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Paul Monach, M.D.

Fibromyalgia

May 15, 2022

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Featured speaker: Paul Monach, MD

- Chief, Rheumatology Section, Boston VA Healthcare System
- Associate Professor, Harvard Medical School

Patricia Woods, RN, Moderator

- MassME Board member and volunteer
- Parent of a person with ME

Fibromyalgia

Paul Monach, MD, PhD
Chief, Rheumatology Section
VA Boston Healthcare System
May, 2022

Disclosures

- Bristol-Myers Squibb: investigator in previous trials of abatacept
- ChemoCentryx, Genentech, GlaxoSmithKline: investigator in previous trials of avacopan, rituximab, and mepolizumab
- Consulting: BMS/Celgene, ChemoCentryx, Kiniksa

A definition of sorts

- Key feature: chronic widespread pain
  - Shouldn’t be only regional pain but that can also be present
- Other symptoms supporting the diagnosis
  - Fatigue (meeting fatigue for chronic fatigue syndrome or not)
  - Abdominal / GI (meeting criteria for IBS or not)
  - Sleep problems (specific diagnosis or not)
  - Cognitive problems (subjective, not always objective)
  - Pelvic / bladder pain (meeting criteria for interstitial cystitis or not)
  - Headaches, jaw/TMJ
  - Paresthesias, neuropathic pain (with or without small-fiber neuropathy)

Criteria - *briefly*

- Numerous proposed criteria but 3 main ones
- American College of Rheumatology 1990
  - Notable for requiring tender points and therefore exam
- American College of Rheumatology 2010 -> 2011 -> 2016
  - Aimed at using patient self-report, revised to ensure 4/5 body regions
- ACTTION Network / AAPT
  - Part of a larger initiative about pain “taxonomy” than has 5 dimensions
- These criteria suggest 2-4% of population is affected

ACR criteria 2016

- Can be used easily in practice!
- Are PROs more empowering for patients?

2016 Fibromyalgia Diagnostic Criteria

1. Widespread pain index (WPI) and symptom severity score (SSS)
   - WPI ≥ 7 and SSS ≥ 5 OR WPI 4-6 and SSS ≥ 9
2. Generalized pain: pain in 4/5 regions
3. Symptoms present ≥ 3 months

The fibromyalgia diagnosis can now be made irrespective of other diagnoses (you do not need to rule out all other conditions that could explain the symptoms, if criteria 1-3 are all met).

1. Widespread pain index (WPI)

In the past week, where have you had pain? (check all that apply)

Left upper region (1)
- ☐ *L jaw*
- ☐ L shoulder girdle
- ☐ L upper arm
- ☐ L lower arm

Right upper region (2)
- ☐ *R jaw*
- ☐ R shoulder girdle
- ☐ R upper arm
- ☐ R lower arm

Axial region (5)
- ☐ Neck
- ☐ Upper back
- ☐ Lower back
- ☐ *Chest*
- ☐ *Abdomen*

Left lower region (3)
- ☐ L hip (buttock/trochanter)
- ☐ L upper leg
- ☐ L lower leg

Right lower region (4)
- ☐ R hip (buttock/trochanter)
- ☐ R upper leg
- ☐ R lower leg

Total: _____ WPI score (add up boxes checked, 0-19)

_____Number of regions checked (excluding items in italics); use this for criterion #2.

Symptoms Severity Score (SSS)

For each of the following, for the past week, rate

	0=No problem	1=slight or mild problem, often mild or intermittent	2=moderate, considerable problem, often present	3=severe, pervasive, continuous, life-disturbing
Fatigue	☐	☐	☐	☐
Waking unrefreshed	☐	☐	☐	☐
Cognitive symptoms	☐	☐	☐	☐

In the past week, have you been bothered by any of the following?

	0=No problem	1=Problem
Headaches	☐	☐
Pain or cramps in lower abdomen	☐	☐
Depression	☐	☐

Total SSS: _____(0-12)

Summary:

☐ **1. Criterion 1 is met if you have EITHER**
- ☐ WPI ≥ 7 and SSS ≥ 5 OR
- ☐ WPI 4-6 and SSS ≥ 9

☐ **2. Generalized pain: met if you checked pain in 4/5 regions (not including items in italics)**

☐ **3. Symptoms present ≥ 3 months**

Fibromyalgia is diagnosed if you meet all 3 criteria 1-3, independent of whether other diagnoses contribute to these symptoms. This is new: FMS diagnosis used to require that there be no other diagnosis to explain the findings.

ACTTION / AAPT

- Maybe not the best to use clinically, but good for understanding FMS
- Core diagnostic criteria
  - Multi-site pain, 6/9 regions
  - Moderate/severe fatigue and/or sleep problems
- Common features
  - Tenderness on exam, stiffness, cognitive, environmental sensitivity
- Common comorbidities
  - Psychiatric (depression/anxiety), somatic pain disorders, rheum diseases
- Neurobiological, psychosocial, and functional consequences
  - Poor QoL, financial costs (employment, healthcare utilization)
- Putative mechanisms, risk factors, and protective factors
  - Trauma especially in childhood, psychosocial stress, medical conditions

Arnold, J Pain 2018

A different sort of “orphan disease”

