Novel treatments for chronic constipation
The St Mark’s Biofeedback Team

Specialist nurses
Brigitte Collins - Lead and hypnotherapy
Ellie Bradshaw - Neurostimulation
Anna Swatton – Body image and psychosexual problems
Rebecca Knox - Adolescents

Physiotherapists
Trish Evans – Anal pain
Rhiann Sunderland – Combined bowel and bladder problems

Dietician
Dianne Brundrett - FODMAP

Psychotherapist
Avril Burns - Psychological problems
New medications

- Prucalopride (Resolor) - $\text{C}_{18}\text{H}_{26}\text{ClN}_{3}\text{O}_{3}$ prokinetic 5-HT$_4$ agonist stimulating colonic mass movements

- Linaclotide (Constella) - $\text{C}_{59}\text{H}_{79}\text{N}_{15}\text{O}_{21}\text{S}_{6}$ activates colonic sensory neurons, reducing pain & activates colonic motor neurons increasing smooth muscle contraction

- Lubiprostone (Amitiza) - $\text{C}_{20}\text{H}_{32}\text{F}_{2}\text{O}_{5}$ increases chloride-rich fluid secretion which softens the stool & increases motility
• Elobixibat (Phase III)

• Colchicine (Phase I)

• Sodium chenodeoxycholate (Phase I)
Whole-body vibration for functional constipation: a single-centre, single-blinded, randomized controlled trial


*Department of Physical Medicine and Rehabilitation, Changhua Christian Hospital, Changhua, Taiwan and †School of Medicine, Chung Shan Medical University, Taichung, Taiwan

6 x 15min sessions on WBV therapy (n=14) vs. standard therapy (n=13)

Reduction in constipation severity Index score (p=<0.005) - obstructive defecation only
Safety and efficacy of the vibrating capsule, an innovative non-pharmacological treatment modality for chronic constipation

Use of a device that applies external kneading-like force on the abdomen for treatment of constipation

Konstantinos Mimidis, David Galinsky, Efraim Rimon, Vassilios Papadopoulos, Yehuda Zicherman, Dimitrios Oreopoulos

**Figure 2.** Average bowel movements/week in baseline and treatment.

- Improved transit
- Improved spontaneous bowel movements
- Improved stool type
Colonic Pacing

A Therapeutic Option for the Treatment of Constipation Due to Total Colonic Inertia

Ahmed Shafik, MD, PhD; Ali A. Shafik, MD; Olfat El-Sibai, MD, PhD; I. Ahmed, MB, BCh, MCh

N= 9 patients

3 failures
3 removals
3 continued to show benefit
Implantable Colonic Electrical Stimulation Improves Gastrointestinal Transit and Defecation in a Canine Constipation Model

Feasible and safe

Stool frequency likely to be governed by nitregic pathways
106 patients randomised 1:1

500ml of Magnesium water daily over six weeks

BUT active group consumed a healthier diet

AND

Study sponsored by Droga Kolinska
Percutaneous tibial nerve stimulation for slow transit constipation: a pilot study

B. Collins*, C. Norton*† and Y. Maeda*

*Sir Alan Parks Physiology Unit, St Mark’s Hospital, Harrow, UK and †Bucks New University and Imperial College Healthcare NHS Trust, London, UK

- 18 patients (17 female)
- 12 sessions
- Wexner score improvement
- PAC-QOL score improvement
- Bowel frequency increased
- Laxative use decreased
- Colonic transit unchanged
Bilateral transcutaneous tibial nerve stimulation for chronic constipation

F. Iqbal*, B. Collins†, G. P. Thomas‡, A. Askari*, E. Tan§, R. J. Nicholls‡ and C. J. Vaizey‡.

*Department of Surgery, St Mark’s Hospital and Academic Institute, Harrow, UK, †Department of Physiology, St Mark’s Hospital and Academic Institute, Harrow, UK, ‡St Mark’s Hospital and Academic Institute, Harrow, UK and §Department of Surgery and Cancer, Imperial College, London, UK

Table 3 PAC-QoL score in 15 patients undergoing TTNS.

<table>
<thead>
<tr>
<th>PAC-QoL domain</th>
<th>PAC-QoL at baseline</th>
<th>PAC-QoL at 6 weeks</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical discomfort</td>
<td>3.50 (1.25)</td>
<td>2.75 (1.50)</td>
<td>0.07</td>
</tr>
<tr>
<td>Psychosocial</td>
<td>2.75 (1.88)</td>
<td>1.75 (1.38)</td>
<td>0.05</td>
</tr>
<tr>
<td>Worries and concerns</td>
<td>3.09 (1.00)</td>
<td>2.54 (0.91)</td>
<td>0.04</td>
</tr>
<tr>
<td>Satisfaction</td>
<td>3.80 (1.00)</td>
<td>3.00 (1.60)</td>
<td>0.283</td>
</tr>
<tr>
<td>Total score</td>
<td>2.95 (1.18)</td>
<td>2.50 (0.70)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Data are expressed as median (interquartile range).

