Management of Chronic Abdominal Pain

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Regulation of Visceral Pain

Injury
Peripheral and central sensitization
Nociceptive Modulation
Aδ or C nociceptive input
Amplified input
Pain Experience

2694

2741
Recovery of Mucosal Barrier Function in Ischemic Porcine Ileum and Colon is Stimulated by a Novel Agonist of CIC-2 Chloride Channel


Effect of Lubiprostone vs. Placebo on Rectal Distension Sensory Thresholds

Effect of Lubiprostone vs. Placebo on Rectal Distension Thresholds for Moderate Pain (AML)


Linaclotide: GC-C Agonist

- Stable peptide analog of guanylin and uroguanylin
- Activates GC-C receptor: increases intracellular and extracellular cGMP
- Extracellular cGMP: inhibits afferent nerve firing
- Intracellular cGMP: activates anion channels
Effects of Linaclotide on Afferent Spike Activity in Viscerally Hypersensitive Mice

Castro J, et al. 2012 DDW Poster

“I’m afraid that your irritable bowel syndrome has progressed.
You now have furious and vindictive bowel syndrome.”
CNS Contribution to GI Pain

- Functional Abdominal Pain (FAPS)
- Functional GI disorders
  - IBS
  - Functional dyspepsia
- Chronic GI disorders
  - GERD
  - IBD
- Acute GI episodes
  - Bowel obstruction
  - Cholecystitis

Pain is a Modifiable Experience

Psychosocial Context
- Pain beliefs
- Cultural schema
- Expectation
- Conditioning

Cognitions
- Hypervigilance
- Attention
- Distraction
- Catastrophizing

Chemical / Structural
- Neurodegeneration
- Metabolic (opioidergic, dopaminergic)
- Maladaptive plasticity

Mood
- Depression
- Anxiety

Genetics

Injury
Peripheral and central sensitization

Nociceptive Modulation
Biopsychosocial Medicine

Visceral Hypersensitivity in IBS, But Not FAPS

Perceptual threshold (mmHg)

Discomfort Pain Maximum


Rectal Sensitivity to Distension in IBS

AML Median pain threshold

SDT Median perceptual sensitivity P(A)

Dorn S et al. Gut 2007; 56:1202

IBS: Lower pain threshold

IBS: Higher response bias

P = 0.0002

Dorn S et al. Gut 2007; 56:1202

P = 0.003

Medial response bias (β)

IBS: Similar perceptual sensitivity

P = 0.69
Moderate vs. Severe FBDSI
Pain Report and Sensation Thresholds

- **Severe (>110) (N=19)**
- **Moderate (37-110) (N=46)**

**Pain self-report (0-100 VAS)**

- **14 Day Diary Cards**
  - **Rectal Sensitivity**
  - **Rectal Sensitivity**

- **Tracking volume (ml) at pain threshold**
- **Tracking pressure (mm/Hg) at pain threshold**

**Moderate (37-110) (N=46)**
**Severe (>110) (N=19)**

**p<0.0001**

IBS - Predictors of Severity

**BDI**
**CAT**
**SIP**
**IBS / QOL Divided by 10**
**Days in bed 3 mos.**
**MD visits 3 mos.**
**Hospital admits 2 yrs.**

**Scores**

**p<0.0001**
**p<0.001**

*Adjusting for: Age, Race, Education*

*Douglas A. Drossman, MD, MACG*

*Drossman Am J Gastro, 2000*
IBS - Ascending Visceral Pain Pathway

Descending Visceral Pain Pathway
Increased dACC in IBS Consistent with Greater Affective Pain Experience

55 mmHg of Distension

45 mmHg of Distension

Verne, et al., Pain, 2003

Naliboff, et al., Psychosom Med 2001;
**IBS + Abuse vs. Others (50 mm Hg)**

- **Pain Covariate (50 mm Hg)**

  - PCC
  - MCC
  - ACC
  - sACC

```
Pain ratings
0
1
2
3
4
5
```

- **IBS / Abuse**
  - n=5
- **All others**
  - n=14

  - p=0.004

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**Severe IBS / Psychological Distress**

