Integrative Medicine Research 12 (2023) 100970

Contents lists available at ScienceDirect

Integrative Medicine Research

journal homepage: www.elsevier.com/locate/imr

Acupuncture treatment for functional gastrointestinal disorders: Identification of major acupoints using network analysis

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ARTICLE INFO

Article history:
Received 10 October 2022
Revised 1 June 2023
Accepted 7 June 2023
Available online 23 June 2023

Keywords:
Acupoints
Functional dyspepsia
Irritable bowel syndrome
Network analysis

ABSTRACT

Background: Using network analysis, we sought to determine the acupoints most commonly used to treat functional gastrointestinal disorders (FGIDs), particularly functional dyspepsia (FD) and irritable bowel syndrome (IBS).
Methods: To explore the acupoint patterns used for FGID, data on acupoint combinations for FD and IBS were gathered from systematic reviews. Network analysis was used to determine the degree, closeness centrality, betweenness centrality, and eigenvector centrality of each acupoint. The most common acupoint combinations for FD and IBS were examined based on the eigenvector centrality.
Results: Network analysis revealed that CV12, ST25, ST36, CV10, and LR3, which had the highest eigenvector centrality values, were the main acupoints for treating FGID. CV12 was the main acupoint for treating FD, while ST25 was the hub acupoint for treating IBS in the abdomen. ST36, LR3, and PC6 were the key peripheral acupoints for FD and IBS.
Conclusions: Using network analysis, we provided data that will aid the selection of both general and specific acupoints for FD and IBS, along with spatial information (i.e., the positions of acupoints on a body map). These findings could be applied in future acupuncture research on therapy for gastrointestinal system dysfunction. They may also help bridge the gap between the traditional meridian theory, which assumes that there is a link between diseases/symptoms and the specific body region being treated, and real-world clinical evidence.

1. Introduction

Functional gastrointestinal disorders (FGIDs), which include functional dyspepsia (FD) and irritable bowel syndrome (IBS), are chronic diseases with a wide range of symptoms and no clear organic pathology[1]; this makes it challenging to pinpoint disease etiology. Over 40% of the world's population has at least one FGID, which is associated with increased healthcare utilization and lower quality of life.[2] Western medicine recommends various medications for stomach symptoms and diseases. However, pharmaceutical treatments, such as prokinetic medicines, proton pump inhibitors, anticholinergics, tricyclics, anti-diarrheals, 5-HT3 antagonists, and antidepressants, are often ineffective or have side effects.[3] Furthermore, because many pharmaceutical agents target only one symptom, they are unlikely to be effective in patients who have symptoms in both the upper and lower digestive tracts, and the simultaneous use of different drugs to treat both upper and lower digestive tract symptoms increases the risk of side effects.

Acupuncture has been used for thousands of years in the East and is effective for treating FGIDs.[4] As a result of dissatisfaction with the side effects of conventional FGID medications, various studies have examined acupuncture as a therapeutic strategy for FGID, especially FD and IBS.[3] Clinicians should be aware of the potential of acupuncture and be open to its use in the treatment of gastrointestinal disorders.[5] For treating FD, acupuncture was comparable to medications, and more or as significantly as sham acupuncture.[6] Although sham-controlled randomized controlled trials (RCTs) found no benefits of acupuncture for reducing IBS symptom severity or improving quality of life when compared to a credible sham acupuncture control, patients reported greater

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https://doi.org/10.1016/j.imr.2023.100970

benefits from acupuncture than from two types of antispasmodic drugs.[7] However, no research has investigated the selection of acupoints for treating FGID.

By representing a holistic system as a graph, network analysis provides mathematical descriptions of complex networks.[8] Many studies have used network analysis to discover the principles underlying the selection of acupoints for various ailments. For instance, Lee *et al.*[9] reported that three acupoint combinations were used for treating low back pain, identified based on mutual information values. Furthermore, using network analysis, key acupoints for pain control were discovered based on a high degree of centrality.[10] A network analysis of acupoint prescriptions for virtual diagnosis of 10 different diseases revealed that some acupoints were common to all diseases, while others were disease-specific.[11] To better understand acupuncture treatment of FD and IBS, network analysis should evaluate both common and disease-specific acupoints.

