Fibromyalgia & Chronic Fatigue Syndrome

Theory and Practice

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A Typical Case

30 yo woman with 8 years of diffuse pain, headache, fatigue, and “brain fog”

- Mood poor
- Sleep fitful and unrefreshed
- PMH: Headaches, IBS, IC
- Exam: Muscle hyperalgesia above and below waist, bilaterally
- Imaging without specific pathoanatomy
Fibromyalgia Pathophysiology

Evidence for both peripheral and central disorders

- Reduced thermal and mechanical pain thresholds
  - Abnormal QST response to heat, cold, electric stimulation
- Increased temporal summation
- Reduced frequency of stimulation to maintain pain
- fMRI data demonstrates:
  - reduced stimulus threshold
  - widespread CNS activation
  - dependence on maintained peripheral input
Chronic Fatigue Syndrome

• Comorbidity ≥ 80% with:
  – Chronic Widespread Pain
  – Irritable Bowel
  – Major Depression

• Poor sleep and sleep disturbances: 70-90%
  “the strong tendency of CFS-like illness to co-occur with these other conditions is unlikely to be an artifact of clinical ascertainment”

Shipley M. Medicine (38) 2010
Central Pain “Neuromatrix”

Pain Processing

Descending Pain Modulation System
Wide dynamic range (WDR) neurons

Central sensitization: impulses from non-nociceptive nerves are perceived as being painful (allodynia)

Emerging Concepts in the Neurobiology of Chronic Pain: Evidence of Abnormal Sensory Processing in Fibromyalgia.
Bennett, Robert
Peripheral Sensation

Normal transduction

Inhibitory interneurons in dorsal horn

Touch becomes pain....

From Woolf 2010
Fibromyalgia

Central Pain Processing Disorder

Woolf CJ, 1991
Brain Imaging in Fibromyalgia

fMRI response to 4 kg/cm² of pressure applied on the R thumb

Fibromyalgia patients vs. Healthy controls

Pujol 2009
Abnormal fMRI in FMS

Correlation map between subjective pain scores and brain activations in fibromyalgia

Pujol 2009
Central Sensitization: Associated Inflammatory Processes

<table>
<thead>
<tr>
<th>Neuromodulators/Neurotransmitters Released by Activated C-nociceptors Presynaptically</th>
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<tbody>
<tr>
<td>Substance P (SP)</td>
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<tr>
<td>Calcitonin-gene-related peptide (CGRP)</td>
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<tr>
<td>Vasoactive intestinal peptide (VIP)</td>
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<tr>
<td>Somatostatin</td>
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<tr>
<td>Galanin</td>
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<tr>
<td>Never growth factor</td>
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<tr>
<td>Glutamate</td>
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<td>Aspartate</td>
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<tr>
<th>Post Synaptic Neuroreceptors/ Neuroeffector Targets</th>
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<tbody>
<tr>
<td>Neurokinin 1 (NK1)</td>
</tr>
<tr>
<td>N-methyl-D-aspartate (NMDA)</td>
</tr>
<tr>
<td>Alpha-amino-3-hydroxy-5-methyl</td>
</tr>
<tr>
<td>4-isoxazolepropionate (AMPA)</td>
</tr>
<tr>
<td>Metabotropic glutamate (mGlu)</td>
</tr>
<tr>
<td>Tyrosine kinase B (Trk-B)</td>
</tr>
<tr>
<td>Protein kinase gamma (PKC-gamma)</td>
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<tr>
<td>Vanilloid subfamily (TRPV-1, TRPVL-1)</td>
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Yunus 2007
Fibromyalgia & CFS

Functional or “Real” disorder

Not “theological” diagnosis requiring “belief”

– “All my tests are negative”
– “My doctor thinks its all in my head”

“Many patients are grateful for an explanation and a diagnosis of their distressing symptoms, which may have been dismissed or passed from one doctor to another. Winning the patient's confidence is an important starting point in any management strategy.”