- **Clinical Recovery (8 months later)**

```
Z=+44  +38  +24  +14  +10  +2
BA 40  MCC  SI  also +38  BA 22  BA 6/44  Ant. ins.
```

- **Drossman et al. Gastroenterol 2003;124:754-761**
Effect of Depressed Mood on Central Pain Registration from Noxious Heat Stimulus in Healthy Subjects

Mood:
- Neutral
- Depressed

Pain

Z scores
-2.3
-4
2.3
4

Berna C et al. Biol Psychiatry 2010; 67:1083

Comparison of Cortical Activation Between Normosensitive and Hypersensitive IBS and Healthy Controls to Expectation and Painful Rectal Distension

Healthy control
Normosensitive IBS
Hypersensitive IBS

Expectation
Distension (45 mmHg)

Larsson MBO, et al. Gastroenterology 2012; 142:463
Effect of Placebo on Pain/Discomfort and Brain Activation with Rectal Distension

Reduced activation in perceived drug group from anticipation of pain (A, B, C) and actual pain (D)


Sex Differences in Regional Activation from Visceral Pain

SMA=Supplementary Motor Area, INS=Insula, CD=Caudate, MCC=Mid Cingulate cortex

Kano M et al. Am J Physiol Gastrointest Liver Physiol 2013; 304:G687
IBS – Brain-Gut Influences on Severity and Treatment

**Afferent excitation**

- Injury
- Infection
- Diet
- Hormones, Peptides
- Life stress
- Psych Dx
- Poor coping
- Abuse

**Disinhibition**

- Mild
- Moderate
- Severe

**Rationale for Antidepressants**

- Treatment of psychiatric co-morbidity
- Peripheral effects
  - Motility / secretion
  - Afferent
- Central pain modulatory effects
Psychiatric Comorbidity in IBS

Subjects with diagnosis (%)

0 25 50 75 100

Anxiety disorders
Affective disorders
Somatization disorder
Other disorders
Any psychiatric disorder

Data adapted from Walker EA et al. Am J Psychiatry 1990

IBS - Antidepressants

TCA (NE effect)  SSRI (5HT effect)

Orocecal transit time (min)

Baseline Imipramine  P<0.05  Baseline Imipramine  P<0.05  Baseline Paroxetine  P<0.05

Baseline Paroxetine  P<0.05

Gorard, Am Pharmicol 1994; 35:203
Response to Noxious Colorectal Distension in Rats

**IBS - Treatment**

![Graph showing response to noxious colorectal distension in rats.](image)

**Su, Pain, 1998; 76:105**

**TCA’s and SNRI’s Reset Dysfunctional Pain Regulation at the Brainstem via Descending 5-HT and NA Activation**

![Diagram showing brain regions involved in pain regulation.](image)

**Important target for drug development**
**Overall Forest Plot of Antidepressant Studies**

<table>
<thead>
<tr>
<th>Tricyclic Antidepressants (TCAs)</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (random)</th>
<th>Weight %</th>
<th>RR (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heefner, 1978</td>
<td>10/22</td>
<td>12/22</td>
<td>5.94</td>
<td>0.83</td>
<td>(0.46, 1.51)</td>
</tr>
<tr>
<td>Myren, 1982</td>
<td>5/30</td>
<td>10/31</td>
<td>2.66</td>
<td>0.52</td>
<td>(0.20, 1.33)</td>
</tr>
<tr>
<td>Ngain, 1984</td>
<td>14/21</td>
<td>21/21</td>
<td>14.74</td>
<td>0.67</td>
<td>(0.49, 0.90)</td>
</tr>
<tr>
<td>Boerner, 1988</td>
<td>16/42</td>
<td>19/41</td>
<td>7.63</td>
<td>0.82</td>
<td>(0.30, 1.36)</td>
</tr>
<tr>
<td>Bergmann, 1981</td>
<td>5/19</td>
<td>14/16</td>
<td>3.82</td>
<td>0.30</td>
<td>(0.14, 0.65)</td>
</tr>
<tr>
<td>Vil, 1991</td>
<td>14/25</td>
<td>20/25</td>
<td>10.67</td>
<td>0.70</td>
<td>(0.47, 1.04)</td>
</tr>
<tr>
<td>Drossman, 2003</td>
<td>60/115</td>
<td>36/37</td>
<td>16.77</td>
<td>0.83</td>
<td>(0.63, 1.08)</td>
</tr>
<tr>
<td>Talley, 2008</td>
<td>0/18</td>
<td>5/16</td>
<td>0.33</td>
<td>0.08</td>
<td>(0.00, 1.36)</td>
</tr>
<tr>
<td>Vahedi, 2008</td>
<td>8/27</td>
<td>16/27</td>
<td>5.02</td>
<td>0.50</td>
<td>(0.26, 0.97)</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>319</td>
<td>256</td>
<td>67.36</td>
<td>0.68</td>
<td>(0.56, 0.83)</td>
</tr>
</tbody>
</table>