This study used network analysis to understand how acupoints have been combined to treat FGIDs, specifically FD and IBS. To examine patterns in the combinations of acupoints, we acquired acupoint data from published systematic reviews, calculated the centrality values of key acupoints, and visualized the network based on the weight of centrality of each acupoint. We also independently assessed the primary acupoints for FD and IBS to explore similarities and differences in acupoint selection between the two diseases.

2. Methods

2.1. Data Sources for Acupoints for Functional Dyspepsia and Irritable Bowel Syndrome

Data on acupoint combinations for FD and IBS were extracted from systematic reviews.[7,12] After eliminating studies that did not use acupuncture or did not report acupoints, 19 and 15 studies on FD and IBS were included, respectively. There were 47 acupoints for FGIDs: 28 for FD and 39 for IBS. The acupoints combinations for FD and IBS were shown in the Supplement 1.

2.2. Network Analysis and Network Visualization

The network analysis of acupoint combinations for FD and IBS was performed using Gephi open source software for graph and network analysis (ver. 0.9.2; http://gephi.org). The degree, closeness, betweenness, and eigenvector centrality values for each acupoint were calculated. Each acupoint network node has one or more edges, and the total edge indicates the degree centrality of the node.[13] The eigenvector centrality of a node is given by the weighted sum of the centralities of all nodes connected to it by an edge, which reflects how important a node is in a network.[14] Closeness centrality is a measure of how accessible a node is to all other nodes in a network; the shortest pathways between any two nodes are summed to obtain this value.[15] The degree to which a node plays a central role in connections with other nodes is determined by its betweenness centrality. Any two nodes can be connected by at least one shortest path, and betweenness centrality is determined according to the number of shortest pathways passing through an individual node.[13] We determined the most important acupoints based on their eigenvector centrality scores, where eigenvector centrality is a measure of a node's impact in a network in graph theory; a high eigenvector centrality score indicates that a node is connected to other nodes with high scores.

To depict the network of acupoints used for treating FD and IBS, we used the Yifan Hu layout based on eigenvector centrality scores. The Yifan Hu layout algorithm is a force-directed method that brings more-connected nodes into the center of the network.[16]

3. Results

3.1. Common Acupoint Combinations for Functional Dyspepsia and Irritable Bowel Syndrome

The most common acupoints used in clinical trials of FD and IBS were visualized using network analysis (Fig. 1). Of the 47 acupoints, the 10 acupoints with the highest eigenvector centrality values were chosen (Table 1).

CV12 (eigenvector centrality = 1.00) and ST25 (0.91) were the hub acupoints in the abdominal region in the treatment network for FGID. CV10 (0.66) also had a significant role in treating FGID. The primary acupoints on the back for treating FGID were BL20 (0.48) and GV7 (0.44), and BL21 (0.44) while ST36 (0.74), LR3 (0.63), and SP6 (0.42) were the key lower extremity acupoints for treating FGID. PC6 (0.47) was the main acupoint in the upper extremities for treating FGID.

3.2. Distinct Acupoint Combinations for Functional Dyspepsia and Irritable Bowel Syndrome

Network analysis revealed unique acupoint combinations for FD and IBS. The main acupoints for FD and IBS are shown on the human body template (Figs. 2A and 2B). The eigenvector centrality values of the 47 acupoints are displayed in a heat map (Fig. 2C).

CV12 (FD, 1.00; IBS, 0.59) in the upper abdomen was the hub in the network for treating FD, while ST25 (FD, 0.33; IBS, 1.00) in the lower abdomen was the hub in the network for treating IBS. In the upper back, BL20 (FD, 0.50; IBS, 0.27) and BL21 (FD, 0.41; IBS, 0.18) were mainly used to treat FD, while in the lower back BL23 (FD, 0; IBS, 0.35) and BL25 (FD, 0; IBS, 0.26) were used to treat IBS. In the peripheral area, ST36 (FD, 0.61; IBS, 0.70), LR3 (FD, 0.47; IBS, 0.57), and PC6 (FD, 0.41; IBS, 0.31) were equally significant in the FD and IBS therapy acupoint networks.

