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Gender Differences in PTSD: Susceptibility and Resilience

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Abstract

Posttraumatic stress disorder (PTSD) is anxiety disorder that has been estimated to affect individuals who are exposed to traumatic events. Women are diagnosed with PTSD approximately twice as often as men. In this review, we outline the evidence of gender differences related to PTSD, and the factors of resilience and susceptibility differ between men and women.

Keywords: PTSD, gender differences, susceptibility, resilience, risk factors

1. Introduction

From previous research, we know that women are diagnosed with posttraumatic stress disorder (PTSD) approximately twice as often as men. Prior studies about gender differences in PTSD have generally focused on prevalence and symptom expression. However, no systematic review has organized the results of studies examining why women developed more PTSD symptoms than men, and what neural basis underlies their different reactions to stress. Understanding these can lead to more targeted and more effective treatments and interventions. In this review, we discuss the susceptibility to, and resilience of, gender differences of PTSD in the existing literatures and the neural mechanisms that underlie them. We propose that investigating the susceptibility and resilience of gender differences in PTSD may help to shed light on the gender-based risk for, or mechanism of, developing PTSD, which may result in long-term treatment gains.

2. Evidence of gender differences related to PTSD

2.1. Gender differences in PTSD prevalence

Most findings of gender differences in posttraumatic stress disorder (PTSD) prevalence found that females are reported to be diagnosed with PTSD after a trauma twice as often as males [1] and developed stronger PTSD symptoms than males [2]. The lifetime prevalence of PTSD in females is higher (10.4%) than in males (5.0%), and that kind of difference become evident in adulthood, peaked in early adulthood, then decreased with age [3, 4]. These findings also show that women experience a longer duration of posttraumatic stress symptoms (4 years duration for females compared to 1 year for males) [5] and display more re-experiencing, avoidance and hyperarousal [3]. In general, women are slightly less likely to experience life traumatic events than men. However, women are at higher risk for PTSD after exposure to a traumatic event because women and men often experience different types of trauma [6]. Meta-analysis showed that men tend to experience traumatic events such as accidents, natural disasters, man-made disasters, and military combat, whereas women tend to experience more incidents of sexual assault and sexual abuse. It is noteworthy that the different types of potentially traumatic events (PETs) only predict a part of gender differences in PTSD [7, 8]. Moreover, the gender differences in PTSD are often cross-cultural, and these kinds of differences were amplified in more traditional cultures [9]. Norris et al. compared gender differences in PTSD in different cultures and suggested that PTSD symptoms such as intrusion and avoidance differences in gender appear to be more evident in more traditional cultures [9]. Also, gender differences in PTSD are not simply associated with biological sex; they may also be due to social gender role [10]. For example, female police officers showed less PTSD prevalence than female civilians, despite greater exposure to traumatic events commonly experienced by female police officers.

2.2. Gender differences in anxiety disorder

From previous literatures, anxiety disorders are much more common among girls than boys [11]. For example, Lewinsohn et al. investigated a large sample of adolescents, which included 1079 who had never met criteria for any disorder, and found that girls were more likely than boys to develop anxiety disorders in early life [12]. The preponderance among females emerged early in life. Data from several investigations indicate that females are twice as likely as males to experience anxiety disorder before age six [11, 12], and this difference lasts throughout adolescence. Many studies also show that adolescent girls are more likely than adolescent boys to make connections between bad events experienced in early life and possible negative events in the future, which could make girls more vulnerable to worry and anxiety [13–15]. As a result, adolescent girls are six times as likely as boys to develop generalized anxiety disorder, and three times as likely as boys to develop obsessive-compulsive disorder (OCD) [16, 17]. The gender differences in prevalence of obsessive-compulsive disorder weaken and even showed an opposite trend with increasing age (males developed more obsessive-compulsive disorder than females) [18, 19]. Similar evidences can be found in studies that were conducted in adults. Data from a large-sample survey suggest that women are at higher risk to be diagnosed with anxiety disorders [20, 21]. A national comorbidity survey found that

women are more likely than men to develop panic disorders, agoraphobia, generalized anxiety disorders and posttraumatic symptom disorders [22]. Moreover, women are twice as likely as men to meet the diagnostic criteria for certain phobias [23]. A similar trend can be found in their Phobia reports [24]. However, gender differences are weak in social anxiety disorder (SAD) and obsessive-compulsive disorder (OCD) in studies of adults [25, 26]. Results from clinical samples show a similar trend in healthy people: The World Health Organization conducted an international survey across 15 countries. It found that more women than men received therapy or are receiving therapy, with a focus on panic disorder with agoraphobia [27]. There is no difference between genders in the number of people who are receiving a diagnosis of SAD, even though more women than men are diagnosed with SAD than men [28].

