Gut-Brain axis and its role in functional gastrointestinal disorders

Essay

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List of Abbreviations

ALT	:	Alanine Amino Transferase
AST	:	Aspartate Amino Transferase
CBD	:	Common Bile Duct
CCK	:	Cholecystokinin
CIC	:	Chronic Idiopathic Constipation
CIN	:	Chronic Idiopathic Nausea
CNS	:	Central Nervous System
CRF	:	Corticotropin Releasing Factor
CT	:	Computerized Tomography
CVS	:	Cyclic Vomiting Syndrome
EI	:	Extraintestinal
ENRD	:	Endoscopy-Negative Reflux Disease
ENS	:	Enteric Nervous System
EPS	:	Epigastric Pain Syndrome
ERCP	:	Endoscopic Retrograde Cholangiopancreatography
ES	:	Endoscopic Sphincterotomy
FAPS	:	Functional Abdominal Pain Syndrome
FD	:	Functional Dyspepsia
FDA	:	Food and Drug Administration
FGIDs	:	Functional Gastrointestinal Disorders
FI	:	Fecal Incontinence
GB	:	Gallbladder
GBEF	:	Gallbladder Ejection Fraction
GERD	:	Gastroesophageal Reflux Disease
GI	:	Gastrointestinal

H2RAs	**:**	Histamine 2 Release Antagonists
HIDA scan	**:**	Hepatobiliary Imino-Diacetic Acid scan
IBS	**:**	Irritable Bowel Syndrome
IBS-A	**:**	Alternating IBS
IBS-C	**:**	Irritable Bowel Syndrome with constipation
IBS-D	**:**	Irritable Bowel Syndrome with diarrhea
IBS-M	**:**	Mixed Irritable Bowel Syndrome
IBS-U	**:**	Unsubtyped Irritable Bowel Syndrome
ICS	**:**	Irritable Colon Syndrome
LES	**:**	Lower Esophageal Sphincter
LFTs	**:**	Liver Function Tests
MRCP	**:**	Magnetic Resonance Cholangiopancreatography
MRI	**:**	Magnetic Resonance Imaging
NERD	**:**	Non Erosive Reflux Disease
NSAIDs	**:**	Nonsteroidal Anti-Inflammatory Drugs
PD	**:**	Pancreatic Duct
PDS	**:**	Postprandial Distress Syndrome
PPI	**:**	Proton Pump Inhibitor
SC	**:**	Spinal Cord
SERT	**:**	Serotonin Reuptake Transporter
SNRIs	**:**	Serotonin and Norepinephrine Reuptake
SO	**:**	Sphincter of Oddi
SOD	**:**	Sphincter of Oddi Disorders
SOM	**:**	SO Manometry
TCAs	**:**	Tricyclic Antidepressants
UK	**:**	United Kingdom
US	**:**	Ultrasound

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Introduction

Throughout recorded history, and alongside structural diseases of the intestinal tract, are maladies that have produced multiple symptoms of pain, nausea, vomiting, bloating, diarrhea, constipation, or difficult passage of food or feces. Although structural diseases can be identified by pathologists and at times cured by medical technology, the nonstructural symptoms that we describe as "functional" remain enigmatic and less amenable to explanation or effective treatment ***(Drossman et al., 1993).***

Historical Background about Functional Gastrointestinal Disorders

There are many references to gut dysfunction in the ancient and early European literature. However, the first credible English language descriptions of irritable bowel syndrome (IBS) appeared in the early 9th century. One such description of the IBS in 1818 ***(Powell, 1818)*** drew attention to three cardinal symptoms of IBS: abdominal pain, "derangement of…digestion," and "flatulence." A few years later, ***(Howship, 1830)*** described a "spasmodic stricture" of the colon reflecting the enduring, but unsubstantiated belief that functional gut disorders are somehow the product of gut spasm. Mid-century brought more sophisticated treatises (and very unsophisticated cures such as purging and "electrogalvanism"). ***Cumming*** **in (1849)** exclaims incredulously, "the bowels are at one time constipated and at another lax in the same person … how the disease has two such different symptoms I do not propose to explain." Were he to return to a modern IBS consensus

meeting, he would discover that this enigma remains! ***Cumming's*** treatise contained one other comment in line with modern thinking about IBS. "One can tell, without more minute examination what the nature of the complaint is".

