Navigating Non-Physical Symptoms in MS

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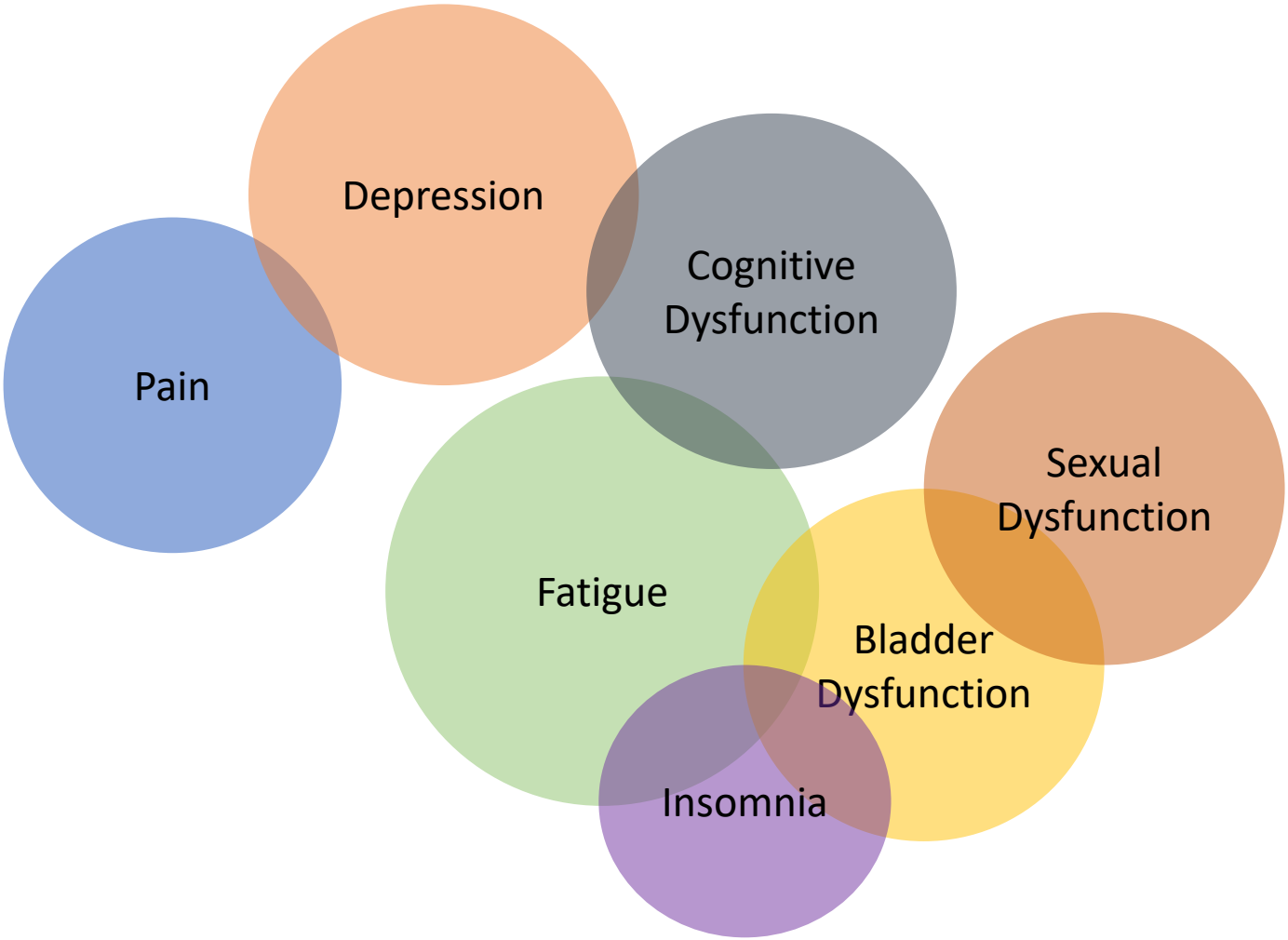
Non-Physical Symptoms



