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Integrated Effects of The Amygdale, Oxytocin, and Vasopressin on Mammalian Social Behaviors

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Abstract. Mammalian social behavior has long been a popular topic in the field of social interaction and cognition, providing insights into the structure formation of human society and the evolution of mammalian behaviors. The importance of the amygdala, oxytocin, and vasopressin in the mediation of sociality has been proved by many previous studies. However, the neurobiological interactions and integrated effects on behavioral regulation are relatively ignored. This review discusses these three determining factors, emphasizing the dissociable interaction at both the biological and behavioral levels. Two main ideas are presented in this review: neuropathways that directly connect oxytocin and vasopressin with the amygdala are unspecified; the mutual relationship between alienate behaviors and prosocial behaviors could be more complicated than expected. Although the influence of oxytocin and vasopressin on the amygdala has been proved by many previous studies, the specific areas and neuropathways that respond to the expression and activation of these two neuropeptides are not distinguished clearly. With more in-depth studies, the previously believed aggression behaviors that drive groups apart could also contribute to the harmony between individuals to some extent.

Keywords: Mammalian social behaviors, Amygdala, Oxytocin, Vasopressin

1. Introduction

1.1. Background of mammalian social behaviors research

Mammalian social behaviors have been in great demand in animal cognition and behavior research. These social processes could provide representative models for human sociality and enlighten the evolution of mammalian social cognition. With a more solid background in neuroscience, studies of those behaviors gradually shift from identifying the correlation between specific brain areas or hormones and social behaviors to the distinct neuro-pathways instead.

1.2. Gaps of current studies

Although the amygdala has long been proposed as a neural center for regulating social interactions and emotional responses, the responsible mechanisms, and circuits that directly influence these behaviors are still little known. This is because many previous studies identify the effects of the amygdala, oxytocin, and vasopressin on different perspectives of mammalian social behaviors, such as maternal behaviors and mating behaviors, but didn’t provide more in-depth information about neural pathways or hormone metabolism.

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One of the commonly used strategies in amygdala-focused experiments is partial lesions, injuring one area of the amygdala and then observing the behavior changes and other biological factors with the intact amygdala group. For oxytocin and vasopressin, many early experiments include several groups of different concentration gradients infused into the amygdala, comparing resulted behaviors within experimental groups. However, these researches on the amygdala, oxytocin, and vasopressin are unable to illustrate the direct relationship between the neurobiological levels and behavior levels. Therefore, the connection between these three influential factors in sociality has been discussed insufficiently.

Moreover, another unavoidable defect of those researches is that the sample size is limited due to the experimental operation and lab capacity. It is almost impossible to collect a large amount of data from rat experiments.

The topic gap in mammalian social behaviors is that studies on mating behaviors, which indeed are easier to conduct experiments or observe, are so dominant that other behaviors are comparatively ignored. Some of the unpopular topics are same-sex interactions and different targeted brain regions of the same hormones under different social behavior situations.

Reviewing mammalian social behavior research from a general perspective, the complexity of social behaviors could be underestimated. With more studies, one of the early beliefs that different categories of emotions and social behaviors are dissociable is gradually shaken and replaced by the new idea that many opposite actions could be reciprocal and inter-connected, such as fights and group harmony. Despite this revolutionary realization, discussion of two more behaviors together is still rare.

1.3. Purpose and the meaning of this review

Even though amygdala, oxytocin, and vasopressin have been proposed to play essential roles in shaping mammalian social behaviors, fever research targets the integrated influence. Therefore, the combined effects would need more attention.

This situation encourages the writing of this review, which considers the amygdala, oxytocin, and vasopressin as a whole, focusing on the close relationships between these three neurobiological factors and the mutual impacts on mammalian interconnections. The review hopefully could discover some gaps in this field, pointing out potential future research directions.

2. Neurobiological bases and connection

2.1. Neural bases of the amygdala, oxytocin, and vasopressin

The amygdala has long been believed the center of emotional reactions and plays an important role in social behaviors. Located near the medial base of the brain, the amygdala has complex and close connections with many brain areas, participating in the adjustment of more advanced activities. The amygdala receives information from the hippocampus, facilitating the production of memories; accepts visceral inputs mainly from the hypothalamus and septal area; gains olfactory information from the olfactory bulb; obtains auditory, visual, and somatosensory signals from the temporal and anterior cingulate cortices [1]. The hypothalamus is also connected with the amygdala through the stria terminalis, which is the major pathway despite the ventral amygdalofugal pathway.

