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Neural Overlap in Sexual and Aggressive Behaviors: Exploring Focal Brain Regions and Implications for Psychiatry

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This paper delves into the identification of focal brain regions governing both sexual and aggressive behavior, with a specific focus on unraveling the neural networks that underlie their shared relation. We begin by providing a brief history on the study of sexual and aggressive behaviors, which further allows for a review of existing literature and empirical studies. We aim to pinpoint the mechanisms in key brain regions, namely the hypothalamus and amygdala, that play roles in the regulation of both sexual and aggressive behaviors. Building on these findings, we explore potential mechanisms that might explain the observed convergence in neural networks and its implications for understanding the complex interplay between sex and aggression. Furthermore, we discuss the broader implications of these findings for the field of psychiatry, proposing that a deeper understanding of the neural substrates of these behaviors could inform therapeutic interventions and shed light on the etiology of certain psychiatric conditions.

Abbreviations: VMH - Ventromedial Hypothalamus, PR - Progesterone Receptor, BNST - Bed Nucleus of the Stria Terminalis, VMHvl – Ventrolateral Subdivision of Ventromedial Hypothalamus, MBN - Mating-biased Network; ABN - Aggression-biased Network; SSRI - Selective Serotonin Reuptake Inhibitor; CSBD - Compulsive Sexual Behavior Disorder; SAJC - Structured Anchored Clinical Judgement Scale; GnRH - Gonadotropin Releasing Hormone

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Introduction

Understanding the intricate connections between sexual and violent behavior is a complex endeavor that delves into the very primal acts of human nature. Prior research has implicated several key brain regions in the regulation of sexual behavior, such as the hypothalamus, amygdala, and prefrontal cortex, as well as hormones such as testosterone, estrogen, and progesterone. Similarly, investigations into the neural basis of violent behavior have identified the involvement of structures like the amygdala, hippocampus, and prefrontal cortex, along with hormones like testosterone and cortisol. It is through this research that scientists have found a discernable overlap between the neural circuitry governing both sexual and violent behaviors. However, an important question that emerges is why there exists an overlap in these neural networks governing seemingly disparate aspects of human behavior. The aim of this review is to identify and map the specific regions within the brain where this convergence occurs and to investigate hypotheses regarding the functional significance of this overlap. By integrating existing neuroscientific knowledge with empirical investigations, we attempt to contribute not only to our understanding of the neural regulation of sexual and violent behaviors but also to shed light on the broader implications for human psychology.

Historical Background

The scientific study of sexual behavior and aggression initially began as distinct and separate fields of study. Early investigations into sexual behavior primarily focused on elucidating the neural mechanisms underlying reproductive processes and biological sex differences, while studies on aggression delved into the circuits governing confrontational and defensive responses. More specifically, aggression research was primarily psychological and clinical in nature, whereas research understanding sexual behavior focused moreso on observing the effect of olfaction and hormones on sexual behaviors and ovulation.

A study published in 1849 is regarded as the first known proof of endocrine functionality and the necessity of the nervous system in modulating behavior (Berthold, 1944). In this study, six roosters were castrated and then half had one teste implanted into their abdomen (Berthold, 1944). For the roosters who had reimplanted testes, there were no deficits in any behaviors such as mating and fighting; this identified the testes as vital for behavior functions through means of some secreted "testicular substance", which would later be identified as hormones (Berthold, 1944). During the 1920s, the importance of the pituitary gland was observed through excising and reimplanting pituitary fragments in rats and observing the changes in sexual receptivity (Beach 1981). This paved the way for future understanding of the influence of the pituitary gland on the hypothalamus.

Lesion studies, rather than physiology studies, have also played an impactful role in understanding the very basis of sexual behavior and aggression. Kluver and Bucy investigated the effects of bilateral temporal lobe lesions in rhesus monkeys through which they observed profound alterations in sexual behavior as characterized by increased exploratory tendencies, indiscriminate mounting, and loss of species-typical mating patterns (Kluver and Bucy, 1937). Through these lesions, they also stopped exhibiting signs of fear and aggression (Kluver and Bucy, 1937) Though this study was rather invasive and nonspecific to a particular region, this was among the earliest lesion studies to identify the temporal lobe as necessary for modulating sexual and aggressive behaviors.