Gender differences were found not only in prevalence of anxiety disorder but also in symptoms of anxiety disorder. For example, the prevalence of Panic Attack between the genders is similar [29], but women showed more typical symptoms such as dizziness, sensations of shortness of breath or smothering [30]. As for the duration of Panic Attack, women showed a more chronic course than men [31, 32]. Women are also more likely to have comorbidity of GAD, somatization and agoraphobia [33, 34]. The most noticeable evidence of gender differences in symptoms of anxiety disorder are those of avoidance in agoraphobia. Females showed more avoidance behavior than males [34, 35]. As for gender differences in OCD symptoms, women diagnosed with OCD tend to have more cleaning behavior and aggressive symptoms of obsessions, while men showed greater obsessive slowness, symmetry obsessions/compulsions, touching rituals and sexual or "odd" symptoms. Besides, the course of OCD in males is more chronic than in females, except in cases of episodic OCD [16].

Gender differences have been found in expression of phobia. For example, girls reported more fear than boys in 9–12 years old children [36]. Similar results can be found in adults, women reports more and stronger fear than men [37–39]. There are also some evidences gender differences in phobia. For instance, Tucker and Bond examined the role of gender in phobia by different surveys and found that femininity is predictive of all categories of animal phobia in general, whereas masculinity is not [40]. Although women were more likely to have an animal phobia, there were no gender differences in social phobia [35]. Fodor and Garrett [41] pointed out that high masculinity and high femininity are assumed to be mutually exclusive traits, phobic behavior of any kind, albeit agoraphobic fears in particular, is consistent with traditionally defined feminine and at odds with the traditional male role, which suggests social gender role is also having significant influence on phobia [41]. Data from a large-scaled survey across 11 countries also found that the role of femininity-masculinity has crucial influence on phobia of animal [42]. Females tend to exhibit higher disgust sensitivity levels than males [39, 43], and cross cultural study of animal fears showed that the disgust-relevant animals were feared significantly more by females than males [44]. However, few studies showed gender differences in phobia associated with social judgments or speech in public [45]. In summary, the gender differences in phobia and expression of fear are not just biological differences, but are it also modulated by social gender role.

2.3. Gender differences in fear and their neural basis

Inconsistent evidences of conditioned fear can be found in animal studies, Baran et al. examined the gender differences of conditioned fear extinction in Sprague-Dawley rats, which indicated that females were resistant to extinction [46]. Milad et al. also found greater fear in female than in male rats during extinction recall [47]. But Chang et al. used the contextual fear paradigm in mice and observed that males showed more freezing both in acquisition and extinction [48]. Gruene et al. [49] conducted a large-sample analysis of fear conditioning and extinction in large cohorts of gonadally intact male and female rats. They found that there were no gender differences in freezing over the course of fear conditioning, fear extinction and extinction recall. But in their retrospective analysis of freezing during fear acquisition and fear extinction, distinct gender differences in susceptible vs. resilient groups have been observed. As a group, females were more easily to be distinguished as susceptible or resilient group in fear conditioning than males. Their findings demonstrated that females might in fact have more distinct neural processes than males [49]. However, a variety of fearful, rather than only freezing behaviors can be observed in response to a conditioned cue. It is a possibility that females, more frequently than males, show freezing behaviors. It is therefore necessary to explore different measurements of fear in future studies [50]. For example, inconsistent evidence has been found when using eyeblink as a measure to detect fear response. Some studies suggested that more female than male rats demonstrated more frequent and stronger eyeblinks in fear acquisition [51–53]. But Toufexis et al. were unable to replicate this difference [54].