One of the most related emotions dominated by the amygdala is fear, especially under emergencies and stress. Therefore, understanding the mechanism and neural connections behind the activation of fear helps us understand more complicated social behaviors. To be more specific, the central nucleus of the amygdala (CeA) forms projections with the brain stem and the hypothalamic structures, evoking defensive behaviors after detecting dangers and organizing fear responses. More updated experiments demonstrate that the CeA controls automatic fear responses with the connections to the midbrain, the profuse reticular formation, and the hypothalamus, mediating stress reactions and evoking defensive mechanisms [2].

The amygdala is also known as an important component in the limbic system, exchanging information with the anterior hippocampus via the uncus. Communication between these two areas is

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essential for the formation of memories and social learning because events with intensive emotions could be more impressive.

Oxytocin (OT) and arginine vasopressin (AVP) are cyclic amino acids that evolved from similar parent compounds during the evolution of vertebrate species. The synthesis regions of these two molecules in the hypothalamus are overlapping, projecting to the posterior pituitary gland for storage and release. Both peptides are believed as critical for mediating varied social behaviors in mammals. Although many studies are still conducted with experiments on rodents, the interest in the modulating effects on humans continuously increased1. In addition, except for the peripheral hormonal effects in mammalian behaviors, oxytocin has also been revealed as acting as the neurotransmitter in the central nervous system, exerting a greater influence on regulating sexual, maternal, and other behaviors [3].

2.2. Connection between the amygdala, oxytocin, and vasopressin

Since the amygdala, oxytocin, and vasopressin all have been discovered to regulate social behaviors in mammals separately, the interest in the intercorrelation between these three factors makes studies in this field more popular. Many pieces of research demonstrate that the amygdala is one of the areas that respond to peptide administration with brain activation patterns the most frequently [1].

The study suggests that oxytocin could serve as a neurotransmitter in related autonomic functions because OT-sensitive neurons in the amygdala also contain OT-binding sites. Moreover, experimental data shows that more than half of the OT-sensitive neurons in the CeA receive sensorial inputs and connect with other nuclei thus concluding that oxytocin could modulate the autonomic responses originating from the CeA3. Interestingly, the experiment on fear with rat models finds out that the receptors of oxytocin and vasopressin are located in distinct regions in the amygdala. For oxytocin, receptors are present in the lateral and capsular areas (CeL/C), while for vasopressin, receptors are restricted to the medial portion of the central nucleus (CeM) but projecting outside [2].

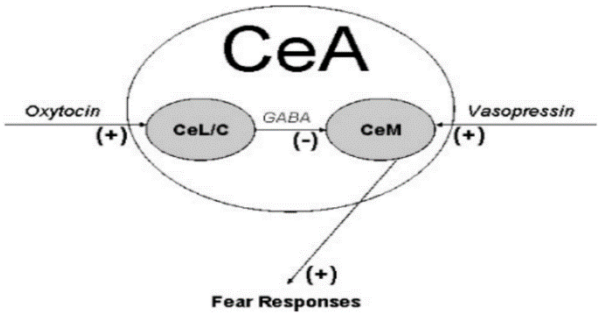


Figure 1. Oxytocin and vasopressin modulate activity of the central nucleus of the amygdala (CeA). Oxytocin excites (+) neurons in the lateral and capsular division of the CeA (CeL/C). Vasopressin excites (+) neurons in the medial part of the CeA (CeM), which plausibly stimulates fear responses. Excitation of CeL/C neurons inhibits (-) CeM activation through GABA-ergic (GABA) projections2.

It is difficult to isolate the effect of the amygdala and oxytocin and vasopressin when discussing the determining factors of mammalian social behaviors because of the tight biological connections between them. Therefore, the integrated influence would be worthy of discussion.

