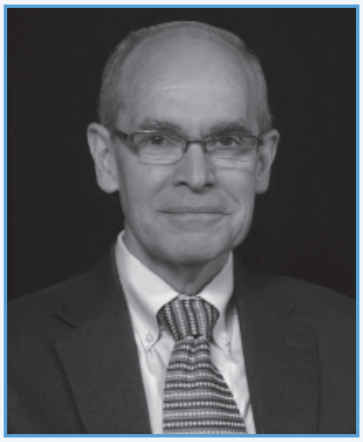
A publication of the University of North Carolina Center for Functional GI & Motility Disorders

Fall 2011

Digest

Our mission is to advance the biopsychosocial understanding and care of patients with functional GI & motility disorders through research, training and education.



Functional Gastrointestinal Disorders in Asia

William E. Whitehead, PhD
Center Co-Director

Two-thirds of the world's population live in Asia – China, India, Korea, Japan, and the Southeast Asian countries – and it follows that most patients with Functional Gastrointestinal Disorders (FGIDs) are Asians. In the last 5 years Asian physicians have become increasingly aware of the importance of the FGIDs in their countries and are asking whether Western explanatory models fit their patients and their circumstances. This article is a brief summary of some of this activity.

Role of the Rome criteria. In the West, the concept of functional gastrointestinal disorders emerged gradually over a period of 150 years from clinical observations that psychological stress has a strong influence on GI function and that many patients have chronic disabling GI symptoms without any infectious or structural cause. The Rome diagnostic criteria developed out of a need for a consensus on research diagnostic criteria and are used in many tertiary care GI clinics, but they continue to be ignored by the majority of primary care physicians. In Asia, the evolution has been quite different: Many Asian physicians became aware of the FGIDs through research and other publications based on the Rome criteria. A major milestone for Asians was the decision by a group of Chinese physicians headed by Dr. Meiyun Ke to translate the book, "Rome III: The Functional Gastrointestinal Disorders" into Mandarin Chinese, and the Rome criteria are used in the clinical diagnosis and management of IBS throughout Asia.

Consensus documents on IBS and FD. Publication of Rome III into Chinese was soon followed by the establishment of the Asian Neurogastroenterology and Motility Association (ANMA) in 2005, which has become a focus for clinical research on the FGIDs. Under the leadership of Kok Ann Gwee of Singapore, the ANMA sponsored working teams to review the published data on the FGIDs in Asia, published an Asian Consensus on IBS (J Gastroenterol Hepatol 2010;25:1189-1205) and is preparing a separate Asian Consensus on Functional Dyspepsia for publication as well. These working teams concluded that the pathophysiology of IBS and FD is identical to what has been reported in the West. However, they also concluded that there are important differences in the symptoms with which Asian patients present for care. Most notably, they concluded that psychological comorbidity is less common and less important in Asian patients compared to Western patients, that reactions to eating play a more important role in Asia, and that bloating rather than pain is the cardinal symptom of Asian IBS. They also concluded that normal ranges for stool frequency and stool form differ for Asians compared to Western populations, probably as a consequence of differences in diet.

Rome Asian Working Team (RAWT). Based on the conclusions of their systematic review of IBS and FD, the leaders of the ANMA considered discarding the Rome criteria and developing uniquely Asian diagnostic criteria for the FGIDs. However, through a series of meetings between Kok Ann Gwee, Doug Drossman, John Kellow, and Bill Whitehead, the decision was to conduct a survey of symptoms associated with FGIDs in Asian countries to determine whether different diagnostic criteria are required or whether modifications to the Rome criteria would meet the needs of physicians caring for Asian patients. This resulted in an agreement to form a Rome-Asian Working Team chaired by Kok Ann Gwee and co-chaired by Bill Whitehead, to design and carry out the survey. Members of the working team are: Andrew Chua (Malaysia), Uday Ghoshal and Nitesh Pratap (India), Sutep Gonlachnavit (Thailand), Minhu Chen and Hou Xiao-Hua (China), Bak Young-Tae (Korea), Hiroto Miwa (Japan), and Reuben Wong (Singapore).

Translation and validation of Diagnostic Questionnaire. The first task undertaken by the RAWT was to develop

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and validate a common survey instrument. The working team first adapted the Rome Diagnostic Questionnaire by adding supplemental questions while preserving all the questions in the standard Rome questionnaire. The supplemental questions addressed additional symptoms the committee believed would be important to Asian patients. The next step was to translate and validate the questionnaire into 7 languages: Mandarin Chinese, Indian Hindi, Indian Telegu, Indian and Pakistani Bengali, Thai, Korean, Malaysian, and possibly Japanese. The translations were done by the technique recommended by Ami Sperber (Gastroenterology 2004;126(Suppl 1):S124-8), which includes two forward translations from English to the target language by independent translators, review by a bilingual physician and resolution of differences between the target language translations, backwards translation into English, and review of differences between the backwards translation and the original English version. The translations were validated for understandability by administering them to small groups of patients with FGIDs and for content validity by comparing questionnaire responses to independent clinical diagnoses. Test-retest reliability was assessed by administering the questionnaire a second time after approximately two weeks. This translation and validation process was completed in most of the target languages by the time of an interim committee meeting in Vietnam on July 1, 2011.

Survey design. The investigators from each of the 6 participating countries have been asked to enroll at least 200 FGID patients from two different sites and to administer the new enhanced Asian FGID diagnostic questionnaire. Data will be transferred to a statistical core at the National University of Singapore for analysis. An interim report on the progress of the study will be presented at the Asian Digestive Disease Week held in Singapore in October, 2011. Sponsors of the survey, in addition to the Rome Foundation, are Abbott and Janssen-Cilag pharmaceutical companies.

There are limitations to the survey being conducted by the RAWT: For example, there is no concurrent comparison group of patients form North America and Europe, and the patients will be clinic attenders rather than representative of the population. Moreover, there are important confounders such as diet and exposure to enteric pathogens which could contribute to East-West differences and these are not addressed by the study. However, this survey will inform the Rome working teams who are tasked with revising the Rome criteria by 2016, and it will provide a foundation for an anticipated multinational survey of FGIDs that the Rome Foundation will undertake. It may also provide some initial insights into the remarkable observation that there has been a 2-3 fold increase in the prevalence of IBS and FD in Asian countries in the past decade.

Over the past decade, the UNC Center for Functional GI and Motility Disorders has enjoyed significant grant support from a number of private foundations and corporations. These grants have ranged from sponsorships of specific events (symposia or CME courses) to unrestricted grants in support of fellowships and the Center's education and training effort. Support for the Digest Newsletter is provided by Takeda Pharmaceuticals North America, Inc.

DIGEST is a quarterly publication of the UNC Center for Functional GI & Motility Disorders, a center of excellence within the Division of Gastroenterology and Hepatology, School of Medicine, University of North Carolina at Chapel Hill.

The Center's co-directors are. **Douglas A. Drossman, MD**, Professor of Medicine and Psychiatry, and **William E. Whitehead, PhD**, Professor of Medicine and Gynecology.

For more information about the Center, please visit our website at www.med.unc.edu/ibs

DIGEST

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REACHING OUT
EXPANDING KNOWLEDGE
OFFERING A RAY OF HOPE

Douglas A. Drossman, MD

Professor of Medicine and Psychiatry
Co-Director UNC Center for Functional GI and Motility Disorders
Division of Gastroenterology and Hepatology
University of North Carolina at Chapel Hill

Dear Friends and Colleagues,

I would like to take this opportunity to inform you of a major transition in my career. As of December 31, I will be leaving full time employment at UNC and the UNC Center for Functional GI and Motility Disorders in order to expand my mission to help physicians and patients on a larger scale. Although leaving UNC may come as a surprise to some, it is something I have considered carefully over the last year and I believe it is the best choice at this time. I plan to broaden my educational and clinical activities from a successful 35 year career in academic medicine to apply my knowledge and skills at a national and global level. While my career path is not fully worked out, there are some things I can share with you at this time.

- I will continue as adjunct Professor of Medicine and Psychiatry at UNC and will be advising and teaching at the UNC Center of Functional GI and Motility Disorders where as you know I am currently co-director.
- I will enhance my international activities as President of the Rome Foundation in order to further develop the Foundation and the Rome IV initiative.
- I will continue to consult in the health care field. This will include:
  - academic programs in medicine, psychiatry and digestive diseases
  - Federal (NIH) or pharmaceutical grants where I will serve as a mentor or consultant
  - gastrointestinal medical practices
  - pharmaceutical advisory boards
  - health care foundations
  - medico legal groups
  - non-profit health care and educational and media companies
- I am also seeking to develop a unique private consultation practice for one day a week or more where I would continue to receive referrals nationally for patients who have complex and difficult to manage functional GI and motility disorders.
- I am looking at the option of traveling to conduct lectures and workshops in the areas of my expertise, and to consult with clinicians about their patients. This would include a patient consultation visit with the clinician present. I would discuss my observations and provide recommendations and remain available by phone to help physicians in the patient's ongoing care. My expertise for these lectures and workshops relate to:
  - the diagnosis and treatment of patients having complex and co-morbid IBS and functional GI disorders
  - clinical trial development
  - epidemiological and outcome studies teaching of communication skills for accurate diagnosis and to enhance the doctor-patient relationship
  - research and clinical mentoring of young investigators

Finally, I am seeking advice and assistance in developing a non-profit organization that would focus on the education of clinicians and patients in biopsychosocial research, education and patient-centered care. I am looking to discuss this further with experts in business development and potential individuals and organizations that might seek to support such an endeavor.

My 35 years at UNC have been enjoyable and productive; now I look forward to the future with anticipation and enthusiasm. I want to thank you for our association over all these years and am hopeful this will continue in the future.

The Role of the Psychologist in the Functional GI Disorders Clinic

Stephan Weinland, PhD
Assistant Professor of Medicine

Psychologists working at the intersection of medicine and psychology often have a sub specialization in the field of "Behavioral Medicine". This area of psychological training examines the role of behaviors, thoughts (cognitions) and emotions as they contribute to the predisposition, onset and perpetuation of illness. While including psychologists into gastroenterology clinics is still in its infancy, this type of integration has been happening in other areas of medicine (cardiology, pain management, diabetes management and cancer care) for some time.

In partnering with medical doctors, psychologists bring a broad understanding of human behavior and a skill set that can inform the medical interaction. In the Functional GI disorders clinic, the psychologist has five important roles.

- ***Education*** – of patients and physicians on how the patient can make changes in their behavior to help improve the clinical response
- ***Assessment*** – the evaluation of coping and symptom management strategies and the detection of psychological diagnoses
- ***Treatment*** – using psychological interventions that complement or enhance the medical care given
- ***Communication*** – within and among the treatment team and patients
- ***Research*** – on the role of psychological factors in the illness experience

Psychologists Foster Understanding of FGIDs and Treatments

For patients, the symptom experiences of Irritable Bowel Syndrome and other FGIDs are very real. Often, patients have an underlying understanding of the relationship between experience and their symptom presentation, but know only limited ways of dealing with or managing their symptoms. Physicians will use the Rome criteria to help diagnose FGIDs, but patients may have difficulty understanding how and why their bodies are reacting with symptoms the way they are. These are areas in which education of both patients and physicians on mind body relationship principles can be particularly effective. Helping patients to develop a grounded understanding of how their symptoms have developed over time, as well as how their clinician is assessing and treating the condition can help patients feel more in control of their symptoms. Positive self-care strategies and implementing behavioral changes can have a positive impact on symptom experience and thereby increase the patients' abilities to engage in effective symptom management. Psychologists are experienced at educating individuals on what it takes to engage in effective symptom management.

Assessing Patient Coping and Symptom Management

Psychologists complete evaluations (assessments) to learn about which psychosocial factors contribute to functional GI diagnoses and how these factors can affect patients. Sometimes a regular length physician appointment is not enough time to understand the contributing factors to a patient's symptom experience. Psychologists have more frequent and longer availability to develop this type of understanding with the patient. We know that GI symptoms often have a considerable impact on moods and behaviors. Psychologists are trained in assessing these effects, and providing recommendations for reducing their adversity. Assessment of coping skills and symptom management strategies are also useful in developing a comprehensive treatment plan.

Conducting Therapy

Dealing with FGID symptoms for a prolonged period of time can have lasting effects on mood. Psychologists are trained to help patients develop clearer strategies for managing those feelings as well. Treatments such as cognitive behavioral therapy (CBT), hypnosis, mindfulness based stress reduction, biofeedback and interpersonal psychotherapy have been shown to be effective in treating functional GI disorders. Not all psychologists will be trained in each modality, but many will have a good understanding of how each may help ameliorate symptom experience. Working with a psychologist can help patients learn to effectively treat the co-occurring mood and behavioral difficulties that can be associated with the illness.

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The Role of the Psychologist in the Functional GI Disorders Clinic

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Facilitating Communication

While therapy discussions with psychologists are confidential, often times treatment relevant factors are brought up during the course of therapy. The psychologist works with the patient to determine how best to communicate treatment relevant information to the treatment team while maintaining patient confidentiality. In this way the psychologist can act as a treatment facilitator. Additionally, the psychologist can serve as another point of contact for the patient while on their own outside of the clinic, facilitating communication on the topic of how treatment is progressing and how symptom experiences change over time.

Engaging in Research

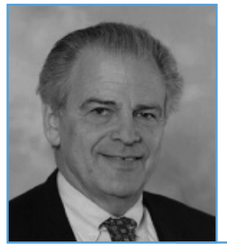
The influence of psychosocial factors in symptom development and management is an important factor in conducting research on FGIDs. With their understanding of how cognitions, behaviors and emotions can influence symptoms, psychologists are able to inform the conduct of research in FGIDs. Current research topics that our center is examining relate to psychological correlates of pediatric FGID, motility functioning, hypnosis research, clinical trials and patient outcomes research.

Putting it all together

Working with a licensed psychologist or mental health practitioner in a gastroenterology clinic need not be distressing, rather, they are often effective members of the treatment team who can help clinicians provide the most comprehensive and effective care to patients. Patients should know that when coming to an initial assessment appointment they may be asked to complete standardized psychological assessments. Patients will then usually meet with the psychologist for a 90 minute new patient evaluation. Topics discussed during this evaluation will include: current symptom experience and the process of symptom onset, exacerbating or ameliorating factors, engagement in self care, sleep/diet and exercise habits. Additional topics of traumatic stressors and substance use history will likely also be discussed. Towards the end of the visit, the psychologist will work with the patient to develop a treatment plan moving forwards. The plan will include either referral to a clinician close to the patient, setting up of follow up appointments and services with the assessing psychologist and engagement in psychoeducation on the topic of FGID's. Any treatment modalities will be agreed upon and discussed with the patient in order to collaboratively develop a plan to improve symptom management strategies.

