Side effects and Symptom management: Neurologic, Ocular, Fatigue and Cognitive Impairment

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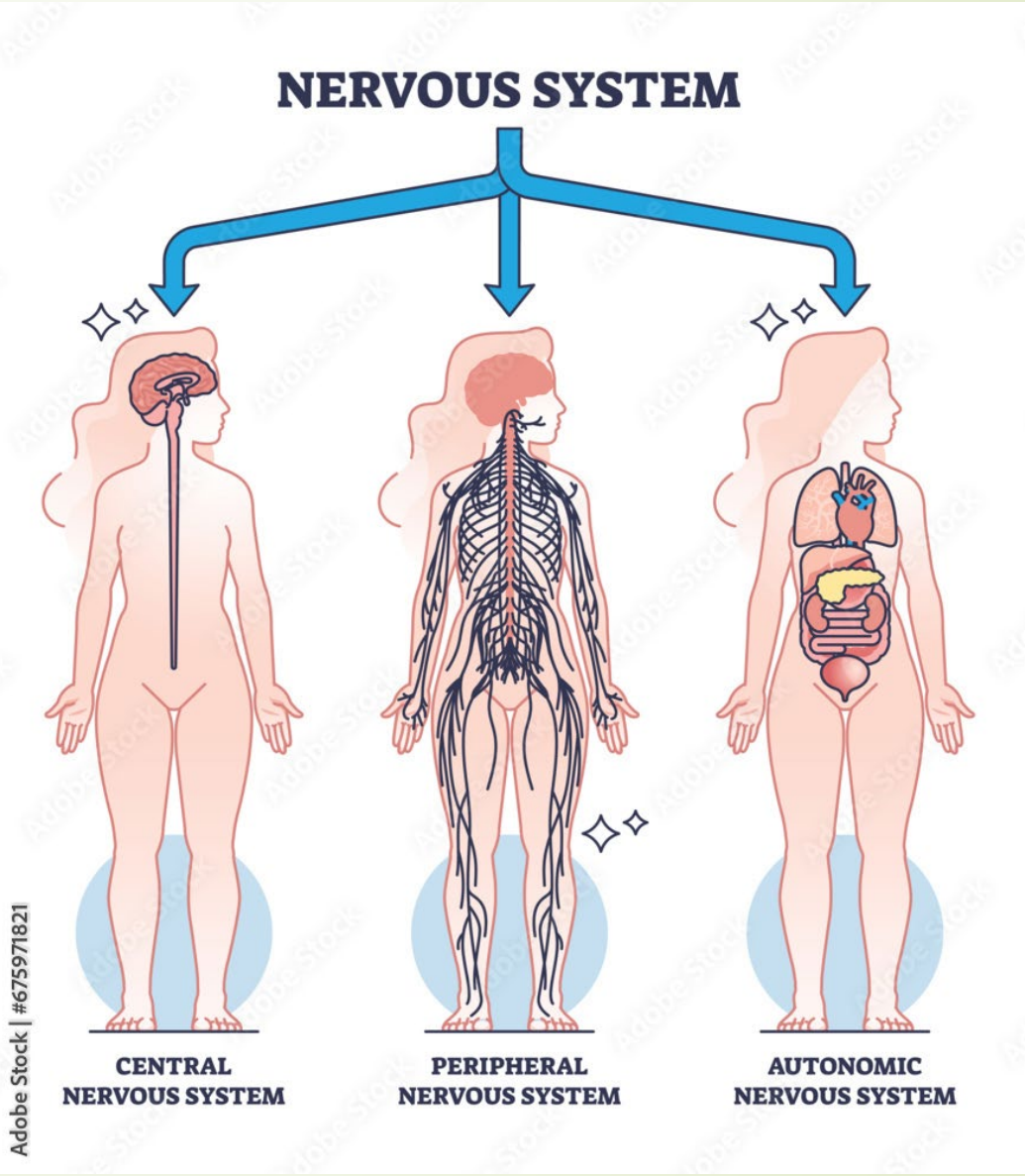
MD Anderson Cancer Center
Making Cancer History®

NEUROTOXICITY AFFECTING THE CENTRAL, PERIPHERAL AND AUTONOMIC NERVOUS SYSTEM



RADIATION TREATMENT

pathophysiology

- Blood vessel damage leads to necrosis
- demyelination

Factors to consider

- Volume of irradiated tissue
- Total dose delivered
- Dose per fraction
- Duration of treatment