4. Discussion

This study used network analysis to analyze the similarity and specificity of acupoint selection patterns between FD and IBS. The most common acupoint combinations for treating FD and IBS were determined based on eigenvector centrality, and included CV12, ST25, ST36, CV10, and LR3. We also found that CV12 was the primary acupoint for treating FD, while ST25 was the primary acupoint in the abdomen for treating IBS. ST36, LR3, and PC6 were key peripheral acupoints for FD and IBS.

The hub acupoints for the therapy of FGID in this study were the abdominal CV12 and ST25 acupoints. According to the traditional East Asian medicine, the function of the GI tract has been controlled using the *front-mu* acupoints belonging to the stomach and large intestine. The CV12 and ST25 acupoints in the abdomen, which are anatomically adjacent to the GI tract, were the hub acupoints for FGID and also had the most edges (Fig. 1). The hub acupoint for FD was CV12, which is in the upper abdomen (4 B-cun superior to the center of the umbilicus, on the anterior median line), and the hub acupoint for IBS was ST25, which is in the lower abdomen (2 B-cun lateral to the center of the umbilicus). According to traditional East Asian medicine, the *front-mu* acupoints for the stomach and large intestine are CV12 and ST25, respectively. The *front-mu* points are located on the abdomen and chest, close to internal organs; thus, they are stimulated to regulate the function of internal organs. According to our findings, the *front-mu* acupoints of the stomach and large intestine play a crucial role in restoring organ function in the treatment of FD and IBS.

We also discovered that the BL20 and BL21 acupoints, which are located lateral to the lower thoracic spinal processes

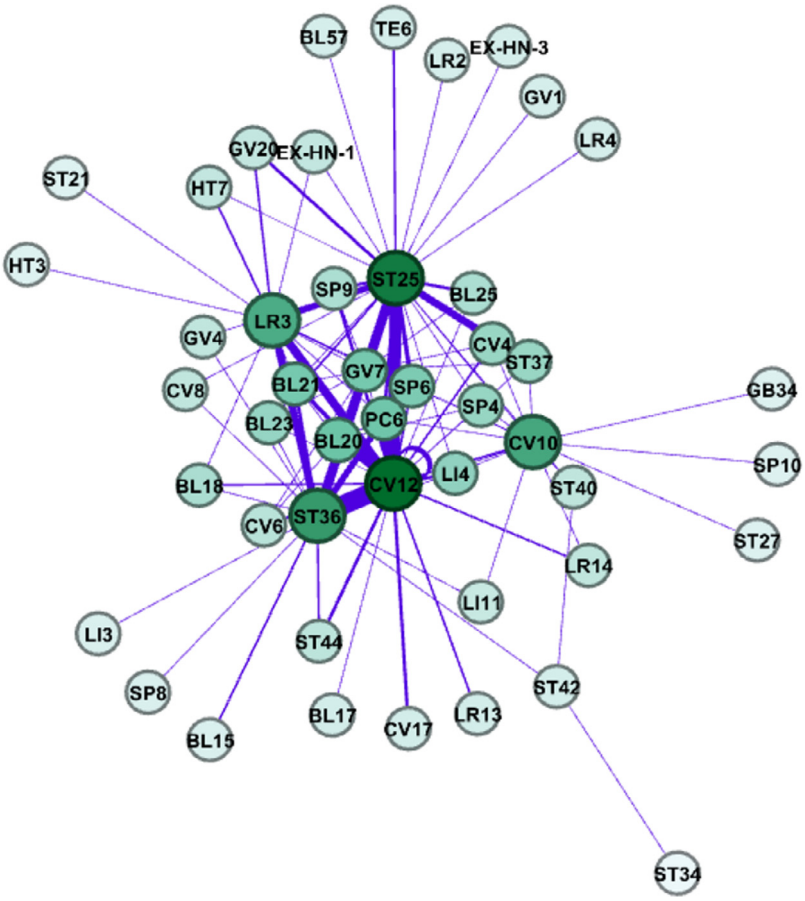

Figure 1. Network analysis of acupoint combinations for treating functional gastrointestinal disorders. The major acupoints for treating functional gastrointestinal disorders were CV12, ST25, ST36, CV10, and LR3, which had the highest eigenvector centrality values. Gephi was used to for the network analysis with the Yifan Hu layout. The eigenvector centrality value was used to determine the color of each node. The weight is represented by the width of the edges, and acupoints with higher eigenvector centrality values are darker. Getphi open source software was usded for network analysis (ver. 0.9.2: http://gephi.org).