Follow up appointments will always start with a discussion of present symptom experience and then move to the active therapeutic modality being worked with at that time (CBT, hypnosis, relaxation training, etc.) The psychologist will communicate relevant treatment issues to the treating clinician – often only in general terms so that the clinician can be aware of contributing factors to care. As members of the same treatment team working to help the patient, these communications are helpful, however confidentiality rules are always observed.

The number of sessions one works with a psychologist is determined by a multitude of factors but is always communicated and established collaboratively with the patient. Typical visit numbers will vary with the degree of symptom experience and typically range from one to twelve sessions. Most insurance plans will cover a portion of or a certain number of psychotherapy sessions.



Management of Fecal Incontinence

Arnold Wald, MD
Division of Gastroenterology and Hepatology
University of Wisconsin School of Medicine and Public Health

Fecal incontinence is one of the most devastating of all nonfatal illnesses, resulting in considerable embarrassment and anxiety to those who suffer from it. It affects 2% to 17% of people living in the community and almost half of all nursing home residents. Many individuals with fecal incontinence are so embarrassed that they do not volunteer this complaint to their physicians and must be asked directly.

The prevalence of fecal incontinence is increased in (1) women; (2) older age groups; (3) those with poor health status or physical limitations, and (4) individuals residing in nursing homes.

The causes of fecal incontinence may be classified into a number of broad categories that occur alone or in combination. Many of these are suggested by a careful history and directed physical examination, including perianal inspection and a digital rectal examination. Such an examination is heavily dependent upon the experience and skills of the examining physician. In selected patients, especially when there is diagnostic uncertainty, tests to assess anorectal structure and function may be performed.

History and Physical Examination

In addition to trying to establish a cause and formulate management, the history should attempt to ascertain the frequency, severity and nature of incontinence, and the impact of incontinence on quality of life. This includes the ability to leave the house for work and social activities. Patients are particularly affected by the unpredictability of episodes of incontinence and often alter both social and professional activities.

Understanding anorectal structure and function provides a road map to the directed physical examination. The technique of performing a digital exam has not been sufficiently emphasized and its assessment has been dismissed by some investigators as inaccurate. As with any test, accuracy depends upon the skill of the examiner. When performed by an experienced and knowledgeable examiner, the following features can be assessed: anal canal tone, external anal sphincter contraction, puborectalis muscle contraction, the presence of a fecal impaction or mass, and large disruptions of the anal sphincter complex.

Anorectal Manometry and Anal Sonography

When fecal impaction with overflow, decreased rectal storage capacity and neurologic causes have been excluded, anorectal manometry is the preferred study to assess anal sphincter function and rectal sensation. When anal sphincter disruption requiring surgical repair is a consideration, anal sonography can assess the structural integrity of the sphincters. If a sphincter tear is discovered, assessment of external anal sphincter and puborectalis muscle with EMG studies is optimal to exclude concurrent denervation which reduces the chances of surgical success (see below). These tests are best done in tertiary centers by experienced individuals.

Management

The management of fecal incontinence requires a multimodal approach and includes modification of both stool consistency and delivery to the anorectum, behavioral interventions, and occasionally, surgery to correct abnormal continence mechanisms. Management of incontinent patients is based upon the following principles:

1. Treatment approaches must be tailored to each patient as there are many different causes of fecal incontinence.
2. Optimal management is based upon accurate assessment of pathogenesis.
3. Modifying bowel habits is often central to effectively managing fecal incontinence.
4. Fecal incontinence is not an inevitable consequence of aging and should never be considered normal or "age appropriate".

Many patients with fecal incontinence can be managed effectively without referral to specialists.

General Measures

Incontinence pads provide skin protection and prevent soiling of clothing and linens; polymers conduct moisture away from the skin. Disposable products are superior to non-disposable products in providing skin protection. Barrier creams such as zinc oxide and calamine lotion (Calmoseptine®: Calmoseptine, Inc.; Huntington Beach, CA) may prevent skin irritation while perianal fungal infections may be treated with topical antifungal agents.

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Management of Fecal Incontinence
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Medical and Pharmacological Treatments

In patients with "overflow" incontinence associated with fecal impaction, disimpaction and colon cleansing provide immediate relief of soiling. Such patients require an ongoing bowel management program. This involves regularly scheduled attempts to defecate with the assistance of osmotic laxatives, such as magnesium salts and polyethylene glycol. Oral stimulant laxatives or bisacodyl suppositories are employed as "rescue therapy" if there is no defecation for 3 days. Short-term success rates of 60-80% have been reported, but high long-term recurrence rates necessitate ongoing vigilance.

When incontinence is associated with decreased colonic and rectal storage capacity or with chronic diarrhea, treatment is directed towards reversing the underlying causes or, if this is not an option, modifying stool volume, consistency, and delivery. It is often beneficial to reduce dietary fiber intake in combination with anti-diarrheal drugs which slow colonic transit. Of the anti-diarrheal agents available, loperamide is preferred as it has no central nervous system effects. Adequate doses and timing are important i.e. 2-4 mg 30 minutes before meals or prior to social occasions to avoid accidents outside the home. In patients with diarrhea associated with irritable bowel syndrome, medications with anti-cholinergic effects, such as tricyclic agents may be effective. Patients with isolated internal anal sphincter abnormalities are characterized by decreased anal canal tone. Characteristically, they have fecal soiling with normal bowel habits. I have found that a cotton anal plug is an inexpensive approach which restores passive barrier function and serves as an absorbent as well.

Biofeedback

Biofeedback has been reported to be effective in many patients with fecal incontinence associated with impaired functioning of the puborectalis muscle and external anal sphincter. In contrast to pelvic floor strengthening exercises such as Kegel exercises which are directed exclusively at re-educating weakened or impaired muscles, biofeedback attempts to improve rectal sensation and sphincter muscle responsiveness to intra-rectal stimuli such as balloon distension. Many believe that improvement of perception of rectal sensation and the synchronization of external anal sphincter contractions to rectal stimulation are important factors associated with improvement.

Surgical Approaches

Anal sphincteroplasty is based on repairing an anatomically disrupted anal sphincter complex. The use of anal sonography to demonstrate sphincter disruptions has largely replaced EMG mapping of the external anal sphincter. Although many studies have reported short term improvement of fecal continence in up to 85% of patients, failure rates of approximately 50% are noted after 40-60 months. In a number of representative series, full continence after sphincteroplasty was maintained in only 28% of patients after a mean follow-up of 40 months, and in only 11-14% of patients followed for over 69 months.

Antegrade colonic irrigation via appendicostomy or cecostomy was initially developed to treat fecal incontinence in children and later was applied to fecal incontinence in adults. The premise of antegrade colonic irrigation is that regularly administered large volume enemas delivered into the cecum produce complete colonic emptying to prevent fecal soiling. The procedure can be helpful in appropriately selected children and adults.

Other surgical approaches

Replacement of a damaged or non-functioning anal sphincter complex involves using nearby muscles (dynamic graciloplasty) or an artificial implanted sphincter. Improved continence occurs in over 50% of patients on intention-to-treat analyses, but with significant morbidity, including infections, device malfunctions, and in the case of the artificial sphincter, a high percentage of explantation of the device. Such procedures are best performed by surgical teams with considerable experience.

For those with severe refractory incontinence, a diverting colostomy may provide dramatic improvement.

Sacral spinal nerve stimulation for fecal incontinence was developed as an extension of its successful use for disorders of urinary voiding and continence. The procedure involves three phases: (i) location of the sacral spinal nerves by percutaneous probing with a needle electrode to identify the nerve root which maximally stimulates anal sphincter contraction; (ii) temporary placement of an electrode to chronically stimulate the nerve root identified as the most efficient during acute testing; (iii) permanent implantation of a neurostimulator for chronic therapeutic stimulation.

In patients who successfully complete the first two phases, clinical improvement of fecal incontinence has been confirmed in both short and long term studies, especially in patients who have fecal incontinence at the first urge to defecate ("urge incontinence"). Objective physiological changes include increases in both resting and squeeze pressures, increased squeeze durations and improved rectal sensation.

On the Physician Patient Relationship

Albena Halpert, MD
Assistant Professor of Medicine
Boston University

Since ancient times, clinicians have recognized that the physician – patient relationship based on trust and compassion has considerable healing power or in modern terms "therapeutic effect." In order for the physician to make accurate diagnosis and provide optimal treatment recommendations, the patient must be able to communicate all relevant information about an illness. Physicians are obliged to honor the special nature of the medical relationship and to refrain from revealing confidential information. The traditional, paternalistic model for the physician-patient relationship involved patient dependence on the physician's professional authority. Believing that patient would benefit from the physician's actions, patient's preferences were generally overridden or ignored. During the second half of the twentieth century, the physician-patient relationship has evolved towards shared decision making. This model respects the patients' rights to hold views, to make choices, and to take actions based on personal values and beliefs. Patients have been increasingly entitled to weigh the benefits and risks of different treatments options, and to select the treatment that best promotes their own values: "Nothing about me without me." (1)

Because of its therapeutic potential, the relationship physicians have with their patients is arguably one of the most powerful, sensitive, and versatile "remedies" they can offer to their patients. However, in the western medical tradition, aside from for mental health professionals, clinicians seldom think of their relationships with patents as a therapeutic tool or even as a placebo. This is not surprising, given that the nature of this relationship today appears to be far more complex than ever before. Varieties of factors within and outside the health care system are constantly molding patient and physician behavior. Among the most important is the prevalence of chronic illnesses, new medical technologies, shifting reimbursement practices, the Internet, government regulations, rising costs, medical litigation and changing social norms. Unfortunately, the once-respected doctor-patient relationship is in great danger. Increasingly, research and anecdotal reports suggest that more and more Americans are loosing their confidence in the medical profession and feel disconnected from their doctors, especially compared to a generation ago. There is now a whole genre of "what your doctor won't tell you" books. The Internet medical blogs and medical support sites are overflowing with frustrated comments from patients about their healthcare experiences. News reports about medical errors and drug industry influence have increased patients' distrust. The rise of direct-to-consumer drug advertising is also contributing to changing physician-patient interactions. Most physicians, motivated to do the best for their patients, feel frustrated and increasingly dissatisfied when dealing with insurance regulations dictating care and fault the rise of medical litigation for practicing "defensive medicine". They also face declining reimbursements and higher costs resulting in significant time pressures often having only minutes to spend with each patient. Perhaps more importantly than any of the above factors is the fundamental disconnect between patients and physicians, who seem to not even talk the same language anymore. Doctors are trained to diagnose disease and treat it, while patients are interested in being listened to and feeling well. This disconnect has deep roots in the western model of medical training which emphasizes treatment of disease rather than taking into account the whole person and his/her disease experience (the illness)

The communication gap between physicians and patients with Irritable Bowel Syndrome (IBS) and other functional bowel disorders may be even greater than for some better defined chronic conditions. These common gastrointestinal conditions with low mortality but very high personal and societal costs have some specific disease characteristics that can strain the physician patient interaction. Two out of five IBS patients report being "not at all" satisfied with the care they are receiving (2). The high prevalence of anxiety and psychological distress associated with severe IBS, de- legitimizes this disease in the eyes of both doctors and patients. Patients often ask themselves "Is this in my head? (3).

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Center Visitor

Hamid Afshar, MD

Associated Professor of Isfahan University of Medical Sciences
Isfahan Psychosomatic Research Center (IPRC)

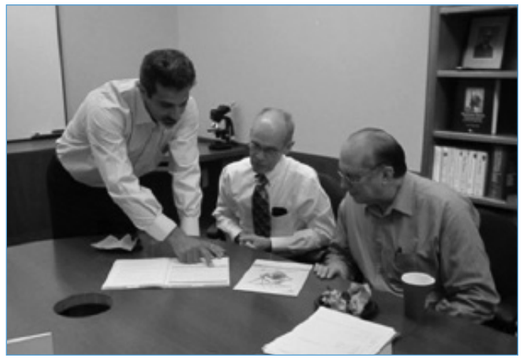
I had a brief but very helpful visit at the UNC Center for Functional GI and Motility Disorders last month. It was a great opportunity for me to learn about the treatment of FGID's in the US. I will never forget the practical training in the biopsychosocial approach to the most common disabling functional disorders in medicine that I received at UNC.

During my stay, I observed wonderful humanistic interviews in clinic, as well as the integration of psychotherapy into GI services. It was fascinating and I feel it would be useful for all medical students of different sectors, and subspecialties to experience these observations as part of their education.

I have been practicing with FGIDs, mainly IBS patients, since 2006, and our most important practical and educational materials came from the UNC Center for Functional GI & Motility Disorders. Although professor Drossman and professor Whitehead were main sources of practice and education for our group, I still had a lot of questions in mind about working with these patients. Questions like - How much education is necessary for the patient? When should we prescribe medication? When is it possible to taper medications?

(Left to right) William E. Whitehad, PhD; Douglas A. Drossman, MD; Hamid Afshar, MD; Christine Dalton, PA-C; Stephan Weinland, PhD; Miranda Van Tilburg, PhD; Ademola Aderoju, MD

I had the chance to join and observe Dr. Drossman and his physician assistant Christine Dalton in their clinic and I found many answers to my questions. Sometimes refractoriness of disorders, stubbornness or difficult problems, limitation of medications in these groups,



(Left to right) Hamid Afshar, MD; William E. Whitehead, PhD; Douglas A. Drossman, MD

slowness of responses and patients' severe suffering makes practicing very hard and challenging. It can therefore cause disappointment in physicians working with FGIDs. This issue was difficult for me before visiting UNC.

Pharmacotherapy for FGIDs is a dilemma. The majority of patients could benefit from antidepressants but many have negative attitude toward pharmacotherapy or medication intolerances. The integration of different skills for education and managing the patients requires a holistic attitude and biopsychosocial approach. I think medical practitioners can find an excellent example of an integrative care model of the biopsychosocial approach by working in Dr. Drossman clinic.

