Effects of Oxytocin, Progesterone, and Estrogen on Disgust and Its Neurophysiological Mechanisms

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Date: 2021-07-27T19:58:20+00:00

Abstract

Disgust is one of the most fundamental emotions in humans and animals, originating from oral rejection of bitter (toxic) substances, often accompanied by nausea and vomiting and a strong desire to avoid eliciting stimuli, and serving the function of avoiding potential disease threats. Extensive animal and human studies have shown that oxytocin, progesterone, and estrogen differentially influence the perception of core disgust stimuli, the generation and expression of core disgust emotion, conditioned disgust learning, and the recognition of disgust expressions. These three hormones primarily affect disgust processing by acting on neurotransmitter receptors such as serotonin, gamma-aminobutyric acid, acetylcholine, and glutamate, and by modulating activity in brain regions including the amygdala, insula, anterior cingulate cortex, putamen, piriform cortex, and middle frontal gyrus. Future research should, based on accurate measurement of hormone levels and control of experimental task difficulty, investigate the effects of each hormone on disgust processing across different sensory modalities and the moderating role of sex; concurrently, by combining brain imaging techniques and animal behavior studies, elucidate the neuroendocrine mechanisms underlying the influence of each hormone on disgust processing.

Full Text

The Influence of Oxytocin, Progesterone, and Estrogen on Disgust and Its Neurophysiological Mechanisms

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Abstract: Disgust is one of the most fundamental emotions in humans and animals, originating from oral rejection of bitter (toxic) substances. It is typically

accompanied by nausea and vomiting and a strong desire to avoid the eliciting stimulus, serving the function of avoiding potential disease threats. Numerous animal and human studies have demonstrated that oxytocin, progesterone, and estrogen differentially influence the perception of core disgust stimuli, the generation and expression of core disgust emotion, conditioned disgust learning, and the recognition of disgust facial expressions. These three hormones primarily affect disgust processing by acting on neurotransmitter receptors such as serotonin, γ-aminobutyric acid, acetylcholine, and glutamate, thereby modulating activity in brain regions including the amygdala, insula, anterior cingulate cortex, putamen, piriform cortex, and middle frontal gyrus. Future research should investigate the effects of each hormone on disgust processing across different sensory modalities and examine their moderating roles of gender, based on accurate hormone measurement and controlled experimental task difficulty. Additionally, studies should combine neuroimaging techniques with animal behavior to clarify the neuroendocrine mechanisms through which these hormones influence disgust processing.

Keywords: disgust, oxytocin, progesterone, estrogen, neurophysiological mechanism
Classification Code: B8426

1 Introduction

Basic emotions are evolutionary adaptive responses to external stimuli that enable individuals to locate food (pleasure), avoid predators (fear), and prevent infection (disgust), thereby surviving within groups (Darwin & Prodger, 1998; Weinstein et al., 2018). In daily life, disgust is elicited by vomit, excrement, rotting matter, certain animals (maggots, flies), dirty environments (garbage dumps, toilets), and uncivilized behaviors (littering, spitting) (雷怡 et al., 2019). Disgust plays a crucial role in the behavioral immune system by regulating avoidance of pathogen-related stimuli and behaviors, thereby reducing infection risk (Cepon-Robins et al., 2021). In the context of the global COVID-19 pandemic, behavioral changes induced by high disgust sensitivity (such as social distancing, handwashing, and disinfection) have effectively prevented further disease transmission (Shook et al., 2020).

Beyond public health, disgust also influences moral judgment (Białek et al., 2021), political decision-making (Shook et al., 2017), and phylogenetic development (O'Shea et al., 2019). Therefore, in-depth research on disgust emotion is significant for both individual survival and social development. Current research on disgust primarily includes: the structure and classification of disgust (Stevenson et al., 2019); its evolutionary functions (Oaten et al., 2009); disgust facial expression recognition (Wicker et al., 2003); conditioned disgust learning and expression (Schier et al., 2019); relationships between disgust and other basic emotions such as fear (Weinstein et al., 2018) and anger (Molho et al., 2017); and associations between disgust and psychiatric disorders including phobias, obsessive-compulsive disorder, and eating disorders (Khalil et al., 2020; Knowles

et al., 2018). Additionally, investigating whether and how hormones modulate disgust processing is crucial for understanding the evolutionary significance of disgust and its neurophysiological underpinnings.