3. Summary of main categories of mammalian social behaviors

The broad range of social systems, complexity, and flexibility led by advanced cognitive abilities makes mammals an ideal model for studying social behaviors. The variation in developmental pace, lifespan, and brain size among mammals also provides more dynamic information compared to other well-studied species such as birds and insects. The social organization of mammals could be separated into three basic categories: the smallest unit, which defines whether individuals live alone or form a group, opposite-sex behaviors, and activities that involve a greater number of conspecific members. In

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addition, mating behavior has been considered a distinct, functionally important subordinate interaction system [4].

This review focuses on social behaviors in mammals, so the first category is not the main target since mammals living as an individual unit have fewer interactions than species that live as a clan. Therefore, mating behavior and behaviors that include the participation of two or more group members are discussed in this review. Considering the different mechanisms and clarity of the structure, the third level of social organization is further divided into sociality and aggression.

3.1. Mating behavior

Studies on mating behaviors tend to focus on the positive interaction between males and females, ignoring the existence of violence. A rat model of intimate partner violence shows that the expression of vasopressin receptors (*avprla*) in the amygdala is enhanced when high anxiety females experience relatively low partner aggression, while the expression of low anxiety females is not affected by partner aggression. The expression of oxytocin receptors (*oxtr*) is also examined in the experiment but does not demonstrate a significant correlation as the vasopressin receptors do. This result indicates that aggressive cohabitation between the opposite sexes is influenced by the female anxious temperament and the vulnerability to depression could be associated with changes in vasopressin signaling in the amygdala [5]. This rat model of violent mating behaviors has further value because the absence of assortative mating corresponds to a common issue in human studies.

The expression of vasopressin in the amygdala also plays an important role in the declined sexual behavior of the aged male rat, though it could not be the only determining factor. The experiment on gonadectomized rats shows that the disappearance of vasopressin immunoreactivity in the amygdala and the reduction of sexual behaviors follow gonadectomy. The significant correlation between decreased vasopressin expression cells in the amygdala, fibers in their projection sites, and the male sexual behavior change is proved by further results [6].

Different styles of mating behaviors have distinct oxytocin neuropathways that influence females' partner preferences. Compared with monogamous prairie voles which have a higher density of oxytocin receptors in the nucleus accumbens and cortical nucleus of the amygdala, polygamous meadow voles have more receptors in other regions. Overexpression of oxytocin in the nucleus accumbens accelerated partner preference in prairie voles but not in meadow voles, indicating that the mating attraction of polygamous females should be accommodated by oxytocin receptors in different regions7.

3.2. Sociality and cooperation

Oxytocin's effects on relieving anxiety and reinforcing sociality are further proved by EEG activity in the amygdala with a mice model of glutamatergic dysfunction introduced by ketamine, with leads to increased fear and social anxiety. Compared with the control group, oxytocin significantly increases sociality and reduces the overall amygdala EEG power during the behavioral tasks. These two indicators refer to oxytocin's influence on prosocial behaviors and social preference [8]. Similar impacts of vasopressin have also been studied on humans in two double-blinded experiments with male participants.

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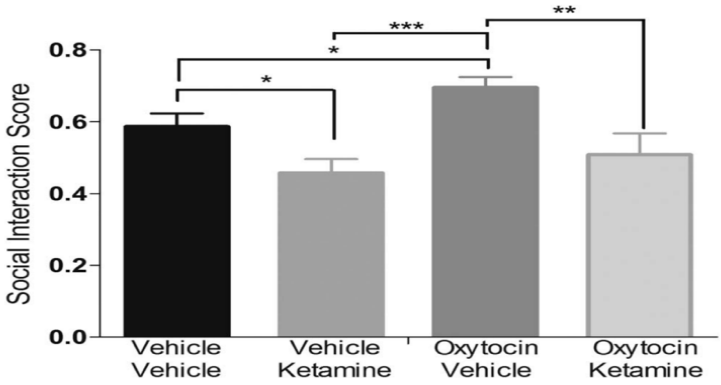


Figure 2. Three-chamber social interaction test behavioral data (n = 9-10/group, means + SEM shown). Ketamine significantly decreased social scores, and oxytocin did not reverse this deficit. Oxytocin increased social interaction score among control mice (*p < .05, ** p < .001, *** p < .0001, factorial analysis of variance with Fisher least significant difference post hoc test)8.