Another valuable experience in UNC clinic was taking part in psychotherapy observation sessions with Dr. Weinland. I observed professional, classic sessions of therapies, which are very helpful for all psychotherapists. To be honest, I would have loved to have video tapes to teach others how to conduct psychotherapy as well!

Two important research projects attracted me, during my observation. The first one was about Narcotic Bowel Syndrome (NBS) that is likely a common FGID in my country because of a high prevalence of opioid abuse and dependency. The other research project was a Seroquel study for refractory IBS cases that was very interesting for me because we have had experience with

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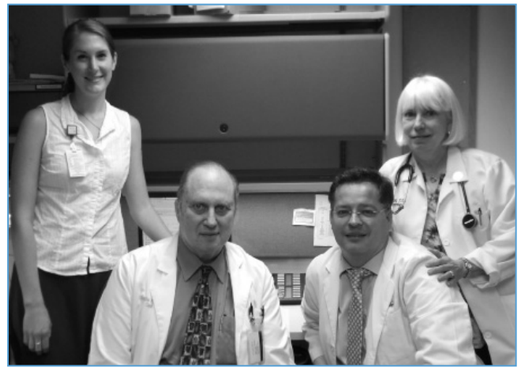
Center Visitor
Personal Reflections About Chapel Hill

Claude Botha, MD

Wingate Institute of Neurogastroenterology
Queen Mary University of London

My first impressions of Chapel Hill were how wonderfully "forestry" the town was. It seemed like everyone built their buildings around the trees as not to disturb the forest, and that was so deliciously refreshing and unlike London where even the gardens can be sculpted. The second thing that really impressed me was how friendly everybody was. From the street vendor all the way up to the company director there was a genuine friendliness and consideration for you.



(Left to right) Emily Brooks, RN; Douglas A. Drossman, MD; Claude Botha, MD; Christine Dalton, PA-C

Upon meeting the UNC team for the first time I was struck at how big both the Drossman and Whitehead teams were compared to the teams that I am used to in Europe. I also appreciated the integrated way pharmacological, preclinical and clinical aspects were dealt with, at all stages of research, from concept to post-analysis. Another thing I envied was the high level of organisation, communication and "team spirit" from all team members. I had the privilege of meeting with certain key researchers, and it was a memorable how each one exuded knowledge and a passion for their work.

When it came to my exposure to some of the clinical activities at the department, I was very privileged on having had the opportunity of joining consultations in the outpatient clinics, both in gastroenterology and psychology. I was also privileged to see some inpatient consultations on the wards. The first thing

(Left to right) William E. Whitehead, PhD; Claude Botha, MD

that impressed me here is how similar our clinical approaches were. But then I don't think I should be as surprised, as our clinical approach (mine in particular) has been heavily influenced by the research and work that was being done here at UNC. I was glad to see that you have similar problems to what we have in London, in that the managers are always complaining about us taking too long with our out-patient consultations, and that our clinics are always overbooked, with long waiting lists. One thing I do covet is the very high level of multi-disciplinary team work that you do during actual clinics and the time you take to consider each patient from different angles even before giving feedback the patient. I had a sense that with a consultation of this intensity, the highest level of patient care was assured.

Christine Dalton, PA-C; Claude Botha, MD

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Center Visitor

Gurpreet Singh, DO

Gastroenterology Fellow
St. John Providence Health System
Madison Heights, MI

I cannot begin to describe my experience at the University of North Carolina Center for Functional Gastrointestinal & Motility Disorders without mentioning the humility that embraces all the faculty and staff. I am truly thankful for your instruction and hospitality. Our program director highly recommended a rotation with Dr. Drossman and having had an interest in functional GI disease, I had hoped to visit UNC.

During my two weeks, I identified the readings from Rome III with my observation of patient interviews and their clinical assessment. I also participated in the following: watching the recorded interview simulation videos by Dr. Drossman, observing the Psychology clinics, and observing manometry procedures. I also attended the research lab meeting, and the biometry research meeting.

Each aspect of my experience was educational. With this foundation, I hope to advance my understanding of management and employment of functional GI disorders as a part of my patient evaluation. Thank you for the opportunity to visit UNC.

Center Visitor – Hamid Afshar, MD

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Olanzapine in a randomized clinical trial for IBS patient in our clinic in Esfahan. Both of these inspired me to perform some more research in our clinical research centers. I wish I could have conducted a research project under the supervision of UNC.

I will never forget the fascinating lecture Dr. Drossman gave at Duke University about FAPS (functional abdominal pain syndrome). It contained the fundamental and advanced discussion about one of the most difficult functional disorders for patients and physicians. I found it beneficial and well laid out.

Finally, my short experience at UNC was very stimulating and informative. I would like to thank everybody for their help in making my visit interesting and educational. In particular, am grateful to Sarah Barrett, Jennifer Layton and Dr. Stephan Weinland for their kind supports, which made me feel like a member of the UNC FGID Center Family.

Thank you to everyone who was involved in my visit.

Center Visitor – Claude Botha, MD

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Finally, I was also privileged to see from 'start to finish', how you approach narcotic bowel syndrome patients. This was the main reason for me coming to visit UNC at this time, and I feel that people went out of their way to discuss and show all aspects of the research and treatment of this condition to me. I feel confident that I can take some of the skills back to the UK, and hopefully implement treatment and even some research on a similar vein to the high standards here at UNC. This reminded me of how much their is to learn and, how rich the academical and clinical experience is here at UNC. It makes me hope that future collaboration would be possible, and that my time before returning to UNC is short. Upon leaving my main recollections is not that of only organised scientists or even that of compassionate healers with a heart for their patients, but was that of friends. My future hope is that there will be many happy returns. Thank you for the possibility of coming to UNC as a visiting scholar; it was a very enriching and highly recommended experience.

On the Physician Patient Relationship

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Health care providers often harbor negative attitudes towards IBS patients (4) thus diminishing their ability to form therapeutic relationships with patients who feel embarrassed by the presence of bowel symptoms, stigmatized, isolated and perhaps worst of all often dismissed by their family members and health care providers (5-7). The impacts of IBS-related isolation and impairment on daily life are far greater than physicians can imagine. Physicians generally trained "to cure" report feeling frustrated with lack of definitive treatment options, time constrains and may even feel emotionally drained from their interactions with IBS patients (8). The communication gap between physicians and patients with functional bowel disorders is further broadened by patients' reluctance to accept the "functional" diagnosis. In a recent study, strikingly, only 1 of 13 patients agreed with or accepted the functional diagnosis, despite all being diagnosed by a specialist as having such (9).

The communication gap between patients and physicians seems to be expanding. There is a tragic irony in this phenomenon in that physicians and patients want the same thing: the best care possible. There is no simple remedy for protecting and restoring the physician-patient bond. It will have to be a mixture of many "potions" among which will be expanded training and assessment of physicians communication skills; joint physician- patient advocacy on behalf of the relationship as well as changing the reimbursement structure so it rewards and incentivizes the relationship aspects of medical care. It is not an easy task to change today's health care system, but there is one thing every one can do - begin the conversation.

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Participate in Research and Clinical Trials

Genetic and environmental factors that cause or influence IBS: Contact: Lenore Keck, RN (919) 966-8329 http://ibsstudy.com	This study involves measuring the relationship between genes, the environment, and various psychological and health factors in men and women with IBS. Individuals who participate will spend one overnight visit in the General Clinical Research Center at UNC Hospital. No additional visits are required.
Tioga: Contact Renuka Kelapure (919) 843-7892	Patients who are eligible for this study should have an IBS-D diagnosis with a minimum of 4 BMs a day. These patients should also have had a recent flex sig or colonoscopy. This is a double blind, placebo controlled study with asimadoline, which is a kappa opioid agonist, which relieves visceral hypersensitivity. This is a twelve week study with six visits. Patients will receive study drug and study–related medical care at no cost. Participants will be compensated up to $400 for their participation.
Ardelyx: Contact Renuka Kelapure (919) 843-7892	Patients who are eligible for this study should have an IBS-C diagnosis per Rome III criteria. These patients should also have had a colonoscopy within 5 years and since the onset of IBS-C symptoms. This is a double-blind, placebo controlled study with RDX5791, which is a NHE3 inhibitor, which reduces Na+ reuptake, increases net fluid volume of GI tract, and facilitates intestinal transit. This is an eight week study with four visits. Patients will receive study drug and study–related medical care at no cost, and will be compensated up to $300 for their participation.
F^3 Study - Finding foods fearful: ***A study of children and adolescents with a fear of trying new foods*** Contact: Miranda Van Tilburg, PhD (919) 843-0688	If you think your child has a fear of trying new foods and/or has such a limited food variety that it gets in the way, join our online registry of parents who have a child who struggles with food neophobia. Your responses will help us learn more about this behavioral pattern so we can develop new treatments, help parents feel less blamed, and learn more about the development of taste preferences in general.
Healthy Controls Needed for Research Study Contact: Lenore Keck, RN (919) 966-8329 http://ibsstudy.com	We are conducting a research study investigating a broad range of factors that may cause or influence IBS. We are looking for subjects without IBS or any other gastrointestinal (stomach or bowel) symptoms to participate.

Participate in Research and Clinical Trials

Narcotic Bowel Syndrome: Contact Megan Bouma (919) 843-4422	Patients with Narcotic Bowel Syndrome have been treated with high doses of narcotics for any number of pain disorders. Initial use of narcotics relieves the pain, but after long term use tachyphylaxis occurs in spite of increasing doses. These patients experience increasing abdominal pain as well as other GI symptoms. Treatment involves gradual detoxification from the narcotics. The study we are performing is purely observational, in an effect to better describe the NBS patient population and their response to detoxification. Contact with the research coordinator will occur at four time periods: 1) Pre-detox 2) Post-detox 3) Three months after detox 4) Six months after detox. Contact will include a series of questionnaires. Patients will be compensated up to $100 for completing the study. Contact Christina Davis pre detox – (919)966-0792 This is an open label study where the patient will take the drug for eight weeks. Drug, physicals, and lab work will be provided at no cost to the patient. Patients will be compensated up to $350 for completing the study.
Seroquel: Contact: Megan Bouma (919) 843-4422	Patients who would benefit most from the Seroquel Study are those with moderate to severe painful functional bowel disorder (which could include IBS, Constipation with pain, chronic functional abdominal pain) who have not responded to antidepressant therapy. These patients will have already been on one of the antidepressants listed below for at least four weeks and have not experienced adequate relief. Seroquel is believed to have a synergistic effect when added to a current regimen of these antidepressants due to its interaction with serotonin, dopamine, histamine, and adrenergic receptors in the brain. Patients not responding to the following therapies would qualify. SNRIs: Cymbalta - Duloxetine; Savella - milnacipran; Effexor - venlafaxine; Pristiq - desvenlafaxine TCAs & Other: Desipramine; Amitriptyline; Remeron - mirtazapine; Imipramine **SSRI's DO NOT QUALIFY** This is an open label study where the patient will take the drug for eight weeks. Drug, physicals, and lab work will be provided at no cost to the patient. Patients will be compensated up to $350 for completing the study

DDW 2011

May 7-10, 2011
Chicago, Illinois

Center faculty and investigators were well represented at Digestive Disease Week 2011. DDW is the premier research and clinical forum for scientists and clinicians within digestive diseases. The abstracts shown on pages 16 - 27 were successfully submitted and accepted for oral or poster presentation.

A Functional Magnetic Resonance Imaging (FMRI) Scanning Environment Enhances Visceral Pain in Patients with Irritable Bowel Syndrome (IBS)

Author: Yang Cao, Xinhua Li , Reuben K. Wong, Khek Yu Ho, Clive H Wilder-Smith

Abstract

Introduction: Several aspects of the CNS processing of pain are dysfunctional in IBS, which is characterized by hypersensitivity and abnormal endogenous pain modulation (EPM). Pain perception and EPM are strongly influenced by psychological factors, such as anxiety, expectation, hypervigilance and stress (1). Brain fMRI is used to study pain processing and has shown aberrant sensory processing in IBS in areas governing these psychological responses, as well as EPM. The scanning environment itself, however, potently stimulates precisely such psychological factors, which may result in altered sensory processing. The effect of the fMRI environment on pain processing in IBS has to the best of our knowledge never been reported.

Aims & Methods: We studied the effect of the fMRI scanning environment on pain perception and EPM in 12 IBS patients (7 female, 5 male). Foot heat and rectal distension sensation and pain thresholds were determined using an ascending method of limits. Subsequently, moderate foot and rectal pain at an intensity between 30-60 (computerized VAS 0-100) were applied separately and together (heterotopic stimulation for induction of EPM) for 30 seconds under identical conditions, except for the testing location being either outside the scanner room or inside the scanner, where 6 randomized imaging blocks were performed. Mean pain scores from out- and inside the scanner were compared by paired Student's t-test, and the correlations between out- and inside data were assessed by linear regression.

Results: Pain intensities out- and inside the scanner with each stimulation condition are shown in the table. Both rectal pain alone and with heterotopic foot pain increased inside the scanner versus outside (both p<0.007). Heterotopic stimulation increased mean rectal pain by 9% (95%CI:-3%-20%) outside and by 7% (-2%-17%) inside the scanner (p=0.82). Pain facilitation was evident in 75% (9/12) of patients in both settings. Foot pain intensity and the change in rectal pain with heterotopic stimulation out- and inside the scanner correlated significantly (r=0.61; p=0.03 and r=0.69; p=0.01, resp.).

Conclusions: The fMRI environment very significantly increased visceral, but not somatic pain, in IBS patients compared to a non-scanner setting. The magnitude of EPM remained similar between settings, with most IBS patients demonstrating abnormal facilitation. This strongly suggests psychological factors independent of EPM selectively affect visceral pain processing in IBS patients in the fMRI. If confirmed, pain processing data gathered inside the scanner may represent a 'stimulated' setting and direct extrapolation to the 'resting' setting outside the scanner may not be advisable. (1) E A Mayer. Gut 2000 (Suppl IV) 47:iv69-72 Study supported by Singapore National Medical Research Council, Individual Research Grant.