In the 1950s, the notable neuroscientist Dr. Paul MacLean began to explore behaviors like sex and aggression to understand the physiological regions responsible for primal behaviors and feelings. Maclean went on further to develop the concept of the visceral brain or the limbic system as a region controlling emotions (1952). It was from the identification of the limbic system that further research was then able to identify the hypothalamus and amygdala as key players in modulating the social behaviors of sex and aggression.

Overlapping Brain Regions for Both Sex and Aggression

Advancements in technology, such as neuroimaging and optogenetic techniques, have further propelled the field forward. Functional magnetic resonance imaging (fMRI) has enabled researchers to observe real-time neural activity during sexual and aggressive behaviors, providing a more dynamic and comprehensive view of the underlying neural processes. Optogenetic techniques have also become extremely important in modulating specific genes, allowing for the ability to knock in or out different neuron types. This has overall allowed for a more comprehensive understanding of the specific brain regions involved in modulating social behaviors, especially in animal trials.

The Amygdala

The amygdala, a complex and evolutionarily ancient structure within the brain, emerges as a crucial modulator in the intricate regulation of both sexual and aggressive behaviors. Functioning as a nexus for emotional processing, the amygdala integrates sensory information and plays a pivotal role in evaluating the salience and emotional significance of stimuli.

Its role extends beyond mere emotional processing, as the amygdala forms interconnected networks with other brain regions, such as the hypothalamus and prefrontal cortex, to orchestrate a nuanced and context-dependent balance between sexual and aggressive responses.

Hormones exert a profound influence on the amygdala, with especially relevant steroid hormones being testosterone and estrogen. Testosterone, predominantly in males, has been linked to increased amygdalar responses to social and aggressive stimuli, implicating its role in shaping emotional and behavioral reactions. Similarly, estrogen, prominent in females, plays a crucial role in modulating amygdalar function, contributing to the regulation of social behaviors. The hormone oxytocin has also been shown to have an inhibitory effect on the amygdala in both humans and rodents, and entirely knocking out this hormone in rats has led to extreme aggression (Kirsch et al., 2005; Ragnauth et al., 2005).

Hyperactivity in the amygdala has been associated with increased aggression and violence. Comparisons of the amygdala volume, which corresponds with prominence of amygdala activity, following temporal lobe resections in epilepsy patients found a positive relationship between contralateral amygdalar volume and positive changes in sexual drive (Baird et al., 2004). This is evidence of the amygdala playing a role in regulating sexual behavior in humans specifically rather than just in rodents.

It has been shown that activity in the amygdala is a precursor to the hypothalamus, in particular "estrogen receptor alpha (Esr1)expressing cells in the posterior amygdala (PA) [act] as a main source of excitatory inputs to the hypothalamus and key mediators for mating and fighting in male mice." (Yamaguchi et al., 2020). Esr1+ neurons have been shown to be essential for mating and fighting behaviors in mice, and especially play a crucial role in other areas of the brain such as the hypothalamus (Wei et al., 2018; Hashikawa et al., 2017).

The Hypothalamus

The hypothalamus was identified as a nexus for neuroendocrine control and autonomic functions, playing a significant role in integrating signals from various brain regions including the amygdala. Through analysis of lesion experiments on guinea pigs and rats, researchers in the 1940s were able to determine that certain regions of the hypothalamus were the most crucial brain region involved in copulatory behavior (Beach, 1947). By lesioning multiple regions within the hypothalamus, it was discovered that the ventromedial region in particular was necessary for copulatory behavior in mice for reasons both related and unrelated to hormone regulation (Kennedy 1964). However, it is still evident that hormones do play a large role in modulating sexual and aggressive behaviors.