The generation and expression of disgust involve multiple hormones, including oxytocin, progesterone, estrogen, testosterone, corticosteroids, and arginine vasopressin. These distinct neuroendocrine systems enable individuals to obtain information about toxins and pathogen cues, evaluate and integrate this information, and subsequently generate appropriate disgust responses and avoidance behaviors (Kavaliers, Ossenkopp, et al., 2019). Among these, oxytocin, progesterone, and estrogen are the most extensively studied hormones in the field of disgust.

Based on this background, this paper reviews recent research on the nature of disgust emotion, evidence for the influence of oxytocin, progesterone, and estrogen on disgust processing, and the neural mechanisms underlying these hormonal effects. The aim is to clarify the evolutionary significance of disgust, explore the neurophysiological mechanisms through which these three hormones influence disgust processing, and further understand the relationship between disgust emotion and the endocrine system.

2 Disgust Emotion

Disgust originates from oral rejection of bitter substances, which often indicate the presence of toxic alkaloids. Its most basic function is to eliminate toxic substances from the mouth and prevent bodily harm (Rozin et al., 2016). Through evolutionary processes, to avoid the substantial health costs of disease, individuals developed disgust responses to pathogen cues such as bacteria, viruses, and parasites, triggering avoidance behaviors and preventing infection. This has established disgust as a disease-avoidance mechanism (Oaten et al., 2009; Weinstein et al., 2018). This characteristic shows phylogenetic continuity, with lobsters, tadpoles, ants, bees, snails, fish, birds, rodents, non-human primates, and humans all exhibiting disgust responses toward infected conspecifics (Behringer et al., 2006; Kavaliers et al., 2020; Kiesecker et al., 1999). In summary, disgust is an evolutionarily formed "behavioral immunity" that detects toxic and pathogen-related cues, eliciting avoidance behaviors (such as nausea, vomiting, and appetite reduction) to expel toxins, pathogens, and parasites from the body or reduce the risk of ingesting them, thereby preventing poisoning or disease.

With the development of human cognition, disgust has interacted with social culture, leading to the generalization of disgust-eliciting objects. Researchers have developed more detailed classifications based on the characteristics of eliciting stimuli. Rozin and Fallon (1987) categorized disgust into five types: (1) oral responses to bitter or sour substances; (2) core disgust, elicited by certain foods (e.g., rotting meat), bodily secretions (e.g., feces), and specific animals (e.g., flies); (3) animal-nature reminder disgust, elicited by reminders of human animality such as bodily injury, unhygienic behavior, and death; (4) interpersonal

disgust, elicited by pathogen-carrying or stigmatized groups (e.g., infectious disease patients, disabled individuals); and (5) moral disgust, elicited by behaviors violating moral norms or perceived as degrading. Subsequently, Olatunji et al. (2009) modified Rozin's framework and proposed three main categories: core disgust, animal-nature reminder disgust, and contamination disgust, where contamination disgust refers to neutral objects becoming disgusting after contact with disgust-eliciting objects (e.g., feces). Additionally, Tybur et al. (2013) reconstructed disgust theory from an evolutionary perspective, proposing the Three-Domain Disgust Theory: pathogen disgust, sexual disgust, and moral disgust. Pathogen disgust arises from threats of bacterial, viral, or parasitic infection (e.g., touching feces), while sexual disgust is triggered by inappropriate sexual behaviors such as incest. Although different classification systems exist, these disgust types overlap substantially. For instance, interpersonal disgust, animal-nature reminder disgust, sexual disgust, and contamination disgust may all contain pathogen cues. Therefore, in practical research, investigators often simplify disgust into core disgust and moral disgust. Core disgust reflects avoidance of media that may indirectly transmit disease, such as rotting food, excrement, and animals like flies and cockroaches, and is equivalent to pathogen disgust. Moral disgust is elicited by violations of social norms and is more abstract, involving greater social cognition (Moran et al., 2019). Chapman et al. (2009) found that moral disgust originates in the oral cavity, similar to disgust elicited by unpleasant tastes and potential disease cues, suggesting that moral disgust may be a social emotion formed on the basis of core disgust.