Stimulations (*, p<0.007 inside vs. outside scanner)	Pain intesity (Computerized VAS 0-100)	
	Outside scanner room	Inside scanner
Rectal pain alone	39 (95%CI: 35 ~ 42)	*53 (43 ~ 63)
Rectal pain with heterotopic foot stimulation	42 (36 ~ 49)	*56 (46 ~ 66)
Foot pain alone	45 (40 ~ 51)	44 (33 ~ 54)

Development and Validation of the Irritable Bowel Syndrome Satisfaction with Care Scale (IBS-Sat)

Author: Spencer D. Dorn, Carolyn B. Morris, Teresa M. Hopper, Susan E. Schneck, Yuming J. Hu, Renuka R. Kulkarni-Kelapure, Stephan R. Weinland, William F. Norton, Nancy J. Norton, Douglas A. Drossman

Abstract

Background: Satisfaction with care is an important measure of quality from the patient's perspective and may also affect outcomes. Currently no standard measure of patient satisfaction with IBS care exists. Accordingly, a multi-item, condition specific instrument is needed.

Methods: Using standard qualitative methods, we conducted focus groups to obtain items that patients identified as associated with satisfaction in their IBS care. These and additional items identified by experts were placed into a preliminary questionnaire, which was refined through pilot testing and cognitive debriefing by additional patients, as well as standard statistical methods. The resulting instrument along with several external validation measures were then administered to 300 adult U.S. patients. Factor analysis was performed to identify clinically relevant subscales and then psychometric properties were assessed.

Results: The final IBS-SAT has 37 items across five clinically relevant subscales (connection with provider, education, benefits of visit, office attributes, and access to care). The IBS-SAT has extremely high internal consistency reliability (Crohnbach's alpha = 0.96). Convergent validity was established by correlations between the IBS-SAT and a single, global satisfaction with care question (r = 0.68; p<0.001), as well as a generic, multi-item satisfaction scale (Physician Satisfaction Questionnaire-18) (r = 0.75, p<0.001). Discriminant (known groups) validity was established across groups stratified based on provider communication (Communication Assessment Tool) (p<0.0001), IBS-Quality of Life (p<0.0001), and number of unmet expectations (p<0.0001).

Conclusions: The IBS-SAT is a reliable and valid measure of patient satisfaction with IBS care. As a new condition specific instrument, it is likely to be a useful tool for quality measurement, health services research, and trials of clinical interventions.

Diffuse Noxious Inhibitory Controls (Dnic) Are Compromised in Patients with Irritable Bowel Syndrome (IBS) Compared to Healthy Controls (Hc)

Author: Steve Heymen, Olafur S. Palsson, Lisa M. Gangarosa, Susan Girdler, William E. Whitehead

Abstract

Introduction: Studies have consistently shown a dysregulation of the endogenous pain modulatory mechanism known as DNIC in IBS patients which may contribute to visceral hyperalgesia. In DNIC, descending serotonergic and opioidergic pain inhibitory signals are initiated by one pain stimulus that then suppresses pain from a second heterotopic pain stimulus. The DNIC effect is defined as the difference between pain ratings from a phasic noxious test stimulus (TS), administered with a concurrent tonic noxious heterotopic conditioning stimulus (CS) compared to the TS pain ratings without a noxious CS. Aim: To compare DNIC in IBS and HC by using somatic TS and CS, and to assess the association between DNIC and visceral pain sensitivity.

Method: Subjects were 40 pre-menopausal females (20 with IBS and 20 age-matched HC, mean age 28 years). The TS were 8 heat pulses [peak=520C, inter-stimulus interval of 2 seconds] applied to the left palm. The CS was submersion of the right hand in painful 100C water. Differences in Average Pain Ratings (APR) of the TS (scale 0-100) during painful CS and the APR during the non-painful CS (hand submersion in 300C water) were compared between groups in a counter-balanced sequence. Water pain ratings (100C) were acquired (0-100) and group differences in psychological measures were assessed. Pain ratings from rectal distensions delivered by barostat were acquired from IBS patients using ascending method of limits.

Results: IBS subjects demonstrated deficient DNIC compared to HC (F=8.9(1,38), p=0.005, effect size:η2=.19). Rather than decrease during noxious counter-irritation (100C), APR increased in IBS, while appropriately decreasing in HC. Although there were group differences in pain ratings for the 100C CS (IBS=66 HC=50 (F=5.3(1,38) p=0.028), when entered as covariates in a Repeated Measures ANCOVA, they did not explain the significant group differences in DNIC (F=5.1(1,37), p=0.03, effect size:η2=.12). DNIC measures were not significantly correlated with visceral pain ratings (r=- .369, p=0.15). IBS subjects also reported greater anxiety, depression, catastrophizing, somatization, and life stress (p<0.05). After controlling for these psychological measures, group differences in DNIC were no longer significant. A larger study is planned to determine whether these group differences in DNIC are explained by group differences in psychological factors.

Discussion: These data support our previous finding of deficient DNIC in IBS. However, a larger sample size will be needed to adequately control for alternative explanations of pain reduction such as psychological factors, rarely addressed in other DNIC protocols. Only by controlling for non-specific effects can evidence of deficient DNIC be attributed to dysregulation in endogenous analgesic mechanisms. [Supported by grants R24DK067664, R01DK31369, and UL1RR025747].

Dysfunctional Endogenous Pain Modulation (Epm) in Patients with Functional Dyspepsia (FD) and Its Clinical Relevance

Author: Yang Cao, Xinhua Li, Reuben K. Wong, Khek Yu Ho, Clive H Wilder-Smith

Abstract

Introduction: EPM is an important aspect of the body's homeostasis and its dysfunction is often associated with abnormal sensory function. Somatic and visceral EPM have been shown to be abnormal in IBS (1, 2), but EPM does not appear to have been studied in FD. Visceral hypersensitivity to capsaicin stimulation has recently been shown in FD (see parallel abstract). We explored EPM in FD patients using an identical technique with heterotopic stimulation, a well-validated method for inducing EPM.

Methods: Moderate gastric pain (intensity 30-60 on 0-100 VAS) was induced on 3 separate occasions by identical titration with capsaicin 0.5mg capsules ingested every 15 minutes in 30 healthy controls (mean age 36 years, 17 female) and 30 FD patients (mean age 40, 15 female). This pain was either applied alone, with heterotopic foot heat pain, or with mental distraction using the STROOP test. Gastric pain was rated by VAS every minute. The differences in intensity of pain at baseline and during the first 5 minutes after the above interventions were compared between groups using the Student-paired-t-test with Bonferroni adjustment. To assess the usefulness of the measure of EPM as a potential biomarker, clinical abdominal pain and discomfort intensity were recorded during one week preceding the sensory testing, for correlation with the magnitude of EPM.

Results: Changes in gastric pain intensity from baseline with heterotopic stimulation and distraction are shown in the table. In healthy subjects, the capsaicin-induced gastric pain was significantly reduced by both interventions (both $p<0.05$), without significant differences between them. In FD patients, the capsaicin-induced pain was greater than in controls ($p<0.008$) and neither heterotopic stimulation nor distraction diminished the pain intensity significantly. There were significant correlations between clinical abdominal pain and discomfort intensities and magnitude of EPM during heterotopic stimulation (both $r>0.54$, $p<0.02$) and mental distraction (both $r>0.65$, $p<0.001$) in patients who reported clinical abdominal pain of at least moderate intensity (n=16).

Conclusion: Healthy controls exhibited normal EPM, with inhibition of gastric pain during heterotopic stimulation. FD patients, however, had abnormal EPM with significantly decreased inhibition of pain both by cognitive and descending modulatory pathways. Importantly, the magnitude of abnormal EPM correlated with the clinical symptom intensity in pain-predominant FD, suggesting the potential usefulness of the described methods in the study of FD-related pain and its treatment. (1) Song G et al. Pain 2006;126:79-90 (2) Wilder-Smith CH et al.. World J Gastro 2007;13:3699-3704 (3) Cao Y et al. Gastroenterology 2010; 138:S1S-375 Study supported by Singapore National Medical Research Council, Individual Research Grant

Stimulations (*, p<0.008 in control vs. FD)	Changes in pain intensity from baseline (VAS 0-100)	
	Control	FD
Capsaicin alone	9.9 (95%CI: 5.9 ~ 13.9)	*24.6 (18.5 ~ 30.6)
Capsaicin with heterotopic foot pain	3.6 (-1.3 ~ 8.5)	*16.7 (8.8 ~ 24.7)
Capsaicin with mental distraction	-1.9 (-5.7 ~ 2.0)	*23.8 (16.3 ~ 31.2)

Dysfunctional Endogenous Pain Modulation (Epm): A Surrogate Biomarker in Irritable Bowel Syndromes (IBS)?

Author: Yang Cao, Xinhua Li, Reuben K. Wong, Khek Yu Ho, Clive H Wilder-Smith

Abstract

Introduction: endogenous pain modulation is a central homeostatic control mechanism closely linked to other non-sensory homeostatic centres. Measures of EPM have in a few recent studies been shown to correlate with clinical measures of somatic and neuropathic pain as well as pain relief, suggesting their potential usefulness as surrogate markers for clinical pain outcomes. Sensory hypersensitivity and abnormal EPM have been demonstrated in IBS by sensory testing with heterotopic stimulation and functional brain imaging studies, but correlations between EPM and clinical pain and other symptoms in IBS have not been reported.

Aims & Methods: We studied correlations between clinical IBS symptom ratings and EPM induced by standard heterotopic stimulation in 12 IBS patients (Rome III, 7 females). Foot heat and rectal distension sensation and pain thresholds were determined using an ascending method of limits. Subsequently, moderate foot and rectal pain individually titrated to an intensity of 30-60 on a VAS of 0-100 were applied separately and together (heterotopic stimulation) six times for 30 seconds in randomised sequence during brain functional Magnetic Resonance Imaging (fMRI). The following were recorded during the week before sensory testing: IBS symptom severity (IBS-SSS questionnaire) and average abdominal pain and discomfort by VAS. Correlations were analyzed by linear regression.

Results: The magnitude of EPM correlated with IBS-related abdominal pain intensity ($r=0.64$, $p<0.02$), abdominal discomfort intensity ($r=0.69$, $p<0.01$), quality of life scores ($r=0.71$, $p<0.01$), as well as IBS-SSS scores ($r=0.84$, $p<0.001$). The duration of IBS pain showed no significant association with EPM.

Conclusions: This data suggests there is a relevant correlation between the magnitude of EPM and clinical pain and symptoms in IBS patients. If confirmed in an ongoing study with a larger group of patients with treatment, EPM measurement may become a useful surrogate biomarker in pathophysiological and therapeutic research of IBS. The current study was support by Singapore National Medical Research Council, Individual Research Grant.

Exploring the Mechanism of a Probiotic Combination VSL#3 in Irritable Bowel Syndrome (IBS): A Randomized Double-Blind Placebo Controlled Study

Authors: Reuben K. Wong, Cao Yang, Claudio De Simone, Guanghui Song, Jennie Y. Wong, Shyam Prakash, Khek Yu Ho

Abstract

Background & Aims: Probiotics have treatment efficacy in IBS, but the exact mechanism remains obscure. One hypothesis is the mediation of melatonin levels, leading to changes in IBS symptoms. This study aims to evaluate the effects of a probiotic, VSL#3, on symptoms, sleep parameters and pain sensitivity in IBS, and relate these parameters to in-vivo melatonin levels.

Methods: 42 IBS patients were randomly assigned to receive 4 capsules of either VSL#3 (n=20) or identical placebos (n=22), twice daily, for 6 weeks. Pre and post-treatment, subjects completed bowel and psychological questionnaires, and underwent rectal sensitivity study as well as saliva and fecal melatonin assays.

Results: VSL#3 and placebo decreased the mean IBS Severity Score from 224.5 to 158.0 ($p<0.05$), and 226.4 to 183.5 ($p<0.05$), respectively. The VSL#3 subjects had a larger improvement (-66.5) than the placebo group (-42.9), and the difference was statistically significant amongst males but not females. Abdominal pain duration decreased (-18.5 vs. -7.3,$p<0.05$) in the VSL#3 arm compared with the placebo controls, as did abdominal distension intensity (-14.5 vs. -12.3, $p<0.05$). Rectal distension pressures needed to induce pain significantly increased in the VSL#3 patients (38.4 to 42.5 mmHg) compared to controls. A correlation between increase in pain tolerance threshold and improvement in abdominal pain scores ($r=0.51$,$p=0.02$) was seen with VSL#3 but not placebo. No significant changes following treatment were observed in psychological indices nor sleep parameters. There was an increase in salivary morning melatonin levels in males (5.43pg/ml to 9.74pg/ml,$p=0.03$) treated with VSL#3, which correlated ($r=0.61$,$p=0.058$) with improved satisfaction in bowel habits. When subjects were grouped into normal vs. abnormal baseline diurnal melatonin levels, the former showed an increase in morning melatonin levels with VSL#3 treatment (3.19pg/ml to 6.58pg/ml,$p=0.07$), which significantly correlated with improved satisfaction in bowel habits ($r=0.68$,$p=0.04$). Similarly, subjects with a normal circadian melatonin had reduced symptom severity scores (-123.8 vs. -45) and abdominal pain duration (-27.8 vs. -12.9) when treated with VSL#3 vs. placebo. They also had significantly improved satisfaction with bowel movements and quality of life.

Conclusions: VSL#3 reduced abdominal pain duration and distension intensity in IBS subjects. Rectal pain thresholds were improved, correlating with an improved abdominal pain scores. The improvement in symptoms correlated with a rise in morning systemic melatonin, which was significant in males and subjects with normal circadian rhythm. We postulate that the probiotic acts by influencing melatonin production, hence modulating IBS symptoms, in individuals with a "normal" diurnal melatonin levels but not in those with a baseline disordered circadian rhythm.

How Good Are Individuals At Predicting Diarrhea Based On Perceived Triggers and Warning Sensations?: A Diary Study

Author: Olafur S. Palsson, Marsha J. Turner, Jeffrey S. Baggish, William E. Whitehead

Abstract

Aim: To assess how accurate individuals are at predicting diarrhea onset based on preceding triggers (e.g., eating something known to cause diarrhea) and warning sensations (e.g., gurgling sounds).