Risk Factors

- Age
- Comorbidities (diabetes, vascular disease)
- Genetic predisposition of the tumor (Li-Fraumeni syndrome)

Acute <4 weeks post RT	Early Delayed 1-6 mos post RT	Late Delayed > 6 mos post RT
• Acute encephalopathy	• Somnolence syndrome • Tumor pseudoprogression syndrome • Lhermitte phenomenon	• Focal brain necrosis • Progressive myelopathy • Cognitive dysfunction • Cerebrovascular disease • RT induced CNS tumor • Plexopathy

Neurotoxic Conditions Resulting from Radiation Therapy	
Neurotoxic Conditions	**Signs and Symptoms**
Acute encephalopathy	drowsiness, dysarthria, fever, headache
Somnolence syndrome	Excessive sleep, fever, headache, transient papilledema
Tumor pseudoprogression syndrome	Worsening of presenting neurologic focal symptoms
Cognitive dysfunction and leukoencephalopathy	Short term memory loss, judgement deficits, visual motor deficits
Radiation induced central nervous system tumors	Headache, nausea, symptoms dependent on tumor location
Plexopathy	Numbness/paresthesias of hands and fingers, motor weakness
Myelopathy	Lhermitte phenomenon, paresthesias radiating down spine and lower extremities
Cerebrovascular disease	Difficulty speaking, motor weakness, mental fogginess

CHEMOTHERAPY

Pathophysiology

- Direct: toxic effects on the nervous system cells
- Indirect: metabolic or cerebrovascular effects

Factors to consider

- Administration of multiple agents
- Dose and route of administration
- Impaired clearance
- concurrent radiation therapy (decrease blood brain barrier integrity)

Risk Factors

- Age
- Comorbidities

CNS

- Meningitis
- Seizures
- Leuko-encephalopathy

PNS

- Altered Sensory Function
- Myalgias
- Altered Motor function

Autonomic

- Postural Hypotension
- Constipation
- Urinary Retention

Chemotherapy induced neuropathy and clinical symptoms		
DRUG	TYPE OF NEUROPATHY	CLINICAL SYMPTOMS
Cisplatin/ Oxaliplatin	Pure sensory	Neuropathic pain in a stocking glove pattern Paresthesia, Dysesthesia
Paclitaxel	Mixed sensory-motor	Neuropathic pain in a stocking glove pattern, Paresthesia, Hypoesthesia, Myopathy, Myalgia
Vincristine	Mixed sensory-motor and autonomic	Neuropathic pain in a stocking-glove pattern, Paresthesia, Hypoesthesia, autonomic dysfunction
Bortezomib and thalidomide	Sensory-motor	Neuropathic pain, Hypoesthesia, Muscle cramps

NEUROTOXICITIES ASSOCIATED WITH CHEMOTHERAPY, BIOTHERAPY AND TARGETED THERAPIES		
DRUG	SIDE EFFECT	CLINICAL CONSIDERATION
Rituximab	Headache, dizziness, paresthesias, myalgia, leukoencephalopathy	Leukoencephalopathy may be associated with viral infections
Tamoxifen	Headache, ischemic stroke, retinopathy	Exacerbation of migraine headaches
Procarbazine	Peripheral neuropathy, confusion, hallucinations, mild encephalopathy	Encephalopathy increases with dose increase Potentiate sedative effects of narcotic analgesics
Vinorelbine	Peripheral neuropathy	Length dependent neuropathy, affects lower extremities more than upper

STEM CELL TRANSPLANTATION

- Neurotoxicities: seizures, stroke, encephalopathy, headache, myelopathy, neuropathy
- Underlying mechanisms:

  antibiotics in pre and post transplantation period can trigger seizures

  Busulfan can freely penetrate the blood brain barrier

  immune mediated neuropathy

  graft versus host disease

Assessment and Diagnostic Tools

- MRI/ CT
- EEG
- EMG/NCS
- Neurologic Examination:
    - mental status
    - cranial nerves
    - motor strength
    - coordination
    - reflexes
    - sensation

NEUROTOXICITY	DIAGNOSTIC TESTING	TREATMENT
Acute encephalopathy	MRI brain	steroids
Plexopathy	MRI of brachial plexus, EMG	steroids
Seizures	MRI brain, EEG	Steroids, anticonvulsants
Neuropathy	EMG	Duloxetine, Gabapentin

Practice Question:

A 76-year-old female with triple negative malignant neoplasm of left breast receiving weekly paclitaxel complains of continuous neuropathic pain in a stocking glove pattern. What is the most suitable drug for this side effect?

