Fibromyalgia and Other Functional Pain Syndromes: Pathophysiology, Assessment, and Management

Peter Pryzbylkowski, MD

Disclosures
- Nothing to disclose
Learning Objectives

- Describe the common comorbid conditions related to functional pain syndromes
- Examine the neurobiological mechanisms contributing to functional pain syndromes
- Explain 2 pharmacologic and 2 nonpharmacologic strategies to manage pain in this patient population

Neurobiology of Functional Pain
The Problem

- In our current medical system when a patient complains of pain and no physiological ("organic") problem is found despite an in-depth work up, their symptoms are deemed functional and they are labeled as having a functional pain syndrome.

Widespread Pain → Fibromyalgia
Abdominal Pain $\rightarrow$ IBS

Bladder/Urinary System Pain $\rightarrow$
Interstitial Cystitis/Bladder Pain Syndrome

The look your Dr. gives you when you mention Interstitial Cystitis.
Different diseases with similar neurobiology/pathophysiology?

Goals
Goals

Review Article

REVIEW

NEUROBIOLOGY OF FIBROMYALGIA AND CHRONIC WIDESPREAD PAIN

KATHLEEN A. SLUKA AND DANIEL J. CLAUW

*Pharmaceutical and Rehabilitation Science, Pain Research Program, University of Iowa, United States

3 Anesthesia, Medicine (Rheumatology) and Psychiatry, University of Michigan, United States

Please cite this article in press as: Sluka KA, Clauw DJ. Neurobiology of fibromyalgia and chronic widespread pain. Neuroscience (2018). http://dx.doi.org/10.1016/j.neuroscience.2018.06.006
**Fibromyalgia**

- Prevalence about 2% in general population
- Symptoms are diverse
  - Widespread pain
  - Sleep disturbances
  - Mood disturbances
- Seen mostly in women
- Significant overlap with other “functional disorders”
  - TMJ
  - IBS
  - Chronic fatigue
- Originally termed fibrositis but changed to fibromyalgia

---

**Diagnosis of Fibromyalgia**

1. Pain and symptoms over the past week, based on the total of number of painful areas out of 19 parts of the body plus level of severity of these symptoms:
   a. Fatigue
   b. Feeling unrefreshed
   c. Cognitive (memory or thought) problems

   Plus number of other general physical symptoms

2. Symptoms lasting at least three months at a similar level

3. No other health problem that would explain the pain and other symptoms
Fibromyalgia—Genetics

- Tenderness is not confined to tender points but it extends throughout the body
- Tender points are influenced by distress
- More sensitive to other stimuli such as heat, cold, electrical stimuli
- Enhanced sensitivity to smell and auditory tone
- Support for amplification of all sensory stimulation on functional imaging studies with the insular cortex consistently hyperactive
So What Lowers The Pain Threshold?

- Reduced Descending Inhibition
  
  VS

- Hyperactivity of Excitatory Afferent Systems

Reduced Descending Inhibition

- Applying a painful stimulus in healthy volunteers leads to generalized analgesia
  - Decreased/absent in fibromyalgia patients
- Thought to be mediated by endogenous opioidergic and serotoninergic/noradrenergic pathways
- Fibromyalgia patients endogenous opioid activity may be elevated at baseline (ie, already working at full levels and thus can’t increase with new pain stimuli)
  - High baseline occupancy of opioid receptors
  - Opioids usually ineffective in most patients with FM
- Unlike the opioid system the serotoninergic/noradrenergic system is hypofunctional
  - Decreased norepinephrine and serotonin metabolites in CSF
  - Efficacy of compounds that raise serotonin and norepinephrine may be effective
    - Duloxetine, Milnacipran, TCA, tramadol
Hyperactivity of Excitatory Afferent Systems

- Central sensitization
- Increased levels of Substance P in CSF of fibromyalgia patients vs controls
- Increased levels of glutamate in CSF of fibromyalgia patients vs controls
- Exercise, a proven therapy for FM, alters endogenous neurotransmission by increasing antinociceptive neurotransmitters and reducing glutamate