Imperial College
London

Figure 1 Placement of the live pad immediately posterior to the medial malleolus.
cankles  verses  ankles
9 patients with slow-transit constipation, stimulation v sham
Caecal manometry measured frequency of propagating sequences (PSs)
Suprasensory SNS significantly increased frequency of colonic PSs, subsensory SNS stimulation did not
In patients with refractory slow transit constipation, SNS did not improve the frequency of complete bowel movements over a 3-week period.
THAT'S ODD  MY ANUS IS RELAXING

EARLY ACUPUNCTURE
Electroacupuncture at ST-36 accelerates colonic motility and transit in freely moving conscious rats

Masahiro Iwa,1,2 Megumi Matsushima,4 Yukiomi Nakade,1 Theodore N. Pappas,1 Mineko Fujimiya,3 and Toku Takahashi1

A

5 min

EA at ST-36

2 g

10 min

B

5 min

EA at ST-36

2 g

10 min
REFLEXOLOGY MAP

Frontal Sinus
Cerebrum
Nose
Hypophysis
Trigeminal Nerve
Cerebellum, Brain Stem
Neck
Hypertension Point
Parathyroid Gland
Esophagus
Thyroid Gland
Stomach
Celiac Plexus
Pancreas
Duodenum
Kidney
Ureter
Bladder
Sigmoid Colon, Rectum
Anus
Insomnia Point
Gonad (Sexual Gland)
Sciatic Nerve

Trapezius
Lung Bronchi
Suprarenal Gland
Heart
Spleen
Transverse Colon
Descending Colon

Caecum, Appendix
Gallbladder
Transverse Colon
Ascending Colon
Descending Colon
Liver

3 month trial
N= 11
Improvement in colonic transit, Constipation severity and CSBM
A single centre blinded randomised controlled trial of trans-abdominal interferential therapy versus trans-abdominal electrical stimulation for slow-transit constipation.
Iqbal F, Askari A, Adaba F et al. St Mark’s Hospital

Powered study- 15 in each arm

6 weeks duration

1 hour post prandial after morning waking

PRIMARY OUTCOME
1 point or more PAC-QOL

Secondary
• PAC-SYM,
• Defecation per week
• SF-36

• Stopped at 15 patients – no effect
CON-COUR study: Interferential therapy in the treatment of chronic constipation in adults: study protocol for a randomized controlled trial

Véronique Vitton¹, Alban Benezech¹, Stéphane Honore³, Patrick Sudour⁴, Nathalie Lesavre⁵, Pascal Auquier⁶ and Karine Baumstarck⁶

Prospective study

Nine centres

Well-powered-200 patients to detect a 20% difference in the proportion of patients who respond between active and sham stimulation

8 weeks of stimulation

Primary endpoint-Achievement of at least 3 SCBM per week
Transcutaneous Sacral Electrical Stimulation for Chronic Functional Constipation

Fareed Iqbal, M.R.C.S., M.B.C.H.B., B.Sc.\textsuperscript{1,2} • Gregory P. Thomas, M.R.C.S., M.B.B.S., M.D.\textsuperscript{1} • Emile Tan, F.R.C.S., M.D.\textsuperscript{2} • Alan Askari, M.R.C.S., M.Sc., M.B.Ch.B.\textsuperscript{1} • Jamasp K. Dastur, M.R.C.S., M.A., M.B.B.S.\textsuperscript{1} • John Nicholls, F.R.C.S., M.S.\textsuperscript{1} • Carolynne J. Vaizey, F.R.C.S., M.B.B.S.\textsuperscript{1}

\textbf{FIGURE 1.} Position of the 4 electrodes, live pads (black lead) were placed over the entire sacrum, ground pads (red leads) were placed on the side.
Is Psycho-social and worries and concern improvement a placebo or representative of improved communication in the neuronal-gut axis?
Efficacy of antidepressants and psychological therapies in irritable bowel syndrome: systematic review and meta-analysis

Table 1. Randomized Controlled Trials of Cognitive Behavioral Therapy for Functional Gastrointestinal Disorders.