Gender differences in human beings are more complicated. Lebron-Milad et al. [55] investigated gender differences in fear learning. They could not find any difference in (Skin Conductance Response(SCR), also known as the electrodermal response, is the phenomenon that the skin momentarily becomes a better conductor of electricity when either external or internal stimuli occur that are physiologically arousing) between females and males over the course of fear learning and fear extinction. But they found different neural activities between women and men in different phases. Women showed increased activation of the right amygdala, right rostral anterior cingulate cortex (rACC) and dorsal anterior cingulate cortex (dACC), compared to men in the fear acquisition phase. In the extinction phase, men showed increased activation in bilateral rACC, while women showed stronger activation in insula [55]. Although there is no evidence of gender differences in physiological arousal levels, there is nevertheless a trend showing that women and men are different in responses to stress because these brain activities are usually associated with stress. Inslicht et al. [56] examined fear acquisition in PTSD patients and found that women demonstrated higher skin conductance response than men in fear acquisition. Even though men have a higher baseline of skin conductance response, women showed higher SCR for conditioned stimuli compared to men [56]. These findings indicate that females acquire fear more easily than males, which in turn might be a risk factor for PTSD.

Gender differences have also been found also in effect of stressors on PTSD. Wood and Shors [51] investigated the response to stressors via the classical eyeblink-conditioning paradigm. They found that exposure to a stressor-facilitated acquisition of a conditioned response in

males, while exposure to the same stressful event dramatically impaired acquisition by females [51]. However, there were some evidences that chronic restraint stress [57], psychosocial stress [58], and early-life stress [59] impaired fear extinction in males. Interestingly, chronic restraint stress can enhance fear extinction in females [60], while environmental stress impaired fear extinction [49]. Although previous stress is a good predictor of PTSD [61], some studies suggested that there is a sex difference. For instance, peri-pubertal stress exposure (predator odor plus elevated platform) impaired fear extinction in men but enhanced fear extinction in women [62]. These inconsistent results might be the influence of gonadal hormones. Increasing evidences suggests that gonadal hormones modulate fear acquisition and fear extinction [54, 63–68].

2.4. Gender differences in attention to negative stimuli and negative emotion processing

The amygdala is part of a workspace in the brain that is significant for creating affective feelings [69]. In general, women and men showed equivalent amygdala responses to novel negative material. However, women tend to have a more sustained amygdala response to familiar negative material relative to men, indicating that women's amygdala responses are more persistent in multiple repetitions of negative stimuli [70]. That might explain why women who have experienced traumatic events are more likely than men to develop PTSD [71], even when the type of trauma experienced is similar for both [72]. Women have been reported to be more sensitive and responsive to threats [73–79]. Researchers have identified that the orbitofrontal cortex (OFC), amygdala and anterior cingulate cortex (ACC) consistently participate in attentive processing of emotional faces [80]. McClure et al. [81] used functional magnetic resonance imaging (fMRI) to examine the developmental and gender differences in the activation of neural structures. They found that in adult women, orbitofrontal cortex and amygdala responses were activated selectively by angry cues, while adult men showed a less discriminating pattern of activation [81].

3. Gender differences in risk factors related to PTSD

According to Blain et al., gender differences have been found in exposure to trauma, PTSD development, as well as in psychotherapy outcomes [82]. Different risk factors are associated with gender differences in PTSD, such as neurohormonal, affective, and social cognition, as well as in coping styles used by females and males to manage distress [83]. Some researchers suggest that gender differences in PTSD are due to these risk factors. In the following paragraphs, we will discuss the possible gender differences in risk factors related to PTSD.

3.1. Gene

Studies have shown that certain genetic characteristics may affect the prevalence of PTSD. For example, PTSD was more prevalent in identical twins than in non-identical twins [84]. And from previous literatures, anxiety-related risk factors are more likely to be inherited in female generations. Lake and his colleagues found that anxiety-related genetic factors influenced