Disgust processing involves three components: disgust stimuli, the disgust evaluation system, and disgust output. Core disgust stimuli can directly trigger disgust output, whereas moral disgust must first be processed through the evaluation system before being expressed through facial expressions (e.g., nose wrinkling, mouth opening), behaviors (e.g., withdrawal), and physiological responses (e.g., nausea) (Rozin et al., 2009). These specific expressions separate external space from the individual's interior, helping to reduce the intake of harmful substances or expel contaminants from the mouth, thereby providing protection. This three-level processing model indicates that while disgust emotion originates from innate instincts, most disgust responses are learned through experience and closely related to social cognition.

In summary, disgust emotion serves a disease-avoidance function and represents one of the most primitive basic emotions shared by humans and animals. Simultaneously, it is shaped by social culture and closely associated with concepts of "cleanliness" and "purity." Any object, behavior, or idea violating these attributes may elicit disgust, typically accompanied by nausea and a strong desire to avoid the eliciting stimulus, along with distinct protective facial expressions and physiological reactions.

3.1.1 Animal Experiments

Animals typically use olfaction to identify infected conspecifics, generating pathogen disgust and avoidance behaviors to prevent infection (Kavaliers et al., 2020). Research has shown that oxytocin (OT) can modulate pathogen-related disgust responses and avoidance behaviors in rodents. For example, OT antagonist administration reduces avoidance of infected female mice by male mice (Kavaliers, Colwell, et al., 2019), and oxytocin gene knockout mice show impaired ability to discriminate between healthy and infected conspecific odors, exhibiting weakened disgust responses toward infected individuals (Kavaliers et al., 2004). These findings suggest that OT may enhance pathogen recognition abilities and strengthen disgust responses to avoid disease (Kavaliers & Choleris, 2011). Additionally, in stressful situations involving unfamiliar environments or exposure to infected conspecifics, OT promotes avoidance of unfamiliar conspecifics in mice (Duque-Wilckens et al., 2018; Kavaliers, Colwell, et al., 2019). Duque-Wilckens et al. (2018) propose that this OT-induced social inhibition does not reduce social motivation but rather increases vigilance toward unfamiliar, threatening social environments, including those associated with pathogens and toxins. This indicates that OT may facilitate the perception and recognition of pathogen cues, enhance core disgust responses, and thereby participate in regulating pathogen-related mate selection, in-group bias, and out-group avoidance.

Furthermore, OT is involved in the acquisition and expression of toxin-induced conditioned disgust. OT antagonist injection attenuates lithium chloride (LiCl)-induced disgust in male rats and reduces active contact with female partners (Boulet et al., 2016). Verbalis et al. (1986) found that rats secrete oxytocin when experiencing taste aversion induced by LiCl or $CuSO_4$. Further research revealed that LiCl-induced conditioned taste aversion is associated with OT neuron activation, and OT antagonist injection impairs acquisition of conditioned taste aversion in mice (Olszewski et al., 2013). This suggests that OT likely participates in taste aversion learning in animals, though the lack of research on other sensory modalities leaves unclear whether OT's effects on animal disgust learning are consistent across channels.

3.1.2 Human Experiments

In human studies, Declerck et al. (2014) found that intranasal OT administration reduced disgust responses to pictures of dirty, bacteria-filled environments in women but not men. Additionally, men receiving OT were more likely to evaluate faces as unhealthy, though this trend was not observed in women. These results indicate that exogenous OT administration does not facilitate pathogen detection based on visual cues and shows significant sex differences in perceiving health and disease cues. The authors suggest that reduced disgust in women may result from OT alleviating infection-related anxiety. This finding appears contradictory to OT's enhancement of pathogen disgust in rodents, possibly because pictures cannot replace real infection environments and deprive partic-

ipants of olfactory input, suggesting that OT may differentially affect visual versus olfactory cues in core disgust generation.

Facial expression recognition is essential for social interaction. A meta-analysis found that intranasal OT administration improves recognition of basic emotions, particularly disgust and fear expressions (Leppanen et al., 2017). In approach-avoidance motor response tasks, OT simultaneously enhanced both approach and avoidance responses to disgust faces but did not affect responses to angry, fearful, sad, or happy faces, indicating that OT accelerates disgust face processing and enhances disgust stimulus salience (Theodoridou et al., 2013). In facial expression recognition tasks, intranasal OT also increased disgust intensity ratings for disgust faces but reduced recognition accuracy (Cardoso et al., 2014). The authors propose that OT reduces disgust face recognition accuracy by focusing attention on the eye region, where disgust is difficult to recognize. Previous studies have also found that OT reduces attentional bias toward disgust faces (Kim et al., 2014) and increases fixation on the eye region (Wang et al., 2020). Therefore, OT's reduction in disgust face recognition accuracy may be related to its modulation of attention.

