International Journal of Medical, Medicine and Health Sciences
ISSN: 2517-9969
Vol:1, No:2, 2007

Relationship between Functional Gastrointestinal Disorders and Risk Factors: A Biomechanical Analysis

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***Abstract*—**Functional gastrointestinal disorders (FGID) affect millions of people spread all age regardless of race and sex. Emotional stress and obesity have been associated with increased reporting of gastrointestinal (GI) symptoms, but the relationship between FGID and risk factors (emotional stress or obesity) is unclear. Our aim was to assess the changes of the mechanical characteristics on the gastrointestinal tracts of the mentally fatigued obese and normal rat models. Finally, using the physical characteristics with micro-indentation test, we made a close investigation into the relation between FGID and risk factors quantitatively.

***Keywords*—**Functional gastrointestinal disorders, Risk Factors, Mechanical Characteristics, Gastrointestinal Tract.

I. Introduction

FUNCTIONAL gastrointestinal disorders (FGID) are clinical syndromes defined by chronic or recurrent abdominal symptoms without identifiable cause [1]. FGID are very common in millions of people spread all age regardless of race and sex; most have been attributed to chronic gastrointestinal disease that is likely a very heterogeneous condition and where risk factors remain poorly defined [2]. In FGID, symptoms are frequently related to meals and stress. Some studies recently found the fact that a strong association between FGID and risk factors (emotional stress and obesity) is appeared [3]-[10]. Obesity is now a major epidemic in the developed world [4]. Moderate body weight changes are generally not associated with gastrointestinal symptom changes over time in the general population. However, obesity has recently been linked to multiple upper and lower abdominal symptoms in [5]-[8]. Reference [9] investigated roles of stress in FGID. Psychological stress is widely believed to play a major role in FGID, including irritable bowel syndrome [10]. However, the mechanism and the physiological characteristic change on the gastrointestinal tract have not been identified explicitly, although it is generally accepted that symptoms related to FGID are likely to arise from motor and sensory abnormalities.

The aim of the current study is, therefore, to identify the mechanism and the physical characteristic change. It is performed by evaluating an alteration of the mechanical characteristic on the gastrointestinal tracts of the mentally fatigued, obese and normal animal models.

Manuscript received February 28, 2007. (Write the date on which you submitted your paper for review.) This research was supported by Regional Research Center Program which was conducted by the Ministry of Commerce, Industry and Energy of the Korean Government.

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II. Material and Methods

A. Animal

Nineteen specific pathogen free Sprague-Dawley (SD) rats (6-week-old, weight of approximately 253g) were housed in an individually ventilated cage under vivarium condition (temperature 22±2°C, humidity 50±10% and 12h light-dark cycle). All rats were randomized into 3 groups: forced diet (FD, n=5) to trigger stress, overeaten diet (OD, n=7) for formation of obesity and normal diet (ND, n=7). During 12 weeks, expanded pellet (Superfeed Co., Korea) was administered to OD group at 23g/day and to ND group at 17g/day, and AIN-93G liquid diet (HanbitBio Co., Korea) was forcedly dosed to FD group at the amount of 165%, compared with the feed of ND group. In the present study, we hypothesized orally forced diet using the gavage needle would be a cause of emotional stress. Body weights of the rats were measured once a week from starting time (Table I).

B. Acquisition of Specimens

The rats on both groups were sacrificed with CO_2 asphyxiation at the final day of 12 weeks, and then gastrointestinal tracts were immediately harvested from the rats under sterile conditions. All specimens were dissected from greater curvature of glandular region for the micro-indentation test below. Dimension of the specimen was then 10mm (width) × 10mm (length) × 1mm (height).

TABLE I
AVERAGE CHANGES OF BODY WEIGHTS IN EACH GROUP

Groups		Weeks												
		0	1	2	3	4	5	6	7	8	9	10	11	12
Weight(g)	FD	262	289	321	338	340	361	371	366	378	393	406	404	411
	OD	262	302	337	363	388	407	424	442	454	466	474	485	492
	ND	261	269	279	295	291	303	302	314	320	322	343	358	365

All procedures were in accordance with approved the National Institutes Health (NIH) Guide for Care and Use of Laboratory animals, under a protocol approved by the Yonsei University School of Animals Care and Ethics Committee.

C. Mechanical Test

Micro-indentation tests were performed for all harvested specimens above using Instron Micro-test System (5848 series, Instron, Norwood, MA, USA) (Fig. 1). The constant load corresponded to $0.001s^{-1}$ strain rate was applied continuously to the specimens. Micro-indentation test was then conducted three times per specimen to identify an error of intra-specimen and to reduce the effect. Stiffness was calculated using the load-displacement data obtained from micro-indentation tests. Three material phases were then considered to represent nonlinearity of the specimen (Fig. 2). In addition, the effective Young's modulus for the first material phase was calculated by using following equation to identify rigorously change of material behaviors at the initial phase. This is a rigorous mathematical solution to the elastic indentation problem of a thin elastic layer bonded to a rigid half-space with a rigid, frictionless cylindrical plane-ended indenter.

$$E = \frac{1-\nu^2}{2a\kappa(\nu, a/h)} \cdot \frac{P}{w} \quad (1)$$

Where ν is Poisson's ratio, P is the applied force, α is the radius of the indenter, h is the tissue thickness, w is the indented depth, and κ is a scaling factor in (1). The scaling factor κ provides a theoretical correction for the finite thickness of the elastic layer, and it depends on both the aspect ratio a/h and Poisson's ratio. Here, 0.49 of Poisson's ratio was used to assume soft tissue to be nearly an incompressible material.

