

**Fibromyalgia is more than pain: a multi-symptom approach**

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OSPA Fall CME 2012

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**Learning Objectives**

- 1) Understand both the 1990 and 2010 ACR criteria for the diagnosis of fibromyalgia
- 2) Identify three main symptom domains in fibromyalgia
- 3) Determine how to develop a treatment plan for fibromyalgia patients

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**Prevalence of FM**

- Estimated 2-3% of U.S. population
- 80-90% female
- Ages 20-50

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### Only pain needed to diagnose

- Diagnostic criteria established in 1990 by American College of Rheumatology
- Widespread muscle pain for greater than 3 months
- Pain in 11/18 tender points on palpation

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### Fibromyalgia tender points



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### Why develop new criteria?

- 1990 ACR criteria are
  - Limited to pain
  - Ignored comorbidities
  - Designed as research classification
  - Never validated for clinical diagnosis

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### 2010 ACR FDC

- **WIDESPREAD PAIN INDEX (WPI): 0-19**
  - Ask about pain in 19 body regions

Jaw, Rt.	Upper Arm, Rt.	Upper Back	Upper Leg, Rt.
Jaw, Lt.	Upper Arm, Lt.	Lower Back	Upper Leg, Lt.
Neck	Lower Arm, Rt.	Hip (buttock, trochanter), Rt.	Lower Leg, Rt.
Shoulder girdle, Rt.	Lower Arm, Lt.	Hip (buttock, trochanter), Lt.	Lower Leg, Lt.
Shoulder girdle, Lt.	Chest	Abdomen	

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### 2010 ACR FDC

- **SYMPTOM SEVERITY SCALE (SSS): 0-12**
  - Symptom domains: Fatigue, Cognition, Pain;
  - 0-3 scale for each (0=none, 1=slight/mild, 2=moderate, 3=severe)
  - Somatic symptoms based on # of other symptom domains;
  - 0-3 scale (0=none, 1=few, 2=moderate, 3=many)

Wolfe F, et al. Arthritis Care Res. 2010;62:600-610.

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### Somatic Symptoms

- Muscle pain, Irritable bowel syndrome, Fatigue/Tiredness, Concentration and memory problems, Muscle weakness, Headache, Pain/cramps in abdomen, Numbness/Tingling, Dizziness, Insomnia, Depression, Constipation, Pain in upper abdomen, Nausea, Nervousness, Chest pain, Blurred vision, Fever, Diarrhea, Dry mouth, Itching, Wheezing, Raynaud's, Hives/Welts, Ringing in ears, Vomiting, Heartburn, Oral ulcers, Loss/Change in taste, Seizures, Dry eyes, Shortness of breath, Loss of appetite, Rash, Sun sensitivity, Hearing difficulties, Easy bruising, Hair loss, Frequent urination, Painful urination, and Bladder spasms.

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**Where to start for treatment?**

- Fatigue
- Pain
- Cognitive Dysfunction

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- Ask patients which of the 3 symptom domains is bothering them the most
- Answer may surprise you: It is not always pain
- Use answer to direct treatment

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**To treat must first understand:**

- Pathophysiology of fibromyalgia becoming clearer
- Gaps in understanding remain

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### What Do We Know about FM?

- Poor deep sleep
- Inadequate growth hormone release
- Dysfunctional stress response
- Central Sensitization

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### Abnormal Sleep

- Alpha-wave intrusion into deep sleep
- Moldofsky reproduced symptoms in healthy volunteers by interrupting deep sleep

Moldofsky H et al. *Psychosom Med* 1975. 37(4); 341-351

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### Non-restorative sleep in FM

- Majority of FMS patients state that sleep is non-refreshing or non-restorative (>90%)
- This is independent of amount of sleep time or sleep efficiency
- Does not seem to be affected by most sleep medications, or proper sleep hygiene
- May have to do with alpha-wave intrusion in deep sleep

Bennett RM, et al. *BMC Musculoskeletal Disorders*. 2007;8:27.