Medicine's understanding of IBS progressed little during the next 120 years.

The first systematic attempt to bring discipline to this area was a 1962 retrospective review of IBS patients at Oxford by ***(Chaudhary and Truelove, 1962)***. The authors reported symptoms that we recognize to be those of IBS (or irritable colon syndrome (ICS) as they termed it). They even separated IBS from what we now call functional diarrhea, and noted that one quarter of their patients' complaints began with an enteric infection. Their report ushered a new era, and scientific publications on functional disorders increased rapidly thereafter (Figure 1).

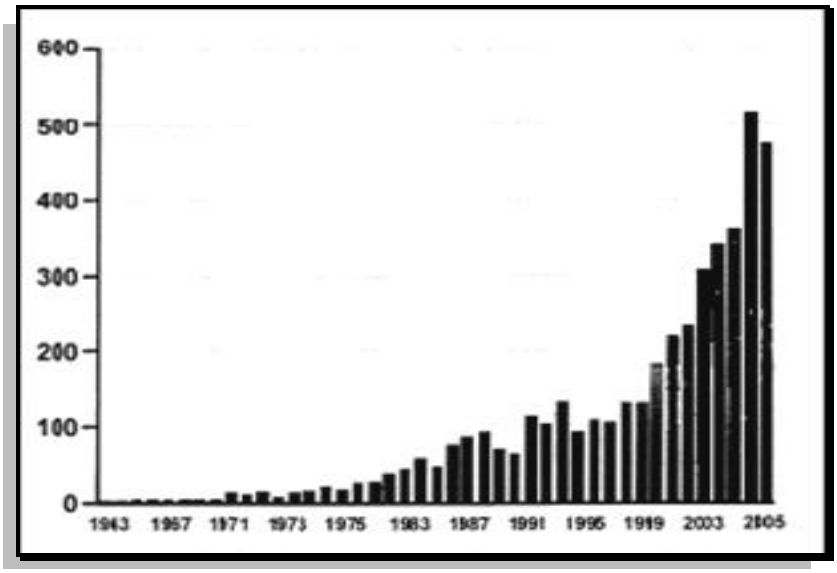

Fig. (1): Annual results of Pubmed literature searches for irritable bowel syndrome (IBS) and irritable colon syndrome (ICS) between the 1962 Chaudhary and Truelove report and December 2005. Note the rapid rise in publications during that period. While half the publications in the 1960s had ICS in their titles, only 1 or 2 do so now exclusively in the non-English literature.

In 1978 ***(Ken Heaton, et al.)*** reported results obtained by questionnaire administered to Bristol outpatients with abdominal pain and disordered bowel habit. They found 6 of 15 symptoms more common in IBS than organic gut disease (diagnosis determined by a chart review a year later) became the ***Manning Criteria***. In 1984, ***(Kruis, et al.)*** from Germany, reported a similar study. Their report recalls the three cardinal IBS symptoms of pain, bowel dysfunction, and flatulence mentioned by ***Powell*** in **1818**, if all three were present, IBS was highly likely. ***Kruis, et al., 1984*** stressed chronicity and other symptoms as well, but their major contribution was to record "alarm" symptoms that should alert the physician to organic disease. These two discriminate function studies in addition to epidemiologic data provided by ***(Drossman and Whitehea, 1982)*** are the basis of the Rome criteria for IBS.

The inspiration for the Rome process was an IBS symposium at the 12th International Congress of Gastroenterology held in Lisbon in 1984.