Total events: 32 treatments; 153 controls
Test for heterogeneity: Chi²=10.94, df=8; (P=0.21), F=26.3%
Test for overall effect: Z=3.86 (P=0.0001)

*Ford AC et al. Gut, Nov 2008; doi:10.1136/gut.2008.163162*

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**Neuroplasticity, Neurogenesis and Augmentation**

- Abuse, FGIDs and other chronic pain conditions are associated with reduced neuronal density in brain pain control areas

- Antidepressants and psychological treatments may reverse this process and regrow neurons → neurogenesis
  - May occur in brain and intestines

- Augmentation, i.e., use of low dose combinations of medications and psychological treatments appear to improve the treatment response for longer periods of time

Drossman DA Am J Gastroenterology 2009;104:2897*
Altered Brain Structure in IBS

Cortical Thinning in Anterior MCC


Cortical thickness of Pain Control Areas: Painful Chronic Pancreatitis vs. Controls

Frøkjær, Clin Gastroenterol Hep 2012; 10:436
Neurogenic Theory of Depression and Antidepressant Treatment

- Genes and early life stress
- Social stress, drug abuse, medical illness
- Antidepressants, Psychological Treatment
- Critical threshold leading to depression
- Uncoupling of affect from context
- Dentate neuron vulnerability

Dentate neuron vulnerability

Stress

Basal neurogenesis

Suppressed neurogenesis

Restored neurogenesis


BDNF Change vs Depression Improvement

BDNF Change vs Days of Treatment

Cohen’s d for depression

Period of depression d

Study analyzed (weighted by inverse variance)

Effect of Imipramine vs. Placebo on Cognitive Function in Traumatic Brain Injured (TBI) Mice

% of time in NOR*

Weeks after injury

* Novel Object Recognition Task


Effect of Imipramine vs. Placebo on Hippocampal Cell Proliferation in Traumatic Brain Injured (TBI) Mice

2 weeks

4 weeks

TBI - vehicle TBI - Imipramine

Ki67 Positive Cells (100x)

Neuroplasticity / Neurogenesis Implications

- Helps explain basis for treatment of depression and chronic pain better than monoamine theory (e.g., longer timeframe to achieve effect and longer effect)

- Implications for GI pain
  - Central pain regulation via ACC
  - Peripheral effects on enteric nervous system:
    - 5HT4 agonists increase enteric neurons developing from precursors, increase neurite outgrowth and decrease apoptosis
    - Effects not seen in 5HT4 deficient KO mice

  (1) Gershon M et al. Neurogast and Motility 2007; 19:19;
  (2) Liu et al. J Neuroscience 2009;29:9683)

IBS - Psychotropic Agents

- Antidepressants
  - Tricyclics (TCAs)
  - Selective Serotonin Reuptake Inhibitors (SSRIs)
  - Serotonin/Norepinephrine Reuptake Inhibitors (SNRI's)
  - Other Agents: Mirtazapine, Nefazadone, Bupropion

- Anxiolytics
  - Benzodiazepines
  - Azapirones (Buspirone)

- Antipsychotics
  - Phenothiazines (eg. Chlorpromazine)
  - Butyrophenones (eg. Haloperidol)
  - Atypicals (eg. Quetiapine, Aripiprazole, Risperidone)

- Mood stabilizers
  - Lithium
  - Anticonvulsants (eg. Valproic acid, Carbamazepine)
  - Lamotrigine
### Antidepressant Receptor Site Effects

