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Evaluating diffuse aches and pains:
It's not all fibromyalgia (but often it is)

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Fall 2009

University of Michigan
Medical School

Case presentation

- A patient presents with diffuse myalgias, fatigue, and weakness

Approach to evaluation

- Does this represent rheumatic symptoms of an endocrinopathy?
  - Hypo- or hyper-thyroidism
  - Hypogonadism, diabetes, acromegaly, adrenal disease, parathyroid disease
- **Could this be a toxic/drug effect?**
  - Hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins)
  - Ethanol
  - Zidovudine, clofibrate, cyclosporine
- Is this a paraneoplastic process?
- Is this a systemic inflammatory rheumatic disease?
- Is this a chronic pain syndrome?

Case 1: HPI

- A 70 year old man presents to your clinic complaining of “aches and pains”. On closer questioning, he notes
  - Gradual onset over the past 6 months
  - Morning stiffness lasting 2-3 hours
  - Symmetric pain predominantly localized in his shoulders and hips, making it difficult to get out of a chair or comb his hair
  - No other systemic symptoms

Case 1: Objective

- Elderly man in mild discomfort
- Decreased active ROM in neck, shoulders, and hip flexors; a little tenderness to palpation in those areas
- Normal strength
- Hgb 11.2 g/dL (nl 12-36)
- CK 40 IU/L (WNL)
- TSH, T4 WNL
- ESR 96 mm/hr (nl 0-20)

Polymyalgia rheumatica

- Never occurs before age 50
- Common: in older persons prevalence approaches that of rheumatoid arthritis (approximately 1 percent)
- F:M 2:1, northern latitudes, Caucasians
- HLA-DR4 association

Polymyalgia rheumatica

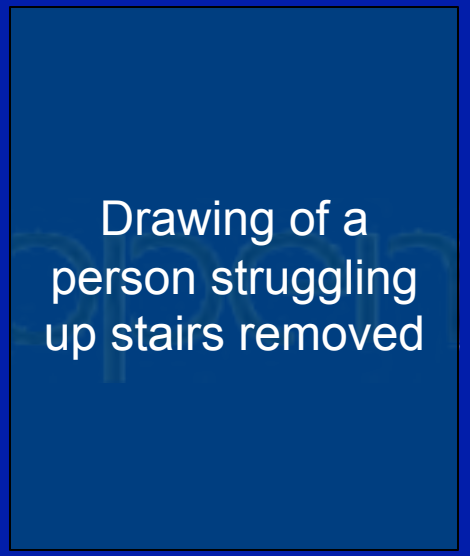
- Diagnosis:
  - Clinical presentation
  - Elevated inflammatory parameters (ESR) – sometimes > 100
- Differential: Some overlap with RA
- Treatment:
  - Exquisitely sensitive to “low” dose steroids (<20 mg/day)
  - Duration of treatment prolonged – 1-2 years

Relationship to giant cell arteritis

- PMR is present in about 50 percent of patients with GCA
- GCA occurs in approximately 15 percent of patients with PMR
- Significant overlap in age of presentation, ethnicity/geography, HLA associations
- Need to screen all PMR patients for GCA signs:
  - headache, scalp tenderness, visual changes, jaw claudication, prominent temporal arteries

Case 2: HPI

- A 55 year old woman presents with “aches and pains”. On closer questioning, she notes
  - Gradual onset over the past 6 months
  - Morning stiffness lasting 2-3 hours
  - Difficulty getting out of a chair, climbing stairs, combing her hair, and reaching for jars in high cupboards; not actual pain with attempting these activities
  - No difficulty holding the comb or standing on toes to get to cupboards



Case 2: Exam & labs

- Minimal muscle tenderness; no joint swelling or tenderness
- Significant proximal muscle weakness in both upper and lower extremities
- No other neurologic abnormalities