Direct empirical evidence for OT's influence on moral disgust remains limited. However, studies have found that both oxytocin gene variation and exogenous OT administration affect moral judgment (Bernhard et al., 2016; Scheele et al., 2014). Thus, OT likely plays a role in moral disgust, though this requires further investigation.

3.2 Neural Mechanisms of Oxytocin in Disgust Processing

The neuropeptide oxytocin is synthesized in the supraoptic nucleus (SON) and paraventricular nucleus (PVN) of the hypothalamus, with receptors highly expressed in the insula, amygdala, anterior cingulate cortex, piriform cortex, and other brain regions, extensively participating in emotion and social behavior processing (Boccia et al., 2013).

Both smelling disgusting odors and recognizing disgust faces activate the insula (Wicker et al., 2003). Electrical or optical stimulation of the anterior insula in mice, monkeys, and humans produces nausea and vomiting, exhibiting typical disgust expressions such as upper lip elevation and nose wrinkling (Caruana et al., 2011; Dolensek et al., 2020; Mazzola et al., 2017). Berret et al. (2019) found that inhibiting the posterior insula eliminated foot-shock-induced disgust in mice, indicating that the insula participates in processing aversive somatosensory information and transmits this information to specific amygdala regions. In summary, the insula plays a critical role in disgust recognition, experience, and expression. Research shows that OT receptors are densely distributed in the insula, which receives OT axonal input from the PVN, enhancing intra-insular excitability, synaptic efficacy, and functional connectivity, thereby modulating approach and avoidance responses to socio-emotional stimuli (Rogers-Carter et al., 2018; Yao et al., 2018). When humans evaluate the arousal level of emo-

tional faces, intranasal OT administration enhances insular responses to disgust faces (Scheele et al., 2014). OT may increase disgust face perception intensity by augmenting insular activity, though whether similar effects occur for non-social disgust stimuli remains uncertain. Additionally, research has found that serotonin (5-HT) in the insula participates in regulating anticipatory disgust and is crucial for disgust learning formation (Limebeer et al., 2018; Tuerke et al., 2012). OT can modulate 5-HT receptor activity while 5-HT release produces nausea (Mottolese et al., 2014; Tuerke et al., 2012). Therefore, OT may promote disgust learning and related behavioral responses by influencing 5-HT in the insula.

The anterior cingulate cortex (ACC) is involved in processing multimodal disgust stimuli, including mild electric shocks, aversive tastes, sounds, facial expressions, odors, and even unfair treatment (Amir et al., 2005; Corradi-Dell'Acqua et al., 2016; Schröder et al., 2019; Wicker et al., 2003). Studies have found that mouse ACC neurons preferentially encode socially aversive cues and transmit this information to the basolateral amygdala (Allsop et al., 2018), while acute OT administration enhances cellular activity in mouse ACC (Pisansky et al., 2017). In fMRI studies of subliminal emotional face processing, OT reduced functional connectivity between the ACC and amygdala during disgust face processing in women (Luo et al., 2017). These findings suggest that OT participates in processing social disgust information by influencing ACC activity and its functional connections with other brain regions.

The amygdala receives disgust cue information from the insula and ACC (Allsop et al., 2018; Berret et al., 2019) and projects to other relevant brain regions (e.g., basal ganglia substantia nigra) to participate in disgust processing (Steinberg et al., 2020). Research has shown that OT is critical for conditioned taste aversion learning, and blocking OT receptors reduces amygdala responses to aversive stimuli (Olszewski et al., 2013). In disgust face recognition, OT also enhances right amygdala responses to disgust faces (Yao et al., 2018). This differs from OT's reduction of amygdala responses to negative emotional stimuli such as fear and anger (Wang et al., 2017), suggesting that OT may have unique effects on the amygdala during disgust processing and reflecting that disgust is a distinct emotion differing from other negative emotions.

Evidence for OT's modulation of disgust processing has also been found in other brain regions. For example, disgust is closely related to olfaction, and Choe et al. (2015) discovered that the piriform cortex, which participates in olfactory processing, contains abundant OT receptors. OT can play an important role in appetitive and aversive social odor learning by directly modulating piriform cortex activity. Huntington's disease (HD) patients are characterized by impaired disgust face recognition, and intranasal OT can enhance activity in the putamen and middle frontal gyri of HD patients, thereby improving their disgust face recognition ability. However, OT reduces putamen and middle frontal gyrus responses to disgust faces in healthy controls (Labuschagne et al., 2018). This suggests that OT may participate in normalizing disgust face recognition

through some balancing mechanism, and that OT misuse may inhibit disgust stimulus recognition.

