## Japanese Acupuncture - Current Research

Basic and Clinical Studies of Acupuncture and Moxibustion Treatment for Irritable Bowel Syndrome Eitaro Noguchi<sup>1)</sup>, Ryota Muranaka<sup>2)</sup> Tomomi Narushima<sup>2)</sup> and Masanori Tojo<sup>1)</sup>
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#### 1. Introduction

In recent years, irritable bowel syndrome (IBS) has begun to be recognized as a common disease. The current prevalence of IBS is conceivably 14.2% of the general population of Japan, representing nearly 31% of outpatients of internal medicine. <sup>1)</sup>

The pathogenesis of IBS has not been elucidated and no reasonable therapy and treatment are established. The abdominal symptoms that patients with IBS complain of are abdominal conditions accompanied by diarrhea or constipation. For IBS diagnosis the Rome III criteria are now adopted.

Although until now it has been thought that acupuncture and moxibustion can work well on these conditions, there is only insufficient evidence to support this. So, domestic and overseas studies on acupuncture and moxibustion relating to IBS will be presented below from both basic and clinical perspectives.

# 2. Basic Research on Acupuncture and Moxibustion Stimulations to Digestive Organs

Experimental medical research of acupuncture and moxibustion treatment for digestive tract has a long history in Japan and has been carried out from much earlier days than in other countries.

In 1912, Tojuro Kashida, et al. reported that they observed bowel peristalsis in house rats by visually inspecting the abdominal wall after causing bowel peristalsis by moxibustion stimulation and they also measured, with a manometer, changes in intra-abdominal pressures after an injection of Ringer's solution into the abdominal cavity to observe inhibitory responses followed by the transient increased motility elicited by moxibustion stimulation to the abdominal region and legs (ashi sanri).<sup>2)</sup> In 1914, Michio Goto observed increased responses in house rabbits of the bowel motility elicited by moxibustion stimulation through visual and stethoscopic inspections of the abdominal wall.<sup>3)</sup> And in 1929, Shuji Fujii visually observed changes in the motilities of the small intestine by making a small hole on the abdomen and reported inhibitory effects of infantile acupuncture.<sup>4)</sup> However, these experiments were intended to find whether the gastrointestinal tract responds to acupuncture and moxibustion stimulations, and they were not referring to the mechanisms of acupuncture and moxibustion treatment.

At the 5<sup>th</sup> International Acupuncture Conference in 1978, Mori, et al. presented the report that gastric motilities in rabbits were observed by the balloon method by stimulating ashi sanri with the sparrow pecking (jyakutaku) technique, resulting in an increased intragastric pressure and disappearance of this response at the cut side of the sciatic nerve on the central side innervating ashi sanri.<sup>5)</sup> Moreover, in 1991, Kudo, et al. reported the results of their observations in anesthetized dogs that the gastric electromyograms of the gastric smooth muscle showed delayed rhythms of gastric motilities and inhibited electrical activities in the gastric smooth muscle when electro-acupuncture stimulation was given to the tan-yu ketsu of the dorsal region.<sup>6)</sup>

In 1993, Sato, et al. observed effects of acupuncture stimulation using similar methods as for basic research and verified that when the rotatory technique was applied to each region of the body, reflex inhibition occurred via the sympathetic nerves in the abdominal region as well as increased reflex motility via the vagus nerves in the four extremities.<sup>7)</sup> (Fig.1)

Yamaguchi, et al. confirmed that the stimulation of electro-acupuncture, with which stable stimulations of various strength levels can be applied, produced inhibitory responses in the abdominal region and increased responses in the hindlimbs and recorded that afferent nerve activities were induced from the intercostals nerves by abdominal stimulation and those from the tibial nerves by hindlimb stimulation.



(refer to the explanation of Fig. 1 on page 7)

And they further indicated that responses occurred from the threshold level at which C-fibers get excited when the abdominal stimulation was given and from the threshold level at which A- and C-fibers get excited when hindlimb stimulation was given, and as a result, the type of nerve fibers to transmit acupuncture stimulation differs between the trunk of the body and the hindlimbs.<sup>8)</sup>

In regard to duodenal motility, Noguchi, et al. observed changes in the motility in anesthetized rats when electro-acupuncture stimulation was applied and reported that the motility was increased via the vagus nerves by the stimulation of hindlimb footpads and a segmental inhibition was induced in the spinal cord by abdominal stimulation.<sup>9)</sup> (Fig.2)