Many different hormone-receptor neurons have been identified as being critical for modulating social behaviors. Estrogen receptor (ER) alpha has shown to be highly expressed in the hypothalamus along with other limbic brain areas (Shughrue et al., 1997; Pinzone et al., 2004). Knocking out ER-alpha in the ventromedial hypothalamus (VMN) reduced both sexual and aggressive behaviors in adult male mice (Sano et al., 2013). Ablation of progesterone receptor (PR)-expressing neuronal populations in the VMH leads to greatly diminished sexual receptivity in females, whereas corresponding ablation in males reduces both mating and aggression (Yang et al., 2013). This sexdifference appears to be related to the differing function of progesterone in males and females, but this study also provided some insight into the mechanism of action of the VMH.

A focal region controlling aggressive behaviors was identified through optogenetic activation of Esr1+ neurons within the ventrolateral subdivision (VMHvl) of the ventromedial hypothalamus, wherein it was observed to induce aggressive behavior in male mice, leading to attacks directed other mice and inanimate objects (Lin et al., 2011). While activation of the VMHvl was initially only observed in male mice, further studies confirmed the presence of this phenomenon in females (Hashikawa et al., 2017). Subsequent optogenetic studies revealed that lower activation of ESR1+ cells in the VMHvL modulated mounting behaviors in mice (Lee et al., 2014). This discovery not only emphasized the multifaceted role of the VMHvl but also connected the two seemingly unrelated social behaviors.

Regional Circuitry

In 1999, researcher Sarah Newman proposed the Social Behavior Network (SBN), highlighting regions of the amygdala, hypothalamus, and midbrain in regulating social behaviors. These specific regions share a commonality in that they are highly reliant on sex horomone receptor expression and are extensively interconnected (Newman, 1999; Guo et al., 2023). The proposition of the SBN laid the groundwork for understanding the larger neural circuits at play.

In a region adjacent to the amygdala, the bed nucleus of the stria terminalis (BNST) PREsr1 neurons have been identified as orchestrating the transition from appetitive (the searching phase) to consummatory (sterotypic behavior completing an innate drive) phases of social behaviors by altering neural representations of sex and behavior in the hypothalamus (Yang et al., 2022). This brings up the question as to whether the observed overlap in the SBN was necessarily correlated with all aspects of sexual and aggressive behavior.

In pursuit of refining the SBN, researchers Guo et al. used cross-regional correlational analysis after multi-site optical records in mice to better establish the functional connectivity during the social behaviors of attack and mating (2023). This has led to the proposal of a mating-biased network (MBN) and an aggression-biased network (ABN) (Guo et al., 2023). The initiation of copulatory and violent behaviors have been characterized by remarkable increases in functional connectivity across various brain regions, indicating a heightened state of coordination; however, as these behaviors progress into its later stages, connectivity at a network level drops significantly (Guo et al., 2023). This suggests that the brain is entering a dissociated network state, which may represent a crucial shift in the neural dynamics governing copulatory and violent behaviors (Guo et al., 2023).

Furthermore, the observed dissociation in network states during the later stages prompts speculation on potential regulatory mechanisms or adaptations that might occur as behaviors progress. This phenomenon invites a closer examination of the temporal dynamics within these neural networks and raises intriguing questions about the functional significance of such convergence and dissociation. As we navigate this complex intersection, there are many philosophical and evolutionary hypotheses, offering perspectives on the integrated nature of these neural networks and their broader implications for our understanding of deviant human behavior.

Evolutionary Theories

David Anderson, a neurobiologist at the California Institute of Technology, notes parallels between sexual behavior and aggression in the animal kingdom. In an interview with Quartz, Anderson said, "[Sex and violence] both involve an initial approach and close investigation, a lot of sniffing and sensing, and in some animals you see that sexual behavior can be accompanied by aggression, for example, biting." (Goldhill, 2016). This observation highlights the connections between the two behaviors in many species. Territorial aggression, mate competition, mate guarding, and complex courtship rituals are among the overlapping factors that contribute to an interplay between sex and aggression, showing strategies that have evolved across species to ensure reproductive success.

