

Research progress on the central mechanism of gut microbiota-mediated acupuncture in improving glycolipid metabolic disorders in the elderly

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ABSTRACT

With global population aging, age-related glucose and lipid metabolic dysregulation has become a critical public health challenge. Acupuncture, a safe non-pharmacological intervention, is widely used to manage such metabolic disorders. Impairment of the gut–brain axis (GBA) is a key pathogenic driver of this condition, and has emerged as a novel target for exploring acupuncture's therapeutic mechanisms. This review synthesizes recent research on acupuncture regulating the GBA in elderly individuals with glucose and lipid dysregulation. Evidence shows acupuncture acts via multiple GBA nodes: reversing gut microbiota dysbiosis, restoring intestinal/blood–brain barrier integrity, inhibiting gut-derived pro-inflammatory factors, and reestablishing hypothalamic metabolic regulation. These findings provide theoretical support for precise clinical application of acupuncture, and offer new directions for targeted intervention research in age-related metabolic disorders.

KEYWORDS

acupuncture, aged, glucose and lipid metabolism disorders, gut–brain axis, microbiota

1 Introduction

Against the backdrop of global population aging, glucose and lipid metabolic dysregulation in the elderly has emerged as a pressing public health concern, with a high prevalence among individuals aged 60 years and above [1]. This condition is closely intertwined with age-related physiological deterioration, including adipose tissue senescence, impaired digestive function, immune-metabolic imbalance, and gut microbiota dysbiosis. By interfering with lipid accumulation and insulin sensitivity [2], it accelerates the onset and progression of metabolic disturbances and readily precipitates multiple severe complications. Notably, it not only acts as a key precursor to type 2 diabetes [3] but also substantially increases cardiovascular disease risk—specifically by elevating triglyceride and low-density lipoprotein cholesterol levels while reducing high-density lipoprotein cholesterol—thereby exacerbating carotid atherosclerosis [4]. Collectively, these consequences severely compromise the quality of life of

elderly individuals.

Currently, clinical management of metabolic disorders in elderly individuals primarily encompasses Western pharmaceutical therapies, lifestyle modifications, and nutritional support [5]. While Western medications—including hypoglycemic agents and lipid-lowering drugs—can rapidly ameliorate metabolic parameters, long-term administration may induce adverse effects such as hepatorenal burden, gastrointestinal adverse reactions [6], and inadequate target organ protection in elderly patients [7]. Lifestyle interventions (e.g., dietary modification, structured exercise) are highly dependent on patient compliance; however, elderly individuals often confront barriers including compromised physical capacity and multiple comorbidities, rendering sustained adherence to standardized regimens challenging [8]. Nutritional support, meanwhile, is hampered by poor individual adaptability, failing to precisely align with the heterogeneous metabolic demands of diverse elderly

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patients [9]. In contrast, acupuncture—a non-pharmacological, minimally invasive physical intervention—boasts distinct advantages including multi-targeted regulation, minimal adverse effects, and long-term tolerability [10]. It not only mitigates age-related glucose and lipid metabolic dysregulation but also modulates overall bodily homeostasis, which is congruent with the physiological tolerance profiles of geriatric populations [11].

However, the underlying mechanisms through which acupuncture alleviates age-related glucose and lipid metabolic dysregulation remain incompletely elucidated. The traditional Chinese medicine (TCM) concept of “unblocking meridians and harmonizing qi and blood” is difficult to reconcile with modern medical pathophysiological pathways. Against this backdrop, the GBA—a pivotal hub integrating intestinal microbiota and central metabolic regulation—provides a novel research paradigm for deciphering acupuncture’s therapeutic mechanisms. As a critical bidirectional communication pathway linking intestinal function to central metabolic control, the GBA transmits signals via three core modalities: neural, humoral, and immune [12]. Its fundamental mechanism hinges on the capacity of gut microbiota-derived metabolites and inflammatory factors to modulate central metabolic networks across the blood–brain barrier (BBB), thereby regulating the maintenance of glucose and lipid metabolic homeostasis [13]. In elderly individuals, age-associated gut physiological alterations—including microbiota dysbiosis and compromised intestinal barrier integrity—can disrupt central metabolic regulation via the GBA, further exacerbating glucose and lipid metabolic disturbances [14].

Acupuncture, a safe and well-validated non-pharmacological intervention, has been shown to improve glucose and lipid metabolism-related parameters in elderly populations, featuring distinct clinical merits including proven efficacy and minimal adverse effects [15]. Nevertheless, substantial research gaps persist: First, direct investigations into the GBA-associated pathological mechanisms underlying age-related glucose and lipid metabolic disorders are scarce. Second, the key targets and specific signaling pathways through which acupuncture modulates the GBA to alleviate metabolic dysregulation in elderly individuals remain elusive. In light of these gaps, this review focuses on the mechanisms by which acupuncture regulates glucose and lipid metabolic disorders in the elderly via the GBA. It synthesizes relevant research progress to provide a scientific foundation and novel insights for expanding non-pharmacological prevention and treatment strategies for age-related glucose and lipid metabolic disturbances.

2 Clinical application of acupuncture in improving glucose and lipid metabolism in the elderly

A growing body of clinical evidence indicates that acupuncture exerts a positive regulatory effect on age-related glucose and lipid metabolic dysregulation, with its clinical utility increasingly validated by evidence-based medicine.

In terms of glycemic control, a systematic review and meta-

analysis by Chen et al. on acupuncture for type 2 diabetes confirmed that needling Zusanli (ST36) and Sanyinjiao (SP6), combined with Neiguan (PC6), Taichong (LR3), and Yanglingquan (GB34), significantly reduced fasting plasma glucose, postprandial plasma glucose, and glycated hemoglobin (HbA1c) levels in middle-aged and elderly patients with type 2 diabetes—with the reduction in HbA1c reaching statistical significance ($P < 0.01$) [16]. Concurrently, acupuncture mitigates insulin resistance (IR), a pathological state characterized by diminished tissue insulin sensitivity that impairs effective glucose uptake, utilization, and storage, thereby precipitating glucose metabolic disturbances [17]. Attenuated IR enhances tissue responsiveness to insulin, enabling insulin to efficiently promote glucose uptake, utilization, and storage—ultimately lowering fasting and postprandial glucose levels and sustaining glycemic homeostasis [18]. A randomized controlled trial (RCT) by Han et al., involving metabolic syndrome patients with a mean age of approximately 50 years, demonstrated that acupuncture at Zusanli (ST36) and Sanyinjiao (SP6), combined with syndrome differentiation-based adjunctive points (Tianshu (ST25), Zhongwan (CV12), Fenglong (ST40), and Taichong (LR3)), directly ameliorates IR, significantly reduces patients’ Homeostatic Model Assessment of IR (HOMA-IR) scores, and concomitantly enhances glycemic control [19].