Additionally, OT administration reduces functional connectivity between the amygdala and insula/ACC in normal individuals (Gorka et al., 2015). During disgust face processing, OT reduces functional connectivity between the right amygdala and left ACC in women (Luo et al., 2017). This indicates that OT may simultaneously influence activities in multiple brain regions that jointly participate in disgust processing.

In summary, oxytocin can influence disgust emotion processing by affecting activity in multiple brain regions including the insula, anterior cingulate cortex, amygdala, piriform cortex, putamen, and middle frontal gyrus.

4.1.1 Animal Experiments

Following evidence from human studies showing progesterone's influence on pathogen disgust, Kavaliers et al. (2021a) first validated this in animals by observing disgust responses of estrous female mice to odors of nematode-infected male mice after acute progesterone administration. However, the results showed that progesterone did not affect female mice's pathogen disgust or avoidance behavior. Yet the avoidance responses in control mice without progesterone injection were already very strong, suggesting that the non-significant results may have been confounded by ceiling effects in the response measures. Furthermore, Bressan and Kramer (2021) argued that Kavaliers et al.'s data analysis was problematic. Using more sensitive methods to reanalyze the data, they found that acutely progesterone-treated mice spent significantly less time investigating infected male odors, demonstrating that progesterone can enhance pathogen disgust and strengthen avoidance of pathogen cues.

The generation of pathogen disgust and avoidance behavior involves three processes: (1) sensory input and perception, reception, and salience of social information; (2) integration and processing of multimodal sensory input; and (3) conversion of pathogen cues into arousal and decisions about whom to interact with and whom to avoid (Kavaliers et al., 2021b). Although existing research confirms progesterone's facilitative effect on pathogen disgust, it remains unclear at which processing stage progesterone exerts its influence, warranting future detailed investigation.

Finally, in rodent disgust learning, progesterone has not been found to affect the acquisition or extinction of conditioned taste aversion (Chambers, 1980; Lin et al., 2015).

4.1.2 Human Experiments

Progesterone is the most important progestogen in humans and a known immunosuppressant that regulates a series of physiological responses ultimately leading to increased disease susceptibility (Shah et al., 2018). Individuals

with weaker immunity show higher sensitivity to disgust stimuli and tend to avoid potential health threats, generating behavioral immunity (Murray et al., 2019). The "compensatory prophylaxis hypothesis" proposes that during pregnancy, to prevent autoimmune attack on the blastocyst or embryo, the maternal body adaptively upregulates progesterone levels, producing immunosuppression. However, to reduce infection risk, pregnant women increase disgust sensitivity to potentially infectious stimuli, compensating for progesterone-induced reduction in immune response (Ackerman et al., 2018; Fessler et al., 2005). Studies on the menstrual cycle in women have verified the close relationship between progesterone and pathogen disgust. For example, women in the mid-luteal phase (high progesterone) show significantly shorter viewing times for nausea-evoking pictures compared to the early follicular phase (low progesterone), indicating higher disgust sensitivity and stronger avoidance of disgust stimuli during the mid-luteal phase (Pilarczyk et al., 2019). Scale measurements have yielded consistent results, with infected women showing significantly higher pathogen disgust scores during the luteal phase than the follicular phase, making them more prone to pathogen disgust (Milkowska et al., 2019). Further research has confirmed positive correlations between luteal phase pathogen disgust sensitivity and progesterone levels, supporting the compensatory prophylaxis hypothesis (Żelaźniewicz et al., 2016). However, Jones et al. (2018) found no significant correlations between progesterone and pathogen disgust, moral disgust, or sexual disgust in a large-sample longitudinal study. Fleischman and Fessler (2018) suggested that Jones et al.'s failure to find relationships between progesterone and disgust may be due to using text-based disgust measures that lack sensitivity to detect changes in disgust sensitivity, or that progesterone may not be the most direct factor causing increased disgust sensitivity but rather interacts with other components in more complex ways.