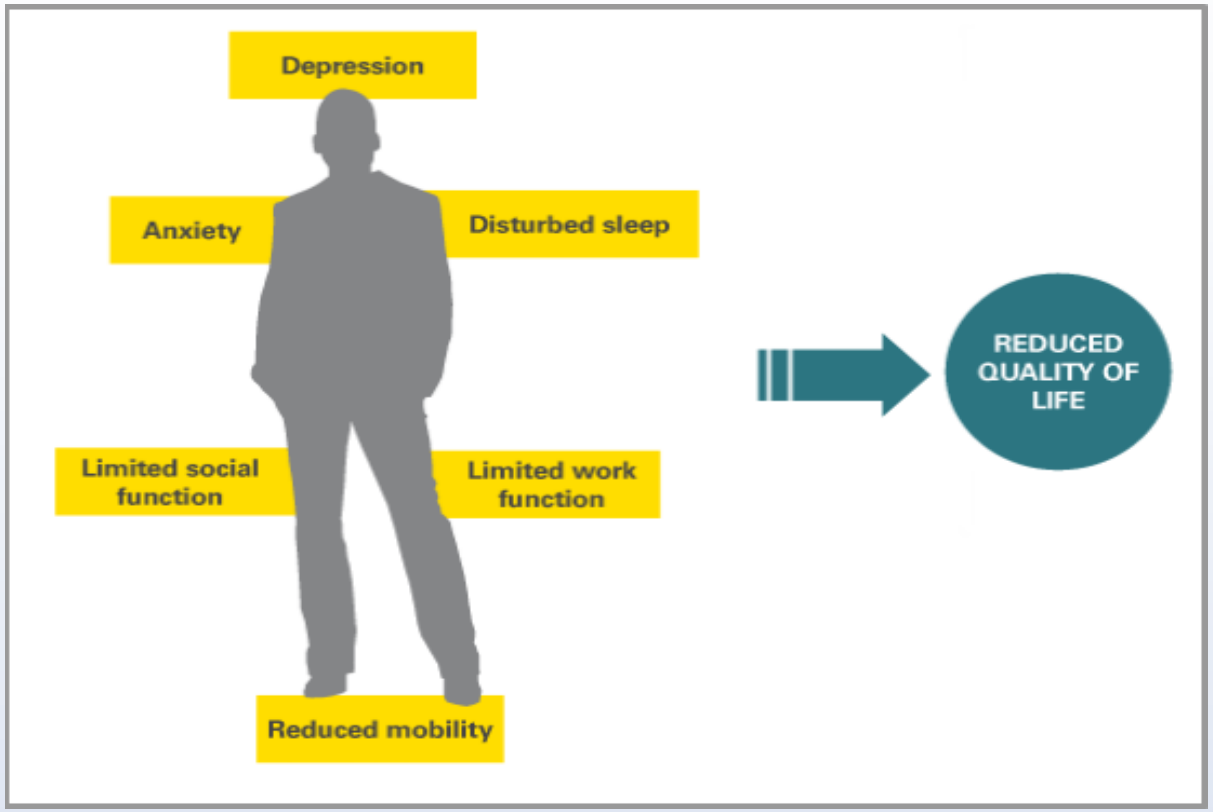
- Who manages fibromyalgia?
  - Primary care
  - Pain management
  - Rheumatology
  - Neurology
- Who refuses?
  - (same list as above, depends whom you ask)
- Who loses out…?

Disagreement and tension within rheumatology

- Academically
  - Many experts in FMS are rheumatologists
  - Some journals publish articles on FMS, some don't
  - ABIM/Rheum exam included only 1 question on FMS – in a patient with lupus
- Opinion
  - Former ACR president: "We need to get FMS patients out of our clinics"
  - Responses included agreement or: "Don't tell me which patients to see" or "I have to make a living and be a good colleague"
- History of nastiness
  - Blank slide for "the pathology of fibromyalgia"
- A possible point of agreement among rheumatologists
  - ***I*** get to decide my role in diagnosing and managing FMS, but ***you don't***