Methods: Individuals 18+ years of age with unexplained diarrhea at least once per week were invited to complete a 60-day diary and a questionnaire about diarrhea warnings and triggers. Excluded were people with inflammatory bowel disease, celiac disease, lactose intolerance, short bowel syndrome, dumping syndrome, GI surgery history other than gall bladder or appendectomy, use in the last month of antibiotics or other drugs with diarrhea side-effect, or diarrhea occurring every day. For a 60-day period, subjects used a printed pocket diary to record the time and nature of the first warning sensations or trigger events alerting them that diarrhea might be coming, rated their confidence (0-100%) in diarrhea actually following these, and recorded the time and stool consistency (Bristol Stool Scale) of every bowel movement (BM). Subjects transferred this diary information to a secure website every night. Diarrhea was defined in analyses as ratings of 6 or 7 on the Bristol scale.

Results: 264 individuals enrolled and began keeping diaries. Sufficiently complete data for diary analysis (i.e., 1 day or less missing per diary month) were obtained from 210 participants (71.0% female; age range 19-70, mean 31.4 years). On average, 31.4% of subject's BMs were diarrhea. Almost all subjects (97.6%) experienced diarrhea warning sensations and most (77.6%) reported triggers; the mean frequency was 1.09 warnings and 0.33 triggers per day. Half (50.5%) of all diarrhea BMs were preceded by a warning but only 25.2% by a trigger. Earliest warnings were most typically reported to be pain/discomfort (44.6%) or rumbling/bowel sounds (29.1%) whereas specific foods or drinks (72.3% of subjects) and stress/anxiety (49.7%) were the most common triggers. Correlation between confidence ratings and diarrhea actually occurring at next BM was moderately strong for warnings (Spearman $rho=0.49$, $p<0.0001$) but modest for triggers ($rho=0.25$, $p<0.0001$). Only confidence ratings of 70%+ for warnings and 90%+ for triggers were associated with better than even chance of diarrhea at next BM. Average time lag until BM was longer for triggers vs. warnings: 15+ min for 81.6% vs. 57.7% of instances, and 30+ min for 68.7% vs. 42.8% of instances.

Conclusions: Diarrhea is preceded by recognizable warning sensations and trigger events at least some of the time for most people with recurrent diarrhea, but warnings are more useful as they occur more frequently and are more likely to be followed by actual diarrhea. Higher confidence in diarrhea occurring after these antecedent experiences is associated with greater accuracy of diarrhea prediction. [Supported by a grant from McNeil Consumer Healthcare]

Inflammatory Bowel Disease Activity and Narcotic Use During Hospitalization

Author: Millie D. Long, Edward L. Barnes, Hans H. Herfarth, Douglas A. Drossman

Abstract

Background and Aims: Narcotics are increasingly prescribed for chronic pain in non-malignant disease. Despite growing evidence for their adverse effects in inflammatory bowel disease (IBD), 5-13% of IBD outpatients and an unknown number of IBD inpatients receive narcotics. We sought to study the relationship between narcotic use, objective measures of disease activity and other associated factors, including prior diagnosis of IBD-irritable bowel syndrome (IBD-IBS), in hospitalized patients with IBD.

Methods: We performed a retrospective cohort study of all adult IBD patients admitted from May 2008 to May 2009 to University of North Carolina. We collected demographic and disease specific information, inpatient narcotic usage (excluding that used for procedural sedation) obtained from billing records and converted to intravenous morphine equivalents, and disease activity measurements (categorized as moderate/severe vs. mild/none) from endoscopic and radiologic reports. Bivariate comparisons were made between clinical characteristics and narcotic use.

Results: 143 unique IBD patients over the one year period were studied. Patients <1 month post-operative (n=5) and those with current intra-abdominal abscess (n=21) were excluded. Narcotics were given to 70.1% of patients during hospitalization. PCA (patient controlled analgesia) pump was used in 7.7%. Median average narcotics per 24 hours was 7.5 mg (IQR 2.5-12.7 mg) intravenous morphine. This was an underestimation, due to the inability to obtain actual PCA dosing from billing records. Factors significantly associated with inpatient narcotic use included: Crohn's disease (CD) (CD 78.6% used narcotics vs. ulcerative colitis (UC) 48.5% used narcotics; p=0.001), duration of IBD (median of 9 yrs IQR 3-16 among narcotic-users vs. 5.5 yrs IQR 1-12 non-users, p=0.02), prior psychiatric diagnosis (24.4% among narcotic-users vs. 5.7% non-users; p=0.02), history of outpatient narcotic use (41.5% among narcotic-users vs. 11.4% non-users; p=0.002), current smoking (39.0% among narcotic-users vs. 11.4% non-users; p=0.003), prior IBD-specific surgery (52.4% among narcotic-users vs. 28.6% non-users; p<0.02), and prior IBD-IBS diagnosis (13.4% among narcotic-users vs. 0% non-users; p=0.02). There were inverse trends for disease severity and narcotic use: 71.4% of non-narcotic users had moderate/severe CT findings as compared to 59.8% of narcotic-users (p=0.23); 65.7% of non-narcotic-users had moderate/severe endoscopic findings as compared to 58.5% of narcotic-users (p=0.47).

Conclusions: A majority of patients with IBD are prescribed narcotics for pain control during hospitalization in spite of data on increased complications with narcotic use. Risk factors for narcotic use include duration of disease, CD and factors related to CD (surgery, cigarette smoking), psychiatric diagnoses, and IBD-IBS.

Irritable Bowel Syndrome Causes Increased Partner Burden: A Comparative Study

Author: Reuben K. Wong, Douglas A. Drossman, Carolyn B. Morris, Stephan R. Weinland, Jane Leserman, Yuming J. Hu, Shrikant I. Bangdiwala

Abstract

Background and Aims: Studies have described the burden experienced by caregivers and next-of-kin of organic diseases. The concept of partner burden in functional GI disorders is novel. Our study aimed to 1) quantify the degree of burden experienced by the partners of IBS patients and 2) describe the factors that affected the perceived burden; comparing these against the partners of non-IBS patients.

Methods: We surveyed 152 Rome III diagnosed IBS patients and their partners from a tertiary GI clinic. The non-IBS partners completed questionnaires including the Zarit Burden Interview (ZBI), Relationship Satisfaction Scale (RSS) and questions on sexual relationships. IBS patients were rated on disease severity using the Functional Bowel Disease Severity Index (FBDSI). 39 healthy volunteers and their partners were also recruited as the control group.

Results: Comparing between the partners of IBS patients and healthy volunteers, there were no significant demographic differences. Relationship burden was significantly higher in IBS partners, with a mean ZBI score of 22.1 compared to 11.5 in healthy volunteer partners (p=0.0002). Those rating their relationship as more burdensome (ZBI) had IBS partners with worse disease severity (FBDSI; p<0.0001). Both the IBS and control partners' ratings of burden (ZBI) were negatively correlated with quality of the relationship (as measured by the RSS) and sexual relationship. When compared, there was no difference in the RSS scores (4.25 vs. 4.19, p=0.78) and sexual relationship (6.47 vs. 6.21, p=0.64), between the partners of IBS patients and healthy volunteers respectively.

Conclusions: IBS poses a significant degree of partner burden, when compared to a healthy control population. Perceived burden is increased with worsening IBS severity, poorer sexual and relationship satisfaction. The fact that relationship satisfaction and sexual relationship were no worse in the IBS partners show that their increased perceived burden was primarily attributable to the IBS. [Supported by R24 DK067674 and Takeda Pharmaceuticals]

Increased Postprandial Colonic Motility Is Associated with Sympathetic Nerve Activity in Patients with Irritable Bowel Syndrome

Author: Yukari Tanaka, Motoyori Kanazawa, Chloé E. Hill, Olafur S. Palsson, Miranda A. Van Tilburg, Marsha J. Turner, Lisa M. Gangarosa, Shin Fukudo, Douglas A. Drossman, William E. Whitehead

Abstract

Background and Aims: It is unclear whether patients with irritable bowel syndrome (IBS) have abnormal autonomic nervous response to visceral stimuli. The aims were (1) to confirm that IBS patients show increased sympathetic activity during colonic distention and postprandial periods, and (2) to investigate whether sympathetic activity is associated with colonic motility and perception in patients with IBS.

Methods: Autonomic measurements were collected from 156 IBS patients meeting Rome III criteria (131 females; mean age, 35±11 years) and 31 healthy controls (24 females; 37±13 years) during rest, pain testing measured by barostat, baseline at individual operating pressure (IOP), sustained colonic distention at IOP+20 mmHg, and following a high-fat meal. Heart rate variability was calculated by frequency domain analysis of 5-minute electrocardiogram segments obtained during each condition. Low frequency (LF) and high frequency (HF) bands were analyzed to assess sympathetic and parasympathetic activity, respectively, and the LF/HF ratio was calculated. Colonic pain threshold was determined by the ascending method of limits (AML) protocol. Motility index was calculated as the sum of the areas of all contractions divided by recording time. Subjective 6-point abdominal pain scores and whole blood serotonin levels were measured before and after the meal. Psychological symptoms were assessed by the Brief Symptom Inventory-18 (BSI-18).

Results: LF/HF ratios during the distention and postprandial periods were significantly higher than that during baseline in both IBS (p<0.001 and p<0.001, respectively) and healthy subjects (p<0.01 and p<0.001, respectively). No significant difference in LF/HF ratio was observed between the groups. In patients with the highest 1/3 of LF/HF ratios (sympathetic dominant, S) during baseline, depression scores were higher (p<0.05) and serotonin was lower (p<0.05) compared with the lowest 1/3 of LF/HF ratios (parasympathetic-dominant, P) patients. There was no difference in the pain threshold between S and P patients. Patients with high LF/HF ratios during the postprandial period had significantly higher abdominal pain scores (p<0.05), higher motility index and lower serotonin concentration (p<0.05) than patients with low post-prandial LF/HF ratios. The postprandial colonic motility was significantly correlated with the post-prandial LF/HF ratio in IBS patients (rho=0.27, p<0.01) but not in healthy subjects (rho=0.10, p>0.1).

Conclusions: A noxious visceral stimulus enhances sympathetic activity in both IBS and healthy subjects. In patients with IBS, greater postprandial sympathetic activity is associated with greater colonic motility, which may contribute to postprandial symptoms. Contrary to expectation, whole blood serotonin was decreased after meal ingestion in the S subjects. [Supported by R01DK36369 and UL1RR025747]

Increased Stomach Aches in Children Are Associated with Parent IBS Status and Maladaptive Parenting in Japan

Author: Motoyori Kanazawa, William E. Whitehead, Rona L. Levy, Shizuka Seino, Nozomi Tatsuta, Olafur S. Palsson, Marsha J. Turner, Yuka Endo, Kunihiko Nakai, Hiroshi Satoh, Shin Fukudo

Abstract

Background and aims: Irritable bowel syndrome (IBS) runs in families. It has been reported that parent IBS status and solicitous response to child's illness impact child gastrointestinal (GI) symptoms in the US [Levy RL, et al. Am J Gastroenterol 2004]. The aims of this study were to determine whether these findings replicate in Japanese children and whether parenting bonding behaviors exert an independent effect on child's GI symptoms and impaired daily activities.

Methods: 311 non-pregnant mothers who had a 7-year-old child were recruited by advertisement from the community in Sendai, Japan. None of the mothers or children had any organic or psychiatric disorder. The mothers were asked to complete the following questionnaires: the Japanese versions of Rome II Modular Questionnaire, Child Symptoms Checklist (CSCL), Illness Behavior Encouragement Scale (IBES), and Parental Bonding Instruments (PBI). Fifty-one mothers were asked to complete the IBES twice within 14 days to confirm test-retest reliability.

Results: The Japanese IBES demonstrated good internal consistency (Cronbach's α; 0.83) and high reproducibility (intra-class correlation coefficient; 0.88, p<0.001). 101 mothers had IBS symptoms (71 diagnosed by Rome II criteria for IBS). Mothers with IBS reported more frequent abdominal pain (43% vs. 31%, p<0.05), more GI symptoms (p=0.01) and more school absences for stomach aches (p<0.05) in their child. Mothers who had a child with abdominal pain (n=104) reported more over-control behaviors toward their child (p<0.05), and less solicitous response to child's GI symptoms (p<0.01) compared with mothers who did not. High solicitous mothers (the highest third of scores) reported more school absences (p<0.01), but lower child's abdominal pain score (p<0.01), compared with low solicitous mothers (the lowest third). A multivariate analysis of variance showed that parent's solicitous response (β=-0.13, p<0.01) and overprotection (β=0.12, p<0.05) were independently associated with a significantly greater impact on child's GI symptom score on the CSCL.

Conclusions: Similar to the US, children of IBS mothers in Japan have more GI symptoms and missed school. In addition, increased child abdominal pain may be associated with maternal over-control and intrusive behaviors. However, in this non-clinic sample in Japan, mothers who have a child with abdominal pain are less likely to report solicitous response to their child's illness.

Influence of Stool Consistency, Urgency, and Obstetric History On Fecal Incontinence

Author: Barbara L. Robinson, Catherine Matthews, Olafur S. Palsson, Elizabeth Geller, Marsha J. Turner, Brent Parnell, Andrea Crane, Mary Jannelli, Ellen Wells, AnnaMarie Connolly, William E. Whitehead

Abstract

Aims: Approximately 9% of women in the United States and 25% of patients with irritable bowel syndrome (IBS) report that they have fecal incontinence (FI). Women with IBS present a unique opportunity to evaluate the cumulative risk factors for FI. The aims of this study are to (1) confirm that fecal urgency and diarrhea are independent risk factors for FI; (2) identify obstetrical risk factors associated with FI; and (3) determine whether obstetric risk factors interact with diarrhea or urgency to explain the occurrence of FI.

Methods: The study is a supplement to a diary study of bowel symptoms in patients with IBS. Inclusion criteria are (a) clinical diagnosis of IBS by a physician and (b) fulfillment of the Rome III criteria for IBS diagnosis. Exclusion criteria are inflammatory bowel disease, celiac disease, lactose intolerance, daily use of IBS medications, and current participation in pharmacologic trials. Subjects are asked to complete daily bowel symptom diaries for 90 consecutive days and to rate each bowel movement (BM) with respect to stool consistency and the presence of urgency, pain, or FI. 164 of the 185 subjects in the parent study were female and 74 (45.1%) reported FI episodes on their symptom diaries. All female participants from the parent study are being contacted by e-mail or mail and interested subjects complete a telephone administered 33-item bowel symptom and obstetric history interview which includes the Fecal Incontinence Severity Index (FISI). Data are analyzed by linear regression to identify risk factors associated with FI severity.