<table>
<thead>
<tr>
<th>Antidepressant</th>
<th>NE</th>
<th>5HT</th>
<th>Histamine</th>
<th>Ach</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TCAs (25-150 mg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline (3°)</td>
<td>+++</td>
<td>+++</td>
<td>++++</td>
<td>++++</td>
</tr>
<tr>
<td>Doxepin (3°)</td>
<td>++</td>
<td>+++</td>
<td>++++</td>
<td>++</td>
</tr>
<tr>
<td>Desipramine (2°)</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Nortriptyline (2°)</td>
<td>+++</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td><strong>SSRIs (1-2 pills)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>nil</td>
<td>+++</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>nil</td>
<td>+++</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>nil</td>
<td>+++</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>nil</td>
<td>+++</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>Sertraline</td>
<td>nil</td>
<td>+++</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td><strong>SNRI’s (variable)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>++</td>
<td>++</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>+++</td>
<td>+++</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>Milnacipran</td>
<td>+++</td>
<td>++</td>
<td>nil</td>
<td>nil</td>
</tr>
</tbody>
</table>

### Functional Dyspepsia Treatment Trial

> 5/12 weeks of adequate relief

- **Placebo**: 40%
- **Amitriptyline**: 53%
- **Escitalopram**: 38%

**Improvement with Amitriptyline associated with:**
- Ulcer like, not dysmotility like dyspepsia
- Normal gastric emptying (p=0.006)

Locke GR et al. Gastroenterology 2013 (Abstract)
### Antidepressant Treatment

<table>
<thead>
<tr>
<th>Potential benefits</th>
<th>TCA (pain) depression</th>
<th>SSRI (pain) depression, panic, anxiety, OCD</th>
<th>SNRI (pain) depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events</td>
<td>Sedation, Hypotension, Constipation, Dry mouth/eyes, Arrhythmias, Weight gain, Sex dysfunction</td>
<td>Insomnia, Agitation, Diarrhea, Night sweats, Headache Weight loss, Sex dysfunction</td>
<td>Nausea, Agitation, Dizziness, Sleep disturbance, Fatigue Liver dysfunction</td>
</tr>
<tr>
<td>Risk from overdose</td>
<td>moderate</td>
<td>minimal</td>
<td>minimal</td>
</tr>
<tr>
<td>Efficacy for IBS</td>
<td>good</td>
<td>not studied</td>
<td>good?</td>
</tr>
<tr>
<td>Dose Adjustment</td>
<td>yes</td>
<td>not usual</td>
<td>varies</td>
</tr>
<tr>
<td>Cost / month</td>
<td>$5-30</td>
<td>$40-80</td>
<td>$60-100</td>
</tr>
</tbody>
</table>

### Other Central Agents with GI effects

- **Mirtazapine**
  - Serotonergic and noradrenergic drug with 5HT₂ and 5HT₃ antagonistic effects – can have pain benefit
  - Use with FD¹, nausea, satiety, weight loss, diarrhea
  - Some sedation
- **Clonidine**
  - α₂-adrenergic against with central (anxiety reduction) and peripheral (pain reduction via bowel compliance)
  - May reduce diarrhea and treat IBS-D²
  - Prevents adrenergic effects of narcotic withdrawal
- **Buspirone**
  - Azapirone with anti-anxiety effects acting on non BZD GABA receptors
  - Has 5HT₁ and 5HT₂ effects
  - Potential benefit for PDS (dyspepsia) due to receptive relaxation of stomach³

Quetiapine

- Atypical antipsychotic with complex effects
- Dopamine ($D_1$ and $D_2$) and Serotonin ($5HT_{1a}$ and $5HT_2$) antagonism with some $\alpha_2$-adrenergic blocking effect

Treatment Effects
- Bipolar disorder and schizophrenia (labelling)
- Augmentation for OCD, PTSD, depression
- Sleep (normal sleep architecture)
- Anxiety reduction
- Some analgesic benefit
- Improves painful FBD refractory to TCA or SNRI

Side effects
- Sedation, somnolence, dry mouth
- Metabolic syndrome (weight gain, glucose intolerance, hyperlipidemia)
- Abnormal LFTs (rare)

Quetiapine for Patients Refractory to SNRI/TCA ($N = 11$)