Something we *should* agree on

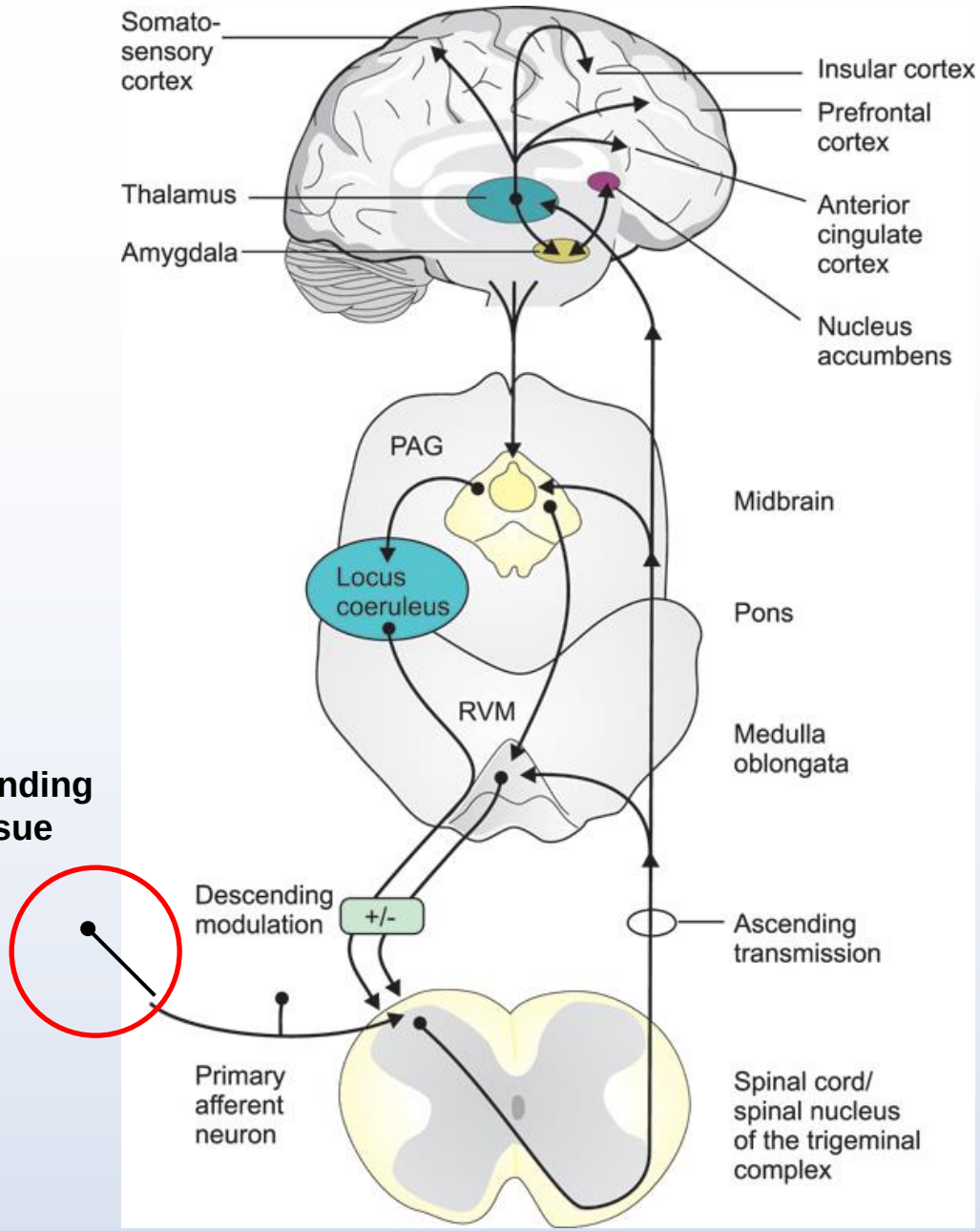
- Patients with fibromyalgia are genuinely suffering



Grunenthal – Change Pain

What causes fibromyalgia?

- FMS is a disorder of pain processing in the CNS as it communicates with the PNS, with central sensitization
- Diverse underlying risk factors or causes
- I prefer “risk factors” for 2 reasons:
  - FMS symptoms occurred (reversibly!) in 1/6 of healthy young people who were sleep-deprived and not allowed to exercise
  - The tender points in FMS are tender in most people relative to other sites in the body – so it’s just easier to detect hyperalgesia in these sites



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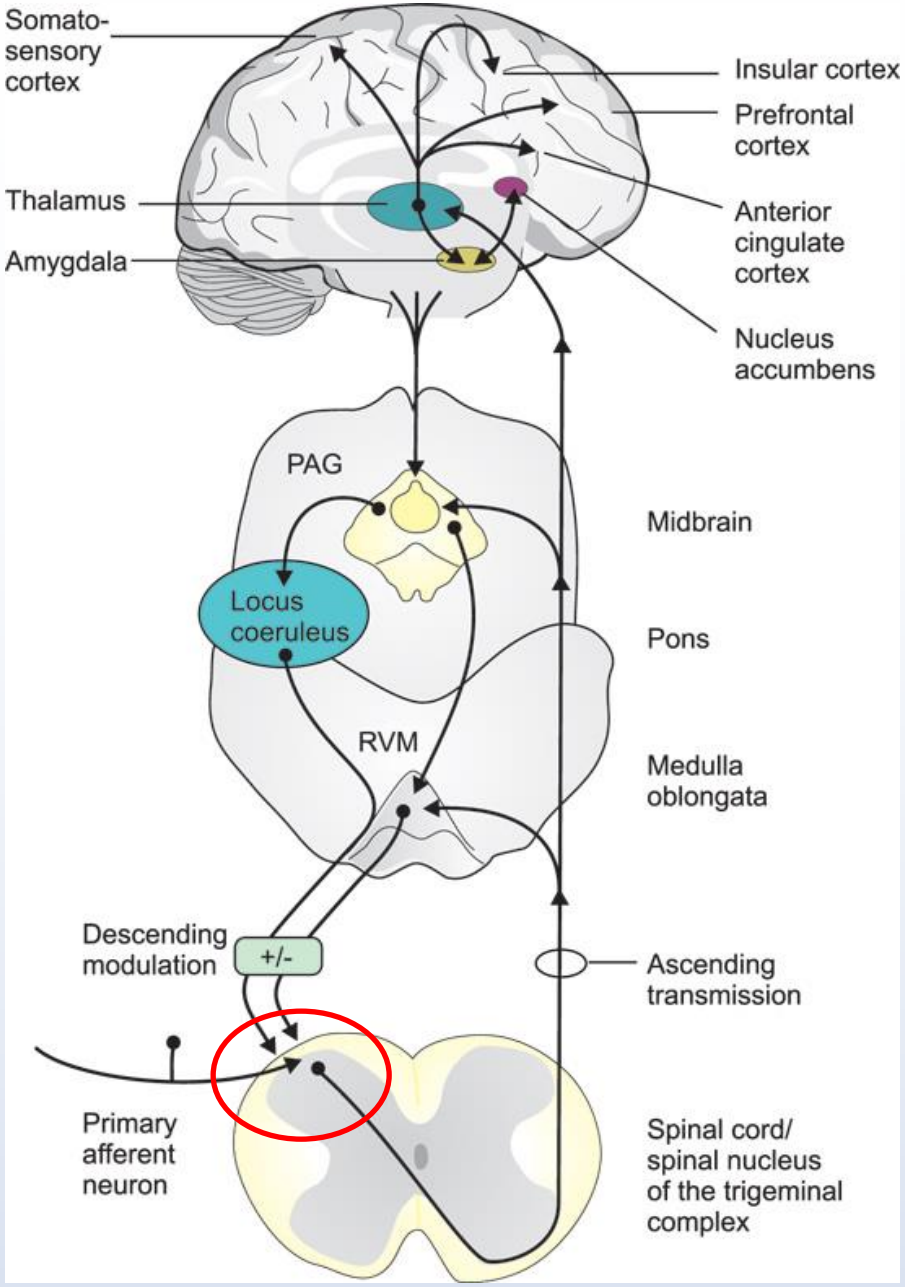

