

## REVIEW

# Trends in psychogenic erectile dysfunction research: a bibliometric and visualized study

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**Abstract**

Psychogenic erectile dysfunction (pED) is more common in the population of young and middle-aged males. Research relating to pED has increased significantly over the past 20 years. However, few studies have performed comprehensive statistical analysis on these publications. In this study, we highlight the current research hotspots and emerging trends relating to pED from 2000 to 2022, as determined by a focused review of the literature. Relevant articles were identified by searching the PubMed and Web of Science databases between 2000 and 2022. VOSviewer and Origin software were then used to analyze and verify emerging trends. A total of 118 articles relating to pED were included in our final analysis. Our analysis showed that research on pED is dominated by clinical studies and concentrated in journals relating to male and sexual medicine. Chinese researchers have produced the highest number of publications. In addition, over the past 20 years, pED research has focused more on pathogenesis, diagnosis and treatment. In this study, we reviewed articles related to pED that were published over the last 20 years; our findings may provide reference guidelines for researchers when designing future research on pED.

**Keywords**

Psychogenic erectile dysfunction; Mechanism; Diagnosis; Treatment

## 1. Introduction

Psychogenic erectile dysfunction (pED) is a type of erectile dysfunction (ED) that is caused by non-organic factors such as depression, anxiety and marital discord [1]. Regrettably, there are no specific biomarkers available for diagnosing this particular type of ED [2]. ED has been shown to be closely related to age in some epidemiological studies [3]. In China, an epidemiological survey involving 5210 ambulatory men aged >40 years from 30 provinces and autonomous regions of China showed an ED prevalence of 40.56% [4]; furthermore, there was a trend for a high proportion pED among this population [5]. pED is usually caused by the lack of sexuality education, psychological trauma of a sexual nature, difficulties in interpersonal relationships, and previous unsuccessful sexual intercourse experiences [6, 7]. Especially during the pandemic caused by COVID-19, psychosexual factors may have influenced sexual activity in males, thus predisposing them to pED [8]. While pED is not life-threatening, it can exert significant impact on a patient's quality-of-life and their partners, potentially causing conflicts within the family.

Bibliometrics is a method used to analyze information relating to countries, journals, authors, keywords and cited journals in the literature. This method can help to quantify the impact of individual research findings and the development of discipline-specific literature, while also assessing trends in scientific

research. Researchers have utilized this method to summarize the current status and trends in specific fields, thus serving as a valuable reference for future research [9]. Over recent years, there has been a notable increase in the number of research studies focusing on pED. However, most published reviews are limited to the clinical research progress of pED; there is scant literature analyzing research hotspots and development trends. In this study, we used VOSviewer and Origin software to analyze the literature relating to pED over the past 20 years. The aim of this study was to analyze the overall trend and gradual evolution of pED research and provide an outlook on challenges that remain. The findings of this study can serve as a reference for future pED research.

## 2. Methods

### 2.1 Literature search strategy

A literature search was performed using the PubMed and Web of Science databases and the subject term "psychogenic erectile dysfunction", as shown in Table 1. The search time-frame was limited to January 2000 to December 2022, and the literature identified were evaluated for subsequent analysis.

### 2.2 Data download

The raw data were downloaded from PubMed or Web of Science and then summarized using Endnote, recording both

**TABLE 1. The strategy used to search literature in the PubMed database.**

No.	Search item
#1	Psychological (Title/Abstract)
#2	Psychogenic (Title/Abstract)
#3	Functional (Title/Abstract)
#4	Non-organic (Title/Abstract)
#5	Nonorganic (Title/Abstract)
#6	Or/#1–#5
#7	Erectile dysfunction (Title/Abstract)
#8	Impotence (Title/Abstract)
#9	Male sexual dysfunction (Title/Abstract)
#10	Or/#7–#9
#11	#6 and #10

complete records and cited references.

### 2.3 Visual analysis of the literature

We extracted a range of key information from the identified literature in the Endnote database (version X9, Clarivate Analytics), including the number of publications per year, country or region, journal name and keywords. Origin (2022, OriginLab, Northampton, MA, USA) and VOSviewer software (1.6.16, Leiden University, Leiden, The Netherlands) were utilized for visual analysis.

## 3. Results

### 3.1 Overview of the literature

A total of 118 papers relating to pED were retrieved from the two databases. These papers consisted of 91 clinical studies, 16 systematic reviews, five animal studies, four case reports and two trial protocols. Of the pED clinical studies, 28 articles focused on mechanistic studies, 25 articles focused on treatment, and 18 articles focused on diagnosis. Although the research on pED is becoming more in-depth, there is still a need to increase the overall number of publications, as depicted in Fig. 1A.

### 3.2 Country/region analysis

When analyzing the 118 publications, we identified authors from 25 different countries and regions. Of these, Chinese scholars had the highest number of publications with 47, followed by Italy, the United States, Japan, Germany, Spain, India, Turkey, Canada and Pakistan (as shown in Fig. 1B). Although collaborative relationships were evident among these countries, there is still potential for further strengthening these connections, as shown in Fig. 1C.

### 3.3 Journal analysis

The 118 papers were published in a total of 62 journals. Fig. 1D shows the top eight journals, with the International Journal of Impotence Research producing the highest number of pub-

lished papers. This was followed by the Journal of Sexual Medicine, Andrology, Andrologia, Sexual Medicine, Urology and PLOS ONE. This suggested that pED, a common male disorder, is predominantly published in the fields of male medicine and sexual medicine.

