

Mechanistic Study of Acupuncture in Polycystic Ovary Syndrome: Insights from the Gut-Ovary Axis

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Abstract: Gut microbiota dysbiosis can induce chronic low-grade inflammation and disrupt metabolic homeostasis and intestinal barrier function, thereby impairing ovarian function and contributing to the development of polycystic ovary syndrome (PCOS). Acupuncture, as a traditional Chinese medicine (TCM) therapy, has been shown to regulate the gut microbiota and modulate multiple cytokines, thereby exerting beneficial effects on ovarian function. Guided by the TCM theories of organs and meridian systems, this study integrates the physiological and pathological correlations between the spleen-stomach-intestine system and the ovary, along with the interconnections of meridians. Taking the gut-ovary axis mediated by intestinal microbiota as a key link, we aim to elucidate the mechanism by which acupuncture improves PCOS by modulating gut microbiota. Acupoint selection is based on the principle of restoring intestinal microbial balance, providing a novel approach to the clinical diagnosis and treatment of PCOS from the perspective of the gut-ovary axis.

Keywords: Polycystic ovary syndrome; Gut microbiota; Gut-ovary axis; Acupuncture; Immune inflammation

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1. Introduction

Polycystic ovary syndrome (PCOS) is a complex and highly heterogeneous endocrine-metabolic disorder characterized by ovulatory dysfunction, hyperandrogenism, and polycystic ovarian morphology. It is commonly accompanied by insulin resistance, chronic low-grade inflammation, obesity, and disturbances in glucose and lipid metabolism^[1]. With a global prevalence of approximately 5–10%, PCOS not only impairs female fertility but also substantially increases the risk of type 2 diabetes and cardiovascular diseases^[2,3]. Its pathogenesis involves a multifactorial interplay of dietary habits, obesity, inflammation, and dysregulation of the hypothalamic–pituitary–ovarian (HPO) axis, all of which contribute to immune-metabolic imbalances^[4]. Recent studies have

indicated that alterations in the gut microbiota (GM) can disrupt downstream metabolic homeostasis, increase intestinal permeability, and elevate circulating levels of lipopolysaccharide (LPS), thereby inducing systemic chronic inflammation and promoting the onset and progression of PCOS^[5]. The maintenance of gut microbiota homeostasis plays a crucial role in overall health and shares therapeutic relevance with acupuncture. As a traditional Chinese medical approach, acupuncture has shown promising effects in managing PCOS, particularly through its anti-inflammatory properties, modulation of gut microbiota, and improvement of metabolic regulation^[6]. This review, grounded in the theory of the “gut–ovary axis,” aims to elucidate the relationship between PCOS and gut microbiota and to explore the underlying mechanisms by which acupuncture may alleviate metabolic and inflammatory disturbances in PCOS. These insights may offer novel perspectives for clinical intervention and provide a theoretical basis for further mechanistic studies.

2. Theoretical connotations of the gut–ovary axis

2.1. Traditional Chinese medicine perspective

In Traditional Chinese Medicine (TCM), the concept of the gut–ovary axis is rooted in the holistic interplay between the organs, meridians, and reproductive function. According to TCM, “the spleen and stomach are the foundation of acquired constitution,” emphasizing their central role in generating Qi and blood. As described in the *Su Wen- Discourse on the Divergent Meridians*, “Food enters the stomach, its essence diffuses and ascends to the spleen, and the spleen disperses it to nourish the organs via the meridians.” Through the processes of digestion and transformation, the spleen and stomach extract nutrients (essence of food and water), which are transported via meridians to the kidneys, replenishing kidney essence. This essence then nourishes the Chong and Ren vessels and, in turn, supports the uterus (*bao gong*), establishing a physiological link between the intestines, spleen, kidneys, and female reproductive system.

In this process, the gut microbiota serves as a microscopic manifestation of the spleen’s transportation and transformation functions, contributing to the digestion and absorption of nutrients. Microbial metabolites influence ovarian hormone regulation, reflecting the TCM principle that “postnatal essence nourishes prenatal essence.” The *Furen Gui* further states, “Menstrual blood is derived from the essence of food and water generated by the spleen and released by the kidneys.” Therefore, impaired spleen function can disturb the distribution of Qi and blood, reduce the nourishment of kidney essence, and disrupt the Chong and Ren meridians’ support of the uterus, ultimately leading to menstrual irregularities and ovulatory dysfunction. On the other hand, the intestines and ovaries are closely connected through the meridian system.