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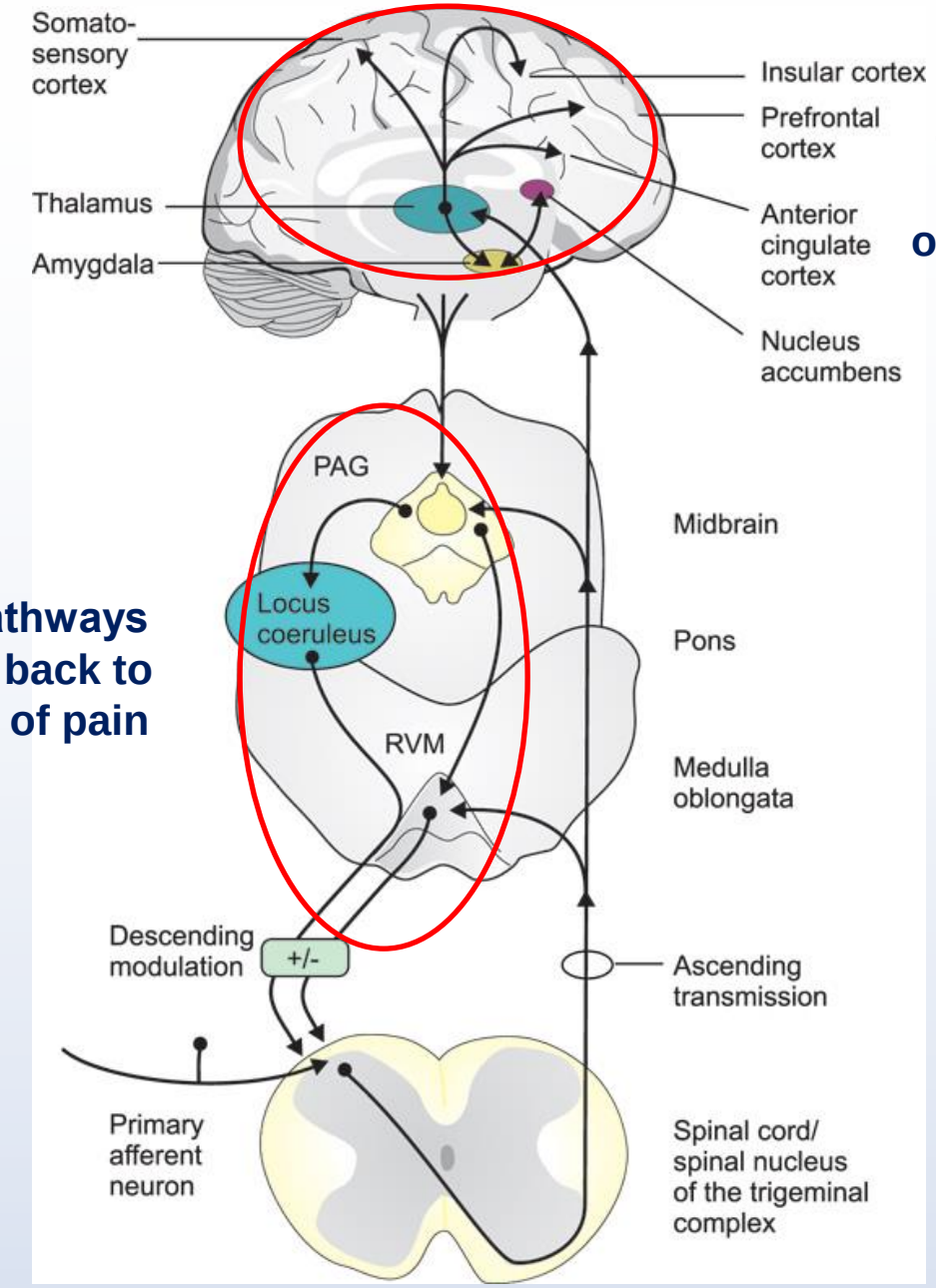
Complex interactions with other parts of the brain!