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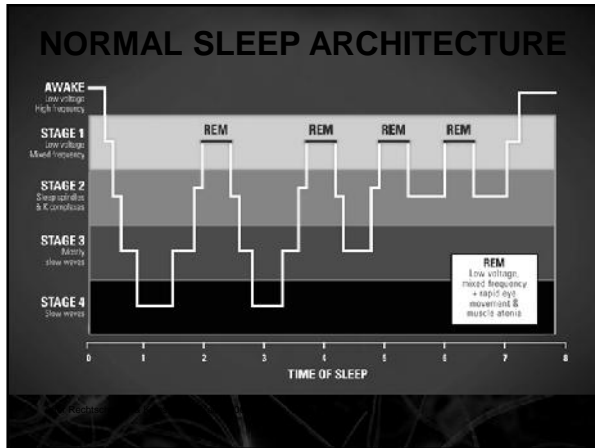
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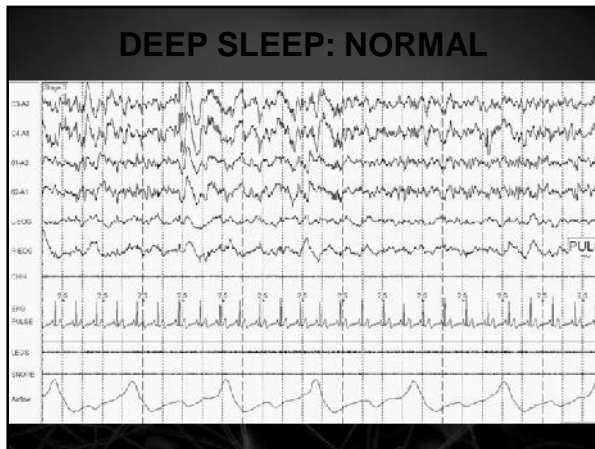
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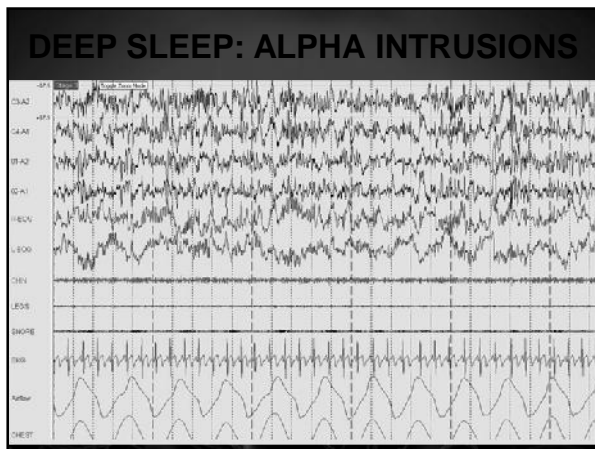
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### Low Growth Hormone

- Bennett at OHSU found low growth hormone in FM
- Symptoms improved after growth hormone supplementation

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### Dysfunctional Stress Response

- HPA axis abnormalities
  - Loss of circadian rhythm of cortisol release
- Autonomic NS abnormalities
  - Decreased heart rate variability evidence of sympathetic NS predominance
  - Stuck in "Fight-or-Flight" mode

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### Central Sensitization

- Amplification of pain signals
- Decreased central inhibition of pain signals
- Leads to exaggerated pain
  - Hyperalgesia
  - Allodynia

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**fMRI evidence of central sensitization**

- Gracely et al, 2002: First functional MRI of fibromyalgia
- fMRI measures cerebral blood flow
- images of FM and controls while varying pressures to thumbnail

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**Results**

- Pressure causing moderate pain in FM causes very mild pain in controls
- 13 additional areas of FM patients brain activated by painful stimulus

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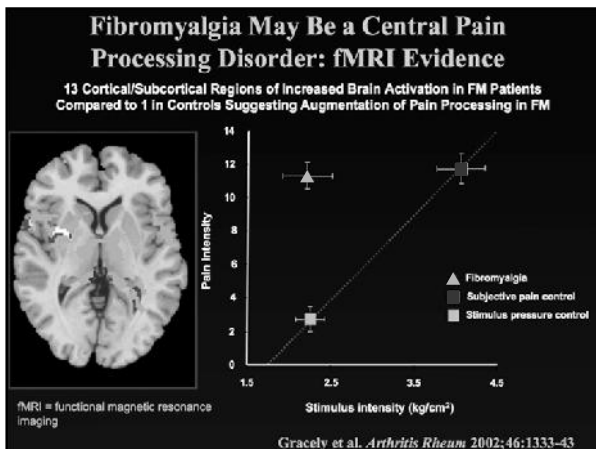
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### Developing Treatment Plan

- Confirm diagnosis
- Ask which symptom domain bothering the most
- Start with that symptom

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### How to Reduce Fatigue

Focus on improving sleep

- Evaluate for, and treat, any co-existing sleep disorders
  - Sleep apnea
  - RLS
  - PLMD

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### Sleep Study

Many patients with FMS have an additional sleep disorder. Studies have found:

- 1/3 of female FMS patients had RLS
- 44% of male FMS patients had OSA
- 26 of 27 women with FMS had at least mild sleep-disordered breathing

1. Shah MA, et al. *J Clin Rheumatol*. 2006;12:277-281; 2. Gold AR, et al. *Sleep*. 2004;27:459-466; 3. May KP, et al. *Am J Med*. 1993;94:505-508; 4. Viola-Saltzman M, et al. *J Clin Sleep Med*. 2010;6:423-427.