Anthropologists have attempted to explain the origin of human warfare using sociological and evolutionary theories but have struggled to find empirical evidence for such developments. One theory investigated is sexual selection theory, expanding from the idea of natural selection. Proposed by Charles Darwin, the sexual selection theory suggests that developed behaviors and traits offered an advantage in the competition for mates. Sexual behavior may have led to a need for combative behaviors, especially inter-male aggression. In a study done by Chang et al. in 2011, the association between mating and warring was neurologically investigated. With proximate cuing of opposite-sex stimuli, heterosexual male participants had a faster response time for warrelated terms than generally aggressive terms (Chang et al., 2011). While these findings offer insight into a neuropsychological relationship between mating and warring, the research emphasizes the need for further neuroscientific exploration on the intricate interplay between war-related mechanisms and mating behaviors.

Another theory, the “Challenge Hypothesis”, suggests that testosterone levels exhibit changes from external cues, particularly during the breeding season. In 1990, while observing male birds’ testosterone levels during different seasons and social challenges, Wingfield and colleagues synthesized this hypothesis to explain the impact of competition on endocrinology. Researchers observed low testosterone levels during the non-breeding season and an increase at the beginning of the breeding season, as well as during social conflict like territory or mate competition (Wingfield et al., 1990). The change is hypothesized by Wingfield et al. as caused by external cues like changes in day length (1990). The testosterone onset results in development of secondary sex characteristics, expression of reproductive viability, and aggressive behavior as an advantage against competition.

Defining Sexual Disorder

The categorization of sexual disorders has undergone significant evolution throughout history. Early perspectives, influenced by religious and cultural views, often pathologized certain sexual behaviors like homosexuality and promiscuity. Sigmund Freud's contributions introduced the notion of the unconscious mind, adding a psychoanalysis perspective. Over time, there has been a notable trend toward depathologization, recognizing the diversity of sexual behaviors, and consideration of boundaries like consent.

During the 19th and 20th centuries, sexual behaviors, particularly in women, were heavily medicalized. The term "nymphomania" was used to label what was perceived as excessive or uncontrollable female sexual desire. Treatment strategies for nymphomania were often drastic, involving oppressive interventions like confinement in mental institutions, forced restraint, dietary restrictions, and even surgical procedures such as clitoridectomy (Goldberg, 1999). These historical approaches reflected patriarchal attitudes and lacked the nuance of contemporary understandings of sexual health.

From an evolutionarily functionalist perspective, purity culture can be viewed as a societal mechanism that addresses the challenge of paternal uncertainty (Kupfer and Gul, 2023). This cultural phenomenon places a strong emphasis on controlling women’s sexuality. By promoting strict sexual norms and discouraging premarital or extramarital sexual relations, purity culture seeks to minimize uncertainty regarding paternal lineage. In ancestral environments, where resources and protection were essential for offspring survival, ensuring accurate parentage held significant adaptive value. While an infant can be easily recognized as related to the mother, asserting who the father is was less secure before genetic technology. Having multiple caretakers plays an impactful role on the child’s survival, as resource acquisition and defense increases. Thus, purity culture, in the forms of male jealousy and mate guarding, may have evolved as a social strategy to enhance reproductive success (Kupfer and Gul, 2023).

In the third edition of the Diagnostic and Statistical Manual of Mental Disorder (DSM-III), the term "nymphomania" was absent, with the concept considered within the broader category of sexual disorders not otherwise specified. Subsequent editions have shown a shift towards more specific diagnoses. In the current DSM-5, Compulsive Sexual Behavior Disorder (CSBD) emerged as a diagnostic category (American Psychiatric Association [APA], 2013). This disorder is characterized by an individual's constant preoccupation with sexual thoughts, urges, or behaviors (APA, 2013). The persistence of these patterns leads to significant distress or impairment in the individual's life, emphasizing the clinical significance and impact on overall well-being (APA, 2013). This transition in definition reflects a move away from vague and stigmatizing terms to more precise and clinicallymeaningful language. The diagnosis of CSBD also utilizes gender-neutral language, indicating a positive change from sexist stereotypes and oppressive norms.