1. Acetaminophen
2. Gabapentin
3. Ibuprofen
4. Lorazepam

Practice Question

- A 40-year-old female survivor of childhood acute lymphoblastic leukemia who was treated with cranial radiation therapy and systemic chemotherapy comes with recurrent headaches and visual disturbances. What is the most likely diagnosis?

1. Migraine headache
2. Radiation induced brain tumor
3. Retinal detachment
4. Retinal migraines

Practice Question

- A 50-year-old woman who is a breast cancer survivor comes with complaints of long-standing neuropathic pain in her lower extremities. The first response of the nurse practitioner should be to:

1. prescribe Duloxetine for neuropathic pain management
2. refer the patient to a pain management specialist
3. perform a thorough neurologic examination
4. order MRI CTL Spine to evaluate for neuropathic complications

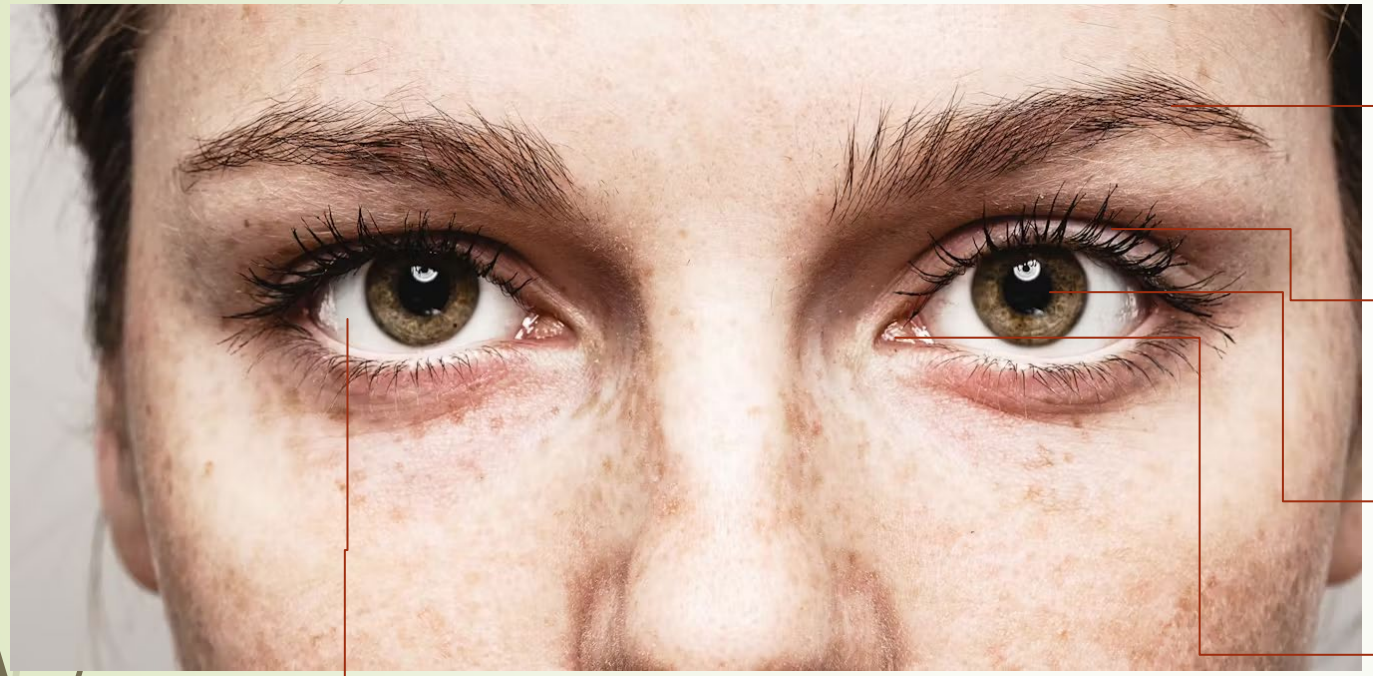
OCULAR TOXICITIES

RADIATION THERAPY

- Ocular side effects: cataract development, retinopathy, keratoconjunctivitis, optic neuropathy, visual impairment
- Correlates to age at time of treatment, total dose, fractionation