Central Sensitization

- Pain/stress in the periphery bombards the CNS. This initially causes changes in CNS neurotransmitter release and gene expression. Dorsal horn receptive fields increase
- Ultimately can lead to neuroplasticity and a memory of pain (ie, after nerve decompression surgery, pain may still be present)
- NMDA receptor and glutamate are important
Augmented Pain and Sensory Processing

Studies Using Experimental Pain/QST Methods

- FM patients are more sensitive to pressure everywhere. Tender points are regions where everyone is more tender
- FM patients were not more expectant or hypervigilant than controls
- Pressure pain thresholds at any 4 points in the body are highly correlated with the average tenderness at all 18 tender points and control points
- FM patients display a decreased threshold to other noxious stimuli, heat, cold, and electrical stimuli
- FM patients are more sensitive to other sensory stimuli such as sound
  - All suggesting…..
Biologic Amplification of all Sensory Stimuli Gains

Brain Region Connectivity

- Increased connectivity between the default mode network (resting brain) and the insula (a pronociceptive region)
- The degree of increased connectivity related to intensity of ongoing spontaneous pain
- There may be hypo-connections between areas associated with antinociception regions in the brainstem in FM patients
CNS Activation/Excitation

- Wind-up of the CNS is seen in some studies of FM patients
- CNS transmitters seen in wind-up are more prevalent in FM patients
  - Substance P, glutamate are elevated in CNS/brain pronociception regions
    - Pregabalin has been shown to decrease glutamme activity in some of these regions and decrease the functional connectivity between the default mode network and insula
    - Some subsets of patients may respond to agents that block NMDA receptors (ie, ketamine)
- These excitatory neurotransmitters may also play a role in some of the other symptoms associated with functional pain syndromes such as sleep impairment and anxiety.
  Patients that have pain improvements with pregabalin/gabapentin usually also report improvements in these other symptoms

Excitation vs Inhibition
Excitation vs Inhibition

- Diffuse noxious inhibitory control (DNIC)
  - Application of intense painful stimulus leads generalized whole body analgesia
    - Consistently reduced or even absent in FM patients compared to controls (but not seen in all FM patients)
    - Also seen in other "functional pain" — TMJ, IBS

- Endogenous opioids
  - Opioid tone is normal or increased
  - FM patients typically have higher levels of CSF enkephalins
  - FM patients without prior exposure to exogenous opioids had reduced baseline mu opioid receptor binding in multiple pain processing regions
  - Some evidence that blocking endogenous opioid release (ie, low dose naltrexone) may help some pts with FM
  - May explain why mu opioid receptors are typically not effective in FM and other functional pain syndromes

Excitation vs Inhibition

- Reduced DNIC may result from reduced serotonergic and adrenergic activity
  - Lower levels of metabolites noted in FM patients CSF
  - Rats given reserpine (depletes biogenic amines) develop widespread muscle and cutaneous hyperalgesia
    - Behavior associated with depression in rats also seen after being given reserpine

- Reasoning behind using agents that raise both serotonin and norepinephrine-SNRI (duloxetine, milnacipran), TCA, tramadol

- TENS unit, sleep, exercise potentiate descending inhibition
Psychological Factors and Fibromyalgia

Psychological Factors

- Various stressors are correlated with severity of functional pain
- Better correlated with personal stressors rather than generalized stressors
- Changes in stress response early in life can predict which symptom free individuals are more prone to develop chronic pain issues
- Studies show hyper/hypo activity in the hypothalamic-pituitary axis in functional pain syndromes
  - Not consistent: did HPA changes come before or after pain?
Some studies note increased circulating inflammatory mediators and enhanced release of cytokines
   - But some also show a decrease and others no differences compared to controls
   - Studies also vary due to low sample sizes and different analysis methods

Some interleukins, cytokines, and tumor necrosis factor alpha may sensitize nerve endings/nociceptors and produce pain in humans. They are also known to produce hyperalgesia in animals

NSAIDS and other anti-inflammatories have not been shown to be beneficial in fibromyalgia or other functional pain syndromes
Central nervous system is thought to be the key player
- Some patients may have a peripheral component
- Mood and sleep disorders contribute to the patients pain experience
- The immune system may also play a role