According to the *Su Wen–Golden Chamber’s Canonical Teachings*, “The north corresponds to the color black, enters and connects with the kidneys, and opens into the two Yin orifices,” indicating that the kidneys, uterus (*bao gong*), and large intestine are linked via the Foot Taiyang Bladder Meridian. The Chong meridian is described as “penetrating Yin and Yang and serving as the sea of the twelve meridians,” while the Ren meridian “governs the uterus and fetus.” Both originate in the uterus and connect directly with intestinal meridians, thereby forming a meridian system that reflects the physiological integration of the intestines, Chong and Ren vessels, and the reproductive organs. As recorded in the *Lingshu–Divergent Meridians*, “The Foot Taiyang branches into the anus, connects to the bladder, and disperses into the kidneys,” suggesting that the intestines and kidney meridian communicate through meridians, enabling the transmission of essential Qi and blood to the uterus. The Chong and Ren meridians, serving as hubs of Qi and blood convergence, convey the refined essence derived from the

spleen and stomach via the intestines to the uterus, thus laying the foundation for menstrual cyclicity and fetal development. As articulated in the Treatise on Blood Disorders-Fetal Qi, “The arrival of menstruation relies on the heavenly water (Tian Gui) reaching the uterus, and the blood of the Chong and Ren meridians responding accordingly.” This statement encapsulates the core of the gut–ovary axis: the essence and blood generated by the spleen and stomach nourish the uterus via the Chong and Ren meridians, thereby sustaining reproductive homeostasis.

2.2. Modern medical understanding of the gut–ovary axis

A close relationship exists between gut microbiota and ovarian function. Studies have demonstrated that the composition of gut microbiota in patients with PCOS differs significantly from that of healthy individuals, providing foundational evidence for the proposed concept of the “gut–ovary axis” [7]. This theory posits that the intestine and ovaries form a regulatory network through metabolic, immune, and neuroendocrine pathways, in which disruptions in gut microbial homeostasis may impair ovarian function via systemic circulation. Accumulating evidence suggests that dysregulation of intestinal homeostasis, comprising gut microbiota, intestinal barrier integrity, and host metabolism, is closely associated with the onset and progression of PCOS [8,9].

The integrity of the intestinal barrier is central to the gut–ovary axis. This barrier, consisting of epithelial cells, tight junction proteins, mucus layers, and commensal microbes, serves as a critical defense against endotoxin translocation and inflammatory responses [10]. Under metabolic or oxidative stress, activation of hypoxia-inducible factor-1 α (HIF-1 α) and nuclear factor- κ B (NF- κ B) signaling pathways downregulates tight junction proteins such as claudin-1, leading to increased intestinal permeability or “leaky gut” [11]. Consequently, LPS and other endotoxins may translocate into the ovarian microenvironment, triggering macrophage-mediated inflammation that disrupts follicular development and hormone secretion, thereby contributing to ovarian dysfunction [12].

3. The intrinsic link between PCOS and the gut-ovary axis

3.1. Regulatory role of gut microbial metabolites

Dysregulation of gut microbial metabolites is a key driver in the pathogenesis of PCOS. Patients with PCOS commonly exhibit reduced microbial diversity and an altered Firmicutes-to-Bacteroidetes ratio, resulting in significantly decreased production of short-chain fatty acids (SCFAs) [13]. SCFAs activate G protein-coupled receptors GPR41 and GPR43, playing critical roles in regulating host energy metabolism, suppressing fat accumulation, and improving insulin sensitivity. A deficiency of SCFAs exacerbates insulin resistance and ectopic lipid deposition [14]. Gut dysbiosis often leads to elevated LPS levels, which trigger chronic low-grade inflammation and contribute to ovarian dysfunction in PCOS, as confirmed by animal studies [15]. LPS activates the toll-like receptor 4 (TLR4) signaling pathway, stimulating macrophages to release pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF- α) and interleukins (e.g., IL-6), thereby promoting both local and systemic low-grade inflammation [16]. These inflammatory mediators impair the function of theca cells and downregulate estrogen receptor alpha (ER α), reducing the sensitivity of follicles to gonadotropins and disrupting folliculogenesis [17]. Furthermore, reduced activity of bile salt hydrolase (bile salt hydrolase, BSH) impairs the synthesis of secondary bile acids, compromising the integrity of the intestinal mucus layer and further aggravating barrier dysfunction [18].