“Descending” pathways that *usually* feed back to reduce signaling of pain



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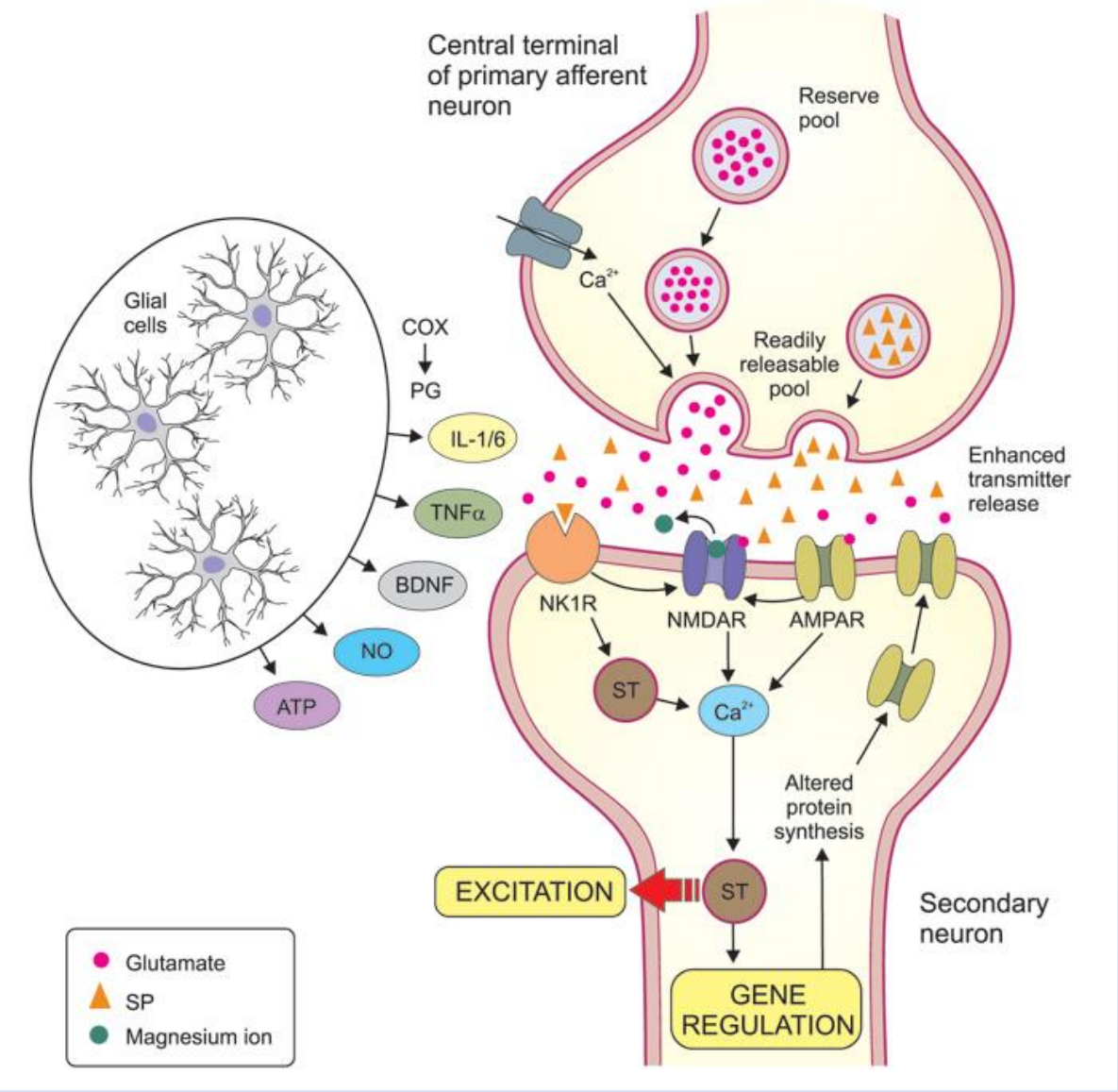
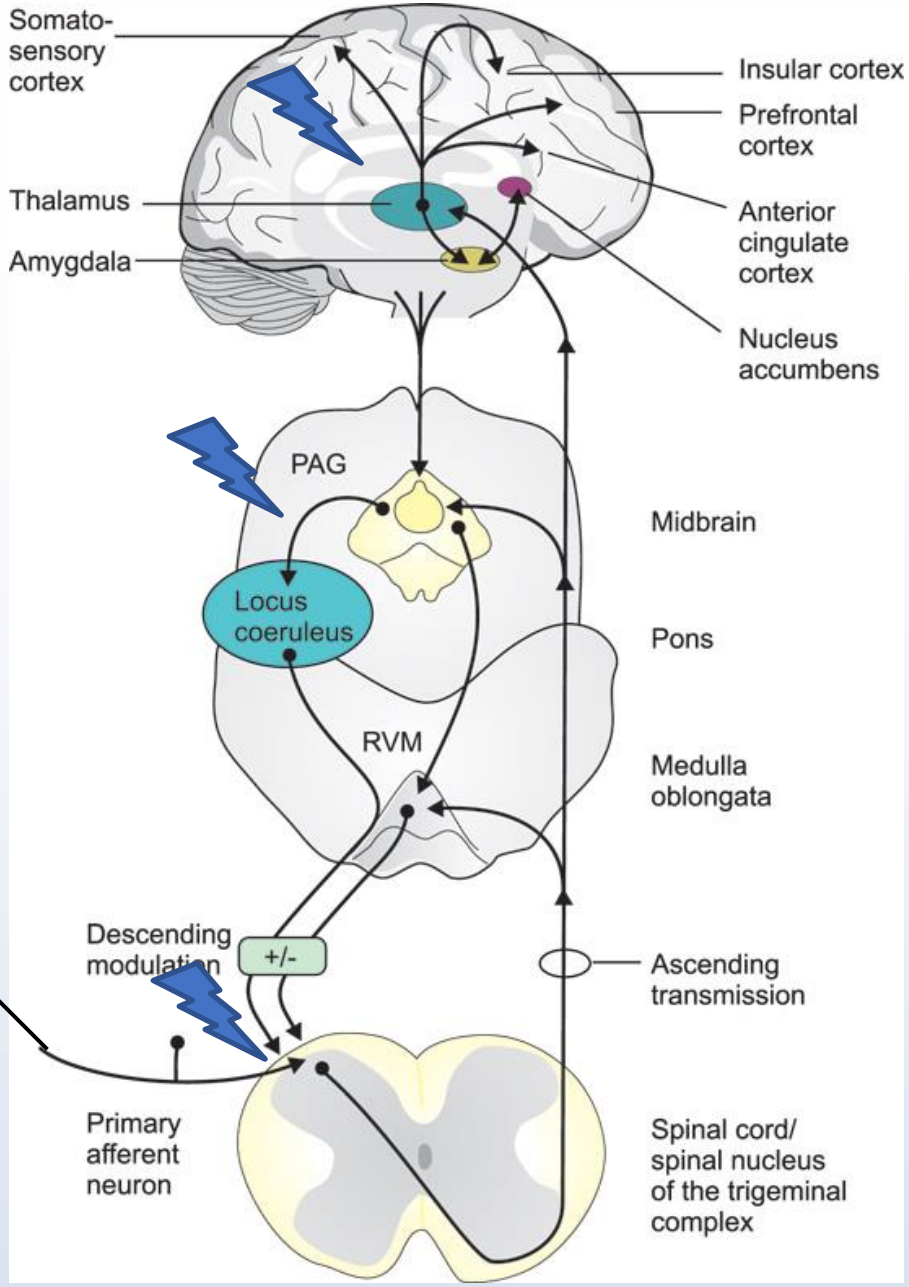