Functional Pain Syndromes:
Pharmacology/Medication Management
**Functional Pain Syndromes**

- Irritable bowel syndrome (IBS)
- Fibromyalgia
- Interstitial cystitis
- Vulvodynia

**Key observations:**

- Outcomes are best with integrated care
- Data supporting use of specific medications may be weak
- Opioid use is subject to adverse selection in these patient populations

---

**Irritable Bowel Syndrome**

- Functional bowel disorder characterized by:
  - Symptoms of abdominal pain or discomfort and changes in bowel function for at least 3 days/month for at least 3 months

- Spectrum of severity
  - Mild IBS patients have few symptoms, report good health related QOL, seek medical care on average once a year
  - Severe IBS have high number of symptoms (abdominal pain, bloating, dietary restrictions), report fair to poor HRQOL, seek medical care 2-7 times a year

- Classification based on stool consistency
  - Constipation-predominant (IBS-C)
  - Diarrhea-predominant IBS (IBS-D)
  - Alternating between constipation and diarrhea (IBS-M)
  - Unsubtyped IBS

Irritable Bowel Syndrome (cont’d)

- Patients with IBS often have significant symptom burden
  - Fatigue (69.3%)
  - Sleep disturbance (47.5%)
  - Back pain (37.3%)

- Patients with IBS are more likely than the general population to have depression and anxiety
  - 38% of patients with IBS have reported thoughts of suicide
  - Psychosocial factors (physical, sexual, psychological abuse, and psychiatric conditions) are reported more commonly in patients with severe IBS

Pharmacology Is NOT First-line Treatment

- Of the medications with demonstrated improvements in IBS symptoms:
  - Lubiprostone
  - Rifaximin
  - Linaclotide
  - Fiber supplementation, and
  - Peppermint oil

- Lifestyle changes
- Dietary modification
- Proper integrated treatment for anxiety and depression
  - Psychological therapies are at least as effective as most medication options

Have the most reliable evidence supporting their use
Medications to Improve Colonic Transit Time (IBC-C)

- Lubiprostone
  - Selective chloride channel activator
  - Studied for treatment of IBC-C
    - Labeled dose is 8 mcg twice daily
    - Studies evaluated response up to 48 mcg twice daily
  - Moderate to significant relief compared with placebo

- Onset of efficacy starts at 1 month of treatment
  - Some symptoms were not improved until 2 months

- Adverse events include
  - Nausea, vomiting, diarrhea, abdominal pain and distension
  - Taking with food and water may help

Targeting Gut Microbiota

- Rifaximin
  - Nonsystemic antibiotic approved for treatment of IBS-D in May 2015
    - Originally approved for travelers’ diarrhea and hepatic encephalopathy
  - 40% patients report global improvement in symptom burden
  - Treatment duration is 2 weeks, and effect can last 3 months

- Adverse effects were no different than placebo
Medications to Improve Colonic Transit Time (IBC-C)

- Linaclotide
  - Guanylate cyclase-C agonist
  - Drug leads to an increase of intestinal fluid in the GI lumen, thus increasing GI transit time
  - Almost 50% of patients report more than 30% reduction in pain

- Approved dose is 290 mcg daily
  - Best taken on an empty stomach 30 min before breakfast
  - Onset of symptom relief may be within first week

- Common adverse events are dose related and commonly occurred within first 4 weeks or treatment
  - Diarrhea
  - Flatulence
  - Abdominal pain

Antispasmodics and Peppermint Oil

- Several antispasmodics improve symptom burden over placebo
  - Otilonium
  - Hyoscine bromide
  - Cimetropium bromide
  - Pinaverium bromide
  - Dicyclomine hydrochloride

- Multiple trials support the use of peppermint oil for improving IBS symptoms
  - 9 trials, 726 patients
  - Product is NOT FDA approved
  - Batch-to-batch consistency may be a problem
Medication Treatment Options for IBS