OCULAR TOXICITIES WITH CHEMOTHERAPY, TARGETED THERAPY AND IMMUNOTHERAPY	
AGENT	OCULAR TOXICITY
Docetaxel	Eye irritation, canalicular inflammation and blockage of tear ducts
5-Fluorouracil	Blurred vision, ocular pain, excessive lacrimation, itching
Imatinib	Periorbital edema, epiphoria, subconjunctival hemorrhage
Cytarabine	Corneal inflammation
Methotrexate	Blurred vision, edema, light sensitivity
Tamoxifen	Cataracts, retinopathy, retinal hemorrhage

ASSESSMENT



Eyebrows: quantity, distribution, dryness

Eyelids: edema, lesions, symmetry with which the eyelids close

Pupils: size, shape, symmetry, reaction to light

Lacrimal sac: swelling, excessive tearing, dryness

Conjuctiva and sclera: color, vascular pattern, nodules, swelling

DIAGNOSIS AND MANAGEMENT OF OCULAR TOXICITIES			
OCULAR CONDITION	SYMPTOM	DIAGNOSIS	MANAGEMENT
Cataracts	Decreased vision	Visual acuity test	Surgical removal
Retinopathy	Visual field changes, blurred vision	Ophthalmic exam, Fluorescein angiography	Laser therapy
Blepharo-conjunctivitis	Red eyes, swelling of conjunctiva, epiphora	Physical exam	Topical or ophthalmic drops
Uveitis	Ocular pain, redness, photophobia, decreased vision	Physical exam, ophthalmic exam	Topical or systemic steroids, discontinuation of therapy

Role of the APP

Baseline ocular exam

- Ocular assessment prior to each treatment

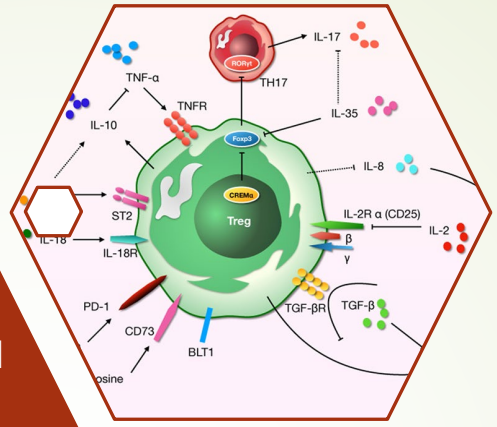
Patient education

- Appropriate referral

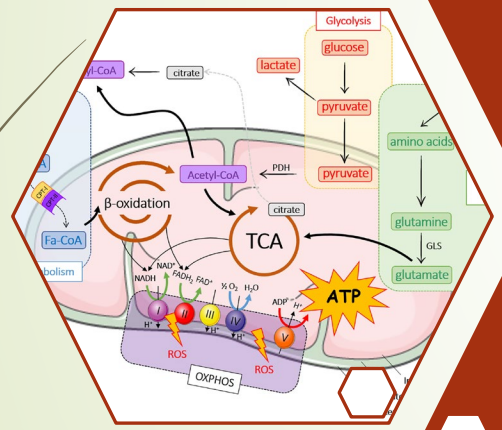
CANCER RELATED FATIGUE

- Subjective sense of tiredness that is not proportional to recent activity and interferes with usual functioning.
- Specific pathophysiology is unknown.
- Prevalent during active treatment, immediate post treatment and long-term survivorship