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## Sleep Disordered Breathing and FMS

- OSA occurs when the upper airway repeatedly collapses during sleep, causing cessation of breathing (apnea), or inadequate breathing (hypopnea), and sleep fragmentation
- Mild sleep apnea may be seen in nearly half of FMS patients
- Moderate and severe sleep apnea is present in at least 15-20% of female FMS patients (more than twice the normal for age-adjusted female population)



Normal



Obstructed

Moldofsky H, et al. *J Rheum.* 2010; 105:465-470.

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## Approaches for OSA in FMS

- CPAP:** Pressure creates pneumatic splint to keep the airway open
  - For moderate to severe OSA
  - Newer masks are more comfortable
  - Newer auto-titrating machines come with expiratory pressure relief
- Oral Appliance Therapy:** Advances mandible
  - Approved for mild to moderate OSA
  - May worsen TMJ
  - Costly
- Positional Therapy:** Avoidance of supine sleep
  - SONA pillow shown effective for mild OSA and snoring



Adapted from American Academy of Sleep Medicine, Clinical Practice Parameters

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## Restless Leg Syndrome

- RLS is a common complaint
  - May represent neuropathy or just pain amplification
  - Periodic limb movement disorder (PLMD) is actually under-represented in sleep studies in FMS population
- 4 cardinal symptoms ("URGE"):**
  - Urge to move legs associated with unpleasant sensation
  - Worsening of symptoms with Rest
  - Improvement of symptoms with movement or Getting up
  - Symptoms tend to increase in Evening and night

American Academy of Sleep. International Classification of Sleep Disorders, Diagnostic and Coding Manual, 2nd ed. 2005.

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### Treating RLS

- Trial iron replacement (goal ferritin >50)
- Dopamine agonists
- Anti-convulsants
- Benzodiazepines

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### Medications to Improve Sleep

- First, minimize medications that cause sleep disruption (eg, opiates, benzos, ETOH)
- Usual sleep medications may help (zolpidem, eszopiclone)
  - useful to treat insomnia
  - can increase quantity sleep
  - don't affect quality of sleep

1. Shaw IR, et al. *Sleep*. 2005;28:677-682; 2. Drewes AM, et al. *Scand J Rheumatol*. 1991;20:288-293; 3. Moldofsky H, et al. *J Rheumatol*. 1996;23:529-533.

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### Meds That Affect Sleep Quality

- Anticonvulsants (pregabalin, gabapentin) have some mildly positive effects on sleep quality
- Sodium oxybate (GHB derivative) increases deep sleep significantly
  - Controversial: "date-rape drug"
  - Not FDA-approved for use in FMS

1. Scharf MB, et al. *J Rheumatol*. 2003;30:1070-1074; 2. Russell IJ, et al; Oxybate SxB-26 Fibromyalgia Syndrome Study Group. *Arthritis Rheum*. 2009;60:299-309; 3. Hindmarch I, et al. *Sleep*. 2005;28:187-193.

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### Treating Fatigue

- Clinically, sometimes a stimulant is helpful for fatigue in FMS
- Several case reports show benefit of modafinil in treating FMS fatigue
- One small study did not show any benefit of armodafinil vs placebo for FMS fatigue
- Not FDA-approved for this indication

1. Schwartz TL, et al. *J Clin Rheumatol*. 2007;13:52; 2. Schaller JL, et al. *J Neuropsychiatry Clin Neurosci*. 2001;13:530-531; 3. Schwartz TL, et al. *Ann Pharmacother*. 2010;44:1347-1348. Epub 2010 Jun 15.

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### Treating Fibromyalgia Pain

- Reduce local pain generators- myofascial trigger points
- Reduce central sensitization
- Gentle exercise
- No evidence for benefit of NSAIDs or opiates
- Tramadol is the only analgesic with evidence of effectiveness in FMS

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### Decreasing Central Sensitization

- Anticonvulsants (pregabalin and gabapentin)
  - Reduce amplification of pain signal
- Serotonin/Norepinephrine reuptake inhibitors (duloxetine, milnacipran, venlafaxine)
  - Increase central inhibition of pain signals

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**Treating “Fibrofog”**

- Hardest symptom domain to treat, limited options
- Often better with sleep improvements
- Have seen improvement with sodium oxybate
  - Not FDA-approved for this indication
- Anticonvulsants can exacerbate

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**Treating “Fibrofog”**

- Speech or cognitive therapies to learn memory strategies, as well as job function strategies, can be helpful
- Stimulants sometimes very helpful

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