- **SSRIs**
  - Pooled data from 7 RCTs documented decreased symptom burden with treatment

- **TCAs**
  - Pooled data from 11 RCTs documented decreased symptom burden

Am J Gastroenterol (2009) 104: 1772-1779

Gabapentin and Pregabalin

- Small studies have demonstrated benefit in patients with all types of IBS

  - Gabapentin dose 200 mg every 8 hours

  - Pregabalin starting dose was 50 mg every 8 hours

Fibromyalgia Medications

Fibromyalgia: Key Points
- Medications are NOT mandatory for the management of fibromyalgia
- Available medications has a modest effect, and patients often discontinue medications due to adverse effects
- Expectations for value (both patient AND physician) are often too high, leading to poor decision making (again, but on the part of the patient and the physician)
Fibromyalgia: First Line Medications

- Amitriptyline (TCAs)
- Duloxetine
- Pregabalin
- Milnacipran

How modest is the effect?

<table>
<thead>
<tr>
<th>Drug</th>
<th>RCT / participants</th>
<th>30% pain reduction (drug vs placebo, %)</th>
<th>Drop out rate due to adverse events, (drug vs placebo, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>duloxetine</td>
<td>5 / 1,884</td>
<td>46.8 vs 34.0</td>
<td>18.7 vs 10.4</td>
</tr>
<tr>
<td>milnacipran</td>
<td>5 / 4,110</td>
<td>36.4 vs 28.1</td>
<td>21.5 vs 11.0</td>
</tr>
<tr>
<td>SSRIs</td>
<td>7 / 414</td>
<td>36.4 vs 20.6</td>
<td>9.5 vs 7.0</td>
</tr>
<tr>
<td>TCAs</td>
<td>9 / 542</td>
<td>48.3 vs 27.8</td>
<td>5.2 vs 6.5</td>
</tr>
<tr>
<td>pregabalin</td>
<td>5 / 3,259</td>
<td>40.0 vs 29.1</td>
<td>19.4 vs 11.0</td>
</tr>
</tbody>
</table>
Impact of Medications on Outcomes Is Limited

- Review of large data sets document that patients often stop medications prescribed for fibromyalgia
  - 150 days with TCAs
  - 25% stop in 1 year and 50% stop in 2.5 years for pregabalin, duloxetine, and milnacipran

- This is likely driven by global impression or change
  - Modest improvement in pain intensity report
  - No significant long-term improvement in fatigue or physical functioning
  - Medications perceived as causing harms

Other Medication Options

- Tramadol
  - 1 study with 313 patients reported lower pain and improved QOL at 12 weeks
  - Open-label safety study demonstrated continued pain relief, no change in HRQOL

- Cyclobenzaprine
  - Meta-analysis of 5 RCTs with 392 patients demonstrated improved pain and sleep at 4 and 24 weeks
  - A recent RCT with 36 patients demonstrated improved outcomes at 8 weeks
Potent Opioids for Fibromyalgia

- There are NO large RCTs evaluating role of opioids in fibromyalgia
  - Small studies report no value
  - A large dataset of 245,758 patients with fibromyalgia documented that 11.3% received chronic opioids
  - Opioid use appears to be associated with negative HRQOL
- Canada and Germany guidelines strongly discourage opioid use
  - Lack of supporting evidence
  - High risk of poor outcomes

Drugs That Have FAILED Fibromyalgia Clinical Trials

- Valacyclovir
- Anxiolytics
  - Alprazolam
- Bromazepam
- Dopamine agonists
  - Pramipexole
  - Ropinirole
  - Terguride
- Hormones
- Tropisetron
- Odansetron
- Calcitonin
- Dehydroepiandrosteron
- Prednisone
- Hypnotics
- Zolpidem
- Interferon
- Ketamine (IV)
- Local anesthetics (IV)
- Ritaneser
Drugs That Might Work

- Cannabinoids
  - Weak evidence to support efficacy

- Growth hormone
  - 3 RCTs of 157 total patients demonstrated benefits on pain and fatigue at 9 and 18 months