D. Statistics Analysis

Statistical analyses were performed using the Statistical Analysis System (SPSS 12.0, SPSS Inc., USA). A one-way analysis of variance (ANOVA) test with *Tukey's-b post hoc multiple comparisons* was used to identify significant difference among the three phases. A paired t-test was used to identify a significant difference, when the FD and OD groups were compared with ND group, respectively. The significance levels for all statistical tests were set at 0.05.

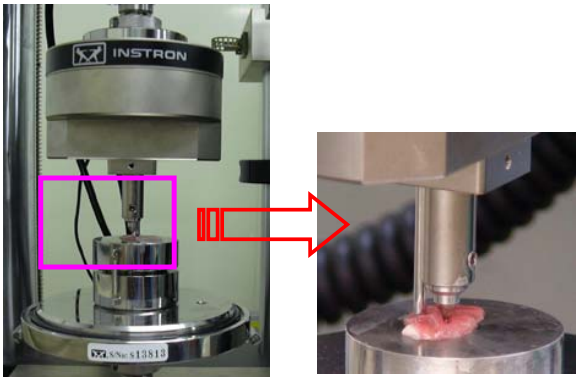

Fig. 1 Micro-indentation test to investigate mechanical characteristic changes on the gastrointestinal tract

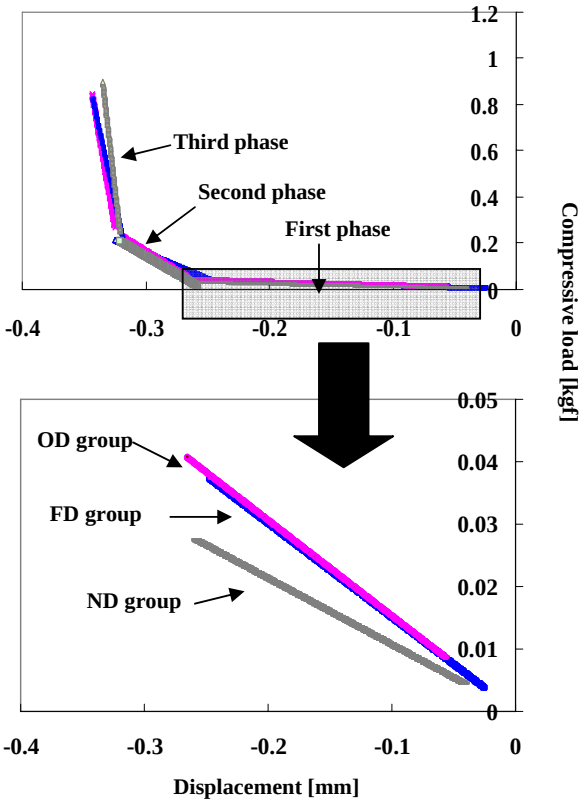

Fig. 2 Average load-displacement curve for the entire material phase (top) and the emphasized first phase (bottom)

III. Results

Average load-displacement curves for each group were shown in Fig. 2. In FD group, stiffness of the first, second, and third phases was 1.6±0.4, 23.8±7.9, and 247.6±77.9N/mm, respectively. In OD group, stiffness of the first, second, and third phases was 1.7±0.4, 29.7±8.0, and 510.6±125.6N/mm, respectively. In ND group, stiffness of the first, second, and third phases was 1.1±0.3, 47.5±1.9, and 372.4±76.8N/mm, respectively. There were significant differences among the material phases for the groups (p<0.05). In comparison of each FD and OD group with ND group, only stiffness in the first material phase except for the second and third material phases was significantly different (p<0.05). The effective moduli for FD, OD and ND groups were 0.32±0.08, 0.34±0.08 and 0.22±0.06MPa, respectively. There was a significant difference among the effective moduli, except for the relation between FD and OD group. Fig. 3 shows the results of micro-indentation test in ND, OD and FD groups. Each result was presented as relative values, normalized by the values for the ND group.

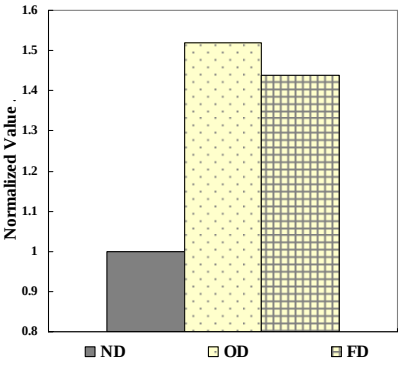

Fig. 3 Results of micro-indentation test in ND, OD and FD groups. Each result was presented as relative values, normalized by the values for the ND group

IV. Discussions and Conclusion

Mechanical characteristics on the gastrointestinal tract with FGID were quantitatively evaluated by using micro indentation test. These results suggest that FGID may be caused by obesity and psychological stress associated with overeating and mentally fatigue, respectively.