<table>
<thead>
<tr>
<th>Study:</th>
<th>Disorder:</th>
<th>Symptoms improved:</th>
<th>Sample Size:</th>
<th>Comparison group(s):</th>
<th>Outcome:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drossman et al, 2003¹</td>
<td>FBD</td>
<td>E,Q</td>
<td>431</td>
<td>education, desipramine, placebo</td>
<td>CBT superior to education and placebo</td>
</tr>
<tr>
<td>Craske et al, 2011²</td>
<td>IBS</td>
<td>G,E</td>
<td>110</td>
<td>stress-reduction, education</td>
<td>CBT superior</td>
</tr>
<tr>
<td>Hunt et al, 2009³</td>
<td>IBS</td>
<td>G,Q</td>
<td>54</td>
<td>waiting list</td>
<td>CBT superior</td>
</tr>
<tr>
<td>Moss-Morris et al, 2010⁴</td>
<td>IBS</td>
<td>G,E</td>
<td>64</td>
<td>usual medical care</td>
<td>CBT superior</td>
</tr>
<tr>
<td>Sanders et al, 2007⁵</td>
<td>IBS</td>
<td>G</td>
<td>28</td>
<td>waiting list</td>
<td>CBT superior</td>
</tr>
<tr>
<td>Ljotsson et al, 2011(a)⁶</td>
<td>IBS</td>
<td>G,Q,E</td>
<td>195</td>
<td>internet-based stress-reduction</td>
<td>CBT superior</td>
</tr>
<tr>
<td>Ljotsson et al, 2011(b)⁷</td>
<td>IBS</td>
<td>G</td>
<td>61</td>
<td>waiting list</td>
<td>CBT superior</td>
</tr>
<tr>
<td>Oerlemans et al., 2011⁸</td>
<td>IBS</td>
<td>G,Q,E</td>
<td>75</td>
<td>usual medical care</td>
<td>CBT superior</td>
</tr>
<tr>
<td>Blanchard et al, 2007⁹</td>
<td>IBS</td>
<td>G</td>
<td>210</td>
<td>educational support group, symptom monitoring</td>
<td>no difference from support group</td>
</tr>
<tr>
<td>Boyce et al, 2003¹⁰</td>
<td>IBS</td>
<td>G,Q</td>
<td>105</td>
<td>relaxation, usual medical care</td>
<td>no difference</td>
</tr>
<tr>
<td>Corney et al, 1990¹¹</td>
<td>IBS</td>
<td>G</td>
<td>42</td>
<td>medical treatment</td>
<td>no difference</td>
</tr>
<tr>
<td>Dulmen et al, 1995¹²</td>
<td>IBS</td>
<td>G</td>
<td>45</td>
<td>waiting list</td>
<td>CBT superior</td>
</tr>
<tr>
<td>Greene &amp; Blanchard, 1994¹³</td>
<td>IBS</td>
<td>G</td>
<td>20</td>
<td>symptom monitoring</td>
<td>CBT superior</td>
</tr>
<tr>
<td>Heymann-Monnikes et al, 2000¹⁴</td>
<td>IBS</td>
<td>G,E,Q</td>
<td>34</td>
<td>self-help support group, waiting list</td>
<td>CBT superior</td>
</tr>
<tr>
<td>Payne &amp; Blanchard, 1995¹⁵</td>
<td>IBS</td>
<td>G</td>
<td>20</td>
<td>usual medical care</td>
<td>CBT superior</td>
</tr>
<tr>
<td>Tkachuck et al., 2003¹⁶</td>
<td>IBS</td>
<td>E,Q</td>
<td>28</td>
<td>symptom monitoring</td>
<td>CBT superior for E and Q changes</td>
</tr>
<tr>
<td>Vollmer &amp; Blanchard, 1998¹⁷</td>
<td>IBS</td>
<td>G</td>
<td>32</td>
<td>waiting list</td>
<td>CBT superior</td>
</tr>
<tr>
<td>Lynch &amp; Zamble, 1989¹⁸</td>
<td>IBS</td>
<td>G,E</td>
<td>21</td>
<td>waiting list</td>
<td>CBT superior</td>
</tr>
<tr>
<td>Kennedy et al, 2005¹⁹</td>
<td>IBS</td>
<td>G</td>
<td>149</td>
<td>antispasmodic (mebeverine)</td>
<td>CBT superior</td>
</tr>
<tr>
<td>Fernandez et al, 1998²⁰</td>
<td>IBS</td>
<td>G,E</td>
<td>90</td>
<td>stress management, placebo, medical treatment</td>
<td>CBT superior to placebo and medical treatment for some bowel symptoms</td>
</tr>
<tr>
<td>Klimes et al., 1990²¹</td>
<td>non-cardiac chest pain</td>
<td>G, E,Q</td>
<td>31</td>
<td>assessment only</td>
<td>CBT superior</td>
</tr>
<tr>
<td>Mayou et al., 1997²²</td>
<td>non-cardiac chest pain</td>
<td>G,E</td>
<td>37</td>
<td>usual medical care</td>
<td>CBT superior</td>
</tr>
</tbody>
</table>
### Table 3. Randomized Controlled Trials of Relaxation Training for Functional Gastrointestinal Disorders.