In terms of lipid metabolism regulation, a systematic review and meta-analysis by Zhang et al. on acupuncture for peripheral neuropathy in elderly diabetic patients demonstrated that acupuncture at Zusanli (ST36), Sanyinjiao (SP6), Yanglingquan (GB34), and Taichong (LR3) significantly reduced serum total cholesterol (TC), triglyceride (TG), and low-density lipoprotein cholesterol (LDL-C) levels in middle-aged and elderly patients with type 2 diabetes—while concurrently elevating high-density lipoprotein cholesterol (HDL-C) concentrations [20]. These clinically meaningful improvements furnish direct evidence for the utility of acupuncture in managing age-related lipid metabolic dysregulation, underscoring the imperative to unravel the underlying GBA-mediated mechanisms.

In view of the frequent selection of ST36 Zusanli, SP6 Sanyinjiao, and ST25 Tianshu in clinical practice, these acupoints demonstrate distinct specificity based on traditional Chinese medicine (TCM) meridian theory. As the He-Sea point of the stomach meridian of Foot Yangming, ST36 tonifies spleen–stomach qi, regulates middle jiao, and resolves phlegm-dampness, which specifically targets qi deficiency and phlegm obstruction underlying elderly metabolic disorders. Such effects may be associated with metabolic regulation, alleviation of intestinal inflammation, protection of the intestinal barrier, and improvement of insulin resistance, possibly via the vagus nerve–cholinergic anti-inflammatory pathway. As the converging point of the liver, spleen, and kidney meridians (three yin meridians of foot), SP6 tonifies spleen qi, nourishes kidney yin, and harmonizes metabolic function. It is particularly suitable for elderly patients with qi-blood deficiency and declined metabolism, and contributes to neuroendocrine and metabolic balance. As the Front-Mu point of the large intestine meridian, ST25 regulates intestinal qi movement and intestinal function. These actions may

contribute to improved intestinal motility, optimized microbiota environment, and enhanced short-chain fatty acid secretion, which may in turn provide important intestinal support for metabolic improvement.

Considering the frail physique, multiple comorbidities, and low tolerance of elderly individuals, acupuncture parameters can be refined following the principles of mild stimulation, low intensity, individualization, and prolonged treatment. Manual acupuncture or low-frequency electroacupuncture (2–10 Hz) is recommended, with gentle manipulation to achieve deqi without obvious pain. Each session lasts 20–30 min, 3–4 times weekly, for 8–12 weeks. For elderly patients with hypertension or osteoporosis, reduced stimulation, shallower needle depth, and alternating unilateral acupoint selection are advised to minimize physical burden.

3 The relationship among gut microbiota, the gut–brain axis, and age-related glucose and lipid metabolic dysregulation in the elderly

The GBA denotes a bidirectional signaling pathway that connects the central nervous system (CNS) and the gastrointestinal tract. It forms an intricate network via three core signaling modalities: neural (predominantly through the vagus nerve), endocrine (mediated by hormones), and immune (driven by cytokines) [21]. The structure and functional integrity of this bidirectional communication system are directly modulated by the gut microbiota and intestinal barrier integrity. Dysregulation of the GBA constitutes a pivotal pathogenic factor in the onset and progression of age-related glucose and lipid metabolic disorders. The subsequent sections will elaborate on this mechanism by focusing on three interconnected processes: age-associated gut microbiota dysbiosis, age-related intestinal barrier impairment, and BBB damage induced by systemic inflammatory responses.

3.1 Age-related gut microbiota dysbiosis

The gut microbiota denotes the collective term for all microbial communities colonizing the human gastrointestinal tract, forming a symbiotic relationship with the host. It is predominantly composed of bacteria, fungi, viruses, archaea, and protozoa—with bacteria (e.g., the phyla Firmicutes and Bacteroidetes) serving as core components. The diversity, abundance, and functional homeostasis of these microbial communities are closely linked to host health [22].

During human aging, the contractile function of intestinal smooth muscle declines, resulting in a marked reduction in intestinal motility. This prolongs the transit time of food in the intestinal lumen, decreases bacterial excretion, and disrupts microbial fermentation processes—thereby impeding the colonization of beneficial bacteria [23]. Concurrently, impaired digestive secretion reduces gastric acid and digestive enzyme levels, increasing the prevalence of conditions such as atrophic gastritis. This further elevates intestinal pH, disrupting the acidic microenvironment favored by beneficial bacteria (e.g., *Bifidobacterium* and *Enterococcus faecalis*) [24]. Alterations in the intestinal microenvironment also involve abnormal oxygen tension: increased local oxygen exposure in the aging gut inhibits the proliferation of obligate anaerobic

beneficial bacteria (e.g., short-chain fatty acid producers), while facultative anaerobic pathogens adapt and colonize more readily [25]. Furthermore, aging is accompanied by a global decline in both innate immunity (e.g., reduced neutrophil and macrophage functionality) and adaptive immunity (e.g., imbalance in T/B cell subsets) [26]. This compromises the intestinal mucosal immune barrier's capacity to recognize and regulate the microbiota [27], failing to effectively constrain pathogenic bacterial overgrowth and ultimately exacerbating dysbiosis [28]. This microbial imbalance is particularly prominent in elderly individuals with metabolic abnormalities [29], whereas healthy centenarians typically maintain high abundances of beneficial bacteria—highlighting the critical role of the gut microbiota in sustaining metabolic homeostasis [30].

Altered gut microbiota composition directly impairs its metabolic functionality, primarily via reduced production of beneficial metabolites (e.g., short-chain fatty acids), increased synthesis of harmful metabolites (e.g., lipopolysaccharides (LPS)), and dysregulated levels of signaling molecules (e.g., bile acids). Short-chain fatty acids (SCFA)—such as butyrate and propionate—not only serve as primary energy sources for intestinal epithelial cells but also directly modulate systemic glucose and lipid metabolism [31]. In contrast, elevated LPS levels compromise intestinal barrier integrity, translocate into the systemic circulation, and elicit chronic low-grade inflammation that contributes to IR [32]. Microbiota perturbations also alter the composition and proportions of secondary bile acids; as signaling molecules, bile acids directly engage receptors in the liver and adipocytes (e.g., farnesoid X receptor (FXR), G protein-coupled bile acid receptor 1 (TGR1)) to regulate glucose, lipid, and energy homeostasis [33]. Imbalances in these key metabolic products represent a pivotal initiating event that concurrently drives peripheral metabolic organ dysfunction and disrupts GBA communication.

3.2 Microbial dysbiosis exacerbates age-related damage to the elderly intestinal barrier

The intestinal barrier integrity serves as a primary defensive mechanism for maintaining host homeostasis, while the aging process itself constitutes an intrinsic driver of its functional deterioration [34]. Studies confirm that with advancing age, the proliferative and self-renewal capacities of intestinal stem cells diminish significantly, leading to delayed epithelial repair and a consequent increase in the barrier's inherent structural fragility [35]. Concurrently, the expression of core tight junction proteins between epithelial cells—such as Occludin and zonula occludens-1 (ZO-1)—exhibits characteristic downregulation in elderly individuals and animal models, further compromising the barrier's physical sealing function [36].