### 3.4 Literature citation analysis

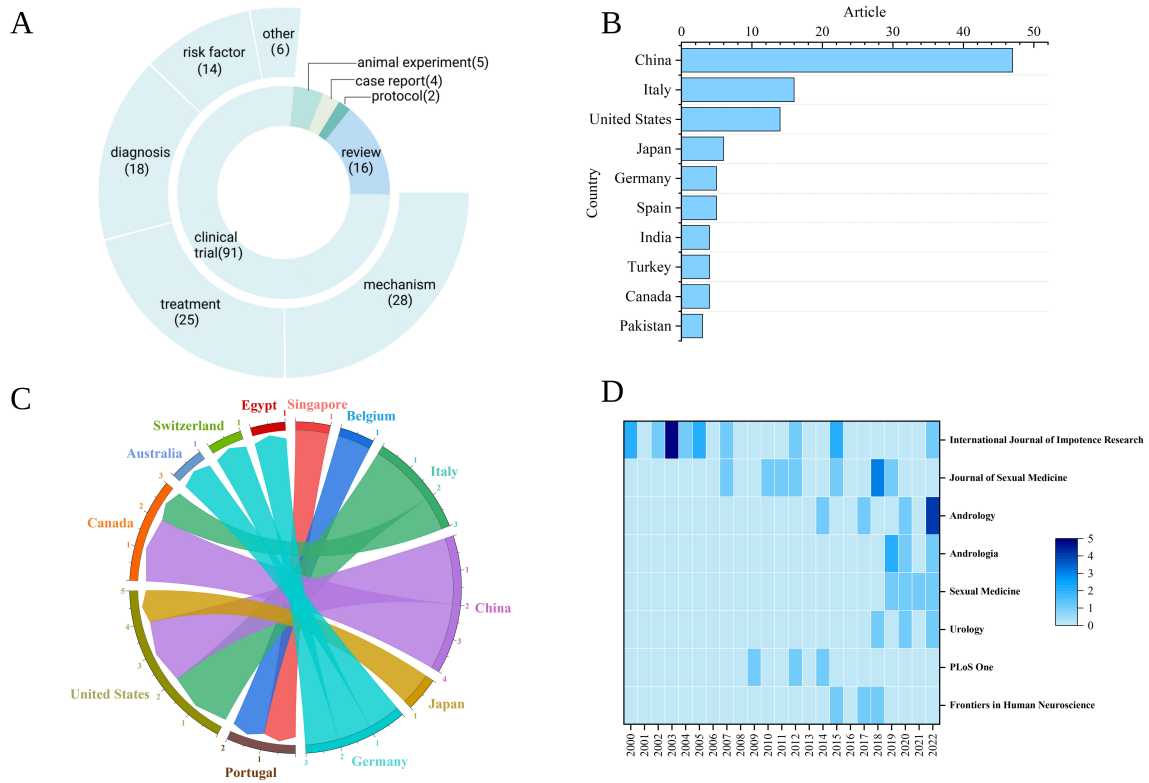
Table 2 presents the top 10 pED-related publications based on citation frequency. The literature mainly focused on clinical studies, with the most cited research areas relating to the treatment of pED by oral phosphodiesterase type 5 inhibitor (PDE5I), cognitive behavioral guidance, and the investigation of pathological mechanisms. Of these, brain activity studies were the most frequent. Rosen *et al.* [10] conducted a systematic review of treatment approaches for pED, including cognitive-behavioral interventions, sexual education and guidance, and couple and psychological counseling. These authors also combined these approaches with oral PDE5I treatment to gain a better understanding of the disease in terms of classification and treatment. Their study was cited 103 times and provided significance guidance for future research on pED.

### 3.5 Keyword analysis

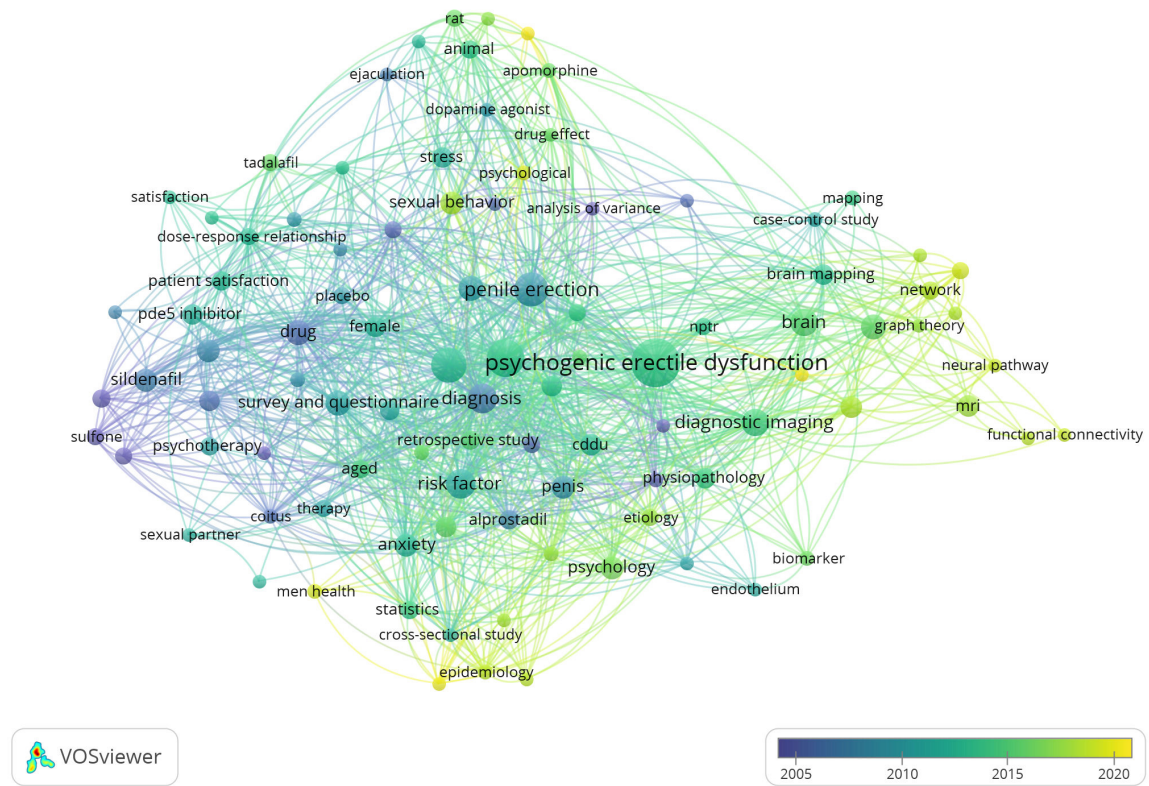
In this study, we used VOSviewer to create a co-occurrence network of keywords in the research area. The co-occurrence network was divided into different clusters based on time nodes, with each cluster represented by a different color. This visualization revealed that earlier research hotspots were primarily centered around the treatment of pED. This included the use of apomorphine, PDE5I, sexual behavior guidance and psychological interventions. As our understanding of this condition deepened, the treatment objectives for pED have shifted towards improving the sexual satisfaction of both men and their partners. In terms of diagnosis, keywords, such as nocturnal penile tumescence and rigidity (NPTR) and color doppler duplex ultrasonography (CDDU) showed that certain tests can be used to diagnose pED. In recent years, a range of other keywords have been associated with pED, including magnetic resonance imaging (MRI), network, neural pathway, functional connectivity and brain mapping. Furthermore, in conjunction with the keywords shown in Fig. 2, research relating to the neurophysiology of the brain in pED patients has grown notably since 2015. This suggests that there may be abnormalities in brain activity, particularly in terms of cortical structure or function. Based on the keywords shown in Fig. 2, we considered that pED research is primarily focused on three areas: mechanisms, diagnosis and treatment.