<table>
<thead>
<tr>
<th>Study</th>
<th>Disorder treated</th>
<th>Symptoms improved</th>
<th>Sample Size</th>
<th>Control groups</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boyce et al, 2003</td>
<td>IBS</td>
<td>G, Q</td>
<td>105</td>
<td>CBT, usual medical care, stress management, placebo, medical treatment</td>
<td>no difference</td>
</tr>
<tr>
<td>Fernandez et al, 1998</td>
<td>IBS</td>
<td>G, E</td>
<td>90</td>
<td></td>
<td>Relaxation training superior to placebo and medical treatment for some bowel symptoms</td>
</tr>
<tr>
<td>Keefer et al, 2001</td>
<td>IBS</td>
<td>G</td>
<td>16</td>
<td>waiting list</td>
<td>relaxation training superior</td>
</tr>
<tr>
<td>van der Veek et al., 2007</td>
<td>IBS</td>
<td>G, Q</td>
<td>98</td>
<td>usual medical care</td>
<td>relaxation training superior</td>
</tr>
<tr>
<td>Blanchard et al., 1993</td>
<td>IBS</td>
<td>G</td>
<td>16</td>
<td>symptom monitoring, antispasmodic</td>
<td>relaxation training superior</td>
</tr>
<tr>
<td>Shaw et al., 1991</td>
<td>IBS</td>
<td>G</td>
<td>35</td>
<td>medication, discussion of food and lifestyle</td>
<td>relaxation training superior</td>
</tr>
<tr>
<td>Shinozaki et al, 2010</td>
<td>IBS</td>
<td>G, Q</td>
<td>21</td>
<td></td>
<td>relaxation training superior</td>
</tr>
</tbody>
</table>

### Table 4. Randomized Controlled Trials of Psychodynamic/Psychoanalytic Interpersonal Therapy for Functional Gastrointestinal Disorders.

<table>
<thead>
<tr>
<th>Study</th>
<th>Disorder treated</th>
<th>Symptoms improved</th>
<th>Sample Size</th>
<th>Control groups</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Svedlund et al, 1983</td>
<td>IBS</td>
<td>G</td>
<td>101</td>
<td>usual medical care</td>
<td>psychodyn. superior</td>
</tr>
<tr>
<td>Guthrie et al, 1991</td>
<td>IBS</td>
<td>G</td>
<td>102</td>
<td>supportive listening</td>
<td>psychodyn. superior for female patients</td>
</tr>
<tr>
<td>Creed et al, 2001</td>
<td>IBS</td>
<td>G</td>
<td>257</td>
<td>paroxetine, usual medical care</td>
<td>no difference</td>
</tr>
<tr>
<td>Hamilton et al, 2000</td>
<td>IBS</td>
<td>G</td>
<td>95</td>
<td>usual medical care</td>
<td>psychodyn. superior</td>
</tr>
</tbody>
</table>
Gut directed psychodynamic-interpersonal therapy for chronic idiopathic constipation
Iqbal F¹, Askari A², Burns A³, Adaba F¹, Tan E⁴, Nicholls RJ¹, Vaizey CJ¹

- 35 patients referred
- 29 completed
- Constipation improvement in 37.9%
- severe anxiety at baseline (p=0.003) if anti-depressant medication was not taken (p=0.033).

<table>
<thead>
<tr>
<th>Table: Symptoms Improvement</th>
<th>N</th>
<th>Before (IQR) severity scale</th>
<th>After (IQR) severity scale</th>
<th>p=</th>
<th>Median reduction in points (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAD-7 Score</td>
<td>23</td>
<td>17 (14-18) 'very severe'</td>
<td>11 (8-14) 'moderate'</td>
<td>&lt;0.01</td>
<td>5 (0.25-7)</td>
</tr>
<tr>
<td>HAD score (Total)</td>
<td>6</td>
<td>28 (25-32) 'Severe'</td>
<td>24 (15-26) 'moderate'</td>
<td>0.005</td>
<td>3 (1-3)</td>
</tr>
<tr>
<td>HAD-Anxiety domain</td>
<td>17</td>
<td>17 (15-19) 'Severe'</td>
<td>13 (11-16) 'moderate'</td>
<td>0.007</td>
<td>4 (1-6)</td>
</tr>
<tr>
<td>HAD-Depression domain</td>
<td>13</td>
<td>13 (10-15) 'Severe'</td>
<td>8 (6-12) 'moderate'</td>
<td>0.011</td>
<td>3 (1-4)</td>
</tr>
</tbody>
</table>