Central terminal of primary afferent neuron
Reserve pool
Ca2+
Readily releasable pool
Glial cells
COX
PG
IL-1/6
TNFα
BDNF
NO
ATP
Enhanced transmitter release
NK1R
NMDAR
AMPAR
ST
Ca2+
Altered protein synthesis
EXCITATION
ST
GENE REGULATION
Secondary neuron
Glutamate
SP
Magnesium ion

Sites of dysfunction in chronic pain



Nerve ending in tissue

http://www.tannlegetidende.no/i/2016/1/d2e1410

Things I won't discuss in detail

- In part because I don't know, and the literature is vast…
- Lab-based studies of:
  - Painful stimuli
  - Sleep
  - Cognition
  - Neuroimaging – connectivity and functional MRI
  - Autonomic testing
  - Biomarkers – in CSF (neurotransmitters), blood (HPA axis, cytokines)
- Conclusion: the majority of studies find abnormalities in FMS vs controls, but results differ across studies

Risk factors for fibromyalgia

Non-modifiable

- Genetics
  - Genetic risk score suggests 25% heritability for age of onset < 50 (Dutta, A&R 2020)
- Female sex
  - Anywhere from 70% to 90% of patients – lower in real practice than in trials
- Autoimmune inflammatory diseases
  - Lupus, Sjogren's, RA, likely others, up to 20-30% risk in those diseases
  - FMS usually doesn't resolve with control of inflammatory disease
- "Other medical conditions"
  - Combination of risk factors and concomitant conditions