## 4. Discussion

In this study, we used Origin and VOSviewer to visually analyze the literature relating to pED from January 2000 to December 2022. Our objective was to demonstrate the international publication of research on this disease, national collaborations, current research trends and hotspots in a visual format spanning over two decades. Fig. 3 provides a detailed representation of our findings. Our results can serve as a valuable reference for future research on pED. Despite an increase



**FIGURE 1. Published literature relating to pED.** (A) type of literature study and the number accounting for the 118 publications; (B) the number of papers by country; (C) the cooperative relationships between country or region; (D) the number of publications by the journals.



**FIGURE 2. Keyword co-occurrence analysis.** The nodes represent keywords. The size of the dots represent the number of keywords. Different node colors represent different times.

**TABLE 2. The citation frequency of pED by ranking.**

Rank	Citations	Type	Journal	Title	Country	Impact factor (2022)	Ref.
1	103	Review	Urologic Clinics of North America	Psychogenic erectile dysfunction. Classification and management	USA	2.4	[10]
2	56	Clinical study	Journal of Sexual Medicine	Integrated sildenafil and cognitive-behavior sex therapy for psychogenic erectile dysfunction: a pilot study	USA	3.5	[11]
3	49	Clinical study	International Journal of Impotence Research	Combined oral therapy with sildenafil and doxazosin for the treatment of non-organic erectile dysfunction refractory to sildenafil monotherapy	Italy	2.6	[12]
4	47	Review	Current Drug Targets	Central oxytocinergic neurotransmission: a drug target for the therapy of psychogenic erectile dysfunction	Italy	3.2	[13]
5	47	Clinical study	European Urology	Brain activation patterns during video sexual stimulation following the administration of apomorphine: results of a placebo-controlled study	Italy	23.4	[14]
6	42	Clinical study	Journal of Sex & Marital Therapy	Psychogenic erectile dysfunction: comparative study of three therapeutic approaches	Brazil	2.5	[15]
7	42	Clinical study	International Journal of Clinical Practice	Sildenafil citrate (Viagra) is effective and well tolerated for treating erectile dysfunction of psychogenic or mixed aetiology	Switzerland	2.6	[16]
8	38	Clinical study	PLOS ONE	Brain networks during free viewing of complex erotic movie: new insights on psychogenic erectile dysfunction	Italy	3.7	[17]
9	35	Clinical study	Clinical Neurophysiology	Combined cardiac sympathetic excitation and vagal impairment in patients with non-organic erectile dysfunction	China	4.7	[18]
10	34	Clinical study	PLOS ONE	Macrostructural alterations of subcortical grey matter in psychogenic erectile dysfunction	Italy	3.7	[19]

in pED publications and national cooperation, further improvement is still needed. Keyword analysis and the frequency of literature citations further suggest that research on neurological aspects for this disease is becoming more common. Previous studies have identified abnormal neurological representations at the local, regional and global levels in pED patients. However, the fragmentation of these studies, along with the lack of systematic analysis of data, pose challenges for researchers in terms of acquiring a comprehensive understanding of the brain abnormalities associated with pED [20]. The definitive diagnosis of this disease remains controversial, making commonly used clinical tests such as NPTR, intracavernosal injection (ICI) + CDDU, and audiovisual sexual stimulation (AVSS) in-

appropriate. Each of these tests has its own characteristics and limitations, thus emphasizing the need for systematic reviews to enhance our clinical understanding of the diagnosis [21]. While oral PDE5I is recommended as the first-line treatment option for ED, guidelines also recommend that individualized treatment should be considered for ED patients [1]. As pED is fundamentally different from organic ED, it necessitates feasible treatment options based on existing clinical evidence [1]. Consequently, unlike other reviews, in the present study, we analyzed 118 publications on pED and primarily focused on publications relating to mechanistic studies, diagnosis and treatment; we analyzed these three aspects in light of the available evidence.