- Quetiapine
  - 4 RCTs (1 published) suggests possible benefit

- Naltrexone
  - Low dose (4.5 mg daily)
  - 2 RCTs with 31 patients demonstrated improvement in pain and mood with low-dose naltrexone (no benefit for fatigue and sleep)

Interstitial Cystitis

Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS)

- New nomenclature and classification system developed by the European Society for the Study of IC/BPS
- Since pain is the fundamental character, they suggested changing the name to BPS
- Diagnostic criteria:
  - Chronic pelvic pain lasting more than 6 months
  - Pressure/discomfort perceived to be related to the urinary bladder
  - One or more urinary symptoms such as urgency or frequency
- American Urological Association requires exclusion of other identifiable causes

Diagnosis and Classification

1. Patient selection
   - Chronic pelvic pain perceived to be related to the urinary bladder

2. Exclusion of similar diseases
   - Cancer, infection, diverticulum, prolapse, endometriosis, among others

3. Classification
   - Cystoscopic findings
   - Biopsy findings*
     - Utility contradictory
IC/BPS May Be a Visceral Neuropathic Pain Condition

- TCAs
  - Have been demonstrated to have an effect in small clinical trials
  - About 40% of patients on amitriptyline 25-75 mg daily reports 30% or better pain relief at 4 months

- Gabapentin/pregabalin
  - Supported via case series reports only
  - About 50% patients report clinical meaningful relief

Interstitial Cystitis

- Anticholinergics
  - Can be used to treat the urinary frequency component of IC
  - Most commonly used agent is hydroxyzine
Vulvodynia

- Persistent vulvar pain in the absence of any obvious disease pathology

- No consensus on the underlying cause of the disorder

- Commonly thought of as a “multifactorial disorder.” Others have advocated that vulvodynia and BPS should be considered as functional pain disorders
Vulvodynia Treatment Options

- Topical therapies
  - Often compounded combination therapies
  - Decisions guided by opinion and not data

Expert Committee Treatment Options

- Committee formed as part of the 4th Annual Consultation on Sexual Medicine
  - Reviewed available data on treatment options
- They basically advised against medications:
  - Topical lidocaine
  - Topical capsaicin
  - Botulinum toxin A
  - Corticosteroids
  - Interferon
  - NSAIDs
  - Hormonal therapy
  - TCAs
  - Anticonvulsants

They advocated for vestibulectomy as the treatment option of choice

### Vulvodynia: a Visceral Neuropathic Pain Condition

<table>
<thead>
<tr>
<th>TCAs</th>
<th>Gabapentin/pregabalin</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Have been demonstrated to have an effect in small clinical trials</td>
<td>- Small trials and case series report benefit with gabapentin</td>
</tr>
<tr>
<td>- Outcome measures were not precise and the true drug effect is not</td>
<td>- Again, limited data on outcomes and the supportive data are</td>
</tr>
<tr>
<td>clear</td>
<td>weak</td>
</tr>
</tbody>
</table>


### Biopsychosocial Approach to Assessing and Managing Patients With Functional Pain Syndromes
Mind-Body Medicine
We believe pain arises in the nervous system but represents a complex and evolving interplay of biological, behavioral, environmental, and societal factors...
Biopsychosocial Approach to CPS

Comprehensive pain management programs based on the biopsychosocial model of pain, typically emphasizing cognitive behavioral therapy, a graded exercise program and appropriate medication management have been shown to significantly improve treatment outcomes (return to work, pain reduction and increase in activity).

Gallagher, 1999
Loeser & Turk, 2000
McCrae & Turk, 2002
Cheatle & Gallagher, 2006

Biopsychosocial Treatment Program for FPS

- CBT
- Functional restoration
- Evidence-based rational pharmacotherapy
- Social support
- Graded motor imagery
CBT/ACT

- CBT focuses on maladaptive thought patterns (catastrophizing) and behaviors (kinesiophobia) that occur frequently in patients with CNCP
- The objective of CBT is to guide the patient in recognizing and reconceptualizing his/her personal view of pain, identifying their role in the process of healing and promoting the patient being proactive rather than passive, and competent rather than incompetent
- CBT include specific skill acquisition (relaxation therapy, stress management, cognitive restructuring) followed by skill consolidation and rehearsal, and relapse training (Turk, Flor, 2006)
Cognitive behavioural therapies for fibromyalgia