<table>
<thead>
<tr>
<th></th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neither agree or disagree</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>I am satisfied with the results of my treatment</td>
<td>-</td>
<td>-</td>
<td>2 (18)</td>
<td>7 (63)</td>
<td>2 (18)</td>
</tr>
<tr>
<td>I am engaging in activities that I would not have prior to treatment</td>
<td>-</td>
<td>-</td>
<td>2 (18)</td>
<td>8 (72)</td>
<td>1 (9)</td>
</tr>
<tr>
<td>Better able to cope up with GI symptoms as a result of treatment</td>
<td>-</td>
<td>-</td>
<td>1 (9)</td>
<td>9 (81)</td>
<td>1 (9)</td>
</tr>
<tr>
<td>Treatment has helped me to cope better in other areas of life.</td>
<td>-</td>
<td>-</td>
<td>2 (18)</td>
<td>9 (81)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>My bowel symptoms have improved as a result of treatment</td>
<td>-</td>
<td>-</td>
<td>2 (18)</td>
<td>8 (72)</td>
<td>1 (9)</td>
</tr>
</tbody>
</table>

**Memantine**

- N-Methyl D-Aspartate receptor (NMDAR) antagonist
  - Amantadine derivative treats Parkinson’s and Alzheimer’s disease via neurogenesis
  - Similar action as ketamine and dextromethorphan
  - Good safety profile: Noncompetitive open channel blocker that dissociates rapidly from channel – limits pathological activity and spares normal synaptic activity
  - Suppresses dorsal horn and CNS excitability
  - Used for chronic pain: FM, CFS, Neuropathic, Phantom Limb

  **Potential Actions**
  - Neuroprotective via downregulation of NMDAR’s
  - Analgesic effects via upregulation of antinociceptive pathways
  - May reduce glutamate induced excitotoxic neurodegeneration and prevent gray matter loss
  - May increase availability of mu-opioid receptors and prevent opioid tolerance

**Augmentation Treatment for Refractory FGIDs**

- Use more than one treatment to enhance benefit
- Can use lower dosages and minimize side effects
- Helpful when one treatment not successful or produces side effects
- Use with refractory GI painful disorders

  **Examples**
  - Add antidepressant to peripheral GI agent
  - Add Pregabalin/gabapentin to antidepressant (abd. wall)
  - Add Buspirone or Bupropion to antidepressant
  - SSRI and TCA
  - Add atypical antipsychotic (e.g. quetiapine) to TCA or SNRI
  - Combine antidepressant and psychological treatment
Combining Antidepressants + Psych Treatments

- **Clinical Observations**
  - Antidepressants improve pain, vegetative signs and hopelessness, and increase motivation for psych treatments
  - Psychological treatments improve coping, cognitive function, and effects of trauma, and increase adherence to medication

- **Brain Imaging**
  - Antidepressants may have “bottom up” effects, acting on paralimbic (cingulate, insula)
  - Psychological treatments may have “top down” effects on prefrontal cognitive areas improving “executive” function

- **Clinical trials show combined treatments > monotherapy for headache, depression and other psych disorders**
Physician - Patient Relationship

**Negotiate - Placing on an Antidepressant**

- Patient with frequently recurring painful IBS
- You recommend an antidepressant
- The patient promptly states:

  “The doctor before you gave me an antidepressant . . . it made me sleepy and didn’t work. Besides, I don’t want something that alters my mind.”
IBS - Treatment

**Approach to Prescribing Antidepressants**

- Address false beliefs or expectations of patients
  - “You think I’m crazy / depressed?”
  - “It will alter my mind”
  - “It’s addicting”
  - “I’ve tried them - made me sick (didn’t work)”

*Drossman et al, Gastroenterology, 2002; 123:2108*
Gate Control Theory

Inhibitory Pathway

Spinal Cord

Intestinal Afferent Receptor

Pain Gate

Midbrain

Pain

IBS

Approach to Prescribing Antidepressants

- Address false beliefs or expectations of patients
- Provide information / rationale consistent with patient interests
- Negotiate a treatment plan
  - Benefit occurs in 4-6 weeks
  - Most side effects diminish in 1-2 weeks
  - Plan to mutually discuss dose range options
  - Consider previous drugs that worked

