Breaking the Cycle of Chronic Pain, Poor Sleep, Depression, and Fatigue

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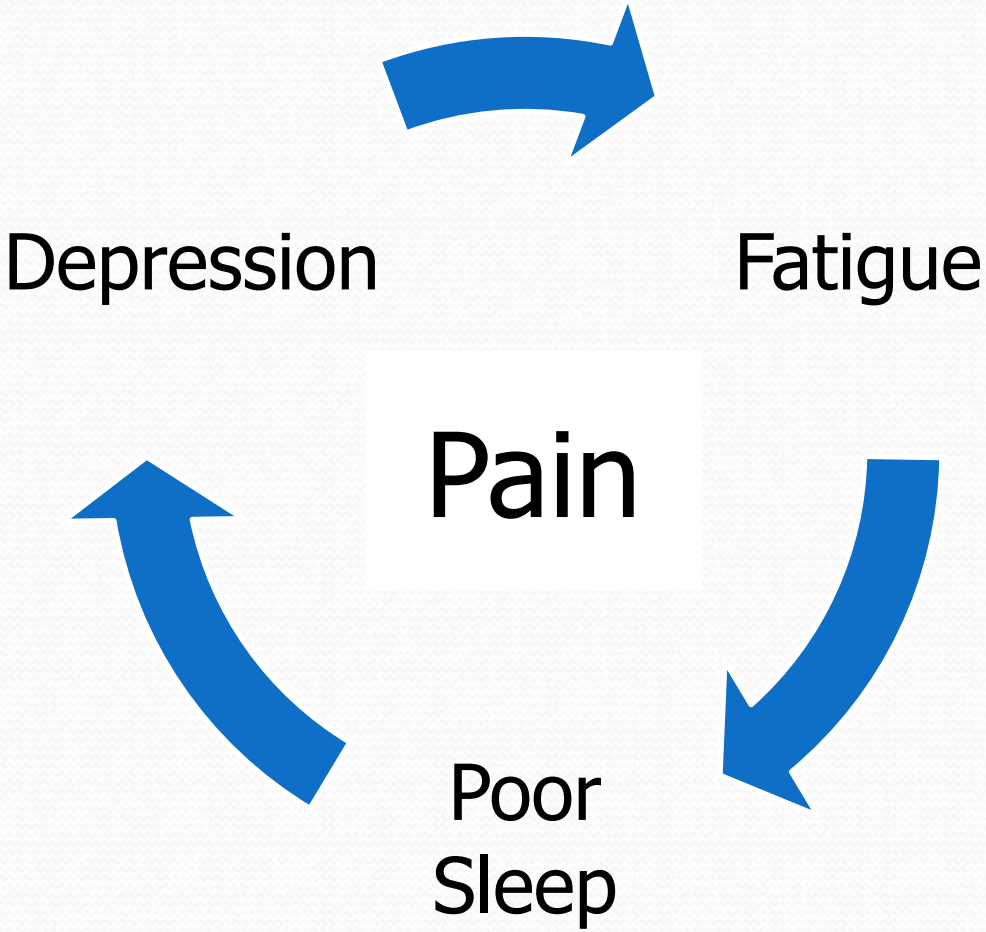
- I have no financial conflicts of interest to disclose
- I will discuss “Off-label” uses of many medications


Depression
Fatigue
Pain
Poor
Sleep

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- “Every patient with chronic widespread pain requires evaluation of sleep, since poor sleep and depression are independently associated with pain.”
  - Dr. Phillip Mease, University of Washington

Address Everything Together

- To break the cycle, you need to address all contributing factors simultaneously, e.g.
- As long as you're in pain, your sleep, your depression, and your fatigue will never get completely better.
- As long as you're depressed your pain, sleep, and fatigue will not improve very much.
- There is no "magic formula."