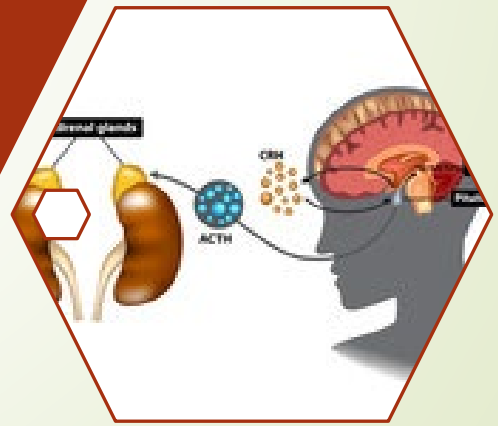
Possible Underlying Mechanisms



Inflammation and peripheral pro-inflammatory cytokine network activation

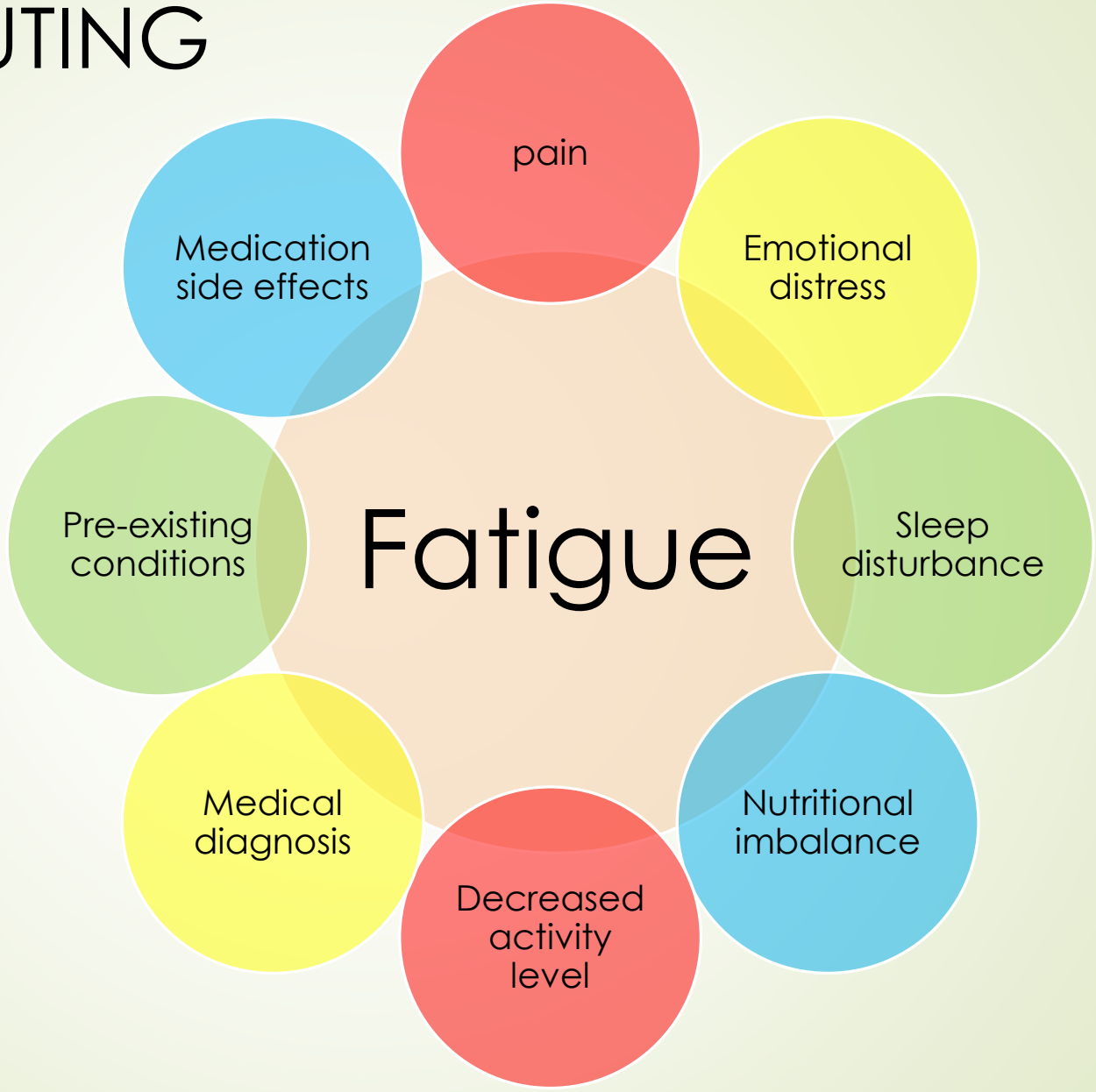


Hypothalamic-pituitary-adrenal axis stimulation



Reduced energy metabolism

CONTRIBUTING FACTORS



SCREENING TOOLS

- MDASI (MD Anderson Symptom Inventory)
- Piper Fatigue Scale
- Brief Fatigue Inventory
- Functional Assessment of Chronic Illness Therapy – Fatigue