CK elevated

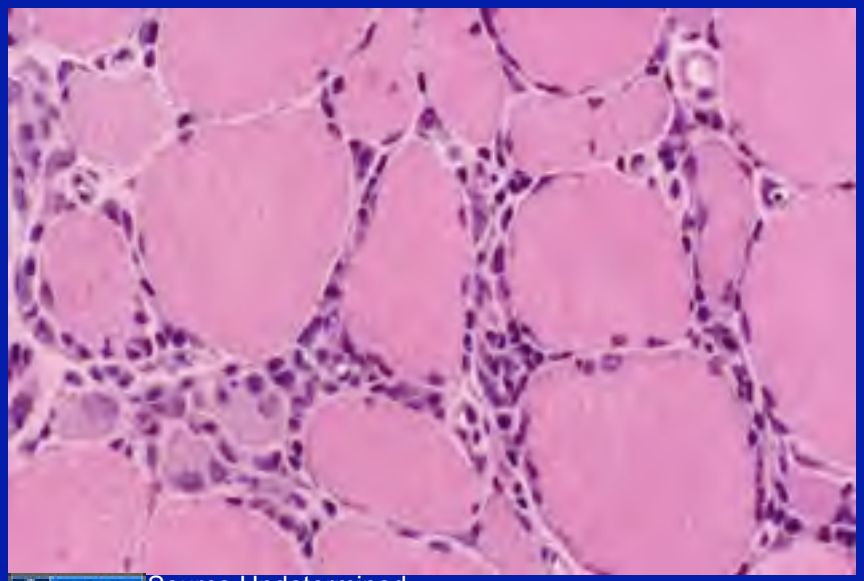
Important

- This could easily be a presentation of statin myopathy or hypothyroidism (and statistically these are the most likely)
- Also a presentation of an inflammatory myopathy, especially if CK highly elevated

Inflammatory myopathy

- Polymyositis, dermatomyositis (inclusion body myositis)
- Bimodal age distribution
- Female predominance; African American
- Proximal muscle weakness

- Diagnosis
  - Elevated muscle enzymes
  - EMG abnormalities
  - Muscle biopsy: inflammation



Dermatomyositis: Gottron's sign

PD-INEL Source Undetermined

PD-INEL Source Undetermined

Dermatomyositis: Heliotrope rash

PD-INEL Source Undetermined

PD-INEL Source Undetermined

PD-INEL Source Undetermined

Shawl sign

Mechanic's hands

PD-INEL Source Undetermined

Periungual erythema

PD-INEL Source Undetermined

Inflammatory myositis

- Treatment
  - Prednisone (1 mg/kg)
  - Methotrexate and/or azathioprine as steroid sparing agents
  - For rapidly progressive or refractory cases, IVIG or rituximab
- Association with malignancy (especially if older onset)

Case: History

- A 48 year old woman presents with diffuse muscle pain, weakness and significant fatigue. She reports
  - Symptoms for over 3 years that have become slightly worse in the past 6 months
  - Generalized pain and fatigue that limit her ability to work
  - Sleep disturbance

Case: Objective findings

- General physical exam:
  - Normal vital signs
  - Diffuse tenderness to palpation
  - Some tenderness around joints, but no obvious synovitis
  - Normal neurologic exam; no objective muscle weakness
- Labs: CBC, ESR, CRP, chemistry profile, TSH normal

History

- 1900s: “fibrositis”: inflammation of fibrous tissue overlying muscles
- 1970s: “fibromyalgia”
- 1990: American College of Rheumatology criteria
  - Chronic widespread pain in all four quadrants of the body and axial skeleton
  - 11/18 tender points (pain with 4 kg pressure)

PD-INEL Source Undetermined

Fibromyalgia

- Central pain syndrome with widespread pain and fatigue
  - Central pain: differs from
    - Nociceptive pain
    - Neuropathic pain
- Part of a larger spectrum of central sensitivity disorders