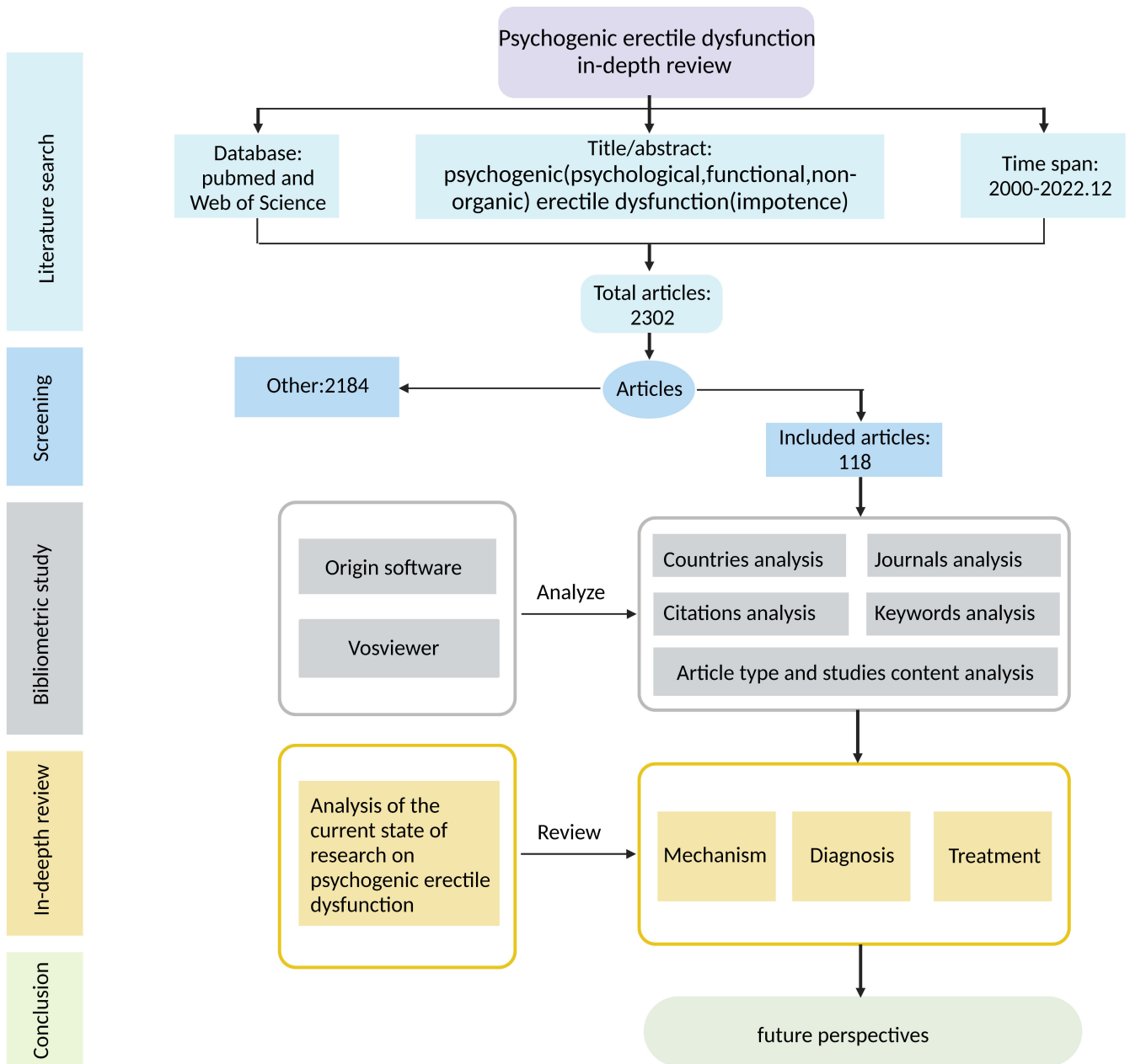


FIGURE 3. Flowchart depicting our research methodology.

#### 4.1 Patients with pED may have abnormalities of the central nervous system

Table 3 summarizes relevant studies on pED that were published over the last decade, including patient sample size, age, international index of erectile function-5 (IIEF-5) (or IIEF), examination modality and study conclusions. By identifying the central neural mechanisms involved in pED, this table provides a comprehensive overview of the abnormal regions and neurological representations found in various brain regions, as depicted in Fig. 4A. Patients with pED exhibit structural brain damage, which is evident from the reduced levels of white and gray matter. Furthermore, pED patients demonstrate dysfunction in multiple brain regions that are primarily characterized by reduced connectivity and abnormal activity. Upon dividing the summary results of Fig. 4A into regions (as shown

in Fig. 4B), we found that these abnormalities were mainly concentrated in the limbic system and frontal lobes.

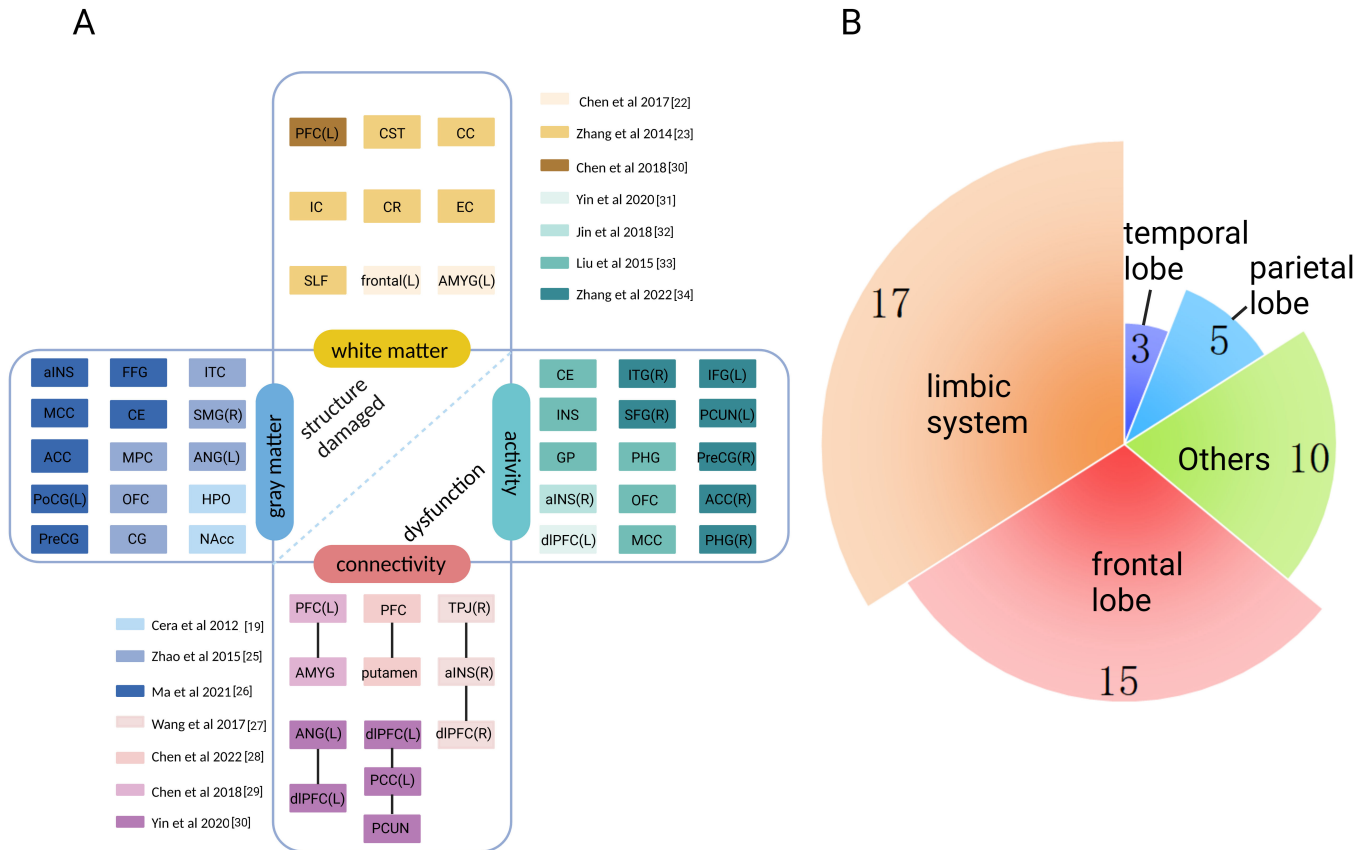
##### 4.1.1 Abnormalities of the limbic system may be closely associated to pED