Progesterone also significantly modulates disgust face recognition. Conway et al. (2007) found that progesterone levels positively correlated with perceived intensity of disgust faces, but this was moderated by gaze direction. At higher progesterone levels, participants perceived averted-gaze disgust faces as more disgusting, but progesterone did not affect perception of direct-gaze disgust faces. The authors proposed that averted gaze implies the presence of contagious sources in the environment, while direct gaze indicates disgust toward the perceiver, suggesting that progesterone increases women's sensitivity to social cues carrying disease threats. This conclusion is supported by Derntl and Kryspin-Exner et al. (2008), who found that women in the high-progesterone luteal phase were more likely to categorize negative facial expressions as disgust. Additionally, progesterone levels show positive relationships with reaction times in disgust face recognition (Hamstra et al., 2017; Kamboj et al., 2015). Enhanced perception intensity and prolonged reaction times may indicate that individuals allocate more attentional resources to disgust faces, increasing sensitivity but reducing response speed. However, findings regarding accuracy are highly variable. Maner and Miller (2014) found that increased progesterone levels during the luteal phase improved accuracy in recognizing disgust expressions,

whereas Mikolić (2016) found that disgust expressions were not recognized more accurately during the luteal phase. These contradictory results across studies may be caused by differences in experimental tasks and progesterone levels in participant populations, highlighting the need for careful attention to task difficulty and precise hormone measurement in future research.

Regarding moral disgust, progesterone appears to have no significant effect. Multiple studies measuring relationships between menstrual cycle progesterone levels and moral disgust scale scores have found no correlations (Jones et al., 2018; Żelaźniewicz et al., 2016). This indirectly reflects that core disgust has a closer relationship with progesterone and deeper evolutionary significance than moral disgust. However, these studies all used scale measures of moral disgust, which may have limited the scope of moral disgust. Future research should attempt alternative approaches.

4.2 Neural Mechanisms of Progesterone in Disgust Processing

Progesterone plays important roles in the nervous system, including neuroprotection, regulation of neurogenesis, and plasticity of astrocytes and synapses (Giatti et al., 2016). Progesterone is highly lipophilic and easily crosses the blood-brain barrier to act in the brain. The amygdala contains the highest concentration of progesterone receptors (Bixo et al., 1997) and is a core brain region for emotion generation, showing significant activation during disgust processing (Diano et al., 2017). Progesterone likely participates in disgust processing by influencing amygdala activity.

Research has found that amygdala excitability is modulated by progesterone (Engman et al., 2018; Ossewaarde et al., 2010). Functional magnetic resonance imaging of healthy women's menstrual cycles revealed that when viewing negative emotional faces (fear and anger), amygdala activation was higher during the high-progesterone luteal phase than during the follicular phase (Gingnell et al., 2012). Oral progesterone administration in follicular-phase women selectively enhanced amygdala responses and modulated functional coupling between the amygdala and other brain regions (Van Wingen et al., 2008). These results indicate that progesterone can enhance amygdala activation, thereby strengthening responses to negative stimuli (Sundström Poromaa & Gingnell, 2014), which may be related to progesterone's enhancement of core disgust stimulus perception intensity. However, these studies did not directly investigate whether progesterone enhances amygdala responses to disgust stimuli specifically. Although disgust and fear are both avoidance-related negative emotions and may share common mechanisms, experimental verification is needed to determine progesterone's effects on the amygdala during disgust processing.

Some studies have also found inhibitory effects of progesterone on amygdala activity. Derntl and Windischberger et al. (2008) directly compared amygdala activity during emotional face recognition between healthy women in the

mid-follicular phase (low estradiol and low progesterone) and mid-luteal phase (high estradiol and high progesterone). They found higher disgust expression recognition accuracy and greater amygdala activation during the mid-follicular phase. The authors proposed that low progesterone promotes amygdala activation, improving disgust face recognition. However, this study could not completely exclude estrogen effects, used a cross-sectional design, and had small sample sizes in each group, potentially introducing substantial error. Additionally, inhibitory effects of progesterone cannot be excluded, as progesterone's neuroactive metabolites pregnanolone and allopregnanolone typically bind to γ-aminobutyric acid receptors (GABA-Rs) to participate in emotion regulation, and GABA is the most widespread inhibitory neurotransmitter in the brain (Sundström-Poromaa et al., 2020). Therefore, more rigorous control of other hormone levels is needed to investigate the relationship between progesterone and amygdala activity and determine whether progesterone impairs disgust expression accuracy through amygdala inhibition.