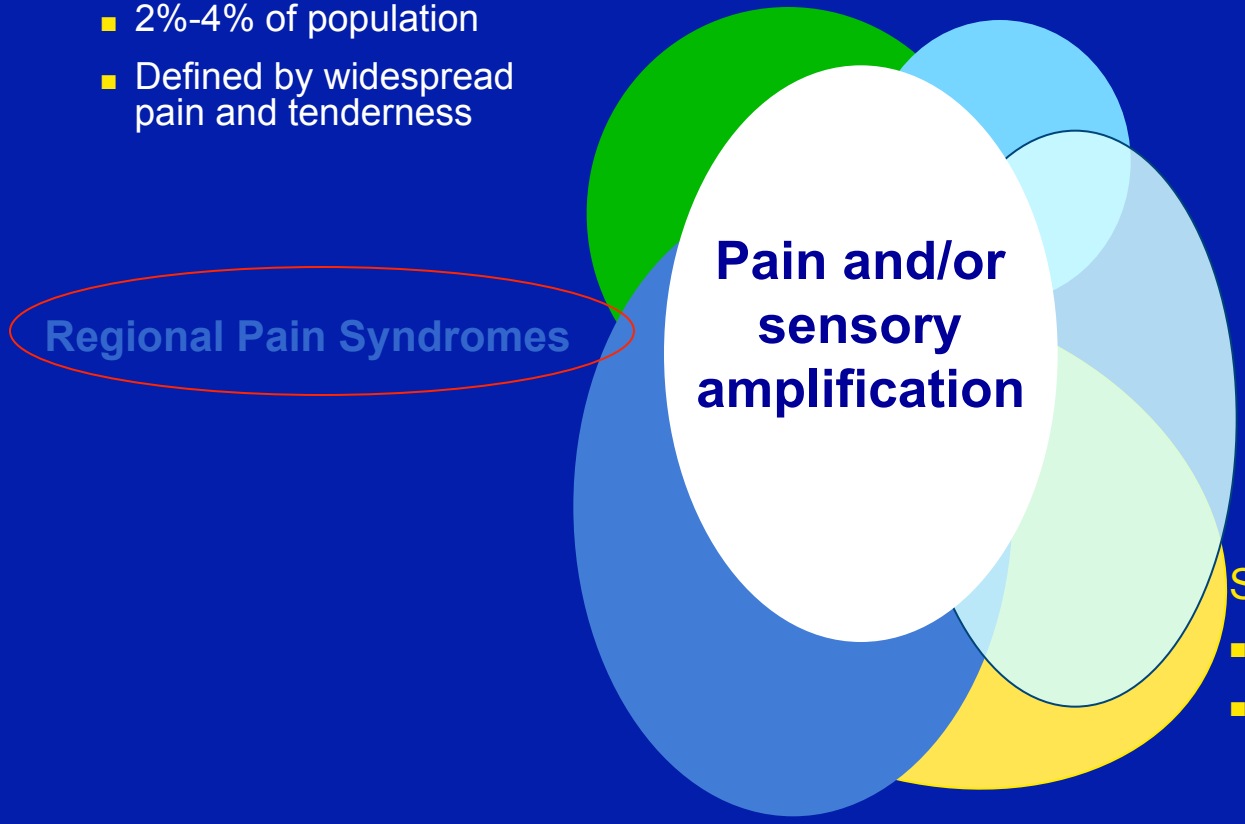
Overlapping Systemic Syndromes

Chronic Fatigue Syndrome (CFS)

- 1% of population
- Fatigue and 4 of 8 “minor criteria”

Fibromyalgia

- 2%-4% of population
- Defined by widespread pain and tenderness



Psychiatric Disorders

- Major depression
- OCD
- Bipolar
- PTSD
- Generalized anxiety disorder
- Panic attack