The limbic system refers to a collection of brain tissues that have evolved from the paleocortex and paleocortex in the central nervous system of higher vertebrates. This system includes several key structures, including the amygdala, nucleus accumbens, corpus callosum, insula, cingulate gyrus and the hypothalamus, which are closely associated with these tissues. Abnormalities in this system may be closely related to pED. The amygdala, along with other limbic areas, plays a key role in cognitive processes, emotions and reward mechanisms, and is also known to regulate penile erection [19, 35, 36]. Primitive instinctual sexual behavior in humans is known to

**TABLE 3. Brain structure and dysfunction related to pED.**

Sample size	Age	IIEF-5	Diagnosis method	Conclusion	Ref.
21	29.38 ± 5.11	9.71 ± 5.71	NPTR	Integrity compromised of the white matter fiber myelin connected by the left frontal (L) lobe and AMYG (L)	[22]
27	33.22 ± 5.92	13.56 ± 3.61	NPTR, CDDU	Morphological changes of white matter in the CC, CST, IC, CR, EC and SLF	[23]
25	28.44 ± 4.77	9.44 ± 5.12	Not mentioned	The white matter integrity changes in the PFC (L) and limbic cortex	[24]
17	34.30 ± 11.00	Not mentioned	NPTR, CDDU	The presence of grey matter atrophy patterns in subcortical structures such as NAcc and HPO	[19]
40	28.45 ± 6.44	Not mentioned	NPTR, CDDU	Decreased cortical thickness in the mPFC, OFC, CG, ITC and decreased interregional cortical thickness correlations from the right lateral orbitofrontal cortex to the SMG (R) and the ANG (L)	[25]
50	32.54 ± 5.41	14.16 ± 3.19	NPTR, CDDU	Decreased gray matter volume in the aINS, PreCG, PoCG (L), ACC, MCC, FFG and CE	[26]
27	26.58 ± 4.89	Not mentioned	NPTR, CDDU	Aberrant connection patterns between the right aINS (R) and the dlPFC (R), as well as the right aINS (R) and the TPJ (R) respectively	[27]
32	42.69 ± 3.95	10.56 ± 5.07	ICI + CDDU	Reduced structural connectivity predominantly located in the PFC and subcortical areas	[28]
21	28.44 ± 4.77	9.44 ± 5.12	ICI + CDDU, NPTR	Lower connectivity degree and strength in the PFC (L)-AMYG pathway	[29]
32	33.16 ± 5.89	13.97 ± 3.60	NPTR, CDDU	Reduced functional connectivity between the dlPFC (L) and ANG (L), and PCC (L) and PCUN	[30]
32	33.16 ± 5.89	13.97 ± 3.60	NPTR, CDDU	Decreased amplitude of low-frequency fluctuation in the dlPFC (L)	[31]
26	26.80 ± 5.00	Not mentioned	NPTR, CDDU	Decreased amplitude of low-frequency fluctuation in the aINS (R)	[32]
27	33.22 ± 5.92	13.56 ± 3.61	NPTR, CDDU	Increased amplitude of low-frequency fluctuation in CE, INS, GP, PHG, OFC and MCC.	[33]
48	27.80 ± 6.40	10.86 ± 3.66	NPTR, CDDU	Increased amplitude of low-frequency fluctuation in PHG (R), IFG (L), ACC (R) and decreased amplitude of low-frequency fluctuation in PCUN (L), ITG (R), SFG (R), PreCG (R)	[34]

*Abbreviations: IIEF-5, international index of erectile function-5; NPTR, nocturnal penile tumescence and rigidity; CDDU, color doppler duplex ultrasonography; ICI, intracavernous injection; L, left; R, right; ACC, anterior cingulate cortex; aINS, anterior insula; AMYG, amygdala; ANG, angular gyrus; CC, corpus callosum; CE, cerebellum; CG, cingulate gyrus; CR, corona radiata; CST, corticospinal tract; dlPFC, dorsolateral prefrontal cortex; EC, external capsule; FFG, fusiform gyrus; GP, globus pallidus; HPO, hypothalamus; IC, internal capsule; IFG, inferior frontal gyrus; INS, insula; ITC, inferotemporal cortical; ITG, inferior temporal gyrus; MCC, middle cingulate cortex; mPFC, medial prefrontal cortical; NAcc, nucleus accumbens; OFC, orbitofrontal cortex; PCC, posterior cingulate cortex; PCUN, precuneus; PFC, prefrontal cortex; PHG, parahippocampal gyrus; PreCG, precentral gyrus; PoCG, postcentral gyrus; SFG, superior frontal gyrus; SLF, superior longitudinal fasciculus; SMG, supramarginal gyrus; TPJ, temporoparietal junction.*