Against this backdrop of age-related vulnerability, gut microbiota dysbiosis emerges as a key extrinsic driver that exacerbates barrier impairment [37]. The imbalanced microbiota orchestrates a coordinated assault on the elderly intestinal barrier primarily through two interconnected pathways: First, metabolic support deprivation. Reduced abundance of beneficial commensal bacteria leads to a marked decrease in SCFA—particularly butyrate—produced via

dietary fiber fermentation [38]. Butyrate not only acts as the primary energy source for colonocytes but also promotes tight junction protein expression and assembly by inhibiting histone deacetylases (HDACs). Consequently, SCFA deficiency directly impairs epithelial cell energy metabolism and active repair capacity [39]. Second, direct toxic insult. Microbiota dysbiosis is often accompanied by an abnormal increase in Gram-negative bacteria, leading to elevated production of the bacterial endotoxin LPS. LPS activates Toll-like receptor 4 (TLR4) on intestinal epithelial cells, initiating pro-inflammatory signaling pathways such as nuclear factor- κ B (NF- κ B). This directly induces phosphorylation and internalization of tight junction proteins, disrupting their structural integrity and function [40]. Further studies suggest that TLR4 expression or responsiveness may be enhanced in aged intestines, rendering them more susceptible to LPS-mediated damage [41].

Under the combined effects of age-related intrinsic frailty and microbial extrinsic assault, the intestinal barrier exhibits pathologically increased permeability. Ultimately, barrier dysfunction facilitates the translocation of intestinal contents into the systemic circulation, resulting in a “leaky gut” phenotype [42]. This process has been identified as the initiating link in triggering and sustaining systemic chronic low-grade inflammation, laying the groundwork for subsequent central nervous system dysfunction. Once intestinal barrier integrity is compromised, gut-derived endotoxins and harmful microbial metabolites can directly enter the bloodstream, disrupting the body’s homeostatic regulation of glucose and lipids [43]. Simultaneously, the absorption and utilization of beneficial metabolites such as SCFA are significantly reduced, abrogating their protective regulatory effects on glucose and lipid metabolism [44]. Furthermore, intestinal barrier damage leads to unregulated absorption of glucose and lipids, causing massive influx of sugars and fats into the bloodstream and resulting in acute elevations in blood glucose and lipid levels [45]. Moreover, pathogenic gut microbiota can directly translocate to key metabolic organs—including the liver and pancreas—directly impairing hepatic lipid metabolism and pancreatic secretory function, thereby further exacerbating glucose and lipid metabolic dysregulation [46].

3.3 Systemic inflammatory damage to the BBB disrupts central metabolic regulation

Intestinal permeability, also termed impaired intestinal barrier function, denotes compromised mucosal barrier integrity that permits the abnormal translocation of irritant molecules, bacterial byproducts, and undigested macromolecules—substances otherwise sequestered—across the intestinal wall into the systemic circulation, thereby activating the immune system and eliciting a systemic inflammatory response [47]. Persistent entry of pathogen-associated molecular patterns (PAMPs) such as LPS into the bloodstream induces sustained upregulation of pro-inflammatory cytokines including interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α). These inflammatory mediators circulate to the CNS, directly targeting the neurovascular units of the BBB [48]. A study by He et al. confirmed that LPS activates the Toll-like receptor 4/nuclear factor κ B (TLR4/NF- κ B) signaling pathway, which

downregulates the expression of tight junction proteins in BBB endothelial cells and markedly increases vascular permeability [49]. This identifies systemic inflammation as the core pathological bridge linking intestinal barrier damage to BBB leakage.

Increased BBB permeability directly disrupts the CNS’s immune-privileged microenvironment, enabling peripheral pro-inflammatory cytokines (IL-6, TNF- α) and microbial metabolites such as trimethylamine N-oxide (TMAO) to cross the barrier and infiltrate the brain parenchyma. This triggers microglial activation and subsequent neuroinflammation [50], which further impairs the function of key central metabolic regulatory hubs including the hypothalamus: it compromises leptin- and insulin-mediated signaling for appetite and energy balance, and suppresses central insulin signaling pathways—markedly reducing the brain’s capacity to orchestrate systemic glucose and lipid metabolism [51]. In mechanistic animal studies using diet-induced obesity (DIO) mouse models of type 2 diabetes, Salameh et al. found that BBB leakage induces aberrant expression of hypothalamic metabolism-related genes, directly precipitating central IR and dyslipidemia. This ultimately disrupts whole-body glucose and lipid homeostasis, with clinical manifestations of hyperglycemia and dyslipidemia [52].

4 Regulatory effects of acupuncture on gut microbiota

4.1 Clinical evidence of acupuncture’s regulation of gut microbiota

The clinical value of acupuncture in modulating the gut microbiota has been validated by numerous RCTs and meta-analyses. As an effective intervention for ameliorating microbiota dysbiosis-associated disorders in elderly populations, acupuncture achieves a gut microbiome reset effect via targeted acupoint combinations—its clinical significance extends far beyond improving the abundance, diversity, and beneficial metabolite production of the gut microbiota. It simultaneously alleviates common geriatric morbidities linked to dysbiosis, including constipation and cognitive impairment. Acupuncture exerts these therapeutic effects through multi-targeted mechanisms, encompassing the targeted promotion of beneficial bacterial proliferation and the inhibition of pathogenic bacterial overgrowth. This clinical evidence furnishes critical support for investigating the mechanistic underpinnings by which acupuncture alleviates age-related glucose and lipid metabolic dysregulation in the elderly via the GBA. Table 1 summarizes representative recent clinical studies on acupuncture-mediated modulation of the gut microbiota in elderly individuals.

Current clinical research on acupuncture-mediated modulation of the elderly gut microbiota is in the preliminary stage, with existing studies mainly focusing on populations with functional constipation and metabolic syndrome.