One ongoing challenge in sexual disorder psychiatry is determining what qualifies as excessive preoccupation or too persistent libido. The criteria for compulsive sexual behaviors are outlined, but cultural norms and individual awareness about such play a crucial role (Levine, 1988). Despite progress in understanding sexual disorders, the neurobiological mechanisms underlying conditions like CSBD remain incompletely understood, so no testable biological marker exists for diagnosis. Ongoing research seeks to clarify the neurological underpinnings of hypersexuality, aiming to shed light on the complex interplay between biology, psychology, and cultural factors in defining and diagnosing sexual disorders.

Dysregulation of Circuits

Intermittent Explosive Disorder (IED) is a psychiatric condition characterized by recurrent, impulsive outbursts of aggression that are disproportionate to the stressors triggering them. While the etiology of IED is complex and incompletely known, research has found that childhood sexual abuse is particularly associated with development of IED (Nickerson et al., 2012). Sexual abuse may lead to alterations in the development and function of the intersecting sexual and aggression neural pathways, potentially causing vulnerability for dysregulation of emotional responses and impulse control.

Neurobiological changes may involve alterations in the functioning of neurotransmitters, such as serotonin, which play key roles in modulating both aggressive and sexual behaviors. In IED treatment, fluoxetine, a selective serotonin reuptake inhibitor (SSRI), was found superior to placebo in causing an antiaggressive effect for patients (Coccaro et al., 2009). However, full or partial remission of impulsive aggressive behaviors occurred in almost half of fluoxetine-treated subjects, raising questions at its long-term efficacy (Coccaro et al., 2009). Dysfunction between the prefrontal cortex and amygdala may also contribute to an increased propensity for aggressive outbursts (Best, 2002). Understanding the neurological basis of IED with awareness of relation to childhood sexual abuse is important for developing targeted interventions that address both the underlying neural circuitry and behavioral issues from a larger context.

Psychiatric Treatment

Before the 1960s, sexually aggressive men were given estrogen therapy, many times without consent in psychiatric hospitals (Laws and O'Donohue, 2008). This practice was based on the early hypothesis that reducing testosterone levels by balancing with the primary female sex hormone might decrease aggressive behaviors. The practice was discontinued due to adverse side effects, inconsistent results, and ethical concerns. In the 1960s and subsequent decades, stereotaxic hypothalamotomies and amygdalotomies were used to treat behavior disorders marked with extreme aggression (Narabayashi and Uno, 1966; Schvarcz et al., 1972). During this period, at least 70 men underwent stereotaxic hypothalamotomy for sexual offense or “deviancy” in West Germany (Rieber and Sigusch, 1979). These surgeries mostly consisted of destruction of the subdominant side of the nucleus ventromedialis hypothalamus, but other regions like the area preoptica and posterior tuber cinereum were sometimes also destroyed (Rieber and Sigusch, 1979). The surgeons regarded the hypothalamus as the “mating center” and control center of sexual feelings. American critics, like Rieber and Sigusch, raised ethical concerns about such procedures, citing results as inconsistent and how the individuals operated on were not all criminal offenders (1979). Post-operation rating systems were utilized to gauge recovery and success but displayed explicit homophobic bias. The most “normal” and “healthy” outcome was described as the ability to maintain a heterosexual relationship (Rieber and Sigusch, 1979). While some individuals operated on were convicted offenders, some individuals only had a history of homosexual relationships with consenting adults, thus showing how the definition of “deviancy” has been subject to change and prejudice (Rieber and Sigusch, 1979).

