Overview of Fibromyalgia: Clinical Features and Treatment Approaches

RAC Meeting

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Presentation Outline

- Nature of Fibromyalgia
  - Clinical features
  - Diagnosis
  - Co-occurring conditions
- Management of Fibromyalgia
  - Complexities of care
  - Behavioral strategies
  - Pharmacological agents

Nature of Fibromyalgia

What's in a Name?

- Documented reports of diffuse pain conditions with associated lethargy in England and France in the 19th century
- Originally termed "fibrositis"
  - "fibr-" = fibers
  - "-itis" = inflammation
- Changed to Fibromyalgia
  - "-algia" = pain

Fibromyalgia and Chronic Widespread Pain

- Prevalence
  - 2-11% lifetime prevalence in the U.S. and U.K.
  - American College of Rheumatology Criteria = 0.5 – 4%
- Demographics
  - 80% women, 20 – 50 years of age
- Co-occurring Symptoms
  - Morning stiffness
  - Fatigue, sleep disturbance
  - Cognitive/information processing disruption
  - Mood disturbance

American College of Rheumatology Definition

- History of chronic widespread pain
  - Pain in 4 quadrants of the body
  - Females 1.5 times more likely to report history of chronic widespread pain
- 11 of 18 possible tender points on examination
  - Females 11 times more likely to meet tender point criteria than men
  - Tender point endorsement highly associated with levels of distress

Tender Point Examination

- 9 paired regions on the body
- Positive point = reported pain when region palpated with 4 kg of pressure
- American College Rheumatology criteria = 11/18 positive tender points

Other Diagnostic Considerations

- Medical rule-out process
  - Thorough medical history
  - Physical examination
- Recent laboratory studies
- Psychiatric evaluation
  - Identify co-occurring, treatable conditions

Physical Examination

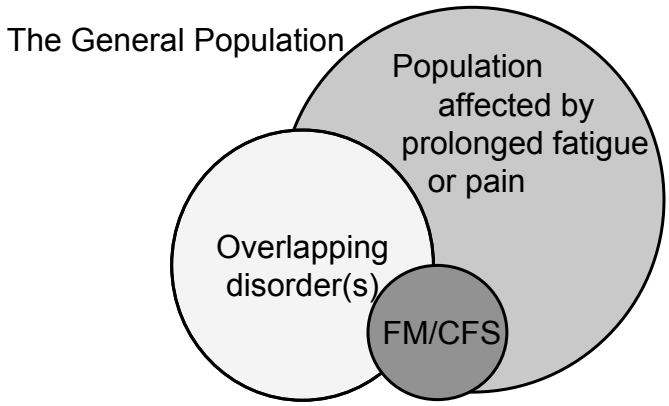
- Besides tenderness, musculoskeletal examination is unremarkable
- Typically no inflammation, connective tissue or neurological abnormalities
- Conduct routine musculoskeletal and neurologic examinations to exclude the presence of co-occurring conditions

Laboratory Testing

- Laboratory testing is usually unremarkable; extensive testing unnecessary and may complicate the situation
- Initial testing
  - Complete blood count
  - Thyroid stimulating hormone
  - Erythrocyte sedimentation rate
  - Muscle enzymes
  - ANA
- Be wary of false positives!

Overlap of Fibromyalgia with Other Disorders

Conceptual Framework of Pain and Fatigue



Complexity of Fibromyalgia: Overlapping Syndromes

- Co-occurrence of unexplained syndromes is common
  - Chronic fatigue syndrome
  - Irritable bowel syndrome
  - Temporomandibular disorder
  - Interstitial cystitis/painful bladder syndrome
  - Migraine headache/tension headache

Overlapping Clinical Conditions

Fibromyalgia	Rheumatology
Chronic fatigue syndrome	General Medicine
Irritable bowel syndrome	Gastroenterology
Temporomandibular disorder	Dentistry
Interstitial cystitis	Urology
Multiple chemical sensitivity	Environmental Medicine
Tension headache	Neurology
Chronic low back pain	Orthopedics
Chronic pelvic pain	Gynecology
Post concussion syndrome	Rehabilitation Medicine
Chronic Lyme disease	Infectious Disease