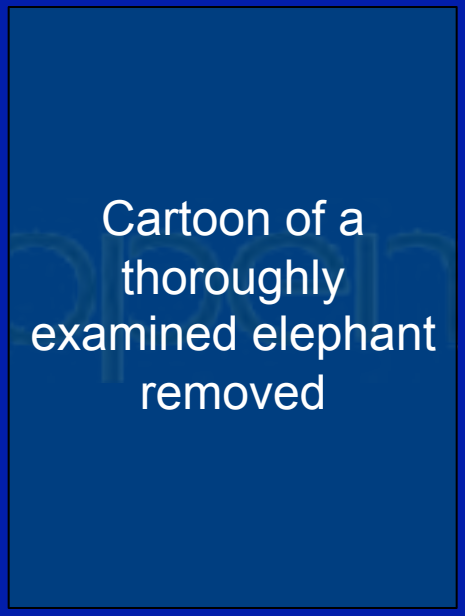
Somatoform Disorders

- 4% of population
- multiple unexplained symptoms without “organic” findings

Clauw, *Neuroimmunomodulation*. 1997

Overlapping regional syndromes

- Tension/migraine headache
- Temporomandibular joint syndrome
- Irritable bowel syndrome
- Interstitial cystitis/ painful bladder syndrome
- Chronic pelvic pain/ vulvodynia/primary dysmenorrhea
- Idiopathic low back pain
- Cognitive difficulties
- ENT complaints (sicca, vasomotor rhinitis)
- Vestibular complaints
- Esophageal dysmotility
- Multiple chemical sensitivity, “allergic” symptoms
- Non-cardiac chest pain



The neurologist sees chronic headache, the gastroenterologist sees IBS, the otolaryngologist sees TMJ syndrome, the cardiologist sees costochondritis, the rheumatologist sees fibromyalgia, and the gynecologist sees PMS.

Epidemiology

- 2-3% general population, 4% of women (using ACR criteria)
- Chronic widespread pain ~10%
- Women more likely to seek treatment ~8:1

Pathophysiology

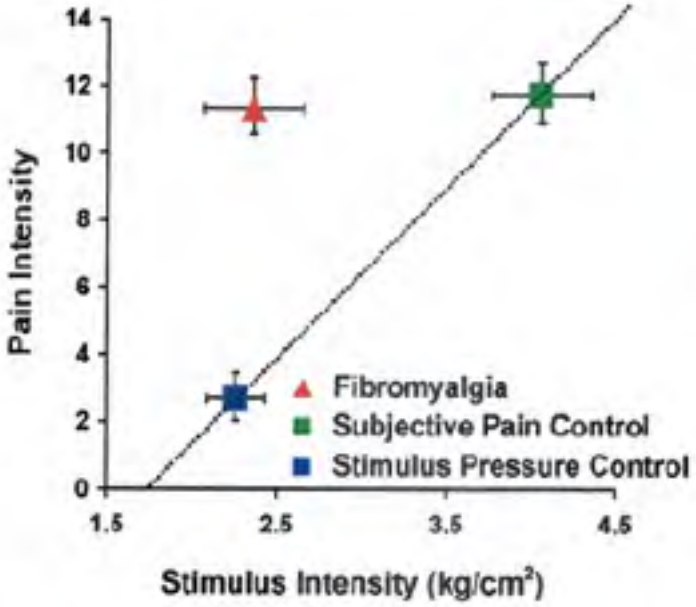
- Genetics
  - First degree relatives have an eight-fold greater risk of developing FM
  - Family members more likely to have other regional pain syndromes
  - Several potentially related polymorphisms affecting metabolism/transport of monoamines

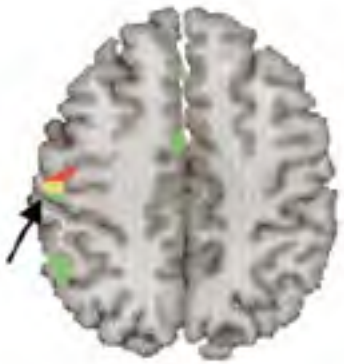
Pathophysiology

- Environmental factors: associated with FM in 5-10% of those exposed
  - Early life trauma
  - Physical trauma
  - Peripheral pain syndromes/autoimmune disorders
  - Psychological stress/distress
  - Certain infections (hepatitis C, EBV, parvovirus, Lyme disease)
  - Certain catastrophic events