Results: Data collection is ongoing. Of 80 subjects who have completed the interview, 26% reported FI on their diary, 97.5% reported urgency, and 91.3% reported one or more episodes of diarrhea. The mean number of FI episodes, urgency episodes, and diarrhea episodes per month were 3.6±5.9, 28.5±24.2, and 13.3±13.9 respectively (mean±S.D.). The mean FISI score was 13.9±10.3. In univariate linear regression analyses, FI was significantly associated with urgency (β=0.245, p=0.038) and a history of 3rd or 4th degree perineal lacerations (β=0.295, p=0.031) but not diarrhea (β=0.091, p=0.444). However, when an alternative measure of FI severity (i.e. proportion of total BMs in the diary associated with soiling) was the dependent measure, urgency and lacerations were no longer significantly associated with FI (β=0.095, p=0.521 and β=0.653, p=0.653 respectively). Interaction of urgency and history of perineal laceration did not affect FI severity (β= -0.206, p=0.436).

Conclusion: In this population of females with IBS, fecal urgency or a history of 3rd or 4th degree perineal lacerations are independent risk factors for FI. Obstetric risk factors do not seem to interact with urgency or diarrhea in development of FI. [Support provided by McNeil Consumer Health]

Molecular Characterization of the Fecal and Colonic Mucosal-Associated Microbiota in Diarrhea-Predominant Irritable Bowel Syndrome Patients

Author: Ian M. Carroll, Tamar Ringel-Kulka, Temitope O. Keku, Young-Hyo Chang, Christopher D. Packey, Sheena K. Neil, Daniel Williamson, Ryan B. Sartor, Yehuda Ringel

Abstract

Background: Alterations of the intestinal microbiota have been associated with irritable bowel syndrome (IBS), however the compositional changes in this complex microbial community in IBS is not clear. Additionally, the microbiota in the lumen of the gut is significantly different in composition and diversity from the microbiota associated with the intestinal mucosa (Durban et al., 2010). In this study we expand our previous preliminary report comparing the composition and diversity of the intestinal microbiota within fecal and colonic mucosal niches between patients with Diarrhea-predominant IBS (D-IBS) and healthy controls (HC) on a larger study population with T-RFLP fingerprints using three restriction enzymes.

Methods: The bacterial 16S ribosomal RNA gene was amplified from fecal and un-prepped colonic mucosal biopsy samples from 16 D-IBS subjects and 21 HC. T-RFLP fingerprints were generated from fecal and colonic mucosal samples by digestion with the restriction enzyme Hha I, and subsequently separated on a capillary sequencer. Further T-RFLP fingerprints were generated for fecal samples using Hae III and Msp I restriction enzymes. T-RFLP community fingerprints were compared by multivariate analysis using PRIMER™ v6.

Results: I. T-RFLP fingerprint analysis revealed a significant decrease in the diversity of microbial groups within fecal samples from D-IBS subjects when compared to HC: 1.2 fold decrease with Hha I-generated fingerprints (P = 0.008), and 1.06 fold decrease (P = 0.015) with Hae III-generated fingerprints. The decrease in microbial diversity in D-IBS fecal samples did not reach statistical significance with Msp I-generated fingerprints (1.05 fold, P = 0.296). No difference in diversity was detected between D-IBS and HC in mucosal samples. II. Multivariate analysis of Hha I-generated T-RFLP fingerprints demonstrated distinct microbial communities between luminal versus colonic mucosal niches in HC and D-IBS groups (HC feces vs. HC mucosa, R = 0.41, P = 0.001; D-IBS feces vs. D-IBS mucosa, R = 0.22, P = 0.001). However, no differences in the global composition of the microbial communities were identified in fecal or colonic mucosal samples between D-IBS subjects and HC. III. Comparison of microbial diversity between fecal and colonic mucosal samples revealed a significant 2 fold increase in fecal samples in HC (P = 0.0001) and a 1.7 fold increase in fecal samples in D-IBS patients (P = 0.001).

Conclusions: We demonstrate a significant decrease in luminal microbial diversity in D-IBS compared to healthy controls. Additionally, the microbiota within the lumen of the intestine displays higher diversity than the colonic-associated microbiota. Our results further support a role for an altered intestinal microbiota in the pathogenesis of IBS and suggest that both luminal and mucosal niches need to be investigated.

Narcotic Bowel Syndrome: Characterization of 30 Patients and Preliminary Results After Detoxification

Author: Douglas A. Drossman, Carolyn B. Morris, Christina E. Davis, Stephan R. Weinland, Ademola O. Aderoju, Renuka R. Kulkarni-Kelapure, Yuming J. Hu, Megan E. Houpe, Joseph Zimmerman, Ceciel T. Rooker, Shrikant I. Bangdiwala

Abstract

Introduction. Narcotic Bowel Syndrome (NBS) is a recently recognized condition characterized by a paradoxical increase in abdominal pain associated with continued or escalating dosages of narcotics. This pilot study evaluated the clinical and psychosocial features of patients with NBS and the response to in-hospital detoxification (detox) treatment.

Methods. Between Nov. 2008 and Sept. 2010, 30 patients seen by the GI consult service at UNC with presumed NBS were placed on a recommended detox program (Grunkemeier D. et al Clin Gastro & Hepato 2007). Clinical, psychosocial, health status and detox related data were obtained pre and post detox. In addition, accessing the NC Controlled Substances Reporting System provided data on whether and when patients from NC may have restarted prescription narcotics. Results. Of the 30 patients detoxed, 63.3% met predefined criteria, and 82.8% were diagnosed by physicians with NBS. Patients had a variety of diagnoses (27% IBS and other functional, 27% IBD and other structural, 13% fibromyalgia and other functional somatic, 33% other: post op, back pain, etc.).They reported high health care use (14.7±9.6 MD visits/6 months; 6.8±6.4 hospitalizations/2 yrs, 6.6±4.1 surgeries/lifetime), and 83.3% were jobless. Despite high dosages of narcotics (total IV morphine equivalent 81.8±85.3mg/day), pain scores were rated severe (52.9±29.2 VAS; 264.1±135.4 FBDSI; McGill Pain 19.7±12.7; greater than labor or post op pain). Multiple symptoms were reported (n=17.0±9.2) and rated as moderate to severe. Psychosocial scores showed high Catastrophizing (20.5±8.2); poor daily function (SF-36 physical 28.4±7.2, mental 33.6±10.8; worse than tetraplegia); 30% were clinically depressed and 33.3% anxious (HADS). Detox (mean 12.2±14.0 days) was successfully completed by 26/30 patients (86.7%); 4 patients were prescribed tramadol by the discharge physician, but only 1 patient requested to leave the hospital on narcotics. At post detox, abdominal pain was reduced 30.6% (p<0.03), and non-abdominal pain 31.1% (p<0.01) on VAS and 34.0% on McGill (p<0.003). Catastrophizing was reduced 19.8% (p<0.01), and general well being was good-excellent in 48.8%. A rigid definition for a clinical responder was met in 52.2% and was predicted by lower predetox depression scores. A 30% reduction in pain occurred in 51.9%, and 66.7% achieved adequate relief. Of the 23 patients from NC who could be accessed on the reporting system, 54.6% went back on narcotics by 43.8±69.7 days later.

Conclusion. Despite severe pain and poor health status and coping, almost all patients with NBS undergoing detox go off narcotics and have significant improvement in pain and coping. However, over ½ are back on narcotics at 6 weeks. Clinicians, patients and the general public need to be educated about the adverse consequences of using narcotics for treating non-malignant pain.

Neuroimmune Regulation of Intestinal Permeability in Inflammatory Bowel Disease (IBD) and Brain-Derived Neurotrophic Factor (BDNF) and Zonulin

Author: Xinhua Li, Yang Cao, Enci Mary Kan, Jia Lu, Reuben K. Wong, Maliha Shaikh, Khek Yu Ho, Clive H Wilder-Smith

Abstract

Background & Aims: Intestinal permeability (IP) changes are among the earliest events in IBD and controlled by inflammatory and neurotrophic mediators, as well as neural input. The neurotrophin BDNF is largely located in neuronal and enteric glial cells and has prominent regulatory functions in neuroimmune signaling, stress responses as well as neuronal plasticity and control of intestinal peristalsis (1). It is abnormally expressed in IBD, but its association with IP changes and a main regulatory tight junction protein, zonulin, are unclear. Zonulin has been implicated in IP changes in other GI inflammatory disorders. In this exploratory study we examined the link between IP and inflammatory mediators, BDNF and zonulin in IBD.

Methods: In this blinded, prospective study, 10 patients with active IBD (6 males, mean age 38y), and 10 matched controls (7 males, mean age 39y) underwent segmental IP testing using ingestion of sucrose, mannitol (M), lactulose (L), and sucralose and measurement of urinary excretion/oral dose in 24-h urine. Serum zonulin, BDNF, cytokines IL-6 and TNFα, and cortisol were quantified. The independent sample t-test and Spearman's rank correlation coefficient were used, means ± SD are shown.

Results: Small intestinal and colonic permeability are higher in IBD than the controls, as assessed by urinary L/M ratio (0.22±0.14 vs. 0.07±0.03%, p<0.01) and sucralose excretion (1.21±0.82% vs. 0.55±0.27%, p=0.03) respectively. Zonulin concentrations correlated urinary L/M ratio in IBD (r=0.86, p<0.01). BDNF correlated with the L/M ratio in healthy controls (r=0.76, p=0.04). IBD patients showed higher cortisol (427.22±113.32 vs. 297.38±114.15 nmol/L, p = 0.03), TNFα (3.12±3.28 vs. 0.99±0.26 pg/ml, p=0.07), and IL-6 (7.63±7.32 vs. 1.26±0.41 pg/ml, p=0.02) than controls.

Conclusion: The increased segmental permeability seen in IBD patients was associated with an uncoupling of the relationship between permeability and BDNF evident in healthy controls and a compensatory correlation with increased serum zonulin levels. As neuronal and enteric glial cells regulating neuroimmune signaling, barrier permeability and neuroplasticity are the main source of BDNF, it is likely that dysregulation of BDNF release from glial cells is directly implicated in the inflammatory changes of IP. The correlation between zonulin and IP changes are of relevance due to zonulin's housekeeping functions, which include regulation of tight junction proteins, bacterial colonisation and host-microbiome-immune interactions, all of which are known to be involved in the pathogenesis of IBD. Further studies are required to extend these preliminary data. Grant support by Defence Science & Technology Agency (DSTA), Singapore (1). Reinshagen, M., et al (2002) Curr. Opin. Investig. Drugs 3, 565-568

On-Therapy Versus Off-Therapy Testing in Patients with Symptoms of Refractory Gastroesophageal Reflux Disease: A Cost-Utility Analysis

Author: Ryan D. Madanick, Stephane Kass, Nicholas J. Shaheen

Abstract

Background: Symptoms of refractory gastroesophageal reflux disease (GERD) despite proton pump inhibitors (PPIs) are highly prevalent among patients presenting to gastroenterologists. pH-impedance (pH-MII) testing is commonly employed in this patient population, however the optimal diagnostic strategy is unclear.

Objective: To evaluate the cost-effectiveness of pH-MII testing on vs. off PPIs in patients with refractory GERD symptoms.Methods: A cost-utility analysis using a hybrid decision tree-Markov model with a 10-year time horizon and third-party payer perspective was conducted to estimate costs, outcomes in quality-adjusted life-years (QALYs), and incremental cost-effectiveness in a base-case cohort of 10,000 patients aged 30-60 with refractory GERD symptoms. After pH-MII testing, patients could undergo surgery (laparoscopic Nissen fundoplication; LNF) or remain on medical therapy. In the base case analysis, patients were assumed to undergo surgery if either pathologic acid or nonacid reflux was noted, and remained on medical therapy if pH-MII was negative. Sources of probabilities and transitions were identified through a search of the medical literature via PubMED. Costs were identified through hospital data for hospital costs, the Physicians Fee Reference for tests, procedures, and physician visits, and through the Master Drug Data Base v2.5. Utility weights were based on previously published data to reflect those used in prior economic analyses of GERD. Costs and QALYs were discounted at 3% annually. One-way and probabilistic sensitivity analyses were conducted of key parameters, including the therapy selected after pH-MII, to account for model uncertainty.

Results: In the base-case analysis, a strategy of pH-MII testing on PPIs cost $44,069 and yielded 6.28 QALYs per person, vs. $50,104 and 5.93 QALYs off therapy. Testing on PPIs dominated testing off PPIs, being both less costly and yielding a larger number of QALYs. In one-way sensitivity analysis, the base-case interpretation was highly sensitive to symptom response to LNF. If this response declined below 50% in patients who had persistent nonacid reflux when tested on PPIs, a strategy of testing off PPIs became dominant. Probabilistic sensitivity analysis revealed that pH-MII on PPIs was the dominant or cost-effective strategy 89% of the time at a willingness-to-pay threshold of $50,000/QALY.

Conclusions: In patients with refractory GERD symptoms, testing on therapy is a cost-effective strategy. As more data regarding the implications of the management decisions based on test results become available, the optimal testing strategy can be further clarified.

Predictive Factors in the Development of Post-Infectious Irritable Bowel Syndrome

Author: Reuben K. Wong, Miranda A. Van Tilburg, David Sweat, Megan Squires, Olafur S. Palsson, Marsha J. Turner, William E. Whitehead

Abstract

Background & Aims: Previous studies suggest that female gender, anxiety, and hypochondriasis are risk factors for the development of PI-IBS, but not all studies find this. Previous studies were limited by focusing on specific outbreaks of gastroenteritis (GE) in a small, defined population of individuals many of whom were genetically related, and by the use of controls who were never exposed to GE. The aim of this study was to evaluate these risk factors in a population-based sample and to control for history of GE exposure.

Methods: Over an 18 month period, all adults aged 18-70 who were reported to the Department of Health and Human Services of the state of North Carolina (NC-DHHS) with a confirmed bacterial GE were mailed a letter containing 4 screening questions and an invitation to participate in a research study 3-12 months after their infection. Those reporting GI symptoms prior to GE on screening questions were excluded; all others were mailed a consent form, more detailed questionnaires, and an Oragene Kit to collect and return saliva for genetic testing.