4.2 Experimental research progress on acupuncture regulation of gut microbiota

In recent years, a wealth of experimental studies using rodent

Table 1 Clinical application of acupuncture in regulating gut microbiota in the elderly

Document Type/Research Subject	Intervention Program	Primary Outcome Measures	Conclusions and Findings	Ref.
RCT/80 top-aged and elderly patients with functional constipation	Acupuncture at bilateral Tianshu (ST25), Fuijie (SP14), and Shangjuxu (ST37) points, administered 4 times per week for a total of 16 sessions over 4 weeks.	Indicators: Gut microbiota abundance, diversity indices, fecal SCFA. Results: Significantly increased abundance of beneficial bacteria such as <i>Lactobacillus</i> and reduced abundance of potentially pathogenic bacteria such as <i>Pseudomonas</i> ; enhanced α and β diversity indices of gut microbiota; markedly elevated fecal butyrate levels.	Acupuncture has been shown to reshape the gut microbiota structure, increase diversity, and promote the production of the beneficial metabolite butyrate.	Ref. [53]
RCT/82 patients with ischemic stroke (predominantly top-aged synchrony) and elderly	Acupuncture was administered using the “brain–gut synchrony” protocol, targeting Baihui (GV20), Tianshu (ST25), Zusanli (ST36), and Dachangshu (BL25) points, 5 times per week for 12 consecutive weeks.	Indicators: Gut microbiota α/β diversity indices, relative abundance of specific bacterial genera. Results: Significant increases in both α and β diversity of gut microbiota; relative abundance of beneficial genera (<i>Bifidobacterium</i> , <i>Lactobacillus</i>) was upregulated, while potential pathogenic genera were downregulated.	Acupuncture modulates the gut microbiota structure in top-aged and elderly ischemic stroke patients via the “brain–gut synchrony” mechanism. This microbiota improvement was positively correlated with the recovery of brain–gut function, confirming acupuncture’s regulatory effect on the brain–gut axis–microbiota pathway.	Ref. [54]
RCT/62 patients with mild cognitive impairment	Acupuncture at Baihui (GV20), Sishencong (EX-HN1), bilateral Fengchi (GB20), Xuanzhong (GB39), Zusanli (ST36), Yanglao (SI6), and Xinshu (BL15), once every other day, 3 times per week, for a total of 12 weeks.	Indicator: Relative abundance of specific gut bacterial genera. Results: Significant increases in relative abundance were observed for the genera <i>Prasollobacter</i> , <i>Clostridium</i> , and the family Ruminococcus.	Acupuncture can specifically regulate the gut microbiota in patients with cognitive impairment, potentially acting through the GBA.	Ref. [55]
Meta-analysis/12 RCTs, 1164 elderly patients with irritable bowel syndrome (IBS)	Acupuncture at points including Tianshu (ST25), Zusanli (ST36), Da Chang Shu (BL25), and Shangjuxu (ST37), administered 2–3 times per week, treatment continues for 4–8 consecutive weeks.	Indicator: Abundance of beneficial and pathogenic bacteria in the gut. Results: Significantly increased abundance of beneficial bacteria such as <i>Bifidobacterium</i> and <i>Lactobacillus</i> , while inhibiting excessive growth of pathogenic bacteria.	Acupuncture effectively improves gut microbiota dysbiosis in elderly patients with irritable bowel syndrome.	Ref. [56]
Clinical observation/68 patients with post-stroke constipation	Acupuncture points including Shuidao (ST28) and Guilai (ST29), once per day; continuous treatment for 2 weeks.	Indicators: Constipation symptoms, SCFA specific microbial populations. Results: Constipation symptoms improved; butyrate and total SCFA concentrations increased; α -diversity index increased; abundance of beneficial bacteria such as <i>Bifidobacterium</i> and <i>Lactobacillus</i> increased; abundance of pathogenic bacteria such as <i>Escherichia coli</i> decreased.	Acupuncture improves post-stroke constipation, with its mechanism potentially involving regulation of gut microbiota composition and increased beneficial metabolites.	Ref. [57]

Note: RCT = randomized controlled trial; SCFA = short-chain fatty acids. Data summarized from Refs. [53–57]. All data are synthesized from publicly available research findings in compliance with academic fair use principles.

models has conclusively demonstrated that acupuncture can effectively modulate the structure and diversity of the gut microbiota in various pathological models via stimulation of specific acupoints. The role of electroacupuncture (EA) in regulating microbial diversity has been corroborated by multiple investigations. For instance, Wang et al. explored EA's effects on the gut microbiota in high-fat diet-induced abdominal obesity rats; via 16S rRNA sequencing, they confirmed that bilateral stimulation at Daimai (GB26) increased gut microbial α -diversity and ameliorated dysbiosis [58]. Similarly, Xu et al. observed in a post-stroke depression (PSD) rat model that acupuncture at Hegu (LI4) and Taichong (LR3) significantly restored gut microbial diversity to normal levels [59].

Building on these findings, numerous studies have further elucidated the specific mechanisms underlying acupuncture-mediated gut microbiota modulation. The core effects encompass promoting the proliferation of beneficial bacteria, inhibiting the overgrowth of pathogenic bacteria, and regulating the relative abundance of specific phyla, classes, and genera—with research focusing heavily on EA in this domain. Yang et al. found that EA at Zusanli (ST36) and Tianshu (ST25) significantly enhanced the proliferation of SCFA-producing bacteria (e.g., Clostridiaceae and Ruminococcaceae families), thereby correcting microbiota dysbiosis [60]. Li et al. also observed that EA at Hegu (LI4) and Taichong (LR3) increased the abundance of beneficial bacteria in the *Bifidobacterium* group (including *Trichoderma* and *Clostridium*) while reducing pathogenic strains (*Bacteroides* and *Bacillus*), bringing the gut microbiota composition closer to that of normal rats [61]. In experiments on senescence-accelerated mouse prone 8 (SAMP8) mice, Jiang et al. demonstrated that EA at Baihui (GV20), Dazhui (GV14), Shenshu (BL23), and Zusanli (ST36) balanced gut microbiota composition—notably decreasing the relative abundance of Delta-proteobacteria and Epsilon-proteobacteria—while suppressing inflammatory responses in both the peripheral and central nervous systems [62].

Beyond EA, conventional acupuncture and warming acupuncture also exert regulatory effects on the gut microbiota. He et al. found that acupuncture at Baihui (GV20) and Yongquan (KI1) in a D-galactose-induced Alzheimer's disease (AD) mouse model significantly increased the abundance of beneficial bacteria (e.g., *Bifidobacterium*) and reduced harmful strains (e.g., *Clostridium*), accompanied by decreased serum levels of pro-inflammatory cytokines (e.g., TNF- α , IL-1 β) [63]. Hao et al. focused on gut fungal communities in APP/PS1 AD mice, confirming that acupuncture at Sishencong (EX-HN1), Fengchi (GB20), and Xuanzhong (GB39) improved fungal dysbiosis. This intervention increased the Sobs, Chao, and Ace indices of fungal communities, reduced the abundance of opportunistic pathogens (e.g., Ascomycota, Aspergillaceae, and *Candida*), and elevated the abundance of Basidiomycota [64]. Zheng et al. employed Weng tong acupuncture to stimulate acupoints including Dazhui (GV14) and Mingmen (GV4) in elderly rats with primary osteoporosis and intestinal dysfunction. Results showed that this therapy increased the abundance of beneficial bacteria (e.g., *Bacteroides*, *Lactobacillus*, and *Enterococcus*), reduced harmful strains (e.g., *Clostridium*),

improved intestinal dysfunction, and enhanced bone mineral density [65].