Overlap Between Chronic Fatigue Syndrome and Fibromyalgia

- 21 – 42% of fibromyalgia patients meet Centers for Disease Control and Prevention criteria for chronic fatigue syndrome
- 25 – 75% of chronic fatigue syndrome patients meet American College of Rheumatology criteria for fibromyalgia

Clinical Importance of Overlapping Syndromes

- Treatment is more difficult and complicated with worse outcomes
- Health care use and costs are higher
- Unemployment and functional impairments are excessive
- Greater risk for psychiatric comorbidity
- Impact on treatment planning (e.g., stepped care)

Psychiatric Comorbidity

- Comorbid psychiatric conditions are common
  - Major depressive disorder
  - Generalized anxiety disorder
  - Posttraumatic stress disorder
- Rates of current conditions range from 30 – 60% among tertiary care patients; lifetime rates as high as 85%
- Community studies of fibromyalgia report much lower rates of psychiatric distress

Psychiatric Comorbidity

Fibromyalgia → Psychiatric Diagnosis

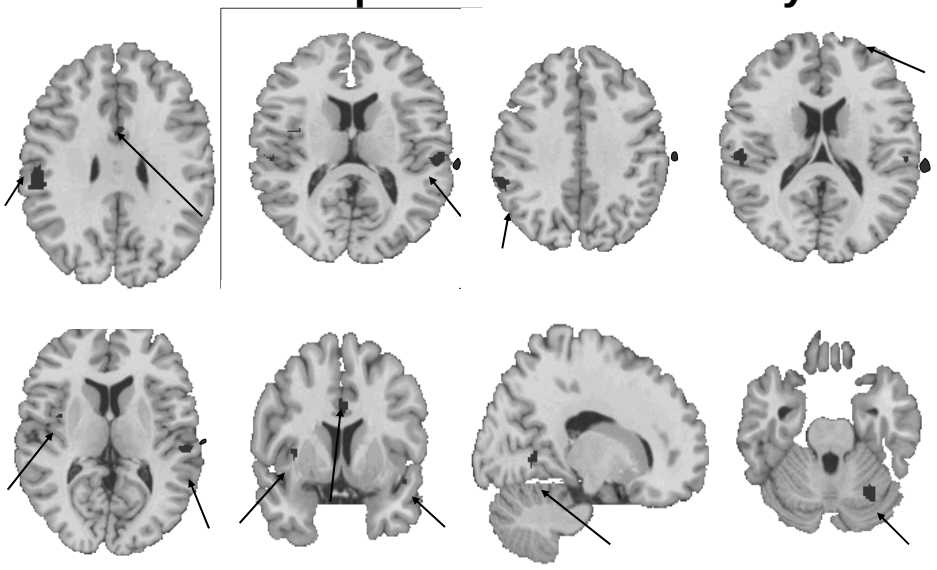
Psychiatric Diagnosis → Fibromyalgia

→ Fibromyalgia →
Psychiatric Diagnosis

Vulnerability Models

- Biological
  - Genetic (familial transmission)
  - Neurobiological (pain processing)
  - Biochemical (norepinephrine, serotonin)
- Precipitating Events
  - Acute physical traumas
  - Infectious diseases (Hepatitis C, Lyme)
  - Emotional stress/victimization

fMRI – Equal Stimulus Intensity



STG=superior temporal gyri; SI=primary somatosensory cortex; SII=secondary somatosensory cortex; IPL=inferior parietal lobule. Gracely. *Arthritis Rheum*. 2002;46:1333-1343.

The Bottom Line…

- No controlled studies have identified a clinically useful biological marker
- Abnormalities in pain perception – central sensitization – are likely mechanism

We also know…

- Certain patient behaviors and systems factors maintain and exacerbate fibromyalgia and functional impairment

Maintaining Factors

- Individual-level
  - Beliefs/attitudes; low confidence
  - Over-exertion cycle
  - Coping strategies
  - Physical de-conditioning
  - Treatment adherence
- Systems-level
  - Changes to support system
  - Disability and compensation; wellness punished?
  - Over-medicalization