Table 1
Common acupoint combinations for functional gastrointestinal disorders.

Label	Eigenvector Centrality	Degree	Closeness Centrality	Betweenness Centrality
CV12	1.00	25	0.66	256.91
ST25	0.91	27	0.70	415.02
ST36	0.74	19	0.63	266.15
CV10	0.66	16	0.60	186.63
LR3	0.63	14	0.58	138.58
BL20	0.48	8	0.51	15.65
PC6	0.47	6	0.53	1.30
GV7	0.44	10	0.46	16.25
BL21	0.44	6	0.51	2.95
SP6	0.42	5	0.52	0

bilaterally (T11 and T12, respectively), were important for treating FD, while the BL23 and BL25 acupoints, which are located lateral to the lumbar spinal processes bilaterally (L2 and L4, respectively), were relatively important for treating IBS. We could distinguish acupoints located on the superior and inferior surface of the back (so-called *back-shu* points; Fig. 2). BL20 and BL21 (upper back) are the *back-shu* points for the spleen and stomach, respectively, while BL23 and BL25 (lower back) are the *back-shu* points for the kidney and large intestine, respectively. These *back-shu* points are used to regulate the functions of internal organs along with *front-mu* points.[17,18] The rationale behind *back-shu* point acupuncture is that these sites activate corresponding segmental autonomic nerves, which control visceral functions of the body.[19] These findings imply that the *back-shu* points for the stomach and large intestine are similarly important in treating stomach and intestinal dysfunction.

In real-world acupuncture treatment, acupoint selection is not restricted to acupoints located close to the site of a disease; acupoints located far from the site are often used. The ST36, LR3, PC6, and SP6 acupoints on the upper and lower limbs ranked highly in the FGID treatment network analysis (Table 1). Unlike acupoints on the abdomen and back, there was little difference in the networks of acupoints on the upper and lower extremities between FD and IBS (e.g. ST36, LR3, and PC6; Fig. 2C). This demonstrates that there are treatment strategies common to both FD and IBS. Stimulation of the ST36, LR3, and SP6 acupoints has general