Aberrant sensory and pain processing

- “Volume control” problem
- Lowered pain threshhold throughout entire body
- Global problem with sensory processing: e.g. loudness sensitivity

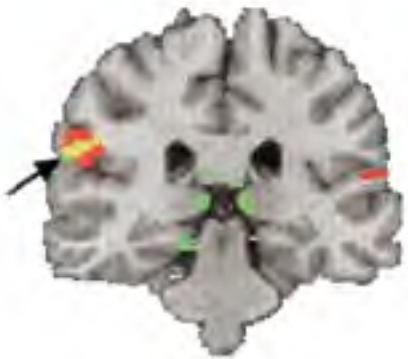




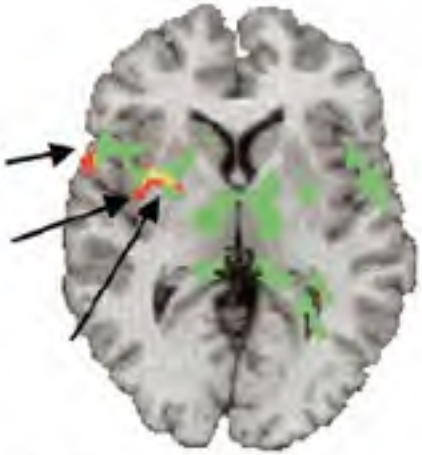
SI

SI (decrease)

IPL



SII



STG, Insula, Putamen

Cerebellum

Gracely, *Arthritis Rheum* 2002

Other biomarkers

- Increased CSF levels of glutamate
- Normal/high levels of CSF enkephalins
- Decreased CSF levels of biogenic monoamines (products of serotonin, norepinephrine)

Diagnosis: History

- Pain
  - Current and lifetime history of widespread pain
  - Involving musculoskeletal and non-musculoskeletal areas
  - Unpredictable, worsened by stress
  - Can also have stiffness, paresthesias
- Fatigue
- Insomnia, sleep disturbance
- Memory difficulties