Management of Fibromyalgia

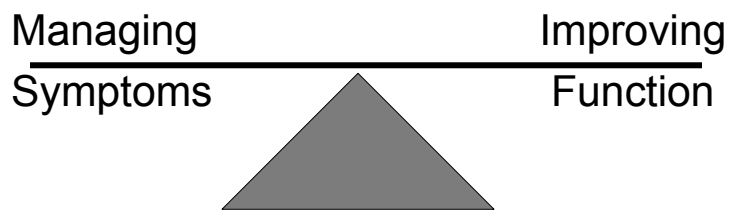
Real-life Complexities of Care

- "Diagnosis-cure" approach
  - Set realistic limits on extent of diagnostic testing
  - Encourage "rehabilitation-coping" model of care
- Limited time to deal with multiple problems
  - Stepwise approach to problems; allow patient choice in prioritizing care of medical issues
- Symptoms, circumstances, and motivation can interfere with the "fair trial"
  - Anticipate difficulties and engage in proactive problem solving

Real-life Complexities of Care

- Numerous medications and providers
  - Consider simplification strategies
  - Open communication with providers; be conservative with referrals
- Competing interventions and non-evidence based treatments
- Illness happens in a system
  - Assess levels of support; enlist family members and friends as coaches
  - Identify resources and barriers to care

Treatment Approach



Treatment Approaches

- Behavioral Strategies
- Pharmacological Interventions
- Augmented Care
  - Complimentary and alternative medicine

Treatment typically involves intervention combinations but MUST involve disciplined physical reconditioning

Behavioral Strategies

- Promote an internal locus of control by modifying maintaining factors at individual and system levels
- Time-limited, skill-based strategies to improve control over the “volume control” of pain
- Emphasis on proactive, not reactive coping
- Interventions
  - Education
  - Exercise and physical therapy
  - Cognitive behavioral therapy

Cognitive Behavioral Therapy

- Education and self-monitoring
  - Identify triggers and maintenance factors
- Behavioral relaxation strategies
  - Diaphragmatic breathing
  - Progressive muscle relaxation
- Challenging negative beliefs
  - Catastrophic beliefs and expectancies for pain
- Graduated exposure

Targets to Self-Monitor

- Situational cues/triggers
- Associations between pain, mood, and behavior

Take Home Messages

- Cause of fibromyalgia is unknown; symptoms are real and can be managed
- Fibromyalgia is chronic, non-life threatening
- Treatment is available, but it will require work; there are no quick cures
- Focus on managing/changing maintaining factors

Activity: Graduated Exposure

- Guarding and resting in response to pain leads to physical de-conditioning
- Over-exertion experiences with physical activity may lead to conditioned fear of pain and anxiety
- Promote gradual re-engagement in physical activity without worsening symptoms and feared consequences

Graduated Physical Activity

- Select low-impact physical activities
  - Walking
  - Stationary biking
  - Yoga, stretching
  - Swimming, water aerobics
- Develop consistency first, then work on duration and intensity

Getting Started

- Select physical activity with patient
- Determine how much they can do without over-exertion and consequences
- Start 10 – 20% BELOW this level and do activity everyday regardless of how they feel
- Write out clear plan for small increase in time/intensity of activity every 1 – 2 weeks
- Use pedometers
- Diversify activities over time

Predictors of Outcome

- Increased sense of control over pain
- Belief that one is not disabled
- Pain is not a sign of damage
- Active problem solving orientation
- Less guarding/resting in response to pain
- Established physical exercise routine
- Pacing activities

Pharmacological Treatment

- Recent area of great interest to pharmaceutical companies
- Anti-inflammatory medications not effective
- Common agents
  - Antidepressants
  - Antiepileptics
  - Analgesics

Antidepressants

- Antidepressants increase concentrations of serotonin, norepinephrine, or both by serving as reuptake inhibitors
  - Act on descending pain inhibitory pathways
  - Can affect other symptoms (e.g., sleep, energy, mood)
- Good support for pregabalin
- Low dose tricyclics have some empirical support
- Novel antidepressants (duloxetine) are generating encouraging results
- Mixed findings regarding predominantly serotonergic agents (fluoxetine)