Kathrin Bernardy¹, Petra Kloé², Angela J Busch³, Ernest HS Choy⁴, Winfried Häusler⁵

¹Department of Pain Medicine, BG University Hospital Bergmannsheil GmbH, Ruhr University Bochum, Bochum, Germany.
²Department of Internal and Integrative Medicine, Klinikum Essen-Mitte, Faculty of Medicine, University of Duisburg-Essen, Essen, Germany.
³School of Physical Therapy, University of Saskatchewan, Saskatoon, Canada.
⁴Section of Rheumatology, Department of Medicine, Cardiff University School of Medicine, Cardiff, UK.
⁵Department of Psychosomatic Medicine and Psychotherapy, Technische Universität München, München, Germany.

Contact address: Winfried Häusler, Department of Psychosomatic Medicine and Psychotherapy, Technische Universität München, Langerstr. 3, München, D-81675, Germany. whaeusler@klinikum-saarbruecken.de.

Editorial groups: Cochrane Musculoskeletal Group.
Review content assessed as up-to-date: 4 September 2013.


Efficacy/Effectiveness

- **Objective:** evaluate the effectiveness of CBT for FM

- **Main results:** 23 studies met inclusion criteria with a total of 2031 patients included. CBT was superior to controls in pain reduction, reducing negative mood and reducing disability both at end of treatment and at 6 month follow up.
Acceptance and Commitment Therapy

- Acceptance and commitment therapy (ACT) is a form of CBT that is a directive and experiential type of therapy based on rational frame theory. The goal of ACT is to experience life mindfully and reinforce psychological flexibility.

- The core processes of ACT include:
  - Contact with the present moment
  - Self-as-context
  - Diffusion
  - Acceptance
  - Values
  - Committed action

- There are 5 randomized control trials on the use of ACT in chronic pain demonstrating efficacy in improving mood and function.

- 171 subjects with chronic MSK completed a course of ACT

- At a 3 year follow up 68% of the cohort noted improvement in key outcomes including pain related anxiety, physical and psychosocial disability, and depression.
Pain and Suicide

Suicidal ideation and the risk of suicide in patients with fibromyalgia: a comparison with non-pain controls and patients suffering from low-back pain

Irene Jimenez-Rodriguez*, Juan Miguel Garcia-Lema, Beatriz Mijares-Lopez, Emilia Cordas-Moreno, Fernando Rico-Villademoros, Elena P. Calandrelli

Abstract: Fibromyalgia is associated with an increased rate of mortality from suicide. In fact, this disease is associated with several characteristics that are linked to an increased risk of suicidal behavior, such as being female and experiencing chronic pain, psychological distress, and sleep difficulties. However, there is a lack of knowledge concerning suicidal behavior and their risk factors in fibromyalgia. The objective of the present study was to evaluate the prevalence of suicidal ideation and the risk of suicide in a sample of patients with fibromyalgia compared with a sample of healthy volunteers and a sample of patients with chronic low-back pain. We also aimed to evaluate the relevance of pain intensity, depression, and sleep quality as variables related to suicidal ideation and risks. Logistic regression analysis was used to evaluate the relationship between suicidal ideation and the risk of suicide adjusted by age and sex. We also used two logistic regression models among age, sex, pain severity score, depression severity, sleep quality, and disease severity. The independent variable and the control group were referenced. Forty-seven patients with fibromyalgia, 32 patients with low-back pain, and 50 controls were included. Suicidal ideation, measured with the Beck Depression Inventory, was almost absent among the controls and was low among patients with low-back pain, however, suicidal ideation was present in patients with fibromyalgia (P = 0.001). The risk of suicide, measured with the Puharic Suicide Risk Scale, was also higher among patients with fibromyalgia than in patients with low-back pain or in controls (P = 0.000). The Beck Depression inventory for suicidal ideation and the risk of suicide were higher among patients with fibromyalgia (odds ratio of 2.9 and 1.8, respectively) than in patients with low-back pain (odds ratio of 0.5 and 1.7, respectively). Depression was the only factor associated with suicidal ideation or the risk of suicide.