Shipley M. Medicine (38) 2010
Fibromyalgia Clinical Presentation

- Characteristic history
  - “FIBRO”
    - Fatigue
    - Insomnia
    - Blues, Rigidity
    - Ow!!

- Frequently headache and sleep problems
- Pain insidious onset
- Frequent co-morbid chronic pain disorders
  - Rheumatologic/Inflammatory
  - Musculoskeletal/Traumatic
  - Other central sensitization disorders
- Family history of chronic pain often present
Multidimensional Features of Central Sensitization

Yunus, 2007
Allostatic Systems

Mayer and Tillisch 2011
Spectrum of Widespread Pain Disorders

Central sensitization

PTSD
Fibromyalgia syndrome
IBS
FUS/IC
Primary dysmenorrhea
Migraine
MCS
PLMS
Restless legs syndrome
TMD
T-T headache
MPS

Yunus 2007
Fibromyalgia Clinical Evaluation

Physical Examination

– Widespread tender-point exam

– Is this still needed?:
  • ≥11/18 bilateral above and below waist, including axial spine

– No other disorder should account for presentation
Fibromyalgia & CFS Evaluation

• “Rule Out Work-up”
  – ANA, RA, CRP, ESR, (CK, aldolase?)
  – CBC, CMP, (HCV, HIV?)
  – Iron, TIBC, ferritin
  – TSH, PTH
  – Vitamin B-12 & MMA, vitamin D, folate
  – TTG/antigliadin?

• Consider tender point exam on *all chronic pain patients* to assess for widespread hyperalgesia related to other disorders
  – Opioid induced hyperalgesia
  – Chronic spinal pain syndromes
Rule-Out Diagnoses
Adverse Childhood Events (ACE)

- Recurrent physical abuse
- Recurrent emotional abuse
- Sexual abuse
- An alcohol and/or drug abuser in the household
- An incarcerated household member
- Someone who is chronically depressed, mentally ill, institutionalized, or suicidal
- Mother is treated violently
- Emotional or physical neglect
Fibromyalgia Diagnostic Criteria 2010
Proposed Revision

- Widespread pain ≥7/19
- 3 Symptoms/severity (0-3)
  - Fatigue Severity
  - Awaken Refreshed
  - Cognition Impaired
  - Plus overall rating of somatic complaints (0-3)

(Wolfe et al Arthritis Care & Research 2010; 62: 600-610)
Fibromyalgia Widespread Pain Index

(Wolfe et al Arthritis Care & Research 2010; 62: 600-610)

Check each area you have felt pain in over the past week.

- Shoulder girdle, left
- Shoulder girdle, right
- Upper arm, left
- Upper arm, right
- Lower arm, left
- Lower arm, right
- Hip (buttock) left
- Hip (buttock) right
- Upper leg left
- Upper leg right
- Lower leg left
- Lower leg right
- Jaw left
- Jaw right
- Chest
- Abdomen
- Neck
- Upper back
- Lower back
- None of these areas

[Diagram of body parts marked with pain areas]
Fibromyalgia & CFS
Treatment Goals

• Restore normal somatosensory response into a disturbed bio-psycho-social milieu
  – Treatments
    • Physical Activation
    • Medication
    • Acupuncture
    • Life-style modification

• Develop patient based exercise/recovery program

• Restore sleep
• Improve mood
  – Counseling
    • Cognitive Behavioral Treatment

• Lessen pain expectancy
• Reduce avoidance of activity
• Improve confidence
• Restore more normally functioning physical activity
Fibromyalgia & CFS Non-Drug Treatments

Cognitive Behavioral Therapy (“Training”)  
Relaxation  
Mindfulness  
Exercise/Aerobic Fitness  
Acupuncture

CFS and Fibromyalgia Self-Help  
www.treatcfsfm.org  
www.cfidsselhelp.org
Fibromyalgia Medications

Tricyclic Antidepressants
SNRI Antidepressants
Anti-Epileptic Drugs
Rarely, if ever, opioids