**FIGURE 4. Diagram depicting brain structure and dysfunction in patients with pED.** (A) brain structure and dysfunction (based on the conclusions in Table 3, the abnormal brain regions were collated and attributed to abnormalities in the white matter, grey matter, function and connectivity of the brain. In the classification of white matter, grey matter, connectivity and activity, the color of the rectangles used for the abnormal brain areas corresponds to the color of the rectangles used for related references); (B) distribution of brain structure and dysfunction (17, 15, 10, 5 and 3 represent the frequency of occurrence in related regions in Fig. 4A, respectively). Abbreviations: L, left; R, right; ACC, anterior cingulate cortex; aINS, anterior insula; AMYG, amygdala; ANG, angular gyrus; CC, corpus callosum; CE, cerebellum; CG, cingulate gyrus; CR, corona radiata; CST, corticospinal tract; dlPFC, dorsolateral prefrontal cortex; EC, external capsule; FFG, fusiform gyrus; GP, globus pallidus; HPO, hypothalamus; IC, internal capsule; IFG, inferior frontal gyrus; INS, insula; ITC, inferotemporal cortical; ITG, inferior temporal gyrus; MCC, middle cingulate cortex; mPFC, medial prefrontal cortical; NAcc, nucleus accumbens; OFC, orbitofrontal cortex; PCC, posterior cingulate cortex; PCUN, precuneus; PFC, prefrontal cortex; PHG, parahippocampal gyrus; PreCG, precentral gyrus; PoCG, postcentral gyrus; SFG, superior frontal gyrus; SLF, superior longitudinal fasciculus; SMG, supramarginal gyrus; TPJ, temporoparietal junction.

be associated with the bilateral amygdala [37]; researchers have detected higher levels of activity in this region when exposed to erotic emotional stimuli when compared to non-erotic emotional stimuli [38]. The amygdala is also known to play a crucial role in the emotional processing of penile sensation [39]. Previous studies indicated that inactivation of the amygdala during penile sexual stimulation results in reduced vigilance during sexual arousal; conversely, an active amygdala may prevent sexual arousal [40]. Furthermore, the nucleus accumbens, which is involved in male sexual arousal, is activated during penile erectile stimulation and serves as motivational component [41, 42]. The release of dopamine in the nucleus accumbens is associated with sexual desire in male rats and is known to influence the central nervous system [43]. Levels of dopamine in the nucleus accumbens of male rats have been shown to increase upon encounters

with female rats. These levels decrease during the post-mating period of inactivity [43]. The corpus callosum plays a role in integrating sensory and cognitive information by connecting different brain areas, such as the occipital and parietal cortices. These areas are known to be involved in somatosensory and visual communication [44]. Abnormal sexual arousal in ED may be related to the corpus callosum [45]. The insula is known to play a vital role in erectile behavior [46, 47] and is involved in the processing of penile input [48], the onset of erection and recognition [49, 50]. In addition, the insula can sustain penile response to erotic stimulation [51]. Studies of animal models have demonstrated that the insula is activated during sex-related processes [52]. The anterior insula is a processing center for sexual stimuli and a relay station for somatosensory signaling and emotion regulation. The insula is also responsible for collecting sexual stimuli and initiating cog-

nitive and behavioral processes to assess subjective sensations and encode stimulus-induced behaviors [53]. In a previous study, Jin *et al.* [32] found that pED patients exhibited lower resting-state spontaneous activity in the left anterior insula. Furthermore, during visual erotic stimulation, the right anterior insula of pED patients was also shown to exhibit reduced functional activation.

The cingulate gyrus is known to play roles in emotion, learning and memory, and is also associated with the abnormal occurrence of sexual arousal [53]. The anterior and middle cingulate cortex have been shown to be closely related to psychosexuality and sexual activity. The anterior cingulate gyrus is responsible for evaluating emotional information and initiating purposeful behavior. Furthermore, the anterior cingulate gyrus is also involved in regulating secretions from the gonads and the adrenal glands. Previous studies have shown that electrical stimulation of the anterior cingulate cortex can lead to the onset of erections in mammals [54, 55]. On the other hand, abnormalities in the middle cingulate cortex have been associated with poor sexual function in males. Along with subcortical structures, such as the nucleus accumbens and hypothalamus, the middle cingulate cortex may mediate the processes that direct behavior towards sexual goals [41, 47]. The posterior cingulate cortex and precuneus are responsible for integrating self-evaluation, perception, memory and attention [56, 57], as well as regulating self-reflexivity and self-reflexive processes during sexual arousal [25]. On the other hand, the hypothalamus plays a vital role in controlling androgenic sexual behavior such as penile erection and may represent the region of the brain that triggers the erectile response induced by pornographic clips [51, 58]. In addition, different subdivisions of the hypothalamus are known to be associated with different stages of penile erection in healthy men [38]. The parahippocampal gyrus, which is part of the limbic system, is located in the emotion regulation sub-network and is also involved in regulating the fundamental drivers associated with sex [59, 60].

#### **4.1.2 The frontal lobe can influence the limbic system and abnormalities in the prefrontal lobe may be associated with pED**

The frontal lobe is responsible for executive brain function, integrating and processing incoming information, and selecting appropriate emotional and motor responses. Within the motor imagery network, the inferior frontal gyrus and precentral gyrus are known to be involved in the initiation of sexual behavior [61], particularly the inferior frontal gyrus which generates conscious “sensual” experiences leading to orgasm through imagery without external stimulation [62, 63]. The prefrontal lobe is an important component of the central emotional pathway and helps to regulate activity of the limbic system [64]. Research has shown that the prefrontal lobe, along with the limbic system including the amygdala and hippocampus, significantly impact the emotional aspect of early sexual arousal models during penile erection [41, 65]. Dysfunction between the prefrontal cortex and the limbic system may result in a patient’s inability to control or regulate their nervous and anxious emotions during sexual activity [66]. Furthermore, this type of dysfunction may also lead to negative

emotions after failed attempts at sexual activity [67]. It is common to observe both structural or functional disorders in the prefrontal lobe and the limbic system in patients with pED [22]. The functions of the prefrontal lobe are performed by different components such as the dorsolateral prefrontal cortex (dlPFC), medial prefrontal cortical and orbitofrontal cortex (OFC); each of these components has its own role in emotional processing.