Keywords: chronic low back pain, suicidal risk, depression
Suicidal Ideation

<table>
<thead>
<tr>
<th>% of population</th>
<th>* p&lt;0.0001</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Control</td>
<td>0</td>
</tr>
<tr>
<td>+ LBP</td>
<td>20</td>
</tr>
<tr>
<td>+ PW</td>
<td>40</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suicidal ideation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>26.889</td>
<td>5.72–126.42</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Low-back pain</td>
<td>4.583</td>
<td>0.826–25.432</td>
<td>0.082</td>
</tr>
<tr>
<td>Risk of suicide</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>48.000</td>
<td>12.929–178.206</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Low-back pain</td>
<td>4.725</td>
<td>1.297–17.209</td>
<td>0.019</td>
</tr>
</tbody>
</table>
Functional Restoration

- Focus on improvement of functional restoration
  - Occupational and physical therapy
    - The most effective treatment option
    - Desensitization and resetting altered central processes of the brain
  - Aquatic therapy
    - Hydrostatic principles and buoyancy component
    - Mild compressive force around affected extremities
      - Decreases edema
      - Assist in weight bearing of the extremity

Social Support
Graded Motor Imagery (GMI)

Pain Is a Disease of the Brain

- Theory of pain modulation based on nociception
- Pain perception involves all areas of the brain
Factors That Influence Nociceptive Inputs to Pain Perception

CNS Plasticity in Pain

CNS reorganization in a variety of chronic pain states: review.
Henry, Chiodo, Yang. PM&R Vol 3 Dec 2011

- CNS reorganization in response to sensory and emotional experiences
- Both structural and functional intrinsic changes are demonstrated
- Changes occur in number/location of synapses
Neuroplasticity Changes in PLP

- Phantom limb pain
  - Remapping of somatosensory cortex
  - Brain activity changes in ipsilateral motor cortex, thalamus, insula, forebrain, ACC

Pain catastrophizing and neural responses to pain among persons with fibromyalgia.

Increased activity in brain areas related to: anticipation of pain (FC), attention to pain (ACC, PFC) emotional aspects of pain (amygdala)
What Is Graded Motor Imagery (GMI)?

- Therapeutic techniques
- Began approximately 20 years ago
- Developed by a group of professional staff at the Neuro Orthopaedic Institute (NOI) group in Australia
- Lorimer Moseley credited with researching and progressing techniques
- Is progressively expanding and is taught internationally
- Research is ongoing

GMI Continued…

- Based on research, the brain is adaptable and changes over the course of our lives
- The brain can be “retrained” to help reduce pain
- GMI uses “brain exercises” to retrain how the brain processes pain

“Graded Motor Imagery is the most up to date rehabilitation program – based on the latest science and clinical trials to treat many complex pain, and movement problems” (noigroup.com)
How is GMI used in therapy?

Three phases:
1. Laterality training
2. Explicit motor imagery
3. Mirror therapy

Laterality Training

Explicit Motor Imagery

Mirror Therapy

Improved Function
**Who is GMI used with?**

- People with:
  - Chronic pain
  - Chronic regional pain syndrome (CRPS)
  - Brachial plexus injuries
  - Amputations
  - Stroke/CVA
  - Arthritis
  - Fibromyalgia

*GMI techniques can be individualized for any diagnosis, depending on the person’s needs*

View Video:

http://noijam.com/2014/10/31/what-is-graded-motor-imagery/

---

**References/Further Information on GMI**

- http://www.bodyinmind.org/
- Lorimer Moseley’s TedX Lecture: “Why Things Hurt?”
  https://www.youtube.com/watch?v=gdw-11dHjs
New Frontiers

Multimodal Approach

- CBT/ACT
- Functional restoration
- Interventions
- Social support
- Pharmacotherapy
- GMI
Thank you !!!

Q and A ?