DIAGNOSTIC TESTS IN FATIGUE WORK UP

TEST	RATIONALE
Complete blood count	Check for anemia and infection
TSH and T4 level	Evaluate thyroid function
Electrolyte levels	Rule out electrolyte imbalance
BUN and creatinine	Evaluate renal function
CT scan, MRI	Rule out metastatic disease
Liver function test	Rule out liver dysfunction

TREATMENT

PHARMACOLOGIC

- Psychostimulants (methylphenidate, modafinil)
- Anti-depressant
- Anti-anxiety
- Pain medications
- Sleep medications

NON-PHARMACOLOGIC

- Exercise
- Nutritional support
- Sleep therapy
- yoga
- Psychosocial therapy

Practice Question

- A patient with cancer related fatigue and anxiety is interested in mind-body approaches. What is the best intervention for this patient?

1. hypnosis
2. relaxation training
3. strength training exercise
4. psychotherapy

Practice Question

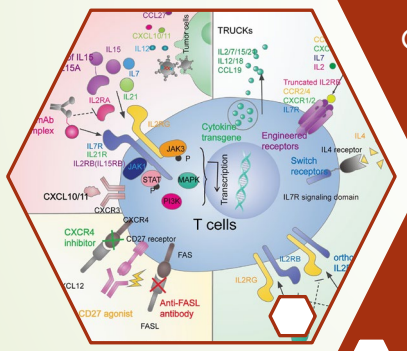
- A patient with advanced brain tumor comes with severe cancer related fatigue that is not responsive to non-pharmacologic interventions. The APP prescribes methylphenidate. What is the mechanism of action of psychostimulants?

  1. suppression of tumor angiogenesis
  2. inhibit the release of excitatory neurotransmitters
  3. activation of the dopaminergic system
  4. inducing anti-inflammatory cytokines

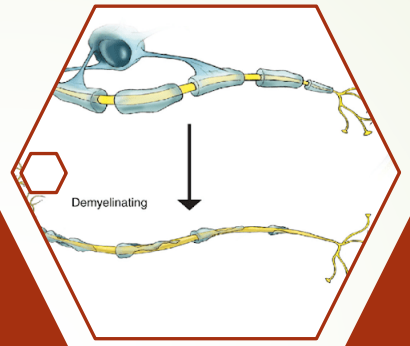
CANCER RELATED COGNITIVE IMPAIRMENT

- "chemobrain"
- impairment of short-term and working memory, attention, executive functions and/or processing speed

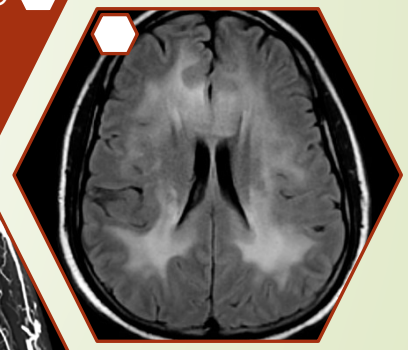
Underlying mechanism



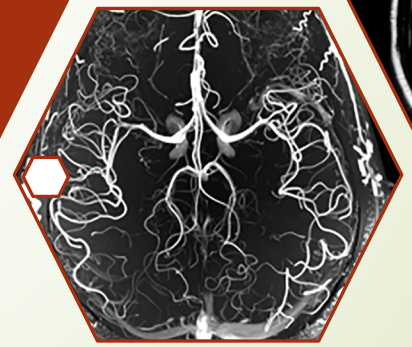
Nerve cell damage and demyelination



Damage to myelin in white matter



Brain blood vessel damage



Cytokines cross the blood brain barrier

ASSESSMENT

- Neuropsychological evaluation
- Physical examination
- Laboratory tests to rule out physiologic causes
- Medication review

TREATMENT

PHARMACOLOGIC

- Psychostimulants (methylphenidate, modafinil)
- Cholinesterase Inhibitor

NON-PHARMACOLOGIC

- Memory Aids
- Physical and Mental Exercise
- Simplification

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