Everybody's Different

- No two patients have identical symptoms.
- Response to symptoms, medications, etc. vary with:
  - Psychological factors
    - Who you are
    - Your life situation
    - Your support system
  - Physiological factors
    - Pre-illness state of health
    - Other medical conditions
    - Pharmacogenetics, other genetic factors

Every Patient Requires a Comprehensive, Individualized Treatment Plan

Different Types of Pain Require Different Treatments

- Accurate diagnosis is the first step
- Pain
  - Muscle/joint
    - Inflammatory, Mechanical, Neuropathic
  - Visceral
    - Inflammatory, Mechanical, Neuropathic, Ischemic
  - Headache
    - Inflammatory, Mechanical, Neuropathic, Vascular, CSF-related

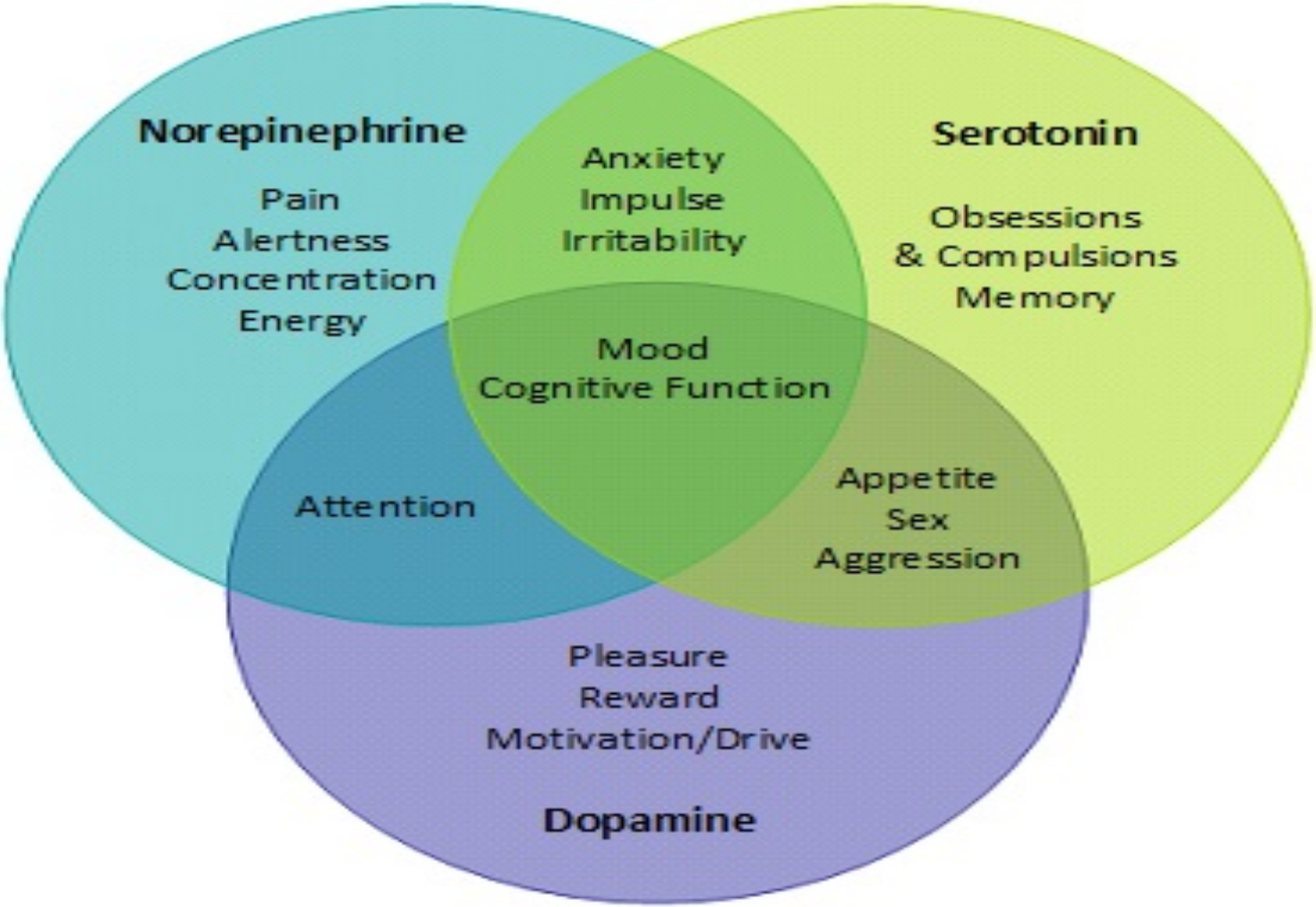
Pain—Don’t Underestimate It

- It’s not that bad
- I’m used to it
- I’ve learned to live with it
- I don’t want to take pain medication

