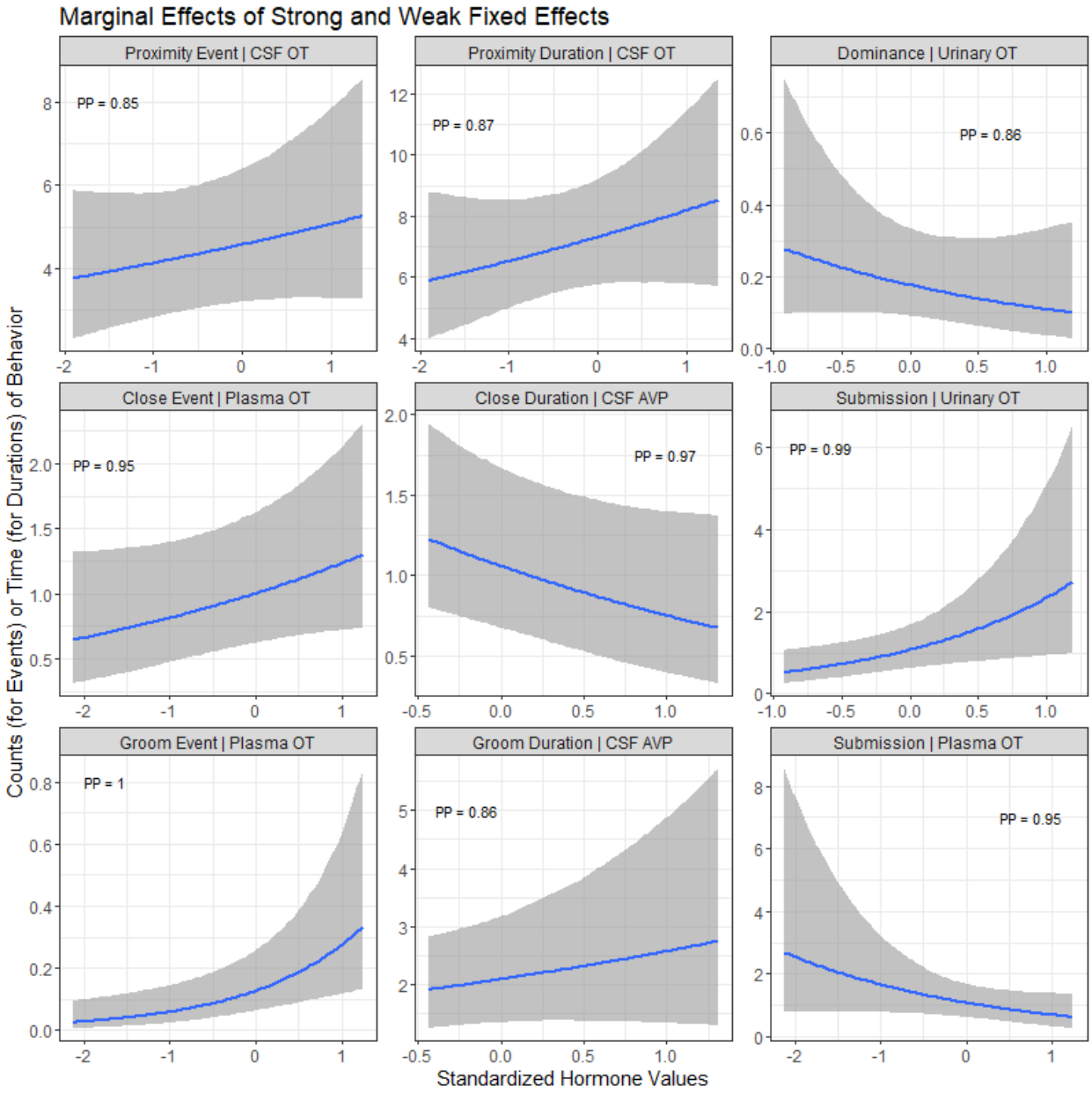

Figure 3 The marginal effects for hormone fixed effects with a proportion of the posterior greater than 0.85. Shaded regions represent 95% credible intervals.

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