females more than males [85]. Similarly, a study of adolescents also demonstrated that fear and phobias are more likely to be passed on in females than in males [86]. Another possible explanation is that extrinsic factors are responsible for men demonstrating lower heredity of anxiety: The higher heredity of anxiety in females is due to the interaction between society and gene. Hettrema et al. [87] conducted personal interviews with 5000 members of male-male and female-female twin pairs from the Virginia Adult Twin Study of psychiatric and substance use disorders. He found that even if the prevalence in anxiety disorders among females is twice that of males, the underlying structure of the genetic and environmental risk factors for the anxiety disorders is similar between females and males [87]. This difference may be explained by a unique environmental factor shared across the disorders and, to a lesser extent, by a common, shared environmental factor. The gender differences in epigenetics may also result in gender differences in PTSD. For instance, research has shown lower plasma cortisol levels in women with a history of prior trauma [88]. Nugent and McCarthy [89] also suggested that the gender differences in DNAm (A type of epigenetic modification involving the covalent coupling of methyl groups to cytosine, a nucleotide found in DNA) might contribute to the gender-different prevalence in PTSD [89]. Uddin et al. [90] explored whether DNAm plays a role in contributing to the observed sex differences in prevalence of stress related disorder, especially PTSD. They proposed that sex differences in DNAm among genes are known to influence brain development and the resilience to developing PTSD [90].

3.2. Physiological response to fear

In previous conditioned-fear studies, men showed generally higher skin conductance response than women. For example, males showed higher skin conductance response in instrumental conditioning fear paradigm [91] and slower habituation for negative acoustic stimuli but were not as reactive as females in skin conductance response to experimental stimuli [92]. However, there was no evidence to indicate gender difference in physiological response to acute stress. Katkin and Hoffman confirmed that more women reported fear than men, but they found no gender difference in autonomic response to shock [93]. The evidence for gender differences in physiological reactivity to stressful situations does not seem to be consistent. Kelly et al. explored the gender differences in reactivity to a social stress challenge by measuring neuroendocrine, autonomic and affective response domains [94]. Their findings demonstrated that cortisol reactivity and the level of autonomic responding failed to discriminate between males and females following the psychosocial stress challenge (i.e., the Trier Social Stress Test (TSST)). Kelly et al. [95] also examined the gender differences in predisposition to panic in individuals without psychopathology. In their study, women showed a similar autonomic response as men but reported more fear and panic than men immediately following a challenge procedure [95]. In summary, observed gender differences in physiological responses to negative stimuli may be due to the gender differences in HPA axis (HPAA) (HPA axis is a complex set of direct influences and feedback interactions among three endocrine glands: the hypothalamus, the pituitary gland and the adrenal glands) stress responses, which may result from sexual dimorphism in brain function and circulating sex steroids [96].

3.3. Hormones

Several studies support the hypothesis that phobias in women are biological, wherein differences are considered to be modulated by the sex hormones [97]. Hedlund and Chambless [98] used an aversive conditioning procedure to test potential sex differences in conditioning ability that may be related to the differential incidence of phobias between the sexes. Their findings suggest that women condition more readily during the premenstrual period [98]. Pearlstein et al. interviewed 78 female patients with late luteal phase dysphoric disorder and confirmed that the luteal phase increases their symptoms and state anxiety levels [99]. Kajantie and Phillips [100] also suggested that although adult women usually show lower HPA and autonomic responses than men of the same age, the HPA response is higher in women's luteal phase, and poststress-free cortisol levels approach those of men [100]. Jin and Zheng [101] examined the effects of female menstrual phases on conditioned fear acquisition and extinction. Their results showed that females in the luteal phase acquired the conditioned context fear response more effectively and extinguished it more slowly than females in the menses phase [101]. Women who are pregnant or in the postpartum period are considered to be at high risk for a diagnosis of obsessive-compulsive disorder (OCD) [19, 102, 103].

3.4. Evolutional factors

Human beings throughout the ages have made evolutionary strategies for survival. Female stress responses have likely evolved in ways that not only protect the female, but also her offspring. The "fight-or-flight" is not that common in females [104]. Their responses to stress are more likely to be marked by a pattern of "tend and befriend" (tending involves nurturing activities to protect themselves and offspring and reduce stress, while befriending involves maintaining social networks that may help in this process). Also, when men and women compete in similar circumstances, they differ in their biobehavioral responses [105] and (women) in responses to maternal frightening behaviors [106]. Females displayed more help-seeking behaviors and experience more fear than men, and males displayed more avoidance and fight behaviors, while experiencing traumatic events [107, 108]. It is noteworthy that gender difference in patterns of reaction to stress are not only modulated by biological factors. The gender role also plays a crucial role [10]. However, Swaab et al. suggested that the HPA axis is affected by both environmental factors and gender role [109].