5.1.1 Animal Experiments

Estrogen has been shown to regulate social cognition, social learning, and avoidance of pathogens/toxins and disgust expression in rodents, behaviors primarily mediated by olfaction (Choleris et al., 2012; Ervin et al., 2015). For example, compared to normal mice, female mice lacking estrogen receptors ERα and ERβ show impaired ability to discriminate infected conspecific odors and exhibit reduced avoidance and disgust responses toward infected individuals (Choleris et al., 2009).

Moreover, estrogen plays an important role in aversive learning in rodents. Female rats show stronger conditioned disgust responses than males, and conditioned disgust significantly increases during estrus, suggesting that elevated estrogen during estrus may enhance the association between toxin-induced nausea and novel environments, facilitating conditioned taste aversion learning (Cloutier et al., 2018; Lin et al., 2015). This indicates that estrogen may also function in taste-based aversive learning.

5.1.2 Human Experiments

In human studies, no effects of estrogen on core disgust or moral disgust processing have been found to date (Jones et al., 2018). Estrogen's influence on disgust processing is primarily manifested in facial expression recognition. Research shows that estrogen affects disgust expression recognition, but unlike its facilitative effects on negative expressions such as sadness, anger, and fear (Guapo et al., 2009; Pearson & Lewis, 2005), estrogen appears to impair disgust expression recognition accuracy. Estradiol is the most potent endogenous estrogen in humans (Gogos et al., 2014). During the high-estradiol follicular phase, women show significantly higher error rates in recognizing disgust faces (Gasbarri et al., 2008). Using dynamic facial expression recognition tasks, Kamboj et al. (2015)

also found negative correlations between estradiol levels across the menstrual cycle and accuracy in recognizing disgust expressions. Some studies have found no effect of estrogen on disgust expression recognition (Gasbarri et al., 2019; Pearson & Lewis, 2005), but these studies did not measure participants' estrogen levels directly, making it impossible to ensure significant differences in estrogen levels across menstrual cycle phases. Therefore, definitive conclusions about the relationship between estrogen and disgust expression recognition cannot be drawn. A review mentioned that increased estrogen during the follicular phase facilitates facial expression recognition to increase mating opportunities (Osório et al., 2018), but estrogen's impairment of disgust expression processing does not appear to have such evolutionary adaptiveness. Future research should more rigorously investigate the relationship between estrogen and disgust expression processing and its underlying mechanisms.

5.2 Neural Mechanisms of Estrogen in Disgust Processing

Numerous estrogen receptors exist in brain regions related to emotion processing (e.g., cingulate cortex, amygdala, hippocampus, hypothalamus). Estrogen can enhance excitatory synaptic transmission in these regions, particularly by positively modulating NMDA (N-methyl-D-aspartate) receptor function (Lymer et al., 2018; Zang et al., 2020).

Research has found that estrogen in the medial amygdala rapidly facilitates social recognition in female mice (Lymer et al., 2018). Disgust emotion is highly related to social recognition (Kavaliers, Ossenkopp, et al., 2019). Estrogen may participate in identifying unfamiliar out-group individuals and infected conspecifics, generating disgust emotion and avoidance behaviors by influencing amygdala activity. Future research could further investigate whether the amygdala mediates estrogen's effects on disgust processing. In aversive learning, Lin et al. (2015) found that estrogen facilitates conditioned taste aversion acquisition in mice, with a possible mechanism being estradiol-enhanced cholinergic and/or glutamatergic activity between the insula and lateral basal nucleus. Additionally, Goldstein et al. (2005) proposed that estrogen may reduce women's arousal to negative emotional stimuli by controlling cortical-subcortical activation in the hypothalamic-pituitary-adrenal (HPA) circuit, which may explain estrogen's inhibition of disgust expression recognition ability.

Pain not only causes physical suffering but also accompanies emotional distress (disgust). Pain stimuli (e.g., knife wounds) and core disgust stimuli (e.g., earthworms crawling on skin) commonly activate the cingulate cortex, left insula, prefrontal cortex, and right parietal lobe (Benuzzi et al., 2008). The anterior cingulate cortex (ACC) is an important brain region for regulating affective pain (Wu et al., 2019), and suppressing ACC hyperactivity can reduce pain-related aversion in rodents (Zhou et al., 2018). Further research has found that brain-derived estrogen in rat ACC is critical for pain aversion formation (Zang et al., 2020), with the mechanism being locally synthesized estradiol in ACC rapidly enhancing excitatory synaptic transmission and synaptic plasticity by activat-

ing NMDA receptors (Xiao et al., 2013). Estrogen may also influence broader disgust emotions by affecting neuronal structure and function in the ACC.