- Disrupt ascending/descending allostasis
  “Disconnects the brain from feeling of the rest of the body”
Clinical Trials of Antidepressant Effectiveness in Fibromyalgia

Tricyclics: NNT 1.7

SNRIs:
  – Duloxetine
  – Venlafaxine
  – Milnacipran

SSRIs:
  – No evidence of benefit

Saarto T, Wiffen PJ. Cochrane Database of Systematic Reviews 2007
NA and 5-HT Reuptake Selectivity

- **Highly noradrenergic**
  - Maprotiline/Bupropion
  - Desipramine/Nortriptyline/Protriptyline
  - Imipramine/Amitriptyline
  - Doxepin/Mirtazapine
  - Tramadol
  - Milnacipran/Tapentadol

- **Mixed**
  - NA/5-HT 3:1
  - Duloxetine
  - NA/5-HT 1:10
  - Venlafaxine
  - NA/5-HT 1:30
  - Citalopram/Fluoxetine/Sertraline

- **Highly serotonin**
  - NA/5-HT only
  - Fluvoxamine

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AEDs for Fibromyalgia Pain

Gabapentin 1200-2400mg

Pregabalin 300-600mg

NNT

>30% improvement: 5-9

>50% improvement: 8-12

NNH: 6-14

Side-effect: edema, sedation, weight gain, tremor

Freeman 2008
Hauser 2009
Muscle relaxers relax:

a) Muscles
b) Patients
c) Doctors
Opioids for FMS?

- No RCT evidence for effectiveness
- Recommend against opioids due to near identical opioid side-effects
  - Hyperalgesia
  - Fatigue
  - Headache
  - Depression
  - Disability
A Framework for Fibromyalgia Management for Primary Care Providers

Arnold LM, Clauw DJ, L. Jean Dunegan LJ, Turk DC

Mayo Clinic Proceedings Volume 87, Issue 5 2012 488 - 496
A Framework for Fibromyalgia Management for Primary Care Providers

A dynamic process
- As patient’s situation improves or changes, treatment priorities and goals will change as well
- However, the core principles—education, goal setting, multimodal management, and outcomes assessment—are employed consistently throughout
A Framework for Fibromyalgia Management for Primary Care Providers

Be proactive and prepared

Know your patient
- Reflect patient’s priorities and preferences in treatment plan

Know your team
- Identify specialists or ancillary health care providers who can work with you in the care of patients with fibromyalgia

Know your community
- Identify community resources the patient can utilize for self-management

Pharmacotherapy to reduce fibromyalgia pain, other symptoms
- Start low/go slow, titrate to efficacious dose
- Manage expectations

Treat comorbid conditions, eg,
- Peripheral pain conditions
- Mood disorders
- Associated pain conditions (IBS, headache/migraine etc)
- Sleep disorders

Nonpharmacological therapies
- Write as “prescriptions”
- Sleep hygiene
- Physical activity
- Self-management support
- CBT (Web-based or referral)

A dynamic process
- As patient’s situation improves or changes, treatment priorities and goals will change as well
- However, the core principles—education, goal setting, multimodal management, and outcomes assessment—are employed consistently throughout
Maintain focus on progress over time vs daily ups and downs

Evaluate on follow-up visits:
- Progress toward agreed-upon treatment goals (using patient assessment tool[s] employed at baseline)
- Physical activity
- Use of self-management techniques and barriers to adherence
- Medication efficacy and adverse effects
- Comorbidities
- Adjustments to the treatment plan

A dynamic process
- As patient’s situation improves or changes, treatment priorities and goals will change as well
- However, the core principles—education, goal setting, multimodal management, and outcomes assessment—are employed consistently throughout
Fibromyalgia & CFS Summary

• FMS & CFS are associated with many other common complex pain syndromes
  – “A disorder of central pain processing”
• Diagnosis is *not* difficult, just need to be thorough
• Believe your patient that they “hurt” & “suffer”
• **CBT and improved fitness most effective and safest**
• Best drugs are TCAs>SNRIs>AEDs
• Avoid opioids