Another concern raised with neurosurgery in addressing sexual disorders was that insufficient preoperative effort was taken before the risky surgery. Most of the patients had no record of any psychothereupetic treatment before surgery (Rieber and Sigusch, 1979). Sexual offender cognitive-behavioral treatment programs have been found to have mixed results on the conclusivity of effectiveness in reducing recidivism. In 2002, Craissati et al. conducted a study on the reconviction rates of child molesters in the United Kingdom based on treatment type and length. Subjects completed the Structured Anchored Clinical Judgement Scale (SAJC), which tests risk of breach, and the Multiphasic Sex Inventory, a psychological assessment tool for sexual function and behavior. While SAJC was moderately accurate in predicting reconviction, Craissati et al. found that there were no significant cognitive changes pre- and posttreatment in prevention (Craissati et al., 2002). Instead, the reconviction rate was more strongly associated with whether the individual had been “sexually victimized” in childhood than any treatment variable (Craissati et al., 2002). This finding is similar to Schweitzer and Dwyer’s 2003 study conducted in Australia, which found no statistically significant recidivism reduction following participation in a cognitive-behavioral program. However, both studies had limitations of small sample size and attrition of posttreatment feedback from participants (Craissati et al., 2002; Schweitzer and Dwyer, 2003). Many other meta-analyses have found that CBT therapies are effective in reducing recidivism of sexual and violent combination behaviors (Alexander, 1999; Furby et al., 1989; Hall, 1995; Hanson et al., 2002).

In recent years, there has been a growing interest in exploring neuropharmacological interventions as a treatment of sexual offenders. This approach involves targeting the specific neurotransmitter systems and neural circuits explored earlier that are related to the manifestation of deviant sexual behaviors. Pharmacological interventions aim to mitigate impulsivity, reduce compulsive sexual urges, and address the underlying neurobiological factors contributing to offending behaviors. SSRIs are noted as having four possible mechanisms of action in clinical treatment of sexual offenders: non-specific inhibition of sexual interest, reduction of impulsivity, decrease in obsessivecompulsive symptoms, and decrease in depressive symptoms (Garcia et al., 2013). SSRIs have been associated with a reduced sexual libido and decreased orgasm in 60-70% of individuals (Montejo et al., 2001). SSRIs therefore offer a regulatory influence on unwanted sexual urges. The concurrent association of paraphilias and obsessive compulsive disorder is a complex and controversial topic, as some psychologists hold theories relating the two disorders (Baylk, 1997), but such models are hypothetical, based on case studies, and lack robust research.

Beyond SSRIs, emerging research has also explored the potential of antiandrogenic medications and Gonadotropin Releasing

Hormone (GnRH) analogs in the pharmacological treatment of sexual offenders. Antiandrogens target the endocrine system, specifically reducing testosterone levels, thereby diminishing libido and sexual drive. While the use of testosterone reducing drugs has shown promise in some cases, concerns about adverse side effects exist. Low testosterone can contribute to bone loss and osteoporosis (Orwoll and Klein, 1995). Other potential side effects of antiandrogens and GnRH include hot flushes, depression, weight gain and gynaecomastia, or the enlargement of male breast tissue (Laws and O'Donohue, 2008). The complex interplay between neuropharmacological interventions and the multifaceted etiology of sexual offending underscores the need for further research to refine treatment protocols and enhance our neurobiological understanding of these behaviors.

Conclusion

The exploration of sexual and aggressive behaviors has evolved from distinct fields into an interconnected study, tracing historical perspectives, physiological understandings, and contemporary applications. Early investigations separated sexual behavior and aggression, focusing on reproductive processes and confrontational responses, respectively. Advances in neuroimaging and optogenetic techniques have allowed a dynamic view of neural processes during sexual and aggressive behaviors. The amygdala and hypothalamus, crucial in modulating emotions and integrating signals, play key roles. Understanding the overlapping brain regions regulating both sexual and aggressive behaviors provides valuable insights into the intricate interconnections within the human psyche and explanations into some of our most universal mechanisms. Drawing from evolutionary theories, the coexistence of these behaviors in our ancestral past meant reproductive success and adaptive advantage. This neural understanding has modern, practical implications, particularly in the context of sexual and aggressive disorders. Recognizing the neural convergence underlying these conditions allows for a more comprehensive approach to psychiatric treatment, but the historical context also brings awareness to the necessity of ethical consideration. As we navigate the complexities of psychiatric intervention, addressing sexual offenders requires a nuanced understanding of the neurobiological mechanisms and psychological patterns occurring. Overall, the exploration unveils a complex interplay of biological, psychological, and sociocultural factors, necessitating ongoing research for targeted interventions.

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