In the experiment, participants need to make decisions regarding financial consequences in a game that requires cooperation. Groups that receive arginine vasopressin are more willing to bare risks regardless of social context and present more trust toward the partner and altruistic concerns [9]. Although arginine vasopressin takes a dominant place in regulating mammalian monogamy and aggression in social interactions, this study reveals its engagement in mutual cooperation. Again, this could be a reminder that more functions of neuropeptides and related neuropathways could remain unknown, and the mechanisms behind alienating behaviors and prosocial behaviors could also be more intercorrelated than expected.

In addition to many studies focused on the targeted effect of oxytocin on the amygdala, the connectivity of the amygdala with cortical regions enhanced by oxytocin, particularly the rostral medial frontal cortex (rmFC) which involves in social cognition and emotion regulation, is also displayed. This enhanced connectivity implicates oxytocin's role in facilitating social-cognitive-affective functions [10].

Besides the frontal cortex, oxytocin and vasopressin also strengthen the connection between the amygdala and the olfactory system. Parental behavior is a critical component in mammalian social behaviors because it describes the tight connection between parents and offspring, providing one of the earliest social interactions for the individual. The prerequisite to establishing parental behavior is parents' ability to distinguish their offspring from others. For small-brained mammals, the recognition heavily relies on the main olfactory system but this dependence decreases in primates with the development of the neocortex and integration of visual cues [11]. Moreover, in sheep and monogamous voles, oxytocin and vasopressin facilitate the formation of selective mother-infant bonds [12].

The olfactory system also helps disease avoidance in small mammals through social odor communication, which enables individuals to distinguish the healthy conspecific odor from the odorant changes caused by pathology in the host. The experiment on rats shows that when rats encountered the healthy conspecific odor, the expression of oxytocin (OT) receptors in the medial amygdala (MeA) increased, while when they are exposed to the sick conspecific odor, the expression of two types of arginine vasopressin (AVP) receptors increased. Therefore, this result supports the belief that OT and AVP receptors in the MeA regulate the approach and avoidance behaviors in mammals with odorant communication. This experiment also hints at the neuropathway of odor detection because the distinguished responses triggered by healthy and sick conspecific odors indicate two differential processing pathways in the MeA [13]. This avoidance behavior regulated by these two peptides and the amygdala could be the evidence for one main idea of the review that there is no clear boundary between behaviors that enhance or alienate social relationships. From a more integrated

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perspective, avoidance behavior also contributes to the harmony of the group because it controls the disease spread among the groups, thus guaranteeing that individuals have a more feasible environment to live in. Therefore, avoidance behaviors facilitate establishing the foundation for other social behaviors.

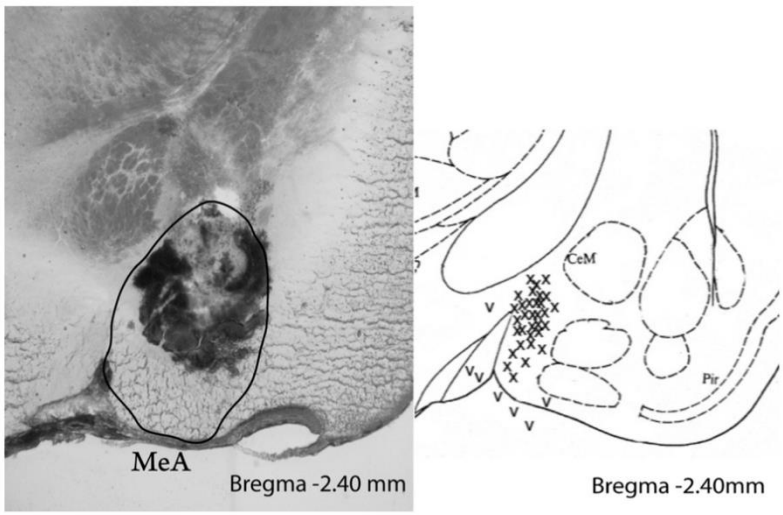


Figure 3. Schematic representation of the sites of cannula implantation within the MeA of rats used in the peptide antagonist microinjection experiments (Experiment 3) as verified by dye injection and histological examination (left panel); MeA, medial amygdala. The "x" indicates individual injector tip placement of the subjects that were used, while the "v" indicates those of the rats that were excluded from the data (right panel); CeM, central amygdala; Pir, piriform cortex [13].