Results: 2622 patients with a documented bacterial GE were contacted, with 738 responding (31% response rate). After excluding individuals with pre-existing GI symptoms based on the screening questions, 542 individuals were mailed the second package of questionnaires and the saliva collection kit; 343 (63%) returned both. After excluding subjects with organic diseases and/or pain at least monthly prior to GE, there remained 234 (125 males, 109 females). At follow-up 3-6 months after GE, 93 met Rome III criteria for IBS, and the other 141 were designated controls. As shown in the table, univariate tests showed the following to be associated with development of PI-IBS: female sex, younger age; GE symptoms of abdominal pain, abdominal distention, and mucus; and psychological symptoms of somatization and anxiety. We used logistic regression to determine which of these are independent predictors of developing PI-IBS and found that female sex, overall psychological distress, and the GE symptom of abdominal distention were significant after adjustment for other variables. Genetic analyses have not yet been performed.

Conclusions: This study replicates previous reports that female gender, anxiety, and somatization (similar to hypochondriasis) are risk factors that predispose to the development of PI-IBS. GI symptoms of pain, distention, and mucus during the GE episode were also significantly associated with PI-IBS. Significant independent predictors were gender, psychological distress, and distention. This study demonstrates the feasibility of a methodology for accruing questionnaire data and DNA from sufficient numbers of subjects to carry out genetic association studies. [Supported by R24 DK067674]

Temporal Summation in Patients with Irritable Bowel Syndrome (IBS) Compared to Healthy Controls (Hc)

Author: Steve Heymen, Olafur S. Palsson, William Maixner, Lisa M. Gangarosa, Susan Girdler, William E. Whitehead

Abstract

Introduction: Visceral hyperalgesia is often observed in IBS. Recent investigations also showing somatic hyperalgesia in IBS suggest the possibility of a dysfunction in central pain regulatory mechanisms. Dysregulation in ascending pain facilitation known as Temporal Summation has been consistently demonstrated in two other chronic pain conditions, fibromyalgia and temporomandibular disorder, which show high comorbidity with IBS. However, Temporal Summation has not been assessed in IBS. Aim: To compare Temporal Summation in IBS and HC using noxious somatic stimuli and to assess associations with visceral pain sensitivity and psychological influences on pain ratings.

Method: Subjects were 40 pre-menopausal females (20 with IBS and 20 age-matched HC, mean age 28 years). Pain ratings (scale 0-100) for 8 heat pulses [peak 520C, inter-stimulus interval 2 seconds] applied to the left palm were recorded. In addition, IBS patients were tested for visceral pain sensitivity using a barostat. Potential psychological (response criterion bias: 1/β) and sensory (perceptual sensitivity: p(a)) determinants of visceral pain sensitivity were acquired using sensory decision theory (SDT): 1/β indicates a tendency to label any stimulus as intense regardless of its strength, p(a) reflects the ability to correctly discriminate between two stimulus intensities.

Results: Temporal Summation, defined as the slope (rate of rise) of pain ratings, showed no significant difference between IBS (slope = 5.2) and HC (slope = 4.4, p=0.5). However, there was a significant negative correlation between slope and the level of the initial pain rating in the series of 8 pulses suggesting a possible ceiling effect. To explore this ceiling effect, post hoc tests were performed: For subjects whose initial pain rating was < 40 (values < the median, n=17) there was a significantly higher slope for IBS subjects (8.3 vs. 4.0 for HC, p = 0.004), but this was not seen when the initial pain rating was equal to, or greater than the median. We also found that psychological response criterion bias predicted the initial pain rating score (F=9.0 (1,18), p=0.008). Perception sensitivity p(a) scores were not associated with initial pain rating scores or Temporal Summation.

Discussion: Ceiling effects appear to have limited the detection of Temporal Summation in IBS patients. IBS subjects were more likely to give a higher initial pain rating and this tendency was associated with a psychological response bias to over-report pain. These data demonstrate exaggerated Temporal Summation in a subset of IBS patients who did not have a psychological bias to over-report pain. This is the first study to assess Temporal Summation in IBS. [Supported by R24DK067664, R01DK31369, and UL1RR025747]

The Effect of Operator Experience On Treatment of Dysplastic Barrett's Esophagus with Radiofrequency Ablation

Author: William J. Bulsiewicz, Sarina Pasricha, Evan S. Dellon, Ryan D. Madanick, Nicholas J. Shaheen

Abstract

Background: Radiofrequency ablation (RFA) is an endoscopic ablation modality that typically requires multiple treatment sessions to fully eliminate dysplastic tissue. It is unclear if increasing experience reduces complications or the necessary number of ablation sessions, and how many ablations are necessary to achieve competence. AIM: To assess the learning curve for physicians performing RFA.

Methods: This was a retrospective study of patients treated with RFA for BE at a tertiary care referral center between June 2006 and November 2010. Pertinent information was extracted from medical records, including: demographics, pre-ablation histology, indicators of GERD activity (symptoms, erosive esophagitis), upper endoscopy findings (Prague criteria, hiatus hernia), ablation outcomes (elimination of metaplasia and dysplasia), and complications (stricture, bleeding). Endoscopist experience was measured by the number of treatment sessions performed prior to initiation of therapy for each patient. Patients with incomplete treatment and those who initiated treatment in the last 6 months were excluded. Patient characteristics and treatment outcomes were examined among 4 quartiles of endoscopist experience by non-parametric tests (Fisher's exact test for categorical variables and Kruskal-Wallis one-way ANOVA for continuous variables). Linear regression and Pearson's correlation were performed to assess the strength of the association between endoscopist experience and number of sessions necessary for complete ablation.

Results: Among 305 RFA treatments by 3 physicians in 113 patients, 245 treatments were in 77 patients who completed therapy more than 6 months prior and were included in the analysis. Over time, there was a significant reduction in the number of RFA sessions and time required to complete therapy, from an average of 4.4 sessions and 226 days in the earliest quartile to 2.3 sessions and 111 days in the most recent quartile (p<0.05 for both). Operator experience and number of RFA sessions to complete treatment were significantly correlated(r=0.38, p<0.001). Linear regression identified operator experience (p<0.001) and Prague M length (p<0.001) as independent predictors of number of treatment sessions to complete eradication of BE. By this model, an endoscopist needs to perform 81 ablations to average 3.0 treatments per patient. Complication rates did not differ significantly dependent on operator experience (p=0.26).

Conclusions: There was a clinically and statistically significant learning curve associated with endoscopic ablation of BE, with initial subjects requiring approximately 2.1 additional treatment sessions for complete ablation. After 81 ablations an endoscopist is projected to average 3.0 treatments per patient. For optimal delivery, this procedure should be performed in high volume.

U.S. Patients with Chronic Abdominal Pain Are Increasingly Prescribed Opioid Analgesics
Author: Spencer D. Dorn, Patrick D. Meek, Nilay D. Shah

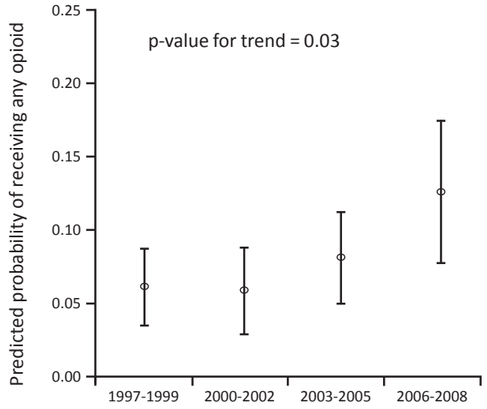
Abstract

Background: Opioids are sometimes used to treat chronic abdominal pain. However, for this condition opioid analgesics have not been proven to be effective, and have been associated with drug misuse, constipation, and worsening abdominal pain. We sought to estimate nation-wide trends and factors associated with opioid prescribing for chronic abdominal pain.

Methods: Chronic abdominal pain-related visits by adults to U.S. outpatient clinics were identified using reason-for-visit and physician diagnosis codes from the National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey (1997-2008). Data were weighted to produce national estimates of opioid prescriptions over time. Logistic regression analyses, adjusted for complex survey design, were performed to identify factors associated with opioid use.

Results: The adjusted prevalence of visits for which an opioid was prescribed increased from 5.9% (95% Confidence Interval [CI], 3.5-8.3%) in 1997-1999 to 12.2% (95% CI, 7.5-17.0%) in 2006-2008 (p=0.03 for trend). Opioid prescriptions were most common in 2006-2008 (odds ratio [OR] 2.2, 95% CI 1.2-4.0) and among patients aged 25 - 40 years old (OR 4.6, 95% CI 1.2-18.4). Opioid prescriptions were least common among uninsured (OR 0.1, 95% CI 0.04-0.4) and African American (OR 0.3, 95% CI 0.1-0.9) patients.

Conclusion: From 1997-2008 opioid prescriptions for chronic abdominal pain more than doubled. Further studies are needed to better understand the reasons for and consequences of this trend.



Utility of Physical Examination and Questionnaire for Identifying Patients Who Do Not Have Dyssynergic Defecation
Author: Giuseppe Chiarioni, Oreste Pieramico, Italo Vantini, Steve Heymen, William E. Whitehead

Abstract

The Iowa group reported that digital rectal exam has a positive predictive value (PPV) of 97% for diagnosis of dyssynergic defecation (DD).

Aims: (1) Reassess the PPV and negative predictive value (NPV) of physical exam for identification of DD. (2) Assess patient awareness of pelvic floor contraction when straining. (3) Determine whether poor rectal propulsion pressures can be detected by abdominal palpation.

Methods: 110 consecutive patients presenting to gastroenterology or surgery clinics for refractory constipation were invited into a one-month study; 4 declined. At enrollment all patients completed symptom questionnaires, underwent balloon evacuation testing (BET), and were then instructed to increase fiber intake up to 30 g per day and keep a daily symptom diary for 30 days. Patients who did not have a satisfactory response to fiber therapy (n=83) were assessed by anorectal manometry (ARM), pelvic floor EMG during straining, and a Sitzmark transit test. Physical examination involved palpation of the abdomen and digital examination of the anal canal during straining to defecate. DD was defined as paradoxical contraction or failure to relax pelvic floor muscles on both manometry and EMG.

Results: Average age was 43.5 years (range 21-72 years), and 13/106 were males. 39.8% (33/83) met criteria for DD. Digital rectal exam had a PPV=61.2% and NPV=91.2% for DD. When asked whether they contracted their anal sphincters when straining to defecate, 93.8% of DD patients were aware of doing so. However, 33.3% of reports of sphincter contraction with straining were not confirmed by manometry; PPV=65.2%, NPV=94.1%. Logistic regression showed that digital rectal exam and self-report of contracting anal sphincters when straining made independent contributions to prediction of DD with overall accuracy 82%. Abdominal palpation showing contraction when straining was associated with higher rectal pressures recorded by manometry: mean±SD 75.6±17.6 vs. 36.2±13.7 mmHg; p<0.001 compared to those without abdominal contraction.

Conclusions: We anticipated that patients would be fearful of passing stool during digital exam resulting in a high NPV and modest PPV; results confirmed this hypothesis. Opposite findings by the Iowa group require further study. We also confirmed that most patients with DD are aware of contracting their pelvic floor muscles when straining, making this a useful screening question. High NPVs for both indicators show that patients who have normal relaxation on digital exam and deny contracting their anal sphincters when straining do not require further testing to exclude DD; however, modest PPVs suggest that ARM and/or BET is required for a confident diagnosis of DD. We also demonstrated that abdominal wall palpation provides a reliable indication of whether patients increase rectal propulsive force when straining. [Supported by R01DK31369]

Utility of the Balloon-Evacuation Test for Identifying Patients with Dyssynergic Defecation
Author: Giuseppe Chiarioni, Oreste Pieramico, Italo Vantini, Steve Heymen, William E. Whitehead

Abstract

Some have suggested the balloon evacuation test (BET) could substitute for anorectal manometry (ARM) in identifying patients with dyssynergic defecation (DD) and save cost.

Aims: (1) Assess test-retest reliability of the BET. (2) Determine its optimal duration. (3) Determine sensitivity and specificity of BET for detecting DD when DD is defined as paradoxical contraction or failure to relax pelvic floor during attempted defecation during ARM. (4) Explore reasons for lack of agreement between BET and ARM.

Methods: 110 consecutive patients presenting to gastroenterology or surgery clinics for refractory constipation were invited into a one-month study; 4 declined. At enrollment all patients completed symptom questionnaires, underwent BET and were then instructed to increase fiber intake up to 30 g per day and to keep a daily symptom diary for 30 days. The BET was repeated after 30 days in all patients. For patients who did not have a satisfactory response to fiber therapy (n=83), a Sitzmark transit study, anorectal manometry (ARM), and pelvic floor EMG during straining were also performed. Defecography was performed in patients who were unable to evacuate the balloon but were not dyssynergic on ARM. The BET test involved insertion of a Foley catheter into the rectum above the level of the anal canal, injecting 50 ml of water at approximately body temperature into the balloon, and instructing the patient to go into a toilet alone and evacuate the balloon. They were asked at 1, 2, 3, 4, and 5 minutes if they had been successful.

Results: Average age was 43.5 years (range 21-72 years), and 13/106 were males. Agreement was 100% between the 2 BETs completed 30 days apart. 44.3% of 106 patients evacuated the balloon in less than 1 minute, an additional 6.6% required up to 2 minutes, and the remaining 49.1% tried for 5 minutes without success. If DD defined by ARM is the gold standard, the specificity of the BET is 100% (no patient who was able to evacuate the balloon was dyssynergic on manometry), sensitivity was 60.2% and positive predictive value (PPV) was 63.5%. The 19 patients who had abnormal BET but were not dyssynergic on ARM included 7 who had rectal prolapse on physical exam and another 7 who failed to contract their abdominal wall muscles when straining (determined by physical exam).