Risk factors for fibromyalgia

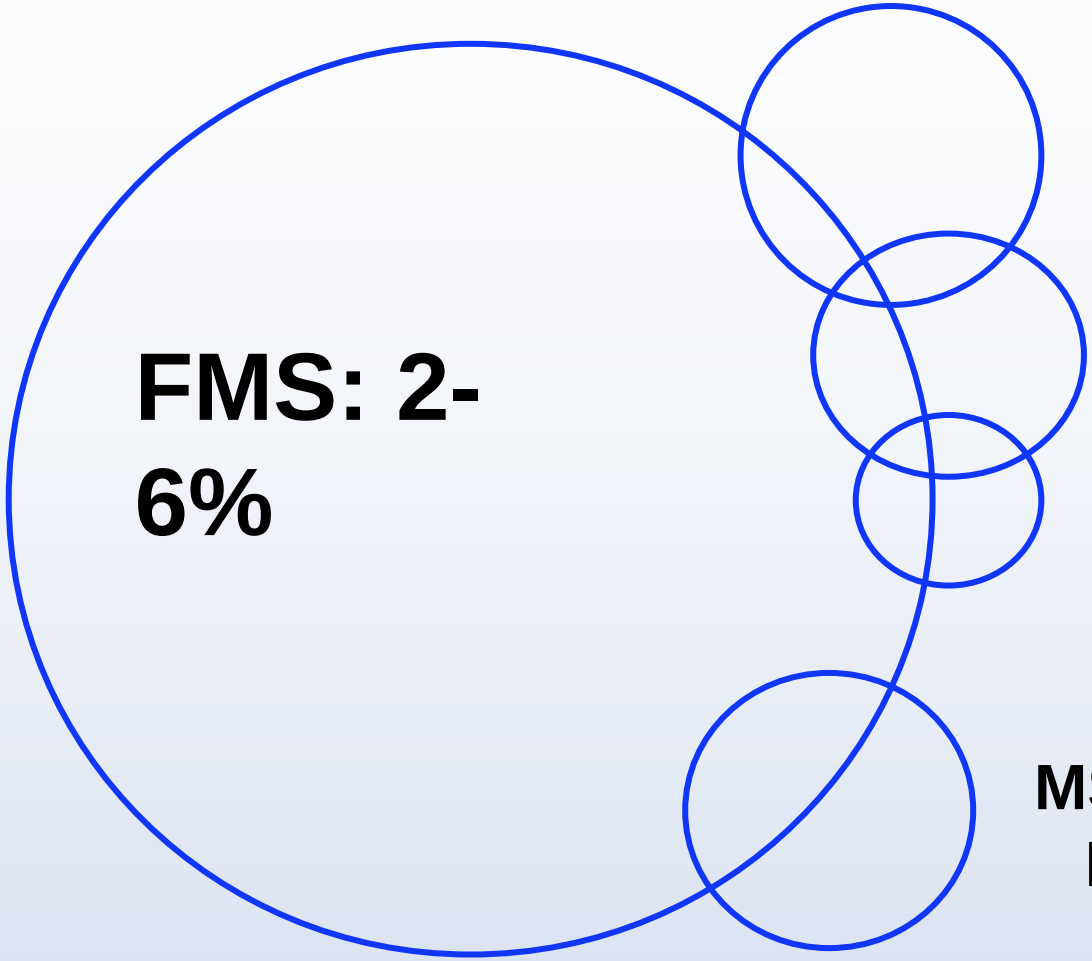
Potentially modifiable

- Anxiety and depression (25-65%)
  - A risk factor or a comorbidity?
  - History of abuse especially in childhood
  - Parallel treatment of pain and anxiety/depression DO help with the other
- Sleep disturbance of diverse causes
  - There probably IS a cause/effect relationship
- Low physical activity
  - Cause and effect difficult to determine – but increasing activity is beneficial
- Excess weight
  - Cause and effect difficult to determine

“Fibromyalgia rheumatica” (© P. Monach)

- Mimic
  - Multifocal mechanical and/or neuropathic pain (LBP, OA, tendonitis, bursitis, radiculopathy, peripheral neuropathy)
  - Spondyloarthropathy
  - Polymyalgia rheumatica
  - Metabolic myopathies
  - Myositis
  - Multiple sclerosis
  - Vasculitis
  - Drug reactions
- Accompany
  - Lupus
  - Sjogren’s syndrome
  - Rheumatoid arthritis
  - Heptitis C, others?

Autoimmune disease? Usually not



RA: 0.5%, 20% with FMS

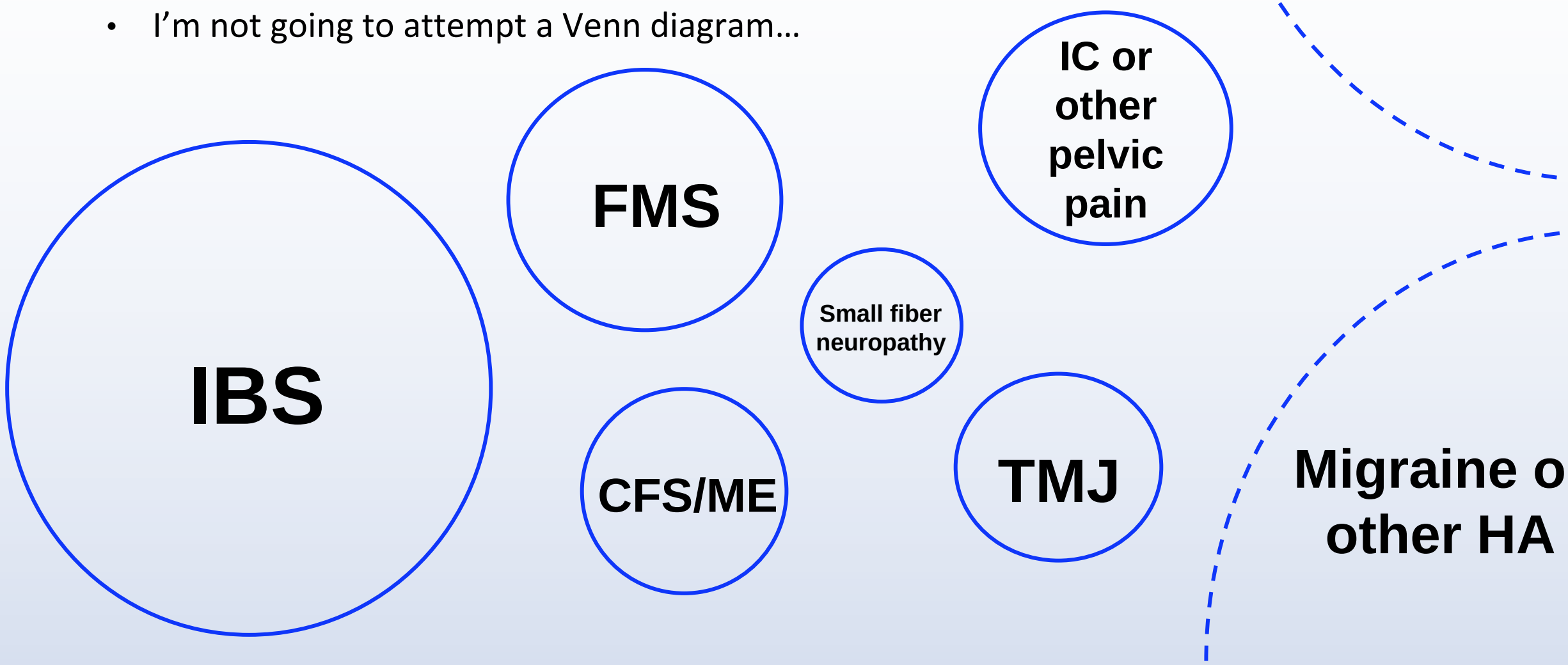
Sjogren's: 0.3%, 30% with FMS

Lupus: 0.1%, 30% with FMS

MS: 0.3%, 30-50% with FMS-like symptoms (mimic)