3.5. Trait anxiety

Women typically report higher trait anxiety levels than men. For example, Chambless and Mason examined the gender differences in agoraphobia and found women scored significantly higher in trait anxiety [110]. They also found that women were slightly more avoidant when alone. But, the results of gender differences in trait anxiety are inconsistent. For example, Turgeon et al. compared 96 women and 58 men who suffered from panic disorder with agoraphobia [34]. Their results showed no gender differences in trait anxiety.

Foot and Koszycki examined gender differences in anxiety-related personality traits in patients with panic disorder with or without agoraphobia [111]. They could not find any gender

differences in trait anxiety level. Some researchers claimed that Chambless and Mason's findings are only statistically but not clinically significant, and that the results may be affected by different anxiety level measurements. For instance, Bander and Betz [112] measured anxiety level with the S-R Inventory instead of STAI-T, with items of S-R Inventory differing in emphasis from those of STAI (STAI items emphasize cognitive and affective indicators of anxiety, and S-R Inventory items emphasize physiological/autonomic responses indicative of anxiety). Using S-R Inventory, they could not find any gender differences in trait anxiety [112]. Similarly, a number of other studies showed that women, compared to men, demonstrate higher anxiety levels in cognitive and affective dimensions but not in physiological and autonomic dimensions [94, 95].

3.6. Life stressors and trauma

It is well documented that women experience less traumatic events than men. Women are at higher risk in potentially traumatic events (PTEs), such as sexual assault, child sexual abuse, attempted rape, sexual coercion [113] and intimate violence [114]. These PTEs are directly related to the high prevalence of PTSD in females [6]. Women are also more vulnerable to the effects of undesirable life events. The emotional impact of undesirable life events is significantly greater among women than men [115]. Moreover, individuals who experienced undesirable life events (life stress) reported greater PTSD symptomatology and the same amount of overall distress as those who had experienced trauma. In fact, individuals who experienced atypical trauma (e.g., death of significant others) reported more severe PTSD symptoms than those who had experienced a typical trauma (e.g., combat or war) [116]. However, females are still more likely than men to develop PTSD, and this did not change when controlling for the type of traumatic events [7, 22].

3.7. The role of control

Evidences from the literature suggest that experience in childhood with diminished control may result in a cognitive style characterized by a greater chance of interpreting or processing subsequent events as out of control, which may play a role in psychological vulnerability for anxiety [117]. Several studies find a gender difference in the sense of control [118–120]. Women are more likely to find themselves in disadvantaged circumstances with less power to control their lives. Moreover, the different behaviors of educators toward boys and girls will affect children's development. Some researchers have found that teachers respond more positively to boys than to girls, which may diminish the feeling of control in girls [121]. And feeling of less control may result in greater likelihood of developing anxiety disorders [121–123].

3.8. Socialized gender role

Girls in general are more likely than boys to report symptoms of anxiety and fear. One of the most common explanations for this gender difference is the expectation of gender role, that is, differences in levels of masculinity and femininity [124]. Girls and boys are socialized to develop gender- or sex-stereotyped feminine and masculine skills, behaviors and personalities. According to theories on gender roles, the feminine gender role is more consistent in expressing

fear and emotional behavior. It is more likely to be accepted, tolerated and encouraged that girls express and acknowledge vulnerability. In contrast, boys are expected to display more frequent traits such as confidence and courage and, consequently, learn how to decrease levels of fear or reduce expression of fear [125]. Many studies suggest that gender role is strongly related to psychopathology (e.g., gender role expectation potentially increases sensitivity to anxiety producing stimuli) [110, 126]. Muris et al. [127] examined the relation between gender role orientation and fear and anxiety using a nonclinically referred sample of children. Their results indicated that femininity and a preference for girls' toys and activities were positively associated with fear and anxiety, whereas masculinity and a preference for boys' toys and activities were negatively related to these emotions [127]. Similar results have been found in a sample of adults, in which femininity was positively associated with a higher level of fear [40, 128] and high levels of trait anxiety [112, 129, 130]. Subjects who displayed higher levels of femininity, but lower masculine traits reported higher levels of fear [131].