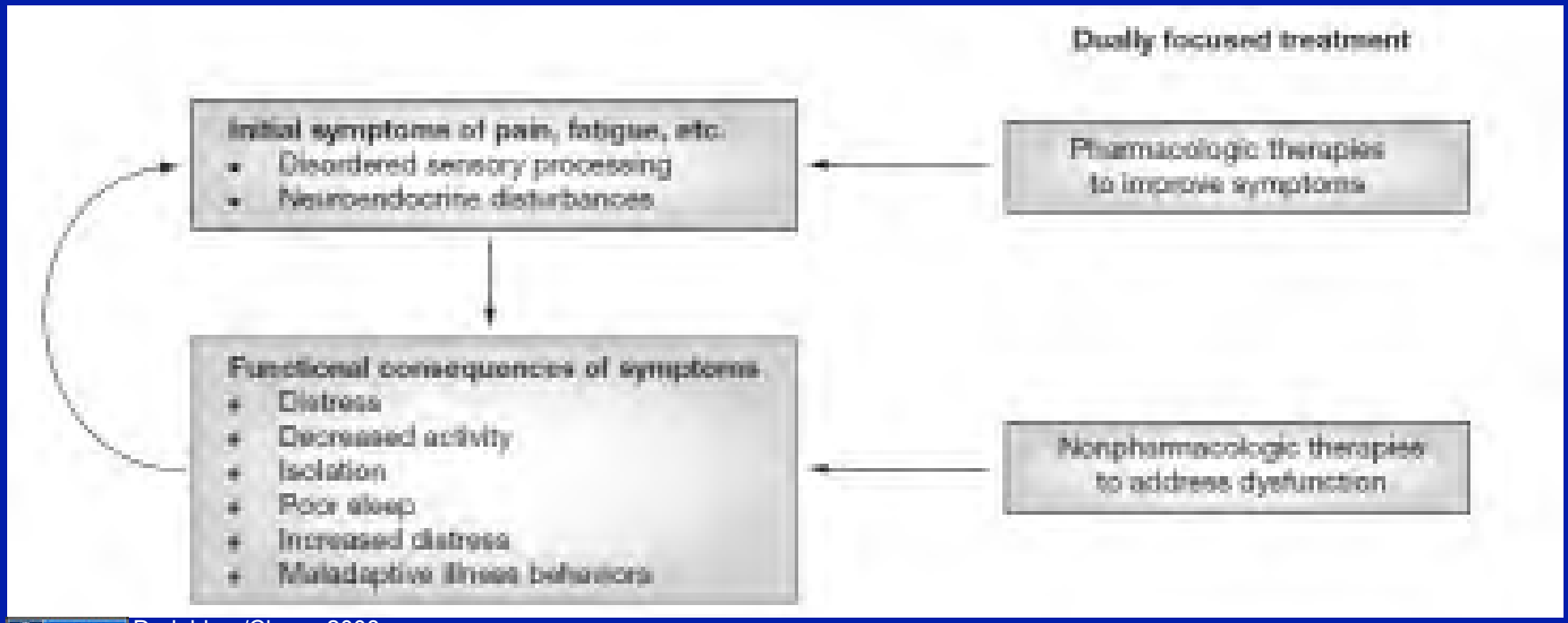
Diagnosis

- PMH: Comorbid syndromes
- FHX: other family members with pain syndromes
- PE: Diffuse tenderness

Evaluation

- If acute/subacute, may warrant further investigation, including
  - Inflammatory markers
  - CBC, chemistry profile
  - TSH, Vitamin D
  - NOT autoantibodies unless clinically indicated
- If chronic, less need for extensive work-up

Treatment: Principles



Dadabhoy/Clauw, 2008

Treatment: Prinicples

1. Education
2. Aerobic Exercise
3. Cognitive behavioral therapy
4. Pharmacologic therapy

Treatment: Education

Screenshot by S. Monrad, UMHS

Treatment: Exercise

- Aerobic
- Highly effective
- Key barriers: tolerance, compliance, adherence
- Recommendations:
  - At least twice a week (more if possible)
  - Start low, go slow
  - Treat exercise as a medication

Treatment: Cognitive Behavioral Therapy

- Teaches patients techniques to reduce symptoms, increase coping strategies, and identify/correct maladaptive behavior strategies
- Especially beneficial for improving functioning

Treatment: Pharmacologic

- Dual norepinephrine-serotonin reuptake inhibitors
  - Tricyclic antidepressants: amitryptiline, nortriptyline
  - Cyclobenzaprine
  - Venlafaxine, duloxetine, milnacipran
- Anticonvulsants
  - Pregabalin
  - Gabapentin
- Other: tramadol, selective serotonin reuptake inhibitors, sedatives

Treatment: Pharmacologic

- Not indicated in fibromyalgia
  - NSAIDs
  - Corticosteroids
  - Opioids

Summary

- Generate a broad differential for the patient presenting with diffuse aches and pains, and eliminate appropriately
- For the diagnosis of FM:
  - Education is KEY
  - Manage symptoms of pain, insomnia, comorbid depression, etc. with appropriate therapeutics
  - Emphasize the essential role of low grade exercise
  - If possible, utilize cognitive behavioral therapy to assist with improved functioning

Additional Source Information

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Slide 15: Source Undetermined; Source Undetermined

Slide 16: Source Undetermined; Source Undetermined

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Slide 35: Dadabhoy/Clauw, 2008

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