In regard to research on the motility of small intestine, Iwa, et al. published their report in 1994, demonstrating acupuncture and moxibustion stimulations caused two-phase responses that acted as an enhancer or an inhibitor of the motility depending on a strained state of the small intestine. They reached this conclusion in the following procedures: Indian ink orally was administered to the stomach in unanesthetized mice and the transfer distance of the ink in the intestinal tract was observed; normally, the motility was increased by abdominal acupuncture stimulation, whereas it was suppressed by moxibustion stimulation; with the administration of Vagostigmin, which promote intestinal motility, abdominal acupuncture and moxibustion stimulations conversely



(refer to the explanation of Fig. 2 on page 7)

turned to a inhibitory response; at the time of inhibition induced by atropine dosing, the increased response was produced; and when sympathetic nerves were stimulated by epinephrine to suppress the motility, no responses were observed – which means two-phase responses.<sup>10)</sup> In 2006 Iwa, et al. further verified that electro-acupuncture stimulation to ST-36 (ashi sanri) in conscious rats significantly increased the motility of the distal large intestine via the pathway of the parasympathetic nerves and that its transfer pathway was mediated by parasympathetic sacral nerves.<sup>11)</sup>

As just described, in recent years basic studies by many Japanese researchers help gradually elucidate the effects of acupuncture and moxibustion treatment on digestive organs and the mechanisms.

### 3. Present State of RCT for IBS in the U.S. and Europe and Clinical Studies in Japan

Searching IBS information on the Internet used in the world civilized societies reveals the actual IBS situation of the world. When IBS is Google searched with the keywords in English and Japanese, the websites retrieved domestically were 368,000 and 8,720,000 on overseas sites (as of January 2010). When compared with the year 2004, the retrieval increased to about 25 times domestically and about 31 times internationally. <sup>12)</sup> (Fig.3) However, when search was made with an addition of acupuncture (hari-chiryo in Japanese) to these keywords, Japanese sites increased to 24 times and overseas English sites increased only 3 times.

In the 2004 search, the number of English sites of IBS in English was 100 times more than Japanese IBS sites, suggesting a high expectation about acupuncture and moxibustion treatment in overseas countries. However, English sites now decreased drastically to nearly 15 times.

A survey, which might be rough, indicates that interest in acupuncture and moxibustion treatment for IBS was toned down in overseas countries.

It was in 1986 that an early literature on IBS with the title of "Alternative medicine consultations and remedies in patients with the irritable bowel syndrome" was published in the journal Gut in England, reporting the results of questionnaires surveyed among the subjects of patients with IBS, patients with organic supragastrointestinal disorders, and patients with Crohn's disease. Herein, Smart, et al. pointed out that most cases of patients with IBS (16%) consulted practitioners of alternative medicine. <sup>13)</sup>



This indicates that in these days, alternative medicine including acupuncture and moxibustion already began to be expected to treat IBS.

Subsequently in 1999, a rapidly increased number of IBS related literatures were published before and after the announcement of Rome II diagnostic criteria.<sup>12)</sup> In conjunction with this, the number of literatures on IBS increased in the field of acupuncture and moxibustion. From 1999 to today, about 50 overseas literatures were retrieved on PubMed and many RCTs and systematic reviews were reported. (Tab.1)

dominant countries, as above.

On the domestic site, although 26 IBS-related literatures can be retrieved, no RCTs are included and the literatures are mostly case reports and commentaries. This may be attributed to the legal status of practitioners engaged in acupuncture and moxibustion treatment: many professionals working on the clinical sites of acupuncture and moxibustion are not M.D. physicians, whose standing is likely to make it difficult to plan RCTs on acupuncture and moxibustion treatment for IBS.

Author	Date of publication	Type of experiment	t Subjects	No. of cases	Results	Name of Journal
Lembo AJ	2009	RCT	IBS patients	230	In IBS procedures, clear evidence was not established to support significance of acupuncture compared to sham needle acupuncture.	Am J Gastroenterol
Lim B	2006	Meta Anna	a 6 RCTs	109	It is not assertive if acupuncture is 109 more effective than sham needle acupuncture in IBS procedures.	Cochrane Database Syst Rev
Schneider A	2006	Syst Rev	IBS patients	566	Acupuncture for IBS is mostly placebo responses.	Gut
Fireman Z	2001	RCT	IBS patients	25	Treatment results of the two groups of acupuncture and sham needle acupuncture showed acupuncture produced significant improvement in abdominal pain and systemic conditions, but no difference between the groups.	Digestion
Kunze M	1990	RCT	IBS patients	143	In comparing five types of treatment for IBS, successful rate of simple mental treatment was 75% against 31% of acupuncture treatment (sham needle acupuncture 17.2%).	Z Gesamte Inn Med.
Table 1: Major literatures on RCT's in the U.S. and Europe						

Kunze reported in his 1990 RCT literature that the effect of acupuncture treatment was about 31% against 17% for sham needle acupuncture but did not exceed 75% for simple mental treatment.