Antiepileptics

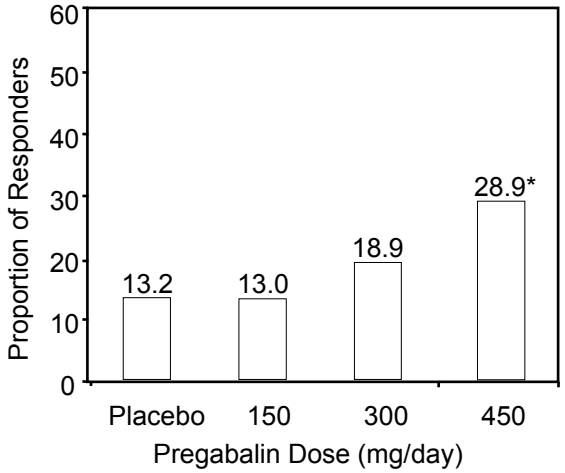
- Pregabalin, gabapentin, tegretol
- Bind to subunit of voltage-gated calcium channels of neurons
- Inhibits release of neurotransmitters (e.g., noradrenaline, substance P)
- Called “anticonvulsants” but effective for neuropathic pain and anxiety

Pregabalin Study

- Randomized, controlled, double blinded trial
- N = 530 fibromalgia patients
- Primary goal: assess efficacy of 3 doses of pregabalin vs. placebo to relieve pain
- Primary outcome: pain rated in a daily diary on a scale of 0 (no pain) to 10 (worst possible pain).
- Secondary outcomes: fatigue, sleep, and global functioning

Crofford L. ACR Meeting; 2002; New Orleans, LA.

Response



- A significantly larger proportion of patients receiving pregabalin 450 mg/day experienced a ≥ 50% reduction in pain from baseline to endpoint

*P = .003 vs placebo.

Summary of Pregabalin Results

	150 mg	300 mg	450 mg
Pain diary			X
McGill Pain Scale			X
Sleep diary		X	X
Multidimensional Assessment of Fatigue		X	X
Patient Global Impression of Change		X	X
Clinician Global Impression of Change		X	X
Short Form-36 General Health Survey	X	X	X

Newer Agents: Milnacipran

- Milnacipran
  - Balanced reuptake inhibitor of norepinephrine and serotonin
  - Approved in Europe and Japan as an antidepressant
  - Double blind, placebo controlled, multi-site study showing dose-dependent efficacy

Newer Agents: Duloxetine

- Duloxetine
  - Balanced and potent serotonin and norepinephrine reuptake inhibitor
  - Antidepressant but also reduces painful physical symptoms associated with depression
  - Examined for treating other chronic pain disorders, e.g., diabetic neuropathy

Opioid Receptor Ligands: Tramadol

- Opioids prescribed to ≈ 15% of fibromyalgia patients
- Variable patient acceptance and physician reluctance
- No good studies of opioids in fibromyalgia
- Tramadol ± acetaminophen show possible efficacy
  - Tramadol functions as μ-opioid receptor ligand and norepinephrine reuptake inhibitor

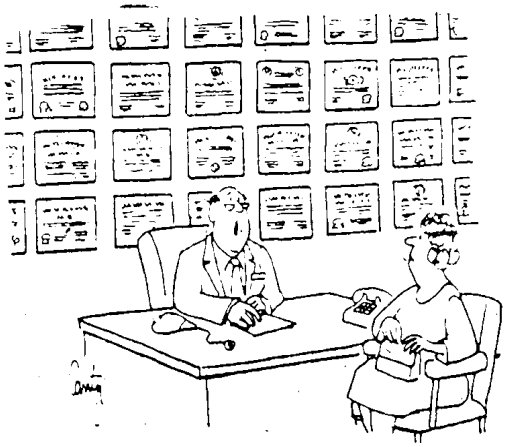
Adjunctive Treatments

- Complimentary and alternative medicine
  - Acupuncture
  - Massage therapy
  - Herbal, naturopathic interventions
- Consider personal and cultural views of illness, health, and wellness

Acupuncture Studies: Summary

- Few randomized, controlled, single blind trials
- Tested directed acupuncture vs. various forms of sham acupuncture, control conditions that varied in needle insertion, location, and stimulation
- All forms of acupuncture are equally beneficial in reducing pain of fibromyalgia
- No effect of needle placement or stimulation

Treatment



"There's so little we know."