3.2. Gut microbiota-associated signaling pathways in the pathogenesis of PCOS

Gut dysbiosis leads to alterations in proinflammatory mediators, involving several signaling pathways known to contribute to PCOS pathogenesis, such as the TLR and NF- κ B pathways. Wang et al. reported that ovarian tissue and peripheral blood from PCOS patients exhibit inflammatory infiltration by macrophages, T cell imbalance, and elevated levels of proinflammatory cytokines such as IL-17 and IL-6^[19]. In addition, overgrowth of *Bacteroides vulgatus* suppresses the synthesis of glycodeoxycholic acid, thereby impairing the secretion of IL-22 by group 3 innate lymphoid cells (ILC3), disrupting the intestinal mucosal barrier, and promoting LPS translocation into the systemic circulation^[20]. Circulating LPS binds to lipopolysaccharide-binding protein (LBP), myeloid differentiation factor 2, and CD14 to form a complex that activates TLR4 receptors on immune cells^[21], thereby triggering the MyD88-dependent NF- κ B signaling pathway and inducing the expression of proinflammatory cytokines, ultimately establishing a chronic inflammatory microenvironment^[22]. These inflammatory mediators impair pancreatic β -cell function, downregulate follicle-stimulating hormone receptor expression in granulosa cells, and activate the HPO axis. This results in aberrant pulsatile secretion of gonadotropin-releasing hormone (GnRH) and an increased follicle-stimulating hormone (FSH)/luteinizing hormone (LH) ratio, exacerbating hyperandrogenism and ovulatory dysfunction. This creates a vicious cycle involving intestinal barrier disruption, systemic inflammation, and hormonal dysregulation^[23]. Moreover, gut microbiota-derived metabolites such as serotonin may reach the hypothalamus via the vagus nerve, interfere with GnRH pulsatility, accelerate follicular atresia, and contribute to neuropsychiatric symptoms such as anxiety and depression in PCOS patients^[24]. These findings underscore the complex interplay between the gut, immune system, and ovarian function in PCOS, highlighting the integrative regulatory role of the gut–ovary axis in disease progression and providing a theoretical basis for targeted therapeutic interventions.

4. Acupuncture regulation of the gut–ovary axis in PCOS

4.1. Regulatory effects of acupuncture on the gut–ovary axis

4.1.1. Acupuncture improves gut microbiota composition

Acupuncture can modulate gastrointestinal motility and enhance intestinal mucosal barrier function, thereby promoting the restoration of gut homeostasis and improving both metabolic and reproductive functions in patients with PCOS. Studies have shown that acupuncture at acupoints such as Zusanli (ST36) and Tianshu (ST25) significantly promotes intestinal peristalsis, reduces intestinal permeability, and improves the ratio of Firmicutes to Bacteroidetes, contributing to the alleviation of energy metabolism disorders and insulin resistance^[25,26]. In addition, acupuncture has a regulatory effect on the gut microbiota, increasing microbial diversity and promoting the production of SCFAs. Li *et al.*^[27] reported that combined acupuncture and herbal medicine treatment significantly increased the abundance of *Bifidobacterium* and *Lactobacillus* in PCOS patients, while reducing the proportion of pro-inflammatory bacteria, potentially through modulation of glucose and lipid metabolism via the TLR4 signaling pathway. In the regulation of gut microbiota, acupuncture not only enhances the spleen and stomach functions responsible for digestion and absorption, thereby improving intestinal nutrient uptake and metabolic capacity, but also regulates the metabolic efficiency of microbial metabolites. These effects result in a coordinated therapeutic mechanism, integrating systemic regulation with local modulation, which contributes to the comprehensive treatment of PCOS.

4.1.2. Acupuncture suppresses inflammatory signaling along the gut–ovary axis

Acupuncture can inhibit inflammatory signaling pathways such as TLR4/NF- κ B, thereby interrupting the

pathological cascade in which intestinal barrier disruption leads to systemic inflammation and subsequent ovarian dysfunction. Zhang *et al.* [28] reported that electroacupuncture significantly reduced both visceral and subcutaneous fat accumulation in PCOS rats, while also improving their estrous cycles and reproductive function. Specifically, electroacupuncture restored the gut microbiota composition toward a more balanced state, an effect potentially associated with suppression of the LPS-mediated TLR4 signaling pathway [29].

Further research by Ding *et al.* [30] demonstrated that acupuncture at ST36 downregulated NF- κ B expression via the SCFA/FFAR3 pathway, thereby correcting dysbiosis, enhancing intestinal barrier integrity, and alleviating systemic low-grade inflammation. In this process, different acupoints may exert distinct anti-inflammatory effects. For instance, Daimai (GB26) may be more effective in regulating the flow of Qi and blood along the Chong and Ren meridians, while Zusanli focuses on modulating metabolic function in the middle jiao. Through its multi-targeted actions, acupuncture can simultaneously repair intestinal barrier dysfunction and attenuate local ovarian inflammation; however, its underlying molecular mechanisms warrant further investigation.