In 2006, Schneider made systematic reviews of accumulated 566 cases and concluded that acupuncture effects were placebo effects.<sup>14)</sup> Furthermore, the meta analysis<sup>15)</sup> of 6 RCTs by Lim (2006), et al. and the RCT by Lembo (2009) showed no differences in effects between sham needle acupuncture and real acupuncture.<sup>16)</sup>

The RCTs conducted up until today in the U.S. and Europe do not indicate that the use of acupuncture for IBS is effective, which might be a cause for the decreased number of IBS-related sites in English In such condition, however, well-planned excellent case reports on acupuncture and moxibustion treatment for IBS have begun to be seen recently.

Matsumoto, et al. of Gifu University employed the reversal study design and studied clinical effects of acupuncture and moxibustion treatment in IBS patients who had 4 years of the disease duration and were resistant to medications. In 4 patients, points/regions to be treated were determined by "sho" and an acupuncture treatment period was alternated with a non-treatment period and during these periods abdominal pain, abdominal fullness, frequency of defecation, stool condition, and psychological state (QOL) were observed with the results that abdominal pain, abdominal fullness, and QOL were improved in 3 out of 4 patients.<sup>17)</sup> (Fig.4)



(refer to the explanation of Fig. 4 on page 7)

While there are case reports showing effectiveness of acupuncture treatment as described above, there may be some reasons for difficulty detecting effective differences in stereotypically designed RCTs in which comparisons are made with sham needle acupuncture.

Complaints associated with IBS are diversified and the state of autonomic nerves in individuals may also be diversified. So, it is considered that effects cannot easily appear from experimental treatments added by stereotypical acupuncture stimulation. In uniform treatments, incompatibility exists between the state of patients and acupuncture treatment. So treatments with acupuncture and moxibustion will become effective when they are administered in response to the complaints and physical conditions of patients of the day.

Practitioners of acupuncture and moxibustion in Japan are placed in the situation where it is not easy for them to conduct RCTs. However, as a matter of course further detailed studies on IBS need to be conducted in the area of investigation for acupuncture and moxibustion and research approaches suited to the realities of our country must be sought.

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#### Legend

Fig. 1 Effect of acupuncture stimulation on gastric motility and its mechanism

A: Stimulated sites and rates of changes in gastric motilities B: Effect of abdominal acupuncture stimulation and activity of the autonomic nerves: Splanchnic nerves get excited (sympathetic) and gastric motility is decreased. C: Effect of hindlimb acupuncture stimulation and autonomic nerve activity: Vagal nerves get excited and gastric motility is increased.

D: Reactive mechanism

a: Abdominal acupuncture stimulation excites sympathetic nerves through the mediation of spinal reflexes. b: Hindlimb acupuncture stimulation excites vagus nerves through the mediation of supraspinal reflexes.

(Alterations/citations were made from the literature of 7 above.)

Fig.2 The effect of electro-acupuncture stimulation on duodenal motility and its mechanism

A: Abdomen and B: Intensity of electro-acupuncture stimulation to hindlimb footpads and the rates of changes in duodenal activity.

A Graph of Inhibitory Responses: The threshold of afferent intercostal nerve activity innervating the

stimulated abdomen, the rate of changes in inhibition of duodenal motility. TI-IV arrows indicate the thresholds of afferent intercostals nerve activities of individual nerves.

Significant inhibitory responses appeared by stronger stimulation than the threshold of group IV fibers.

Inhibitory responses are not affected by a vagus nerve cut and spinal cord myelination but they disappear by a greater splanchnic nerve cut.

B Graph of Increased Responses: The threshold of afferent tibial nerve activity innervating stimulated hindlimb footpads and inhibitory rate of changes in duodenal motilities.

TII-IV arrows indicate the threshold of afferent tibial nerve activity for each nerve. Significant inhibitory response appeared when giving stronger stimulation than the high threshold group III or the excitatory threshold of the excitatory threshold group IV fibers.

Inhibitory responses disappeared by a vagus nerve cut and spinal cord myelination and are not affected by a greater splanchnic nerve cut.

(Alterations/citations were made from the literature (9) above.)

Fig.3 Changes in the number of IBS-related sites on the Internet

The graph above is the comparison of the number ('000) of websites retrieved with the key word of "irritable bowel syndrome" between 2004 and 2010.

The graph below is the comparison of the number ('000) of websites retrieved with the key word of "irritable bowel syndrome" +"acupuncture treatment" between 2004 and 2010.

Fig.4 Changes in Abdominal Symptoms in 4 Cases A: Abdominal pain, b: Changes in Bloating Sensations. The axis of ordinate shows averages of points recorded in the diaries, the axis of abscissas shows time of the treatment period and the non-treatment period.

(Alterations and citations were made from the literature 17 above.