3.3. Social anxiety, aggression, and fear

Context-conditioned fear is the simplest form of learning from the operational perspective and one type of aversion learning that helps individuals remember the danger and escape on time. The basolateral amygdala (BLA) and central amygdala (CeA) each involves in the expression and extinction of context-conditioned fear in rats separately. The activation of CeA during the experiment is observed to be stimulated by oxytocin receptors specifically, which also exert a bidirectional effect on the production of CeA OT signaling. In the BLA, the acquisition of context-conditioned fear is also impaired by the infused oxytocin before context-shock pairings with the fear suppressed. Later, the result also shows that long-term extinction is enhanced by BLA activity [14].

For the alleviation of more general fear, the physiological significance of oxytocin released within the central amygdala is examined by the forced swimming experiment. The examined result shows that oxytocin contributes to the passive stress-coping strategies not only through the physiological significance acted on the amygdala but also through the local release of selected amino acids that modulate emotion processing [15].

Other than the fear and anxiety aroused by the context stimulation, the behaviors of other individuals could also be considered stress sources. One common example is the attack under territorial defense and offspring protection. This type of aggressive behavior is studied by a resident-intruder testing experiment with adult and juvenile mice, concluding that modulation of hostile aggressive behaviors the associated with the medial amygdala and the immediate expression of oxytocin and vasopressin neurons in specific areas [16].

Behaviors related to pair binding, such as territorial defense and opposite-sex preference, stand out from other social interactions in mammalian groups because it is easier to study and unique in mammals, but other types of binding are also valuable. Besides the affiliation and behaviors that connect individuals in a group, anxiety and aggressive actions almost weigh the same in social behaviors. The sociality of mammals is more complex than expected because sometimes fights are

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aimed at long-term group harmony [17]. Moreover, in the relationship between female parents and offspring, oxytocin enhances maternal behavior but increases attacks toward intruders simultaneously. However, the direct effects of OT release on maternal aggression remain obscure [18]. Again, this could weaken the existing belief that aggression is the behavior leading to estrangement.

4. Conclusion

Studies in mammalian social behaviors have significant contributions in the understanding of human society structure and the evolution of social interactions in mammals. The effects the amygdala, oxytocin, and vasopressin on social behaviors in mammals have been proved by many previous studies, though the corresponding neuropathways are unspecified due to the limitation of visualizing neural activations during the experiments. Moreover, the influence of these three essential factors has been discussed individually, having the integrated influence on mediating social behaviors comparatively ignored. With more comprehensive studies, the neuropeptides and mechanisms behind aggression and prosocial behaviors could be found more intercorrelated; the boundary between these two seemingly opposite behaviors could be less absolute. For the future direction, the identification of responsible amygdala areas in different types of mammalian social behaviors and the relationship with oxytocin and vasopressin would require more efforts. The integrated perspective could also be strengthened with more solid understanding of these three factors separately. Social behaviors in mammals could be more complicated and dissociable than expected, asking for more dedication in the related fields.

References

[1] Baribeau, D. A. and Anagnostou, E., Oxytocin and vasopressin: linking pituitary neuropeptides and their receptors to social neurocircuits, Frontiers in neuroscience, 9, 335 (2015).

[2] Debiec, J., Peptides of love and fear: vasopressin and oxytocin modulate the integration of information in the amygdala, BioEssays: news and reviews in molecular, cellular and developmental biology, 27(9), 869–873 (2005).

[3] Condés-Lara, M., Veinante, P., Rabai, M. and Freund-Mercier, M. J., Correlation between oxytocin neuronal sensitivity and oxytocin-binding sites in the amygdala of the rat: electrophysiological and histoautoradiographic study, Brain Research, 637(1-2), 277–286 (1994).