4.1.3. Acupuncture modulates systemic immune function

Acupuncture modulates systemic immune homeostasis by activating the HPO axis, thereby achieving neuro–endocrine–immune regulation through acupoint stimulation [31]. Studies have shown that warm acupuncture can regulate the secretion of GnRH, LH, and FSH, reduce inflammatory responses, and promote follicular development and endometrial growth [32]. Moreover, acupuncture facilitates the proliferation of beneficial gut microbiota such as *Lactobacillus* and *Bifidobacterium*, enhancing mucosal immune barrier function, suppressing LPS translocation and endotoxemia, and mitigating chronic low-grade inflammation associated with PCOS [33]. Jiang *et al.* [34] found that acupuncture at Zhongwan (CV12) and Sanyinjiao (SP6) significantly increased the proportion of regulatory T cells and inhibited the overactivation of Th17 cells, thereby improving the local ovarian immune microenvironment. Additionally, the meridian effects of acupuncture can alleviate abnormal visceral tension caused by functional dysregulation, thereby enhancing ovarian blood flow and optimizing the follicular development microenvironment [35]. Therefore, acupuncture exerts a bidirectional immunomodulatory effect—suppressing excessive inflammation while enhancing immune tolerance—which is particularly relevant in addressing the chronic inflammatory state of PCOS.

4.2. Acupoint selection

In acupuncture treatment for PCOS, acupoint selection is guided by the principles of strengthening the spleen and stomach to enhance transformation and transportation [5], and regulating local Qi and blood [36], with attention to local and systemic effects. Common local points include Guanyuan (CV4), Zhongji (CV3), Guilai (ST29), and Zigong (EX-CA1), which act directly on the uterus to improve Qi and blood flow in the ovaries and uterus. In addition, middle jiao points such as ST25, GB26, ST36, Shangjuxu (ST37), and Xiajuxu (ST39) are selected to restore the spleen and stomach's ascending and descending functions and help rebalance the gut microbiota.

ST25, the Front-Mu point of the Large Intestine on the Foot-Yangming Stomach Meridian, is also connected to the Chong and Ren vessels. According to the Qian Jin Fang, it is traditionally used to treat lower abdominal pain and prolonged or irregular menstruation caused by blood stasis and uterine dysfunction. Acupuncture at Tianshu helps to clear turbidity and promote the ascent of clear Qi, facilitating gut microbiota metabolism. It is also effective for irregular menstruation and pelvic pain. Studies have shown that acupuncture at Tianshu can indirectly reduce androgen levels, promote follicular development, and restore ovarian function, possibly through

downregulation of hypothalamic Kisspeptin expression and improvement of HPO axis function ^[37]. GB26 is a key acupoint for resolving phlegm, dampness, and blood stasis. Shen *et al.* ^[38] found that electroacupuncture at Daimai improved insulin resistance in PCOS rats, potentially by modulating NF- κ B signaling protein expression in the hypothalamus. Furthermore, pairing ST36 with the lower he-sea points ST37 and ST39 enhances the spleen and stomach's transformative functions, promotes the descent of intestinal Qi, and clears damp-heat. Electroacupuncture at these points has been shown not only to regulate gut microbiota composition but also to alleviate ovarian dysfunction caused by chronic inflammation. The underlying mechanism may involve reduced serum levels of TNF- α and IL-1 β ^[39,40]. These synergistic effects of multiple acupoints help improve the reproductive microenvironment and modulate metabolic and immune imbalances via the gut–ovary axis, reflecting the holistic and dual-target (root and symptom) approach of acupuncture therapy.

5. Conclusion

According to TCM, the spleen, stomach, and intestinal organs are functionally connected to the ovaries through meridians and the circulation of Qi and blood. Disruption of Qi dynamics in the six fu-organs can lead to gut microbiota imbalance, resulting in the downward flow of damp-heat and phlegm-turbidity along the Chong and Ren meridians, which impairs ovarian function. Modern research has revealed that dysbiosis of the gut microbiota interacts bidirectionally with ovarian function via microbial metabolites and compromised intestinal barrier integrity. This interaction promotes chronic inflammation and metabolic disturbances, both of which are recognized as key contributors to the pathogenesis of PCOS. Acupuncture exerts therapeutic effects by modulating the composition of gut microbiota, suppressing inflammatory pathways, and improving metabolic homeostasis, thereby regulating the gut–ovary axis. In clinical practice, acupoint selection should integrate both local and systemic approaches—combining points such as CV4 and EX-CA1 with middle-jiao points like ST36, ST37, and CV12—to help restore intestinal microbial balance. Despite growing interest in gut microbiota and acupuncture, studies focusing on their interaction in PCOS are still scarce. Future studies should further investigate the mechanisms by which acupuncture regulates the gut microbiota to treat PCOS to provide a solid theoretical foundation and practical guidance for precision therapy.

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