5 Mechanisms of acupuncture regulation of gut microbiota in improving glycolipid metabolism in the elderly

5.1 Acupuncture reverses age-related gut microbiota dysbiosis

Restoring gut microbiota homeostasis is crucial for alleviating age-related glucose and lipid metabolic dysregulation in the elderly. Acupuncture modulates the gut microbiota primarily by enhancing intestinal motility and optimizing microbial community composition. EA stimulation at specific acupoints such as Zusanli (ST36) effectively activates local nerve fibers; signals are transmitted via afferent nerves to the spinal cord and brainstem (e.g., nucleus of the solitary tract (NTS)), thereby activating the dorsal vagal nucleus (DVN) that innervates the gastrointestinal tract. This subsequently promotes the release of acetylcholine (ACh) from vagal nerve terminals [66]. The released ACh binds to muscarinic acetylcholine receptors (mAChRs) on intestinal smooth muscle cells and enteric neurons, directly enhancing the contractility and rhythmicity of intestinal smooth muscle [67]. This markedly increases intestinal transit rates and restores the normal emptying rhythm of intestinal contents, facilitating the timely elimination of excessively proliferating facultative anaerobic pathogens in the aging gut while reestablishing a favorable microenvironment for obligate anaerobic beneficial symbionts (e.g., SCFA-producing genera *Faecalibacterium* and *Ruminococcus*) [68]. This mechanism holds significant potential for reversing age-related reductions in beneficial gut microbiota abundance in elderly individuals.

5.2 Acupuncture repair of the elderly intestinal barrier and BBB

Acupuncture's dual protective effects on the intestinal barrier and BBB, coupled with its systemic anti-inflammatory activity, constitute key mechanisms for alleviating age-related glucose and lipid metabolic dysregulation in the elderly. As critical barriers that prevent pathological signal transmission to the CNS, these two barriers are simultaneously protected by acupuncture through the synergistic effects of systemic anti-inflammation and barrier repair [69].

First, acupuncture can suppress the release of enteric and centrally mediated pro-inflammatory cytokines (e.g., TNF- α , IL-6) [70]. In a study exploring acupuncture's regulation of intestinal macrophage polarization and inflammatory factors, Liu et al. found that EA at Zusanli (ST36) in mice modulated intestinal macrophage polarization (M1/M2 balance), reduced the release of pro-inflammatory cytokines TNF- α and IL-6, and significantly enhanced the secretion of the anti-inflammatory cytokine interleukin-10 (IL-10) [71]. Concurrently, Zhao et al.'s clinical study on acupuncture regulating the Th17/Treg balance in Crohn's disease (CD), an inflammatory bowel disease (IBD), revealed that needling bilateral Zusanli (ST36), Shangjuxu (ST37), Sanyinjiao (SP6), Taixi (KI3), and Gongsun (SP4) modulates the balance between Th17 and Treg cell subsets. This intervention

reduced the number of pro-inflammatory Th17 cells and their associated pro-inflammatory factors (IL-17, ROR γ t), while increasing Treg cell counts and the secretion of anti-inflammatory factors (TGF- β , IL-10), thereby suppressing pro-inflammatory responses [72]. A clinical controlled study by Lyu et al. on patients with post-ischemic stroke cognitive impairment found that acupuncture at Baihui (GV20), Shenting (GV24), Fengfu (GV16), Dazhui (GV14), and Yintang (EX-HN3), supplemented with Neiguan (PC6), Shenmen (HT7), Taixi (KI3), and Sanyinjiao (SP6), significantly reduced serum levels of enteric endotoxin (LPS), barrier damage marker (DAO), and pro-inflammatory cytokines (TNF- α and IL-6) [73], thus inhibiting systemic low-grade inflammation.

Another RCT by Ye et al. on elderly patients with diabetic peripheral neuropathy (DPN) confirmed that the “Root-Branch Point Prescription” acupuncture technique—targeting EX-B3 (Pancreas Shu), Pishu (BL20), and Shenshu (BL23), combined with syndrome differentiation-based acupoints (Zusanli (ST36), Sanyinjiao (SP6), Yanglingquan (GB34), Taixi (KI3))—significantly reduced serum levels of IL-6, IL-1 β , and TNF- α in elderly DPN patients [74]. Furthermore, Liang et al. found that acupuncture at Zusanli (ST36) modulates experimental autoimmune encephalomyelitis (EAE) by regulating B-cell function, indicating its broad immunomodulatory potential [75]. Regarding the BBB, Oh et al. demonstrated that acupuncture at Zusanli (ST36) in rats and mice activates the dorsal motor nucleus of the vagus nerve (DMV), which triggers the vagus nerve-cholinergic anti-inflammatory pathway (CAP) and promotes acetylcholine (ACh) release. ACh then activates α 7 nicotinic acetylcholine receptor (α 7nAChR) on microglial surfaces, inhibiting the NF- κ B pathway to suppress systemic and central inflammatory responses, thereby preserving BBB integrity [76].

Second, acupuncture can upregulate the expression of tight junction proteins (e.g., Occludin and ZO-1). For the intestinal barrier, this process may involve activating the SCFA receptor FFAR2/3 pathway and promoting mucin synthesis [77], thereby reducing serum endotoxin and diamine oxidase (DAO) levels to ameliorate “leaky gut” [78]. For the BBB, it may enhance the expression of brain-derived neurotrophic factor (BDNF) and vascular endothelial growth factor (VEGF), promote tight junction protein synthesis, maintain BBB integrity, and reduce vascular permeability [79]. In a study investigating EA’s mechanism in a diarrhea-predominant irritable bowel syndrome (IBS-D) rat model, Hou et al. found that EA at Zusanli (ST36), Tianshu (ST25), and Taichong (LR3) upregulated the expression of intestinal tight junction proteins (ZO-1 and Occludin) ($P < 0.01$), reduced intestinal permeability [80], and improved intestinal ultrastructure. Yang et al. observed in senescence-accelerated mouse prone 8 (SAMP8) mice (a model of accelerated aging and dementia) that EA at Yintang (EX-HN3) and Baihui (GV20) increased the mRNA expression of BBB tight junction proteins (ZO-1 and Occludin) [81]. Concurrently, Jin et al. conducted an RCT on elderly patients with mild cognitive impairment (MCI), showing that acupuncture significantly reduced serum DAO levels and the cerebrospinal fluid (CSF)/serum albumin ratio (QAlb) [82], with a positive correlation observed between decreased QAlb and reduced

DAO levels [83]. Serum DAO is a sensitive indicator of intestinal mucosal barrier integrity [84], while QAlb is a widely used marker for BBB permeability [85]. These findings confirm that acupuncture restores intestinal barrier integrity and reduces BBB leakage risk, providing structural support for maintaining central metabolic homeostasis.