Pain

- Neurogenic – 50%-70%[1,2]
  - Paroxysmal – trigeminal neuralgia, Lhermitte's, tonic spasms, radicular pain
  - Persistent – burning dysesthesias limbs/trunk
    - Dysfunction of spinothalamic pathways
    - Damage to brain or spine - central pain
  - Pharmacologic Rx
    - Anticonvulsants, SNRI, TCA
    - Cannabinoids – subjective benefit to pain/spasticity large study[3]
  - Non-pharmacologic
    - Spinal cord stimulation
    - TENS, FES & rTMS[4]
- Non-neurogenic
  - Musculoskeletal or soft-tissue pain
  - May be related to spasticity

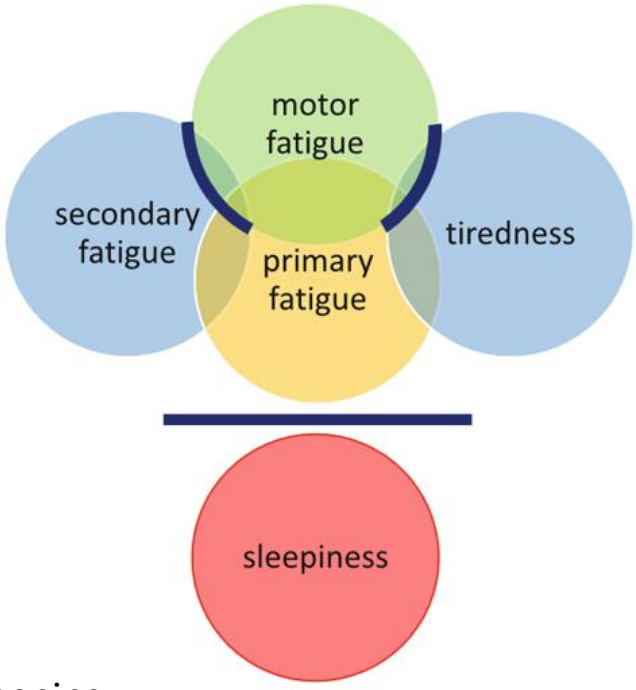
[1]Hirsh AT, Arch Phys Med Rehabil 2009;90:646–651; [2]Hadjimichael O, NARCOMS data. Health Qual Life Outcomes 2008;6:100;
[3]Zajicek JP, MUSEC trial. J Neurol Neurosurg Psychiatry 2012;83:1125–1132; [4]Cruccu G, Eur J Neurol 2007;14:952–970

Depression

- Multifactorial causes*
  - Psychological reaction to effects of disease
  - h/o depression
  - Fatigue
  - Lack of social support/social stress
  - Brain changes (ie. lesions/atrophy)
  - Immune dysregulation/endocrine abnormalities
  - DMTs – interferons
- Pharmacologic Rx
  - TCA, SSRI/SNRI
- Non-pharmacologic
  - CBT
  - Counselling/support structure

*Wilken JA, Sullivan C, Neurologist 2007;13:343–354

Fatigue



- Common symptom; severe in up to 74% patients[1]
- Mechanism unclear
  - Patients with active relapsing MS have severe fatigue more often than stable[1]
  - No clear relationship to progression[2]
- Fatigue vs. sleepiness
  - Sleepiness: propensity to fall asleep & effort to avoid sleeping
    - Sleep disorders
    - Polysomnogram required
- Motor fatigue: associated with but out of proportion to muscle weakness[3]
- Pharmacologic Rx
  - Amantadine
  - Modafinil
  - Aminopyridine
  - Amphetamine
- Non-pharmacologic
  - CBT
  - Treat underlying sleep d/o

[1]Hadjimichael O, NARCOMS data. Health Qual Life Outcomes 2008;6:100; [2]Koch M, MSJ 2008;14: 815–822; [3]Sehle, J Neuroeng Rehab, 2011;8:59