Drossman et al, Gastroenterology, 2003; 123:2108
"Side Effect" Symptom Severity
(wk2-wk0 mean score +/- 95% CI)

- Dizzy (9.58-49.16)
- Lightheaded (10.77-50.11)
- Dry mouth (24.68-128.8)
- Flushing (15.86-53.86)
- Tremors (0.52-20.14)
- Nausea (-13.89-12.27)
- Fever (-6.15-24.29)
- Headaches (-9.58-2.85)
- Blurred vision (-6.15-7.0)
- Rash (-5.73-3.42)
- Insomnia (-2.68-45.38)
- Poor appetite (-12.65-20.68)
- Ear ache (-16.11-6.56)
- Tired (-41.14-0.59)

Increased Severity
- Decreased Severity

Thiwan S et al. DDW 2005

IBS

Approach to Prescribing Antidepressants

- Address false beliefs or expectations of patients
- Provide information / rationale consistent with patient interests
- Negotiate a treatment plan
- Continue dialog for 4-6 weeks
  - Phone call first week is critical
  - Assess compliance
  - Involve patient in treatment decisions
  - Gauge response by behaviors and function
  - If side effects:
    - First reduce dose
    - May switch within same class

Drossman et al, Gastroenterology, 2002; 123:2108
Typical Clinical Presentation for NBS

- Patient presents with chronic or recurrent abdominal pain which is treated with narcotics
- Narcotics may have relieved pain initially but then tachyphylaxis occurs
- Pain worsens when the narcotic effect wears off
- Shorter pain-free periods result in increasing narcotic doses
- Increasing doses further alter motility and aggravate pain
- Can occur with in patients FGID, organic disease or otherwise health subjects (e.g., post operative)
Neuron-to-glia chemokine
Fractalkine

Sensory afferent neuron
ATP, NO, SP, CGRP

Immune / infectious challenges
Virus, bacteria, trauma

CNS signals

Chronic opioid use
Pro-inflammatory cytokine, dynorphin release

Other glial cells

Pro-inflammatory cytokines, PG, NO excitatory amino acids

Enhanced pain

Neuron excitability upregulates NMDA release

Narcotic Withdrawal Protocol

Accept pain as real and treatable
Elicit patients concerns/expectations
Provide information through a dialog
Present the withdrawal program
Gauge the patient’s response

Morphine equiv. Dose (mg) 220 200 180 160 140 120 100 80 60 40 20 0

Clonidine 0.1mg PO q 6 hrs.
Lorazepam 1mg PO q 6hrs.
TCA or SNRI
PEG 3350 17g PO BID

Physician – Patient Relationship

Day of taper -3 -2 -1 0 1 2 3 4 5 6 7 8 9 10 ... 21

Grunkemeier, DMS et al., Clin Gastroenterology and Hepatology 2007; 5:1126
Abdominal Pain Scores

![Graph showing VAS (0-100) pain scores for different groups: Pre-detoxification (n=39), Post-detoxification (n=37), Stayed off narcotics (n=15), Went back on narcotics (n=10).]


Risk of Refilling Narcotics by Days Since Detoxification

![Graph showing survival distribution function with censored observations and product-limit estimate curve.]

**Relationship of COMM Scores* to Detoxification and Responder Status**

- **Successful detoxification**
  - Score 0: 29 Yes, 4 No
  - Score 1: 20 Yes, 12 No
  - p<0.06

- **Responder**
  - Score 0.5: 29 Yes, 4 No
  - Score 1: 20 Yes, 12 No
  - p<0.02

* = Higher COMM scores indicate greater drug abuse potential


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**The Rome Foundation/AGA Institute Lectureship at Digestive Disease Week 2014**

"Understanding and Treating the Brain’s Contribution to Pain"

- **Irene Tracey, PhD**
  - Oxford Centre for Neuroethics
  - Central mechanisms of pain

- **Laurie Keefer, PhD**
  - Northwestern University
  - Behavioral interventions for pain management

- **Douglas A. Drossman, MD**
  - Center for Biopsychosocial Patient Care and UNC
  - Centrally-targeted pharmacotherapy for chronic abdominal pain

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