5.3 Acupuncture restores central metabolic regulation in the elderly

Acupuncture effectively alleviates age-related glucose and lipid metabolic dysregulation by targeting the structural and functional homeostasis of the hypothalamic metabolic center. The hypothalamus—particularly nuclei including the arcuate nucleus (ARC), ventromedial hypothalamic nucleus (VMH), and paraventricular nucleus (PVN)—acts as the central hub for integrating peripheral metabolic signals and regulating energy balance and glucose-lipid homeostasis [86]. During aging, the hypothalamus commonly exhibits chronic low-grade inflammation, elevated oxidative stress, and functional impairment of key neurons (e.g., proopiomelanocortin (POMC) neurons, agouti-related peptide (AgRP) neurons). These changes induce leptin and insulin signaling resistance, thereby triggering central metabolic dysregulation [87]. Acupuncture intervention synergistically restores the regulatory capacity of the aged hypothalamus via two pathways: direct modulation of neuroendocrine networks and indirect improvement of GBA function—an effect validated in numerous preclinical studies. Wang et al. found in an aged mouse model that EA at Baihui (GV20) significantly suppressed hypothalamic pro-inflammatory cytokine expression (e.g., TNF- α and IL-1 β), alleviated neuroinflammation, increased superoxide dismutase (SOD) activity, and reduced malondialdehyde (MDA) levels. This effectively mitigated oxidative stress-induced hypothalamic damage, creating a favorable microenvironment for neuronal functional recovery [88]. In terms of improving neuronal function, Li et al. demonstrated that EA at bilateral Zusanli (ST36), Zhongwan (CV12), Tianshu (ST25), and Sanyinjiao (SP6) specifically activated POMC neurons in the hypothalamic ARC while inhibiting excessive AgRP neuronal activity in diet-induced obesity (DIO) rats. This rebalanced the output of orexigenic and anorexigenic signals, correcting dysregulation in food intake and energy expenditure [89]. Furthermore, acupuncture plays a pivotal role in regulating key hypothalamic hormone signaling pathways.

Zhuang et al. found in a type 2 diabetes rat model that EA at Zusanli (ST36) and Sanyinjiao (SP6) significantly upregulated hypothalamic insulin receptor substrate-1 (IRS-1) protein expression while downregulating suppressor of cytokine signaling 3 (SOCS3) protein expression. This intervention reduced fasting plasma glucose, fasting insulin levels, and the homeostatic model assessment of IR (HOMA-IR) index in rats, while improving pancreatic morphology and β -cell function. Enhanced hypothalamic insulin signaling sensitivity alleviated IR, thereby rectifying systemic glucose and lipid metabolic dysregulation [90]. Jing et al. observed in a type 2 diabetes rat model that EA at bilateral Zusanli (ST36) and Neiting (ST44) significantly upregulated hypothalamic leptin receptor and signal transducer and activator of transcription 3 (STAT3) expression while enhancing STAT3

phosphorylation. This increased central leptin sensitivity, suppressed appetite, regulated energy metabolism, and ameliorated systemic glucose and lipid metabolic disturbances [91]. The subsequent sections elaborate on the mechanisms by which acupuncture alleviates age-related hypothalamic functional decline and restores its central metabolic regulatory function—these mechanisms act via multiple pathways, including the direct and indirect modulation of key neuronal activity, the restoration of impaired metabolic signaling pathways, and the mitigation of inflammatory and oxidative stress responses in the hypothalamus.

5.3.1 Direct regulation: activation of neural pathways and remodeling of signal transmission

Acupuncture can directly transmit regulatory signals to the hypothalamus by activating specific somatic-autonomic reflex pathways. Experimental studies by Lubaczeuski et al. revealed that after vagus nerve transection, the regulatory effects of acupuncture on glucose and lipid metabolism in aged animal models were significantly attenuated, suggesting the vagus nerve serves as a key pathway for acupuncture signal transmission [92]. Research confirms that EA at points such as Zusanli (ST36) effectively stimulates local sensory nerve fibers, activating the dorsal vagal complex and the NTS, which subsequently projects signals upward to the hypothalamic energy balance center [93].

Upon reaching the hypothalamus, these projected signals precisely regulate two key neuronal populations: first, proopiomelanocortin (POMC) neurons that promote satiety and energy expenditure, and second, agouti-related protein (AgRP) neurons that stimulate appetite and conserve energy [94]. The bidirectional regulatory effect of acupuncture is manifested as the promotion of POMC neuronal excitation alongside the inhibition of AgRP neuronal activity [95]. Activated POMC neurons release alpha-melanocyte-stimulating hormone (α -MSH), which, by activating the melanocortin 4 receptor (MC4R), exerts two main effects: on the one hand, it transmits signals downward to the brainstem NTS to induce satiety, directly inhibiting feeding behavior and reducing exogenous glucose and lipid intake; on the other hand, it activates the sympathetic nervous system to directly stimulate white adipose tissue lipolysis, brown adipose tissue thermogenesis and skeletal muscle activity, thereby increasing the basal metabolic rate [96]. Meanwhile, inhibited AgRP neurons reduce their antagonism of POMC neurons and their excitatory output to the feeding center, further consolidating a state of negative energy balance [97].

Simultaneously, autonomic signals emitted by the hypothalamus through the aforementioned regulatory mechanisms can directly influence peripheral metabolic organs [98]. In the liver, they suppress the expression of key enzymes involved in gluconeogenesis, reducing endogenous glucose production. In adipose tissue, they activate hormone-sensitive lipase, promoting the breakdown of triglycerides into free fatty acids for energy supply [99]. These signals do not rely on complex humoral feedback loops, enabling rapid and direct reduction of blood glucose and lipid levels [100].

Additionally, acupuncture can protect neuronal functional integrity by regulating hypothalamic oxidative stress levels, thereby maintaining glucose and lipid metabolism regulation

capabilities [101]. During aging, excessive accumulation of reactive oxygen species (ROS) in the hypothalamus damages the structure and function of POMC and AgRP neurons, leading to disrupted feeding regulation and impaired insulin and leptin signaling. This subsequently promotes gluconeogenesis and fat accumulation [102]. Xu et al. demonstrated in animal studies that acupuncture at Baihui (GV20) and Zusanli (ST36) can upregulate hypothalamic superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) activity, reduce malondialdehyde (MDA) levels, effectively scavenge excess ROS, mitigate oxidative stress damage, and thus protect key neuronal functions, maintain precise regulation of glucose and lipid metabolism, and directly improve blood glucose fluctuations and lipid deposition in the elderly [103]. Concurrently, acupuncture modulates hypothalamic–pituitary–adrenal (HPA) axis function [104]. Excessive activation of this axis serves as a central trigger for age-related glucose and lipid metabolism disorders. In aged states, hyperactivity of the HPA axis increases cortisol secretion, promoting hepatic gluconeogenesis, lipogenesis, and peripheral IR, thereby elevating blood glucose and lipid levels [105]. Acupuncture reverses HPA axis hyperactivation by inhibiting the secretion of corticotropin-releasing hormone (CRH) in the hypothalamus, thereby reducing the release of adrenocorticotrophic hormone (ACTH) from the pituitary and cortisol from the adrenal cortex [106]. This mechanism subsequently suppresses hepatic lipid synthesis and hepatic glucose output while enhancing peripheral tissue insulin sensitivity, ultimately achieving central regulation of glucose and lipid metabolism.