The dlPFC, a core region of the central executive network [68], is known for its role in response inhibition, cognitive control and attention [39]. It also plays a role in the processing of sexual information, particularly in guiding the inhibition or induction of sexual responses [69]. Abnormal functional activity in the dlPFC may represent a significant neuropathological feature of pED. Previous studies have indicated that pED patients exhibit an abnormal activity pattern in the left dlPFC, thus leading to reduced spontaneous activity [28]. Furthermore, healthy men showed greater activation of the dlPFC when viewing explicit sexual scenes [70, 71]. The ventromedial prefrontal cortex (vmPFC) is closely connected to the amygdala, which regulates emotions [72]. The vmPFC plays a significant role in processing self-related emotional information. Abnormalities in the neural network of the vmPFC may lead to mood disorders and negative psychological effects associated with adaptive cortical plasticity, potentially influencing sexual arousal in males with pED [25]. The OFC, considered a central node in the brain’s emotional circuitry, is an important hub associated with emotions. The OFC has rich connections to many emotion-related brain regions, and significant changes in emotional regulation may indicate damage or dysfunction within the OFC [73, 74].

#### **4.2 The diagnosis of pED often involves three different modalities, each with its own clinical application**

Distinguishing between pED and organic ED requires a comprehensive evaluation for patients on first presentation. This evaluation involves taking a medical and sexual history, conducting a physical examination and laboratory tests. It remains challenging to differentiate the type of ED using IIEF-5 alone [75]. Therefore, clinicians often choose a combination of treatments, such as oral PDE5I with audiovisual sexual stimulation (AVSS), intra-cavernosal injection (ICI) with CDDU and NPTR testing.

The NPTR test is a non-invasive method that effectively distinguishes between organic and pED. This test is considered the primary modality for differentiating pED from organic ED, which is often misdiagnosed as pED in individuals with normal NPTR [21]. However, there may be situational factors during the examination that can cause patient discomfort and tension during wear, potentially affecting the accuracy of the results [76]. Therefore, it may be necessary to gather data over consecutive nights to confirm the diagnosis [77]. Both sexually stimulated erections and those occurring during sleep involve the same vascular and penile structures, but they are regulated by different neural mechanisms. The mechanisms responsible for initiating and maintaining sleep-related erections remain unclear [78, 79]. In addition, Hatzichristou *et al.* [80] found



that erectile events lasting at least 10 minutes and occurring in up to 60% of the head of the penis could be considered abnormal according to the parameters of a normal NPTR test. However, this study only evaluated 12 men aged 21–24 years and therefore suffers from certain limitations, including the small sample size and the small age distribution. In contrast, Liu *et al.* [21] established the diagnostic parameters for this test as normal by referencing previous studies [81, 82]. These parameters include at least 70% of the head and base, an increase in swelling of at least 2 cm in the head and 3 cm in the base, and an event lasting not less than 10 minutes [14]. However, there is still no commonly accepted gold standard for the normal parameter values of the NPTR test.

ICI testing is often combined with CDDU [80, 83, 84]. The ICI + CDDU is highly correlated with NPTR with regards to diagnosing pED and is preferred in cases of ED involving vascular lesions [85]. Some studies suggest that there may be a delayed response after ICI for pED, and that sufficient sexual stimulation is necessary to improve erectile hardness. Re-dosing may be an option for those who do not achieve an erection after leaving the hospital [86, 87]. Santi *et al.* [88] proposed a two-step approach to identify pED. The first step involves the evaluation of medical history and hormone levels. Subsequently, an intra-penile injection of 5  $\mu\text{g}$  of prostaglandin E-1 (PGE-1) is administered. If a full pharmacological erection is not achieved, a CDDU evaluation is performed after administering another 10  $\mu\text{g}$  of PGE-1 to measure intra-penile blood flow and diagnose pED. This approach has a sensitivity of 97% and a specificity of 100% and therefore helps to avoid further unnecessary retesting [88]. The accuracy of ICI + CDDU as an invasive test may be influenced by psychological and environmental factors, leading to false negatives. In addition, its accuracy is controversial, particularly with regards to the determination of venous abnormalities based on reduced systolic maximum flow rate combined with abnormal diastolic minimum flow rate [89, 90].

According to research, the AVSS, based on RigiScan, is a relatively simple, economical and less time-consuming method that closely mimics erection during normal intercourse and is not affected by sleep [91]. However, Mizuno *et al.* [92] found that the AVSS is associated with a high false negative rate, with a sensitivity of 71% and a specificity of 92%. To further evaluate the accuracy of AVSS in identifying pED, Wang *et al.* [93] conducted a study featuring 1169 ED patients. These authors found that when the AVSS was combined with PDE5I and RigiScan tests, the sensitivity and specificity were 87.7% and 93.4%, respectively, when differentiating between psychogenic and organic ED [93]. Combining oral PDE5I with AVSS can help to mitigate the influence of vascular factors when diagnosing patients with pED. This approach offers higher levels of accuracy and can confirm the diagnosis of normal sexual desire and erectile function, even in patients with normal AVSS test results. However, factors such as the level of sexual desire, environmental and psychological factors during the examination, and the potential of adverse effects arising from a single high dose of PDE5I, can still influence the results [94]. Some researchers have attempted to minimize the influence of environmental factors by utilizing techniques such as three-dimensional head-mounted displays [95]. Data arising

from AVSS testing studies is limited and may be subject to bias. Moreover, there is a lack of standardized reference values for men in different countries. Nevertheless, considering the standards set by the European Association of Urology, AVSS may be more suitable as a primary screening tool.