W. Grant Thompson collaborated with ***Doug Drossman (USA), Ken Heaton (UK), Gerhard Dotteval (Sweden), and Wolfgang Kruis (Germany)*** for 2 years. In 1987, they met in Rome to debate a draft proposal and reach consensus and sent the penultimate draft to 16 expert colleagues in seven countries. The working team considered their comments and suggestions and presented the first Rome criteria at the 13th Congress in Rome in 1988. The guidelines were published the following year and known as the ***Rome-2 IBS Criteria***, and attracted much interest among researchers and pharmaceutical companies (Table 1).

Table (1): History of the Rome Diagnostic Criteria

The Manning Criteria for IBS (1978)
The Kruis Criteria for IBS (1984)
The Rome Guidelines for IBS (1989) **(*Rome-2 IBS Criteria*)**
The Rome Classification System for FGIDs 1990 **(*Rome-1*)**
The Rome I Criteria for IBS (1992) and the FGIDs (1994)
The Rome II Criteria for IBS (1999) and the FGIDs (1999)
The Rome III Criteria (2006)

In 1990, ***Torsoli, Enrico Corrazziari and Doug Drossman*** met in Rome to classify the functional gastrointestinal disorders into 21 entities in 5 anatomical regions of the gut. This was the first time that diagnostic criteria were proposed for all the functional gut disorders, included the first revision of the 1988 IBS criteria, and could be considered *Rome-1*. In 1994, their collective work was updated and published and this work is now known as *Rome I.*

The *Rome II* process included 4 years of deliberations by over 50 investigators from 13 Western countries organized into 10 committees. The working teams met together in Rome in 1998. This permitted interaction and harmonization among the committees. The Rome II criteria and essential supporting information were published in a *Gut* supplement in 1999. In addition to the anatomically determined criteria and clinical trials working teams, new teams addressed basic science, neurogastroenterology, psychosocial issues, and pediatric functional gut disorders.

The Rome III Board selected 87 participants from 18 countries in 14 committees. Members were added from developing countries including

China, Brazil, Chile, Venezuela, Hungary, and Romania. New working teams were created for gender, society, and social issues. Functional abdominal pain was split from functional bowel disease. Rome III culminated in a meeting in Rome in November/December 2004. The results of the process are published in the summer of 2006 (Table 2).

Table (2): Rome III Functional Gastrointestinal Disorders

A. Functional esophageal disorders
A1. Functional heartburn
A2. Functional chest pain of presumed esophageal origin
A3. Functional dysphagia
A4. Globus
B. Functional gastroduodenal disorders
B1. Functional dyspepsia
B1a. Postprandial distress syndrome
B1b. Epigastric pain syndrome
B2. Belching disorders
B2a. Aerophagia
B2b. Unspecified excessive belching
B3. Nausea and vomiting disorders
B3a. Chronic idiopathic nausea
B3b. Functional vomiting
B3c. Cyclic vomiting syndrome
B4. Rumination syndrome in adults
C. Functional bowel disorders
C1. Irritable bowel syndrome
C2. Functional bloating
C3. Functional constipation
C4. Functional diarrhea
C5. Unspecified functional bowel disorder
D. Functional abdominal pain syndrome
E. Functional gallbladder and Sphincter of Oddi (SO) disorders
E1. Functional gallbladder disorder
E2. Functional biliary SO disorder
E3. Functional pancreatic SO disorder
F. Functional anorectal disorders
F1. Functional fecal incontinence
F2. Functional anorectal pain
F2a. Chronic proctalgia
F2a1. Levator ani syndrome
F2a2. Unspecified functional anorectal pain
F2b. Proctalgia fugax
F3. Functional defecation disorders
F3a. Dyssynergic defecation
F3b. Inadequate defecatory propulsion

Aim of the Work

The aim of this essay is to review the literature to clear the role of gut-brain axis in controlling functional gastrointestinal disorders.