At the molecular level, acupuncture significantly enhances the hypothalamic sensitivity to key metabolic hormones. Animal studies have indicated that acupuncture upregulates the expression of hypothalamic leptin receptors (LepRb) and insulin receptor substrates (IRS), improving the transduction efficiency of the JAK2/STAT3 and PI3K/Akt signaling pathways, thus reversing central leptin and IR [107, 108]. The restoration of central insulin and leptin sensitivity exerts a cascade amplification effect: the hypothalamus exhibits an increased responsiveness to circulating insulin, thereby suppressing hepatic glucose output more effectively; meanwhile, the enhanced sensitivity to leptin signaling suppresses appetite and promotes energy expenditure with higher efficiency [109]. Concurrently, acupuncture modulates the hypothalamic levels of ghrelin and its receptors, balancing the hunger-satiety signaling network in the hypothalamus [110]. Collectively, these effects strengthen the metabolic homeostatic capacity of hypothalamic neurons themselves, providing robust evidence for the direct central regulatory effects of acupuncture in ameliorating metabolic disorders.

The regulation of hypothalamic lipid metabolism-related genes by acupuncture also constitutes a key molecular mechanism underlying its direct improvement of glucose and lipid metabolism [111]. Lipid dysregulation accumulates in the aging hypothalamus, suppressing neuronal activity and exacerbating IR [112]. Acupuncture downregulates the expression of lipid synthesis-related genes, such as fatty acid synthase (FAS) and acetyl-CoA carboxylase (ACC), in the hypothalamus [113], while simultaneously upregulating the

expression of lipid catabolism-related genes, such as carnitine palmitoyltransferase 1 (CPT1). This reduces hypothalamic lipid accumulation, alleviates neuronal damage induced by lipotoxicity, and restores the hypothalamus's regulatory capacity for systemic glucose and lipid metabolism. Consequently, it directly lowers serum triglyceride and cholesterol levels, as well as fasting blood glucose concentrations [114].

5.3.2 Indirect regulation: blocking gut-derived inflammation from targeting the hypothalamus

Age-related “leaky gut” and systemic inflammation act as key peripheral drivers of hypothalamic neuroinflammation. As discussed in the preceding sections, acupuncture effectively interrupts the transmission of gut-derived inflammatory signals to the central nervous system CNS by reshaping the gut microbiota, enhancing SCFA production, repairing the intestinal barrier, and mitigating systemic inflammation (reducing LPS, IL-6, and TNF- α levels). Furthermore, SCFA such as butyrate not only directly cross the BBB but also establish an anti-inflammatory microenvironment in the hypothalamus by suppressing excessive activation of microglia and reducing the release of pro-inflammatory cytokines [115].

Butyrate, the SCFA with the most pronounced central regulatory effects, also directly participates in the central regulation of glucose and lipid metabolism by activating the hypothalamic AMP-activated protein kinase (AMPK) signaling pathway [116]. The AMPK pathway acts as a core switch for systemic energy metabolism. Diminished hypothalamic AMPK activity during aging induces energy metabolic imbalance and enhanced hepatic glucose and lipid synthesis [117]. When gut-derived butyrate, whose production is promoted by acupuncture, enters the hypothalamus, it specifically triggers the phosphorylation of the AMPK α subunit. This process promotes glucose uptake and lipolysis in peripheral tissues including the liver and skeletal muscle, while simultaneously inhibiting hepatic gluconeogenesis and de novo lipid synthesis, thereby directly lowering circulating blood glucose and lipid levels [118].

Simultaneously, acupuncture modulates the secretory balance of hypothalamic orexins via the GBA, further strengthening its regulatory control over systemic glucose and lipid metabolism. Gut microbiota dysbiosis and intestinal barrier impairment lead to an abnormal elevation in hypothalamic orexin A secretion, which promotes feeding behavior, suppresses energy expenditure, and exacerbates glucose and lipid accumulation [119]. By repairing the intestinal barrier and regulating microbial composition, acupuncture inhibits excessive hypothalamic orexin A secretion while facilitating the normal expression of orexin B [120]. This normalization of the orexin system corrects age-related feeding dysregulation in the elderly, reduces carbohydrate and lipid intake, enhances energy expenditure, and ameliorates systemic glucose and lipid metabolism disorders.

Additionally, acupuncture indirectly preserves the function of metabolic regulatory neurons in the hypothalamus by suppressing astrocyte activation [121]. Aging and enteric inflammation induce the proliferation and activation of hypothalamic astrocytes, leading to the excessive release of

pro-inflammatory and neurotrophic factors that disrupt the normal function of POMC and AgRP neurons, thereby exacerbating glucose and lipid metabolic disorders [122]. By interrupting gut-derived inflammatory signaling pathways, acupuncture markedly suppresses hypothalamic astrocyte activation, downregulates the expression of glial fibrillary acidic protein (GFAP), and alleviates the infiltration of inflammatory factors into hypothalamic neurons [123]. This preserves the structural and functional integrity of the hypothalamic metabolic regulatory network, thus stabilizing glucose and lipid homeostasis in the aging organism.

Beyond the mechanistic interpretations outlined above, statistical correlations between metabolic parameters and biomarkers in clinical studies further corroborate the intrinsic link by which acupuncture improves age-related glucose and lipid metabolic disorders through the GBA. Available clinical and experimental evidence indicates that reduced abundance of butyrate-producing bacteria in the elderly is closely associated with aggravated insulin resistance, and acupuncture can significantly upregulate the abundance of such bacteria to alleviate metabolic imbalance [124]. Acupuncture at Zusanli (ST36), Sanyinjiao (SP6), and other points effectively elevates short-chain fatty acid levels including butyrate and propionate, whose changes are significantly negatively correlated with glycemic and lipid profiles [125]. Meanwhile, acupuncture decreases serum levels of pro-inflammatory factors such as LPS and tumor necrosis TNF- α ; the reduction in LPS is positively correlated with the improvement in TG and TC [59]. Furthermore, the decrease in serum DAO is positively correlated with the reduction in inflammatory indices [126]. The above regulatory mechanisms are summarized in Fig. 1.

6 Summary and outlook

This review elucidates the mechanisms by which acupuncture ameliorates age-related glucose and lipid metabolic disorders via the GBA. Accumulating evidence demonstrates that acupuncture, as a multitargeted, systemic non-pharmacological intervention, modulates GBA function across multiple levels and pathways. Specifically, its therapeutic effects are achieved through reshaping the gut microbiota, alleviating systemic and central neuroinflammation, and repairing the intestinal barrier and BBB. Consequently, acupuncture enhances central and peripheral metabolic homeostasis, thereby exerting a potent regulatory role in mitigating age-related glucose and lipid metabolic disorders.