Insomnia

- Dysfunctional sleep architecture
  - RLS, OSA or other sleep-related breathing d/o
  - Poor sleep hygiene
- Nighttime arousals
  - Frequent urination
  - Muscle spasms/pain
- Pharmacologic Rx
  - Short-acting sedative-hypnotics
  - Ramelteon
  - Melatonin
  - Trazadone
  - Sedating antihistamines
- Non-pharmacologic
  - Sleep hygiene
    - Relaxing routine 1 hr prior to bed
    - Cold environment
    - Regular morning exercise
    - Avoid late heavy meals
    - Avoid daytime napping
  - OSA
  - Sleep restriction for sleep-onset insomnia

Insomnia – Sleep Restriction

- Designed to eliminate prolonged middle of the night awakening
- Restrict time in bed to actual sleep time
- Slowly increase time in bed
- Sleep restriction example
  - Person goes to bed at 11:00 pm and gets up at 8:00 am but only sleeps on average 6 hours per night
  - First step: restrict time in bed to only 6 hours (11:00 pm – 5 am)
  - Next step: gradually extend time spent in bed by 15-30 minutes as long as nighttime wakefulness remains minimal

Cognitive Dysfunction

- Prevalence of 40%-80%[1]
- Areas of dysfunction[2]
  - Attention, processing speed & working memory
  - Executive dysfunction
  - Learning and memory
- Pharmacologic Rx
  - Memantine, donazepil, modafinil, amphetamine, dalfampridine[3]
- Non-pharmacologic
  - CBT/cognitive rehab
    - BrainHQ
    - COGNI-TRAcK
  - Physical exercise[4]

[1]Potagas C, J Neurol Sci 2008;267:100–106; [2]DeLuca J, Nat Rev Neuro, 2020;16:319-332; [3]Amato, J. Neurol. 2013;260:1452–1468; [4]Motl, Mult Scler 2011;17:1034–1040

Bladder Dysfunction

- Bladder
  - Control regions in frontal lobe, brainstem and spinal cord
  - Causes
    - Detrusor hyperactivity – urgency, frequency and urge incontinence
    - Detrusor Inefficiency – incomplete emptying, residual urine and frequency
    - Detrusor-sphincter dyssynergia – hesitancy, interrupted stream and incomplete emptying
  - Pharmacologic Rx
    - Anti-muscarinic Rx – oxybutynin, tolterodine
    - β-adrenergic agonist - mirabegron
    - Botox injection in sphincter
  - Non-pharmacologic
    - Implanted electrical stimulation
    - rTMS of frontal pathways*

*Centonze D, Neurology, 2007;68:1045–1050

Bowel Dysfunction

- Present in up to 2/3 patients[1]
  - Impaired mobility, drug side effects, altered diet
  - Constipation, fecal incontinence or both
- Pharmacologic Rx
  - Bulking agents – fiber supplements + hydration
  - Osmotic/stimulant laxatives
  - Pro-kinetic agents - linaclotide
  - Suppositories
- Non-pharmacologic
  - Kegel isometric exercises[2]
  - EMG biofeedback[2,3]
- Nutraceuticals
  - Swiss Kriss herbal laxative
  - 4 oz prune juice + slice of butter

[1]Preziosi G, Expert Rev Gastroenterol Hepatol 2009;3:417–423; [2]Lucio AD, Clinics. 2011;66:1563–1568; [3]Opara J, Fizjoterapia. 2011;19:41–49

Sexual Dysfunction

- Causes
  - Female – reduced libido and/or vaginal dryness
  - Male – erectile dysfunction and/or reduced libido
    - Seen in up to 60% males with MS[1]
- Pharmacologic Rx
  - Phosphodiesterase-5 (PDE5) inhibitors – sildenafil, tadalafil
    - Several studies show benefit for male ED
    - Few studies show benefit for vaginal dryness[2]
  - α2 antagonist – yohimbine
    - Not evaluated in controlled trials
  - SSRI may contribute
    - Bupropion may reduce sexual dysfunction caused by SSRI

[1]Zorzon M, Mult Scler 1999;5:418–427; [2]DasGupta R, J Urol 2004;171:1189–1193

Conclusions

- Non-physical symptoms of MS are common
- Represent a large component of factors impacting quality of life
- Overlap between many non-physical symptoms
- Both pharmacologic & non-pharmacologic interventions