3.9. Social support

It is generally accepted that a lack of social support during and after a trauma present a significant risk for developing PTSD [132], and some studies have found it to be a reliable predictor for developing PTSD [133]. Women tend to seek more social support than men, but nevertheless have a higher risk than men for developing PTSD [134]. The explanation may be the difference in both levels and benefits of social support received by females and males in response to trauma [135]. Social support was found to be more strongly protective against traumatization among women than among men. Women with low social support were more likely to experience symptoms of PTSD [133, 134, 136, 137]. Christiansen and Elklit [133] explored the effects of social support in PTSD on men and women. They found that women in a stabbing sample (subjects who saw dead body inside a school) felt more let down than the men. Also the predictive power of social support in PTSD symptoms was stronger in women in the stabbing sample, but not in an explosion sample (subjects who experienced explosions in a fireworks factory) [133]. Therefore, the effect of gender on the relationship between social support and PTSD is further complicated by the possibility that different types of trauma and social support modulate the PTSD symptomatology [10, 138].

4. Gender differences in responses to PTSD

Across various studies, women are about one-third less likely than men to report having experienced a trauma [6, 139]. However, women are approximately twice as likely as men to meet criteria for PTSD following such events, and they are more than four times as likely as men to develop chronic PTSD. These results suggest that the higher rate of PTSD among women cannot be attributed to a greater overall risk of trauma. Coping style for dealing with trauma has been proven to play a critical role in PTSD development [83]. The different coping styles between men and women may be one of the explanations for gender differences in PTSD. Men and women are known to have different coping styles. Women are more likely to exhibit an emotional reaction to stressors (emotion-focused), and are believed to spend more time

seeking support and discussing problems with friends or family. Unlike women, men are more likely to use direct problem-focused coping strategies to deny or avoid stressors [135]. However, emotion-focused strategies may not always be adaptive. Focusing on emotions can impede adjustment and also distract people from making active coping efforts [140]. Blake et al. [141] examined psychological coping styles and mental health treatment histories in veterans with PTSD. They found that subjects with PTSD showed a significantly greater use of emotion-focused coping [141]. Moreover, women have been found to be significantly more likely to report a lack of alternative coping strategies than men [142, 143]. Female trauma victims are also more likely to self-blame and to hold negative views about themselves and the world than male victims, as well as to view the world as dangerous. Such negative cognition about self and the world are important predictors for PTSD symptoms [144].

There are a variety of effective treatments for PTSD, including Cognitive Behavioral Therapy (CBT) and pharmacotherapy [145]. Overall, the literature suggests that females are somewhat more likely to seek therapy for PTSD than males [146]. However, there is evidence that women and men may respond differently to the same PTSD therapy [82], and they may also prefer different treatments for PTSD. It has been suggested that gender socialization plays a role in the treatment of PTSD, and that males express less affect and are more cognitively oriented toward treatment than females [147]. However, results of various studies have been inconsistent, Başoğlu et al. examined treatment for PTSD patients who experienced natural disasters and found no gender differences in effectiveness of treatment [148]. Felmingham and Bryant [149] examined potential gender differences in responses to Cognitive Behavioral Therapy (CBT) and found there were no significant differences between men and women in treatment response immediately after treatment. However, they found that men displayed more severe PTSD symptoms than women in the exposure only group [149]. Gender differences have been found in PTSD patients treated with medication. A study search of electronic bibliographic databases showed that gender differences have been identified in response to PTSD medication-based treatment [150]. Nugent et al. [151] found a gender difference regarding pharmacological PTSD prevention: girls receiving propranolol reported more PTSD symptoms relative to girls receiving placebo, while boys who received propranolol showed a nonsignificant trend toward fewer PTSD symptoms than boys receiving placebo [151].

5. Conclusion

In conclusion, women are approximately twice as likely as men to develop PTSD after a trauma, and certain risk factors may account for why they reported PTSD more often than men. To date, existing studies have focused on prevalence, and the description of gender differences in PTSD symptoms. However, most researchers in this area primarily paid attention to men. More research is needed to address questions related to how and why females develop PTSD at a higher rate than males, how gender acts as a susceptibility or resilience factor. As for the possible explanations of gender differences in PTSD, most researchers attributed these differences to biological differences (e.g., gene, hormones). Future studies are needed to delineate more precisely the ways in which culture, and gender role, alone and in combination,

shape the gender differences of PTSD. Further research is also needed to improve PTSD prevention and treatment in women.

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