Are not helpful approaches to managing chronic pain

Different Types of Depression Require Different Treatments

- Depression
  - Serotonergic Symptoms
  - Noradrenergic Symptoms
  - Dopaminergic Symptoms
  - Symptoms that Suggest a Bipolar Disorder



Source: Deplin™ pamphlet

Depression—Don’t Underestimate It

- It’s not that bad
- I’m used to it
- I’ve learned to live with it
- I don’t need counseling
- I don’t want to take antidepressants

Are not helpful approaches to managing depression

Remember:

- You don’t have to be sad to be depressed.
- *Neurotransmitter deficiency can be significant even in the absence of clinical depression*

Different Types of Sleep Problems Require Different Treatments

- Difficulty getting to sleep
  - Anxiety
  - Pain
  - Something else, e.g. restless legs
  - "Environmental" factors—uncomfortable mattress, noise, light, restless or noisy bed partner
- Trouble staying asleep
  - Pain, sleep apnea, snoring, vivid dreams
- Hard time getting back to sleep
  - Any of the above

Don’t Underestimate How Bad Your Sleep Is

- It’s not that bad
- I’m used to it
- I’ve learned to live with it
- I don’t want to take sleep medication

Are not helpful approaches to managing sleep disorders

Sleep "Misperception"

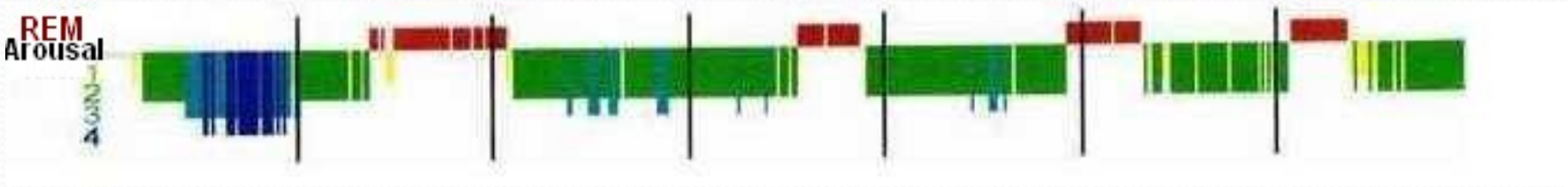
- Perhaps even more than pain and depression, sleep is often misperceived:
- "I'm a great sleeper"
- Up to 90% of patients with sleep apnea don't know they have it
- Many patients with periodic limb movements also are unaware that they're moving at night
- Frequent arousals and lack of deep sleep, two common causes of non-restorative sleep, don't cause any particular symptoms except fatigue on waking

Sleep Studies

- Sleep studies are usually very helpful, *if carefully interpreted*
- Home sleep monitoring, if available, can also be very helpful, though currently available monitors have significant limitations