### 4.3 Treatment options for pED often involve multiple therapeutic modalities

Patients with pED can be administered with a range of treatment options, including psychosexual therapy, oral medications, ICI and traditional Chinese medicine. Although 32.3% of ED patients experience an improvement in erectile symptoms after receiving a definitive pED diagnosis, many still seek treatment [96]. PDE5I, known for its convenient oral administration, effective therapeutic results, and good safety profile, has become widely accepted and is recommended as a first-line treatment for pED by multiple guidelines [97–99]. In a study involving 141 ED patients, 23% were diagnosed as having pED; of these patients, 87% benefited from sildenafil treatment [100]. However, another study reported a high failure rate of 30–40% when treated with PDE5I [101]. The reasons for failure may have included inadequate sexual stimulation, incorrect dosing and the inappropriate timing of intercourse. In a study conducted by Li *et al.* [102], 90 patients with pED were randomly assigned to either a tadalafil step-down group or a tadalafil 5 mg group. The tadalafil step-down group received a dosage of 20 mg/day for the first month, 10 mg/day for the second month, and 5 mg/day for the third month. The results showed a more significant improvement in IIEF-5 and erectile hardness score in the tadalafil step-down group when compared to the tadalafil 5 mg group [102]. Similarly, Huang *et al.* [103] conducted another study using a step-down treatment regimen with tapered discontinuation of the drug. Patients were administered a daily dose of tadalafil (5 mg) in the first month; this resulted in high efficacy and increased self-confidence in their successful sexual experiences. In the second month, the treatment continued with 5 mg of tadalafil every other day; this maintained good efficacy and achieved a cure rate of 85.71% [103]. While PDE5I can restore erectile confidence in patients with pED, the temporary use of ICI in patients who did not respond to PDE5I can also lead to immediate erection [104, 105]. Lidawi *et al.* [106] demonstrated the effectiveness of a short course of ICI therapy involving 1 to 2 self-injections. Most patients used 0.5 mL of the therapy, combined with opium poppy alkaloids (6 mg) and 6 mg of prostaglandin D<sub>1</sub>. This treatment effectively addressed psychological barriers related to sexual performance anxiety but did not result in abnormal erections. Pharmacotherapy for pED may not be accepted by some patients due to cultural and other reasons, as they believe this strategy only provides a temporary solution to the problem. In countries such as China, acupuncture is a common alternative for treating pED. While it may not result in immediate erection, acupuncture can improve IIEF-5 scores and overall sexual satisfaction. In addition, acupuncture can also alleviate symptoms such as anxiety, depression and insomnia, which are often experienced by pED patients. As a multi-targeted non-pharmacological therapy, acupuncture can be considered a viable option for the

treatment of pED [107].

pED is often attributed to a range of factors including anxiety, depression, a lack of sexual education, sexual trauma, relationship issues and previous unsuccessful sexual experiences [3, 6, 7]. In cases where treatment with PDE5I is ineffective, patients may turn to psychotherapy. However, in clinical practice, pED patients may deny the presence of psychological factors, making it challenging to obtain the patient's cooperation for psychosexual therapy alone [103]. Some studies suggest that the efficacy of psychotherapy alone is comparable to that of psychotherapy when combined with PDE5I [15]. Recently, a protocol that combines cognitive-behavioral sex therapy (CBST) with oral PDE5I has been adopted in some clinical settings [11, 108]. This protocol integrates traditional sex therapy with modern cognitive-behavioral therapy. CBST includes psychosexual education, sexual role-playing exercises, cognitive reframing of attitudes related to sexual behavior, Socratic dialogue towards sexual activity, and the development of sexual communication skills [11, 109, 110]. Previous studies have shown that patients with pED can benefit from CBST and the combination with sildenafil [108]. This combination of CBST and PDE5I may be effective in helping couples to improve their relationships and reduce the psychological distress associated with pED. This treatment approach focuses on the couple as a whole rather than solely addressing the individual symptoms of sexual dysfunction in males [111]. This highlights the importance of considering the role of the sexual partner [112]. Therefore, pED may not be solely caused by organic factors, and the treatment of pED aims to boost the patient's self-confidence and address the psychological factors that contribute to sexual intercourse difficulties by applying various therapies [113]. This approach differs from the treatment of organic ED and aligns with the European Association of Urology guidelines on ED treatment, which emphasize a holistic approach to curing the patient's symptoms [1].

## 5. Limitations

This review aimed to analyze trends in pED research and provide an update on current progress in the mechanisms, diagnostics and therapeutics of pED to inform future in-depth studies. However, it is important to note that due to the inclusion of a broad range of literature, we did not apply the Preferred Reporting Items for Systematic Reviews statement and the PICO (Participant, Intervention, Comparison and Outcomes) framework in our methodology. In addition, the insufficient evidence described in the existing literature may lead to the fact that our discussion of central nervous system abnormalities, and the diagnosis and treatment of pED, are not adequate for patients with pED.

## 6. Conclusions and future perspectives

In this study, we investigated the progress of pED research and aimed to identify new research hotspots. Based on a specific literature search, we performed an in-depth and comprehensive review that provides a new perspective on the mechanisms of occurrence, diagnosis and the treatment of pED in the future.

According to the results of this study, it was evident that pED research hotspots are targeted to central neurological mechanisms, diagnostic methods and existing treatment strategies. Given our findings, we put propose four key research priorities for the future: (a) further investigation of the pathogenesis of pED with regards to the limbic system and frontal lobes of the brain; (b) normal parameters for the NPTR testing of different races should be established as soon as possible; (c) oral PDE5I combined with sexual behavioral guidance and psychotherapy may be beneficial in the treatment of pED, and (d) pED research needs to expand to provide guidance on the direction and predictive trends of future research efforts.

## AVAILABILITY OF DATA AND MATERIALS

The data are contained within this article.

## AUTHOR CONTRIBUTIONS

HW and DYM—wrote the manuscript; HW—collected the data; ZWZ—visualization; DYM and AMW—edited the manuscript; JWZ and FW—designed the scheme. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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