The present study identified that the gastrointestinal tract with the FGID became more rigid than normal gastrointestinal tract. This may be explained by the pacemaker mechanisms underlying the gastrointestinal autonomic rhythmic motility. It is widely accepted that Interstitial Cells of Cajal (ICC) drives spontaneous rhythmic motility in the integrative control of the gastrointestinal function [11], [12]. Here, this ICC form networks widely distributed within the submucosal, intra-muscular and inter-muscular layers of the gastrointestinal tract from the esophagus to the internal anal sphincter. Considerable researchers reported the ICC affected intracellular Ca^{2+} handling, which plays a critical role in generation of pacemaker for the spontaneous rhythmic motility, although respective players such as the Ca^{2+}-ATPase of the sarcoplasmic reticulum (endoplasmic reticulum), IP3 receptors, ryanodine receptors and plasma membrane ion channels might have divergent roles in the Ca^{2+} release-refilling cycles [13], [14]. Based on these facts, it may be expected that abnormalities of the ICC induced by a toxin absorbed into the gastrointestinal tract well generate abnormal function of intracellular Ca^{2+} handling. This may result in a rigor of the gastrointestinal tract by abnormally successive contraction of the smooth muscle composed the tract. It is because the contraction of the smooth muscle is controlled by the excitation-contraction coupling mechanism regulated by Ca^{2+} pump [15].

The study may be valuable as first attempt to identify the relationship between risk factors (emotional stress and obesity) and FGID in the mechanical point of view. The occurrence mechanism of FGID related to obesity and stress will be explained in our ongoing study incorporated with molecular biological studies.

Acknowledgment

This research was supported by Regional Research Center Program which was conducted by the Ministry of Commerce, Industry and Energy of the Korean Government.

References

[1] S. Haag, “Symptom patterns in functional dyspepsia and irritable bowel syndrome: relationship to disturbances in gastric emptying and response to a nutrient challenge in consulters and non-consulters,” *Gut*, vol. 53, pp. 1445-1451, 2004.
[2] N. J. Talley, “Symptom patterns in functional dyspepsia and irritable bowel syndrome: relationship to disturbances in gastric emptying and response to a nutrient challenge in consulters and non-consulters,” *Am J Gastroenterol.*, vol. 99, pp. 1807-1814, 2004.
[3] F. Cremonini, “Relationship between upper gastrointestinal symptoms and changes in body weight in a population-based cohort,” *Neurogastroenterol Motil.*, vol. 18, pp. 987-994, 2006.
[4] K. M. Flegal, “Prevalence and trends in obesity among US adults,” *JAMA*, vol. 288, pp. 1723–1727, 2002.
[5] M. Nilsson, “Obesity and estrogen as risk factors for gastroesophageal reflux symptoms,” *JAMA*, vol. 290, pp. 66–72, 2003.
[6] J. Lagergren, “No relation between body mass and gastro-oesophageal reflux symptoms in a Swedish population based study,” *Gut*, vol. 47, pp. 26–29. 2000.
[7] M. Nilsson, “Body mass and reflux oesophagitis: an oestrogen-dependent association?” *Scand J Gastroenterol.*, vol. 37, pp. 626–630, 2002.
[8] G. R. Locke, “Risk factors associated with symptoms of gastroesophageal reflux,” *Am J Med.*, vol. 106, pp. 642–649, 1999.
[9] H. Mönnikes, “Role of Stress in Functional Gastrointestinal Disorders Evidence for Stress-Induced Alterations in Gastrointestinal Motility and Sensitivity,” *Digestive diseases*, vol. 19, no. 3, pp. 201-211, 2001.
[10] R. L. Levy, “Psychosocial Aspects of the Functional Gastrointestinal Disorders,” *Gastro.*, vol. 130, pp. 1447-1258, 2006
[11] K. W. Min, “Interstitial Cells of Cajal (ICC) and Gastrointestinal Stromal Tumor (GIST): facts, speculations, and myths,” *J. Cell Mol Med.,* vol. 10, pp. 995-1013, 2006.
[12] M. Takaki. “Cut pacemaker cells: the interstitial cells of cajal (ICC),” *J. Smooth Muscle Res.,* vol. 39, pp. 137-161, 2003.
[13] K. D. Keef, “Basal release of nitric oxide induces an oscillatory motor pattern in canine colon,” *J. Physiol.,* vol. 499, pp. 773-786, 1997.
[14] T. K. Smith, “Interaction of two electrical pacemakers in the muscularis of the canine proximal colon,” *Am. J. Physiol.,* vol. 252, pp. 290-299, 1987.
[15] A. C. Guyton, *Textbook of medical physiology*. 10 ed. W.B. Saunders, Philadelphia, 2000.