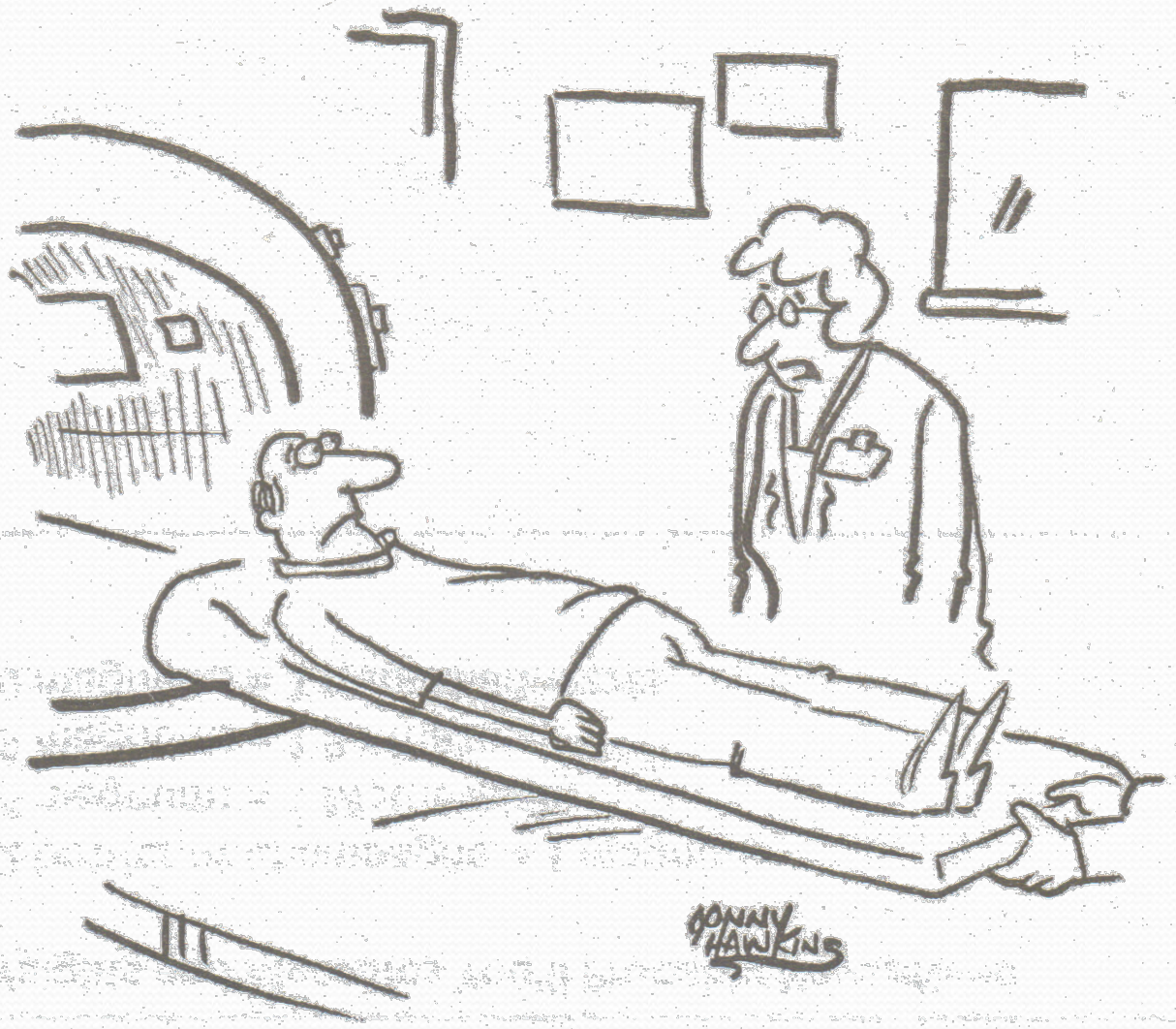
Non-Restorative Sleep in EDS

- Frequent arousals and awakenings
- Little or no deep sleep



Normal Sleep

Non-Restorative Sleep



"The MRI reveals that your head is riddled with conventional wisdom."

Different Causes of Fatigue Require Different Treatments

- Much of the Fatigue in EDS comes from:
  - Poor Sleep
  - Chronic Pain
  - Depression
  - Autonomic Dysfunction
- But that doesn't mean that these are the ***only*** causes of fatigue. Common metabolic factors need to be looked for, too.