6 Summary and Outlook

Oxytocin, progesterone, and estrogen differentially influence disgust processing, with similarities and differences summarized in Table 1. However, current findings contain many contradictions. For example, Żelaźniewicz et al. (2016) found positive correlations between progesterone levels and disgust sensitivity, and Kamboj et al. (2015) found that high estradiol increased disgust expression recognition speed, but Jones et al. (2018) did not support these findings. Inconsistent results may stem from differences in hormone measurement methods, disgust assessment approaches, and experimental tasks. Moreover, most current research remains at the descriptive and correlational stage, with limited understanding of underlying mechanisms. Future studies should improve internal validity by ensuring accurate hormone measurement and conducting longitudinal tracking studies across menstrual cycles, while avoiding ceiling or floor effects when measuring emotional responses. Based on these foundations, research should focus on the following aspects.

6.1 Effects of Each Hormone on Disgust Processing Across Different Sensory Modalities

In animal models, previous research has primarily investigated oxytocin and estrogen's effects on olfactory-based pathogen disgust perception (Choleris et al., 2009; Kavaliers, Colwell, et al., 2019) and taste-based conditioned aversion expression (Boulet et al., 2016; Cloutier et al., 2018), as well as estrogen's modulation of touch-based pain aversion (Zang et al., 2020). In human subjects, research has been more limited to the effects of these three hormones on visual disgust stimulus processing, particularly disgust face recognition (Hamstra et al., 2017; Kamboj et al., 2015; Leppanen et al., 2017). Disgust emotion can be triggered through multiple sensory modalities including taste, smell, vision, hearing, and touch. Research has shown that these three hormones have differential modulatory effects in olfactory, gustatory, visual, auditory, and somatosensory systems (Grinevich & Stoop, 2018; Shuster et al., 2019; Tomás et al., 2019). Thus, different hormones may have different effects on information processing across sensory modalities, and future research should further investigate the roles of these three hormones in processing disgust stimuli from different sensory channels.

6.2 Effects of Each Hormone on Disgust Processing Across Different Sexes

From rodents and non-human primates to humans, females show cross-species consistent advantages in disgust processing, with higher disgust sensitivity, better disgust cue recognition, and stronger disgust experiences (Al-Shawaf et al.,

2018; Cloutier et al., 2018; Poirotte et al., 2019). These sex differences may partially originate from differential sex hormone levels, and hormonal effects on disgust processing are likely moderated by sex. For example, Declerck et al. (2014) found that OT reduced disgust in women but not men. At the neural level, OT enhances amygdala activation to threatening stimuli in women but has opposite effects in men (Lieberz et al., 2020). Given the side effects of estrogen and progesterone administration, current human research has primarily examined how endogenous progesterone/estrogen changes across the menstrual cycle affect disgust processing, using only female participants. Whether these hormones' effects on disgust processing are sex-dependent remains unclear. Future research could combine animal studies with exogenous hormone administration to investigate sex moderating effects on hormone influences on disgust processing, with particular focus on the mechanisms underlying these sex differences.

6.3 Investigating Neuroendocrine Mechanisms of Hormonal Effects on Disgust Using Multiple Techniques

Through the preceding review, we found that oxytocin influences disgust emotion processing by affecting activity in multiple brain regions including the insula, anterior cingulate cortex, amygdala, piriform cortex, putamen, and middle frontal gyrus. Progesterone may primarily participate in disgust recognition by modulating amygdala activity and its functional coupling with other brain regions. However, direct evidence for estrogen's neural mechanisms in modulating disgust processing remains limited. Future research should employ techniques such as event-related potentials (ERPs), functional magnetic resonance imaging (fMRI), and functional near-infrared spectroscopy (fNIRS) to explore the neural mechanisms through which these three hormones modulate disgust processing. Simultaneously, through animal behavior studies combined with immunohistochemistry and live cell detection methods, researchers should investigate the modulation of neurotransmitter systems including 5-HT, GABA, NMDA, and acetylcholine by these three hormones to further clarify their neuroendocrine mechanisms in regulating disgust processing.

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