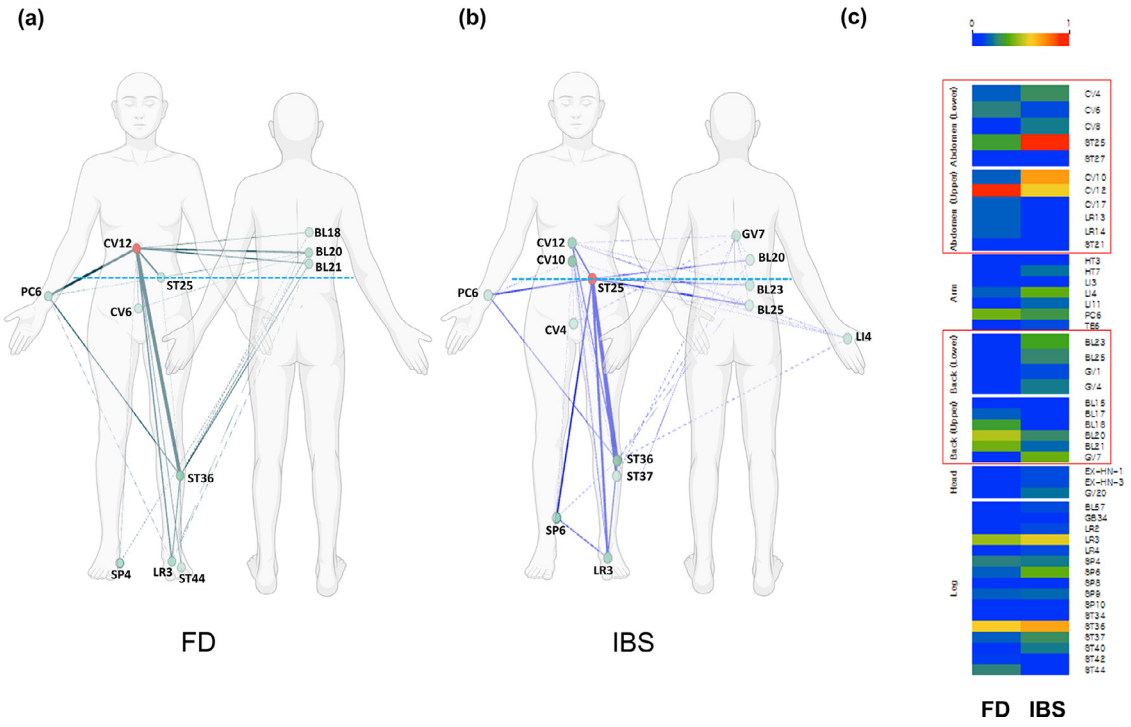

Figure 2. Distinct acupoint combinations for functional dyspepsia (FD) and irritable bowel syndrome (IBS). (a) The main acupoints for FD plotted on the human body template (n = 11; 39.29% of all acupoints with K-core ≥ 2). (b) The main acupoints for IBS plotted on the human body template (n = 14; 35.9% of all acupoints with K-core ≥ 3). The dotted line is the standard line (umbilicus line). BioRender.com was used to develop the human body template. (c) The eigenvector centrality value for each acupoint for FD (left) and IBS (right). Orange Software was used to create the heatmap (version 3.28.0; http://orangedatamining.com).

neurological effects, including descending analgesia and central regulatory effects.[10] Acupuncture had a reasonably consistent effect on gastrointestinal motility, with ST36 and PC6 being the main acupoints.[20] Patients with FD may benefit from the antiemetic effect of acupuncture at PC6, while patients with visceral hypersensitivity may benefit from the antinociceptive effects of acupuncture at PC6 and ST36.[21] An epidemiological study suggested that there is over 60% overlap between FD and IBS.[22] In addition, they appear to have similar underlying pathophysiological mechanisms, including visceral hypersensitivity, possible immunological dysfunction, dysbiosis, and increased mucosal permeability.[23,24] As a result, similar peripheral acupoint combinations can be used to treat both FD and IBS.

Several limitations of this study should be considered. First, due to the small number of studies included, we did not assess the effectiveness of acupuncture treatment. Acupuncture at some stomach meridian acupoints, including ST36 and ST40, had a much higher overall response rate in FD patients than other acupoints on the trunk, and in other meridians, as well as conventional treatment.[25] Given the effectiveness of acupuncture treatment, it is important to identify the major acupoints for treating FGID. Second, due to the limited number of studies describing distinct acupoint prescriptions for different patterns of symptoms/signs, we were unable to analyze acupoint combinations for treating FD and IBS based on pattern identification. Acupuncture prescriptions are usually based on pattern identification for individual patients, and different acupoint combinations are chosen for FD patients.[26] Further research should identify critical acupoints based on pattern identification for personalized therapy.

In conclusion, using the network analysis method, we obtained information on the similarity and specificity of acupoint selection patterns for FD and IBS. Our findings shed light on the relationship between traditional theories and real-world treatment. The results could help researchers understand the mechanisms underlying gastrointestinal dysfunction in FGID patients treated with acupuncture.

Conflict of interests

The authors declare that they have no competing interests.

Funding

This work was supported by Korea Institute of Oriental Medicine (KSN1812181), by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HF22C0023) and by Institute of Information & communications Technology Planning & Evaluation (IITP) grant funded by the Korea government(MSIT) (No.RS-2022-00155911, Artificial Intelligence Convergence Innovation Human Resources Development (KyungHee University)).

Ethical statement

Not applicable.

CRediT authorship contribution statement

Heeyoung Moon: Conceptualization, Methodology, Investigation, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Yeonhee Ryu:** Visualization, Writing – review & editing. **In-Seon Lee:** Investigation, Formal analysis, Writing – review & editing. **Younbyoung Chae:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing.

Data availability

The authors can provide the data upon reasonable request.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.imr.2023.100970.

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