[4] Kappeler, P. M., Barrett, L., Blumstein, D. T. and Clutton-Brock, T. H., Constraints and flexibility in mammalian social behaviour: introduction and synthesis, Philosophical transactions of the Royal Society of London. Series B, Biological sciences, 368(1618), 20120337(2013).

[5] Poirier, G. L., Cordero, M. I. and Sandi, C., Female vulnerability to the development of depression-like behavior in a rat model of intimate partner violence is related to anxious temperament, coping responses, and amygdala vasopressin receptor 1a expression, Frontiers in behavioral neuroscience, 7, 35 (2013).

[6] Van Zwieten, E. J., Kos, W. T., Ravid, R. and Swaab, D. F., Decreased number of vasopressin immunoreactive neurons in the medial amygdala and locus coeruleus of the aged rat, Neurobiology of aging, 14(3), 245–248 (1993).

[7] Ross, H. E., Freeman, S. M., Spiegel, L. L., Ren, X., Terwilliger, E. F. and Young, L. J., Variation in oxytocin receptor density in the nucleus accumbens has differential effects on affiliative behaviors in monogamous and polygamous voles, The Journal of neuroscience: the official journal of the Society for Neuroscience, 29(5), 1312–1318 (2009).

[8] Sobota, R., Mihara, T., Forrest, A., Featherstone, R. E. and Siegel, S. J., Oxytocin reduces amygdala activity, increases social interactions, and reduces anxiety-like behavior irrespective of NMDAR antagonism, Behavioral neuroscience, 129(4), 389–398 (2015).

DOI: 10.54254/2753-8818/4/20220617

[9] Brunnlieb, C., Nave, G., Camerer, C. F., Schosser, S., Vogt, B., Münte, T. F. and Heldmann, M., Vasopressin increases human risky cooperative behavior, Proceedings of the National Academy of Sciences of the United States of America, 113(8), 2051–2056 (2016).

[10] Sripada, C. S., Phan, K. L., Labuschagne, I., Welsh, R., Nathan, P. J. and Wood, A. G., Oxytocin enhances resting-state connectivity between amygdala and medial frontal cortex, The international journal of neuropsychopharmacology, 16(2), 255–260 (2013).

[11] Broad, K. D., Curley, J. P. and Keverne, E. B., Mother-infant bonding and the evolution of mammalian social relationships, Philosophical Transactions of the Royal Society of London. Series B, Biological sciences, 361(1476), 2199–2214 (2006).

[12] Lim, M. M. and Young, L. J., Neuropeptidergic regulation of affiliative behavior and social bonding in animals. Hormones and behavior, 50(4), 506–517 (2006).

[13] Arakawa, H., Arakawa, K., and Deak, T., Oxytocin and vasopressin in the medial amygdala differentially modulate approach and avoidance behavior toward illness-related social odor, Neuroscience, 171(4), 1141–1151 (2010).

[14] Campbell-Smith, E. J., Holmes, N. M., Lingawi, N. W., Panayi, M. C. and Westbrook, R. F., Oxytocin signaling in basolateral and central amygdala nuclei differentially regulate the acquisition, expression, and extinction of context-conditioned fear in rats, Learning & memory (Cold Spring Harbor, N.Y.), 22(5), 247–257 (2015).

[15] Ebner, K., Bosch, O. J., Krömer, S. A., Singewald, N. and Neumann, I. D., Release of oxytocin in the rat central amygdala modulates stress-coping behavior and the release of excitatory amino acids, Neuropsychopharmacology: official publication of the American College of Neuropsychopharmacology, 30(2), 223–230 (2005).

[16] Wang, Y., He, Z., Zhao, C., and Li, L., Medial amygdala lesions modify aggressive behavior and immediate early gene expression in oxytocin and vasopressin neurons during intermale exposure, Behavioral brain research, 245, 42–49. (2013).

[17] Caldwell, H. K., Oxytocin and Vasopressin: Powerful Regulators of Social Behavior (2017). The Neuroscientist: a review journal bringing neurobiology, neurology, and psychiatry, 23(5), 517–528.

[18] Campbell, A., Attachment, aggression and affiliation: the role of oxytocin in female social behavior, Biological psychology, 77(1), 1–10 (2008).