Related / overlapping conditions

- I’m not going to attempt a Venn diagram…



Diagnosing fibromyalgia

- Evidence in favor of FMS
  - Questionnaire or equivalent
  - Muscle tenderness – tender points from 1990 criteria or simply compare joints to nearby soft tissues
- Evidence against other things
  - “Joint-specific pain”
    - Especially with swelling but can be without
  - Muscle/tendon strain
    - Isometric resisted use is good for diagnosing focal muscle/tendon strain
  - Rash, neuropathy, other organ systems if indicated
  - Labs… depends whom you ask

Lab work-up to address differential diagnosis?

- Large difference of opinion, ranging from none to several
- In order of reasonableness (my opinion):
  - ESR and CRP
  - CK
  - Vitamin D, Ca, Mg, Phos
  - Creatinine and urinalysis (because absent symptoms in kidney disease)
  - CBC/diff, LFT, TSH (to round out assessment of internal organs)
- Things to generally NOT send unless there's high suspicion:
  - ANA (lupus, Sjogren, "UCTD")
  - RF, CCP (rheumatoid arthritis)
  - HLA-B27 (ankylosing spondylitis and other spondyloarthropathies)
  - ANCA, myositis antibodies, TTG antibodies (or let GI decide)

Treatment

- Non-pharmacologic
- Pharmacologic
- Both of these include varying levels of evidence

Non-pharmacologic approaches

- Education!
  - Realistic goals focused on self-management -> better function
- Exercise
  - Individualize to the patient, gradually increase intensity
  - Aerobic is mentioned the most but isn't the only evidence-based approach
  - Strength training, water exercise
  - Tai chi, yoga
- Cognitive-behavioral therapy
  - Ideally supervised, but there are online courses
- Sleep hygiene
  - May need help in diagnosis and management of sleep disorders

Pharmacologic approaches – good evidence

- Tricyclics: amitriptyline, cyclobenzaprine
- SNRIs: duloxetine, milnacipran
- Gabapentinoids: pregabalin, gapapentin
- Usual recommendation is to start with very low doses and titrate up gradually

Other pharmacologic approaches

- Low-dose naltrexone
  - Supported by 2 small trials
  - Not FDA-approved and requires compounding, unlikely to be covered
  - 4.5 mg/day in evening, 3 mg or even lower is an alternative
- SSRI's – not clear that they work in FMS
- Cannabinoids – needs more study
- NSAIDs – don't work for FMS but could help with simultaneous mechanical causes of pain
- Tramadol – avoid stronger opioids, don't work in FMS and risky

Other non-pharmacologic approaches

- Non-invasive electrotherapy
  - TENS
  - Transcranial direct current stimulation (tDCS)
- Acupuncture, massage
- Chiropractic
- Balneotherapy (mineral water), aromatherapy
- Mindfulness training, spiritual therapy
- Pilates, Zumba, other specific exercise regimens
- Diet changes, green tea, fish oil
- The time and money that >90% of patients put into such efforts is a good indicator of motivation to “get better”…

My own non-evidence-based additions

- Therapeutic alliance
  - Frequent, short visits if possible
  - Do “something” in the treatment realm
  - Trying to use the placebo effect is still respectful to the patient!
- Be aware of separate, concomitant problems but don’t search for them, examples
  - Psych referral for depression or anxiety but not automatically
  - Consider mechanical causes of pain but don’t do widespread imaging

Prognosis

- Most studies are from referral centers and under-estimate the percentages of patients who improve
  - Studies have reported ~0 – 65% with moderate improvement over years
- Partial but significant improvement over a long time should be the goal – unless there is a dramatic discovery
- Although patients often feel left out in practice, they should find some reassurance that FMS and related conditions are widely studied

References

- Bair MJ and Krebs EE. Fibromyalgia. Ann Int Med (In the Clinic) 2020; ITC 34-48. Includes “Tool Kit” for clinicians and information sheet for patients.
- Clauw DJ. Fibromyalgia: a clinical review. JAMA 2014;311:1547-55.
- Borchers AT and Gershwin ME. Fibromyalgia: a critical and comprehensive review. Clin Rev Allergy Immunol 2015;49:100-151. 647 references.

Two patient stories

Elizabeth Alexander

- Fibromyalgia since childhood

Vicki Kneale

- Diagnosed with FM in 2019

Please join us next month!

Dr. Maria Vera Nuñez

"A whole-person health approach to Myalgic Encephalomyelitis/Chronic Fatigue Syndrome – Lessons for Post-COVID conditions"

Sunday, June 19, 2022, 4 p.m. EDT

Co-Presented with the New Jersey ME/CFS Association

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