However, this review identifies several limitations in current research: First, model constraints—existing basic studies predominantly rely on young obese rats or adult animal models, lacking elderly-specific models of naturally aged metabolic syndrome. This impedes the simulation of age-specific pathological hallmarks such as immunosenescence and neurodegenerative alterations, resulting in inconsistencies between clinical efficacy and experimental findings [127]. Second, fragmented mechanistic investigations—current studies focus primarily on isolated components (e.g., individual microbiota taxa or inflammatory factors), lacking systematic analysis of the integrated pathway encompassing “gut microbiota-intestinal barrier-systemic inflammation-

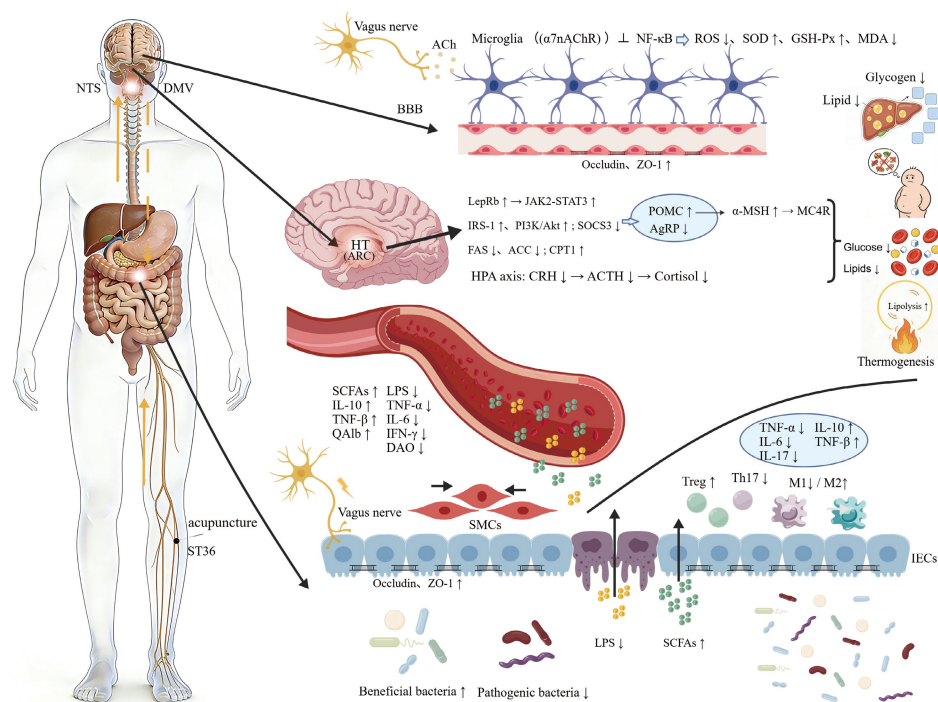


Figure 1 Regulation of glucolipid metabolism disorders by acupuncture via the GBA.

blood–brain barrier–central regulation.” The synergistic regulatory networks among these components remain elusive [128]. Third, ambiguity in acupoint specificity and target identification. Comparative studies on acupoint specificity for the elderly population are scarce, and the regulatory effects of different acupoints on key GBA molecules (SCFA, LPS, and TMAO) and signaling pathways (IRAK1/NF-κB, PI3K/Akt) remain undefined [129]. Additionally, standardized protocols for acupuncture stimulation parameters (frequency, duration, and treatment course) are lacking. Fourth, most clinical studies neglect geriatric-specific confounding factors including multimorbidity, physical frailty, and polypharmacy. Potential interactions between acupuncture and common medications (hypoglycemics, lipid-lowering drugs, and antihypertensives) remain underexplored, reducing the clinical reliability of current evidence. Fifth, few studies adopt rigorous designs to quantify the net effect of acupuncture, leading to uncertainty in mechanistic attribution. Sixth, inadequate clinical evidence. Existing clinical studies are characterized by small sample sizes (mostly < 100 cases) and a paucity of multicenter, large-scale, long-term follow-up RCTs. Efficacy evaluation systems focus primarily on glycemic and lipid profiles, with limited concurrent monitoring of GBA biomarkers, highlighting the need for higher-quality evidence [130]. Furthermore, notably, current clinical research on acupuncture-mediated modulation of the elderly gut microbiota remains in its preliminary stages, with existing studies primarily focused on populations with functional constipation and metabolic syndrome. A scarcity of large-scale targeted studies in elderly individuals with glucose and lipid metabolic disorders further limits the translational application of these findings.

Therefore, future research should focus on the in-depth integration of basic and clinical studies, prioritizing the following initiatives: At the basic research level, it is

imperative to establish age-specific animal models of natural aging combined with metabolic syndrome (e.g., aged diabetic rat and aged obese mouse models) [131]; integrate metagenomics, metabolomics, transcriptomics, and single-cell sequencing technologies to systematically decipher the molecular network linking “acupuncture-gut microbiota-metabolites-signaling pathways-central nervous system” [132]; and identify specific acupoint targets that regulate core pathways such as IRAK1/NF-κB and PI3K/Akt [133]. At the clinical translation level, future studies should systematically assess geriatric confounders and concomitant medications, and evaluate potential drug–acupuncture interactions. Rigorous methodologies including sham controls, standardized protocols, and confounder adjustment are required to accurately quantify the net effect of acupuncture and enhance mechanistic reliability. Future directions should be concrete and feasible, focusing on biomarker validation and elderly-adapted acupuncture protocols. Standardize acupuncture regimens based on acupoint specificity research and optimize stimulation parameters [134] (e.g., 2/100 Hz sparse-dense wave frequency, 30-minute session duration, 12-week treatment course) [135]; conduct multicenter, large-sample, long-term follow-up RCTs to establish a comprehensive efficacy evaluation system integrating “metabolic indicators (blood glucose, blood lipids, HOMA-IR) + GBA biomarkers (microbiota abundance, SCFA, DAO, LPS, inflammatory factors, QALb)” [136]; and explore personalized acupuncture protocols tailored to elderly patients’ gut microbiota profiles (e.g., Bifidobacterium abundance), Traditional Chinese Medicine (TCM) constitutional types (Yang deficiency, Qi-Yin deficiency), and metabolic phenotypes to enhance treatment precision and efficacy [137]. Particularly, targeted clinical studies should be prioritized for elderly individuals with glucose and lipid metabolic disorders, to clarify the specific regulatory effects of

acupuncture on their gut microbiota and its underlying mechanisms. Through the synergistic advancement of basic and clinical research, more robust scientific evidence can be generated to support acupuncture for age-related glucose and lipid metabolic disorders, establishing it as a core non-pharmacological intervention for managing metabolic diseases in the aging population.

Author contributions

Xincan Lan: Conceptualization, literature search, writing original draft; Jing Cao: Literature analysis, visualization, writing-review & editing; Yuwei Qu: Literature search; Chunyang Xia: Literature sorting; Liya Zhu: Reference management; Lian Yang: Supervision, writing-review & editing; Deguang Ding: supervision, writing-review & editing

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Conflict of interests

There is no conflict of interest to declare.

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