Conclusions: The appropriate duration for the BET is 2 minutes, and the test is 100% reproducible. Specificity of BET is 100%; a normal BET rules out dyssynergic defecation. The PPV is only modest because 36.5% of subjects with an abnormal BET are not dyssynergic. However, ¾ of these discordant cases (14/19) could be explained by physical exam findings. [Supported by R01DK31369]

Visceral Hypersensitivity in Functional Dyspepsia (FD) Demonstrated By Individual Capsaicin Titration
Author: Yang Cao, Xinhua Li, Reuben K. Wong, Khek Yu Ho, Clive H Wilder-Smith

Abstract

Background: The dyspeptic symptoms in patients with FD are often food-related, suggesting that abnormal chemosensitivity (sensitization) may contribute to the etiology of FD. TRPV1 -receptors on chemoceptive afferent neurons are known to play a prominent role in the regulation of multiple GI functions, including visceral sensitivity. A TRPV1 gene polymorphism (G315C) has in Japanese FD patients been shown to influence upper gastrointestinal sensation (1). TRPV1 pathways can be selectively activated using the ligand capsaicin and are implicated in sensory sensitization. Gastric sensation in healthy controls and FD patients has been studied using a fixed dose of capsaicin, albeit with wide variability in largely non-painful sensations (2). However, the study of sensitization mechanisms involving high-threshold C-fibers rich in TRPV1-receptors requires adequately intense stimulation levels of pain.

Aims & Methods: A standardized, double-blind, randomized gastric pain model with good reproducibility (3) was used to induce moderate pain intensity in 30 FD patients (mean age 40 years, 15 female) and 36 healthy volunteers (39 years, 26 female). They swallowed one capsule containing either capsaicin 0.5mg or nocebo (induction of pain by expectation when inert substance is given in blinded fashion) every 15 minutes until stable moderate pain intensity (30-60 on a VAS of 0-100) was reported for at least 5 minutes. Abdominal pain was rated every minute. Student t and CHI2-tests were used for group comparisons of the dose required to achieve stable moderate pain and pain intensity.

Results: The median dosage to induce stable moderate pain was 1 capsule (IQR: 1-1) in patients and 2 capsules (1-3) in controls (p=0.03). The endpoint of moderate pain was reached with 1 capsule in 77% (23/30) of FD patients and in 53% (19/36) of control subjects (p=0.002). The average intensity of pain in the 5 minutes following the onset of moderate pain was 55±3 in FD and 42±2 in controls (p=0.03). With nocebo titration up to a maximum of 4 capsules, 10% (3/30) of FD patients and 3% (1/36) of controls reported moderate pain (p=0.5).

Conclusions: Patients with FD demonstrated visceral hypersensitivity to stimulation with capsaicin, with increased dose-responses during individual capsaicin titration. The titration methodology used is simple and well-tolerated, with a low nocebo rate and has previously shown high reproducibility (3). TRPV1 pathways are implicated in the hypersensitivity in FD. Activation of this polymodal receptor may be via inflammation (inflammatory mediators, neurotrophins, protons) or food ingredients (e.g. lipids). (1) Tahara T et al.. J Clin Gastroenterol. 2010;44:1-7 (2) Hammer J et al. Neurogastroenterol Motil 2008;20:125-133 (3) Cao Y et al. Gastroenterology 2010; 138:S1S-277 Supported by Singapore NMRC Individual Research Grant

Legislation to Bolster Functional GI Research Introduced in the U.S. House of Representatives

Dane Christiansen
Health and Medicine Counsel of Washington

June 16th, 2011 will forever mark a watershed moment in the effort to advance our scientific understanding of functional gastrointestinal and motility disorders (FGIMDs). On this date, the *Functional Gastrointestinal and Motility Disorders Research Enhancement Act* (H.R. 2239) was introduced in the U.S. House of Representatives. This legislation, which was crafted by the International Foundation for Functional Gastrointestinal Disorders (IFFGD) to expand research in this field and improve the development of treatment options, was introduced on a bipartisan basis by Congressman F. James Sensenbrenner, Jr., a Republican from Wisconsin, and Congressman James Moran, a Democrat from Virginia.

Beyond raising critical awareness of FGIMDs on Capitol Hill, H.R. 2239 seeks to establish a Centers of Excellence program in FGIMDs at five academic medical centers in the U.S. The legislation would also grant NIH new authority to expand its research portfolio in this area and coordinate research activities with the Department of Defense and the Veterans Administration. H.R. 2239 also calls on the Food and Drug Administration to improve review, approval, and oversight of treatments developed for FGIMDs.

While the introduction of this legislation represents meaningful progress after years of congressional outreach by FGIMDs advocates, such as Dr. Douglas Drossman, Co-Director of the UNC Center for Functional GI & Motility Disorders, more needs to be done to ensure H.R. 2239 is passed into law. In order for this legislation to move forward in the legislative process, additional House Representatives need to support it by becoming "co-sponsors." Every American has a House Representative, and the only way they will become a co-sponsor of H.R. 2239 is if one of their constituents (you) reaches out to their office and asks them to do so. Below please find talking points to assist you with reaching out to your House Representative to ask them to cosponsor H.R. 2239.

Additional, official information on H.R. 2239 can be found at: http://iffgd.org/HR2239.

To Call Your Representative

- Identify your House Representative by visiting www.congress.org and entering your zip code in the prompt underneath the "Get Involved" heading on the right hand column of the page. Your U.S. Representative will be the name/link, under "Representatives" within the left column. Click on their name, and then click on their tab labeled "contact" to view their contact information.
- Call your Representatives' Washington, DC office (the 202 number) and ask to speak to the staff member who handles health issues; you will likely receive their voicemail. Be prepared to leave the following message or make the following request over the phone.
- [Please note, congressional staffers are very busy and they receive multiple requests a day. In order to ensure they follow through on your request, you may want to call multiple times and leave multiple messages. For example, calling once Monday, Wednesday, and Friday in a week.]

> My name is _____ and I am constituent from [your town or neighborhood]. I ask that your office become a cosponsor of the bipartisan Functional Gastrointestinal and Motility Disorders Research Enhancement Act, bill number H.R. 2239, by contacting Amy Bos in the office of Congressman F. James Sensenbrenner, Jr. at Amy dot Bos at mail dot house dot gov or 225-5101. Very briefly explain your FGIMDs story (how they impact or affect you). Thank you for your time and your consideration of this request.

To E-mail Your Representative

- Go to www.house.gov and enter your zip code in the search field at the top of the page underneath the heading "Find Your Representative." Then, click on the name that appears in the left hand column to visit your Representatives' personal webpage.
- On your Representatives' personal web page there will likely be a "contact me" button. This button may send you to a page with a general e-mail address, but it will likely send you to a webform that needs to be submitted to e-mail the Representative. Please send the following message via e-mail or submitted through the web form.
- [Please note, in order to ensure your request is acted upon, follow-up is often needed after an e-mail is sent. Consider calling the office a couple times to follow-up on and reiterate your request with the staff.]

> I write you today as a constituent from [your town or neighborhood] to ask that you please cosponsor the bipartisan Functional Gastrointestinal and Motility Disorders Research Enhancement Act (H.R. 2239). To become a cosponsor of this important legislation, please contact Amy Bos in the office of Congressman F. James Sensenbrenner, Jr. at Amy.Bos@mail.house.gov or 225-5101. Very briefly explain your FGIMDs story (how they impact or affect you). Thank you for your time and your consideration of my request.
>
> [Name]
> [Address]

To Write Your Representative

- This is the most effective form of outreach to ensure that your Representative responds to your request and becomes a cosponsor of H.R. 2239. If you would like to write to your Representative, please contact the IFFGD's Development Coordinator at dchristiansen@iffgd.org. The Foundation will e-mail you a draft letter that includes the official request and you will simply need to add your story and personal information to that letter and e-mail it back to us. We can then have our Washington Representatives hand deliver your letter to the appropriate staff in your Representatives' Washington, DC office.
- [Please note, do not mail your letters directly to your Representatives' office. For security reasons they do not arrive for over a month and they have been subjected to many tests, such as for anthrax, that may have damaged them or made them unreadable.]

Tribute to Steve Heymen, PhD

Article by William E. Whitehead, PhD
Center Co-Director

Steve is retiring from the University and our Center on October 31 after an amazing 13 years. During that time he completed and published two large randomized controlled trials on pelvic floor biofeedback – one on dyssynergic defecation type constipation and another on fecal incontinence. These were seminal publications which have changed clinical practice for these disorders by demonstrating that biofeedback is a highly successful treatment. As a follow-up to this work, Steve played a key role in persuading UNC Hospitals to establish a dedicated pelvic floor biofeedback laboratory, and he recruited Mary Schultz to staff this clinic. This Biofeedback Clinic is absolutely unique in gastroenterology and has been a tremendous success; it has had a waiting list of 2-3 months almost since its inception and brings new referrals from many departments within UNC and from outside of the university.

Although Steve's research shows that biofeedback is a highly effective treatment for fecal incontinence, he was concerned that biofeedback services are limited to a few academic medical centers and are not available to most patients. Therefore he led an effort to develop a standardized conservative treatment for fecal incontinence that can be learned and used by nurses in primary care to treat this disorder. He showed this approach to be very effective, but randomized clinical trials have not yet been conducted.

While actively working on these research accomplishments, Steve also enrolled in and completed doctoral studies in Biological Psychology here at UNC, receiving his Ph.D. in 2007. In the process of his doctoral research, Steve inaugurated a new line of research on visceral pain. For his PhD dissertation he tested central nervous system (CNS) contributions to visceral pain perception in patients with Irritable Bowel Syndrome (IBS). Normally the brain sends out signals to the spinal cord to down-regulate pain perception, but Steve's doctoral research showed that IBS patients are deficient in the ability to do this. This may help to explain the chronic nature of IBS pain and may provide a new target for treatment of IBS.

Steve is very young to retire from academic research. However, in response to the cut-back in research funding by the NIH, he decided to start a clinical practice for biofeedback in the community. He will see patients in Pittsboro and Cary, and will accept referrals of patients with pelvic floor disorders as well as those in need of anxiety and stress management. He is a good friend to many of us, and we will miss him. He will continue to be affiliated with our division as an adjunct faculty member. We wish Steve much success in his private practice. We are grateful for his many contributions to the successes of our team's research over the years and look forward to continued connections with him in the future.

Farewell Letter from Dr. Heymen

Dear Colleagues,

I wanted to say goodbye to everyone with an expression of my deep appreciation for my experience working with you all during my twelve years in the Division. In 1999 Bill recruited me to UNC to run his NIH Biofeedback grant treating patients with fecal incontinence or constipation. With exceptional support from Yolanda Scarlett, Doug Drossman, and all of the Faculty and Fellows, and with the outstanding assistance of our research nurses, Jane Tucker and Lenore Keck, we were able to successfully demonstrate the efficacy of Biofeedback for these challenging disorders. Many of our colleagues have described these as definitive investigation in our field. As a result, this well designed RCT is being cited to challenge insurance carriers regarding reimbursement for FI and PFD constipation, which we hope will lead to improved access, and many more patients benefitting from this effective treatment. Our treatment protocol has been adopted by the Pelvic Floor Disorders Network of NIH for use in a large multicenter RCT trial comparing Biofeedback to Loperimide for patients with FI. These accomplishments alone would have satisfied my goals for relocating to NC from Florida, but included in the offer from Bill and Doug was the opportunity to complete my education. As I managed both Biofeedback studies, I was able to complete a PhD in Biological Psychology at UNC. There are not many bosses that would provide so much flexibility and support to allow for such a thing. Bob Sandler and David Brenner were also supportive and I will always be very grateful for the opportunity that they have provided to me. Please forgive me for my absence at meetings and lectures and if I seemed preoccupied from 2002 to 2007, I was. I also want to thank Marsha Turner for listening to my frequent rants about the difficulty of performing both tasks simultaneously. I couldn't have made it with you Marsha. It has been a fulfilling phase of my career here at UNC and I want to thank all of you for your well wishes as I transition to the next thing.

My future is full of challenges and opportunities. As some of you know, I will be opening a private practice in October, returning to my clinical role that I had at the Cleveland Clinic, providing Psychotherapy and/or Biofeedback for patients with anxiety, pain, or pelvic floor disorders. We continue to pursue funding for our conservative treatment for FI protocol, and I am hopeful to continue that work with Bill and his team on a part-time basis.

Best Regards to you all,
Steve

Upcoming Chat Schedule

Every month the Center offers an "Evening with the Experts" chat room series. This monthly event features a pre-recorded presentation given by an expert in the field of functional GI disorders, followed by a general interactive question and answer discussion with the presenter and audience. Most chats are scheduled the first Tuesday of every month from 8:00 - 10:00 PM, EST. On the night of the chat, log onto our website at www.med.unc.edu/ibs, and access the chat portal on the left side of the homepage. This is a unique opportunity to get answers to questions about specific gastrointestinal issues of interest to you. We hope to see you there!

December 6, 2011	*IBS Beyond the Bowel: Why Do Some IBS Patients Have So Many Non-gastrointestinal Symptoms and What is the Impact of Those Extra Symptoms*	Olafur Palsson, PsyD
January 10, 2012	*The Role of the Psychologist*	Stephan Weinland, PhD
February 7, 2012	*Dietary Approaches and Probiotics*	Spencer Dorn, MD

Save the Date!

2012 Research Day

7th Annual UNC Center for Functional GI & Motility Disorders Research Day
January 28, 2012 in Chapel Hill, NC

Featured Topics:

- Physiological Mechanisms for IBS
- Psychosocial Mechanisms for IBS
- Treatment Studies
- Pelvic Floor Disorders
- Cross-cultural Studies

Research Day is a non-CME event for faculty, investigators and students at UNC and other universities in North Carolina. It is open to anyone with a professional interest in FGID research. The event is supported through educational grants from various sponsors, for whom we are grateful for support for the Center's ongoing clinical, educational and training activities.

For more information, please contact Sarah Barrett at slbarret@med.unc.edu.

2012 Patient Symposium

June 23-24, 2012 in Chapel Hill, NC

Expert Update on Treatments for Functional GI Disorders

The Patient Symposium is a unique opportunity for individuals with Functional GI problems to learn about new perspectives and treatments. Each plenary session will feature a panel discussion with symposium faculty.

For more information, please contact Sarah Barrett at slbarret@med.unc.edu.

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Contributions from individual donors and grants from foundations and corporations are essential to enhancing and expanding the Center's comprehensive and multi-disciplinary approach to clinical care, research, training and education in functional GI and motility disorders.

Memorial Research Fund
The Alan Wayne Ducoff Memorial Fund provides an opportunity for families and friends to remember and honor their loved ones by making a designated contribution to the Center's research program. To make a donation to the Alan Wayne Ducoff Memorial Fund, please check off the appropriate box on the donation form.

For more information about supporting the Center, please contact Sarah Barrett at ***slbarret@med.unc.edu.***

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