Autonomic Dysfunction

- Autonomic nervous system regulates all functions that occur automatically, e.g. circulation, breathing, digestion, etc.
- Sympathetic—"fight or flight," the accelerator
- Parasympathetic—"rest and digest," the brake
- Sympathetic hyperactivity can aggravate pain and sleep problems, and mimic anxiety, panic, even hypomania
- Parasympathetic overactivity can cause nausea and aggravate fatigue, malaise

Common Metabolic Factors in Fatigue in EDS

- Anemia, hypothyroidism, and other "common" problems
- Micronutrient deficiencies, especially Vitamin D, Vitamin B12, and Magnesium
- Hormone deficiencies, especially cortisol, DHEA/testosterone
- Salt/fluid imbalance, usually inadequate salt and/or excessive water intake
- Mast cell dysfunction

Basic Metabolic Testing

- Chemistry Profile
  - Rule out liver and kidney problems
  - Look for low sodium and chloride, high or low glucose
- CBC
  - Rule out anemia, abnormal white blood cell counts
  - If anemic, check B12, folate, and iron studies
  - Watch out for “dilutional” anemia
  - Be mindful that “normal ranges” apply to most people, but maybe not to you! e.g. ferritin

Hypothyroidism

- Clinical hypothyroidism can occur with thyroid hormone levels in the "normal" range
- However, routinely administering thyroid supplements to patients complaining of fatigue who have normal thyroid function tests is not recommended
- Similarly, although conversion of T4 to T3 is often impaired in acute illness and sometimes impaired in chronic illness, routine administration of T3 is also not recommended.

Micronutrient Testing

- Serum 25OHVitamin D levels generally do reflect tissue levels, except when high-dose supplements are used.
  - Deficiency usually requires MILLIONS of units of Vitamin D to correct.
  - Just because the normal range is 30-100 doesn't mean that a level of 31 is good.
- B12 deficiency can occur even in the presence of "normal" serum B12 levels, i.e. serum levels don't always accurately reflect tissue levels

Micronutrient Testing

- Magnesium even harder to measure than B12
  - Only 1-2% of body magnesium is in the bloodstream
  - Clinical deficiency can occur with normal serum levels
  - Deficiency is very hard to correct, since oral magnesium is not absorbed well, and has a laxative effect
  - Magnesium is absorbed well through the skin, eg. via Epsom salts and topical formulations
  - Magnesium deficiency is even harder than D deficiency to correct
- Calcium blood levels also don’t reflect deficiency

Micronutrient Testing

- “High-tech” nutrient panels, e.g. Spectracell, can be very helpful
- B Vitamin levels are often marginal or low in EDS
- Trace element deficiencies, including not only calcium and magnesium but zinc, selenium, and chromium are fairly common
- Assays for glutathione, carnitine and Coenzyme Q10, alpha lipoic acid, insulin sensitivity can not only detect deficiency but provide clues to metabolic problems.

Hormone Deficiency/Supplementation

- "Birth control" hormones can reduce autonomic dysfunction, improve mood and sleep, and sometimes even reduce pain
- Androgen deficiency appears to be unusually common in EDS
  - Most often caused by oral contraception or narcotics, but often seen without these
  - Often DHEA, total and free testosterone all are low (with conventional normal ranges)
  - Telltale symptom is inability to build muscle despite appropriate exercise and good nutrition
  - Often DHEA supplementation is helpful, but not always

Assessing Salt-Fluid Balance

- Serum Osmolality=Total Concentration of Electrolytes, Proteins, etc. in the Blood
  - Normal ranges usually 280-300
  - Most people with orthostatic intolerance are around 280
- Urine Osmolality=Total Concentration of Urine
  - Normal ranges usually 300-1000
  - Many people with orthostatic intolerance are below 300, often way below!

Treating Salt-Fluid Imbalance

- Most People with Orthostatic Intolerance, told to drink lots of water and eat lots of salt, are getting too much water and not enough salt!
- Electrolyte drinks are the best "solution," but be careful, because many have lots of sugar
- Limit plain water to less than half of your daily fluid intake
- Forget the conventional wisdom that salt is bad for you
- Most people don't need more than 2-3 liters of fluid a day

Mast Cell Dysfunction

- Now clearly associated with EDS
- Can cause respiratory, skin, and digestive problems
- Mast cell overactivity also can aggravate autonomic problems, fatigue, and pain
- Dietary measures and pharmacological measures are usually both necessary to control symptoms

So How Do You Break The Cycle of Chronic Pain, Poor Sleep, Fatigue and Depression?

By identifying and as many contributing factors as we can, and addressing as many as possible in a comprehensive treatment program

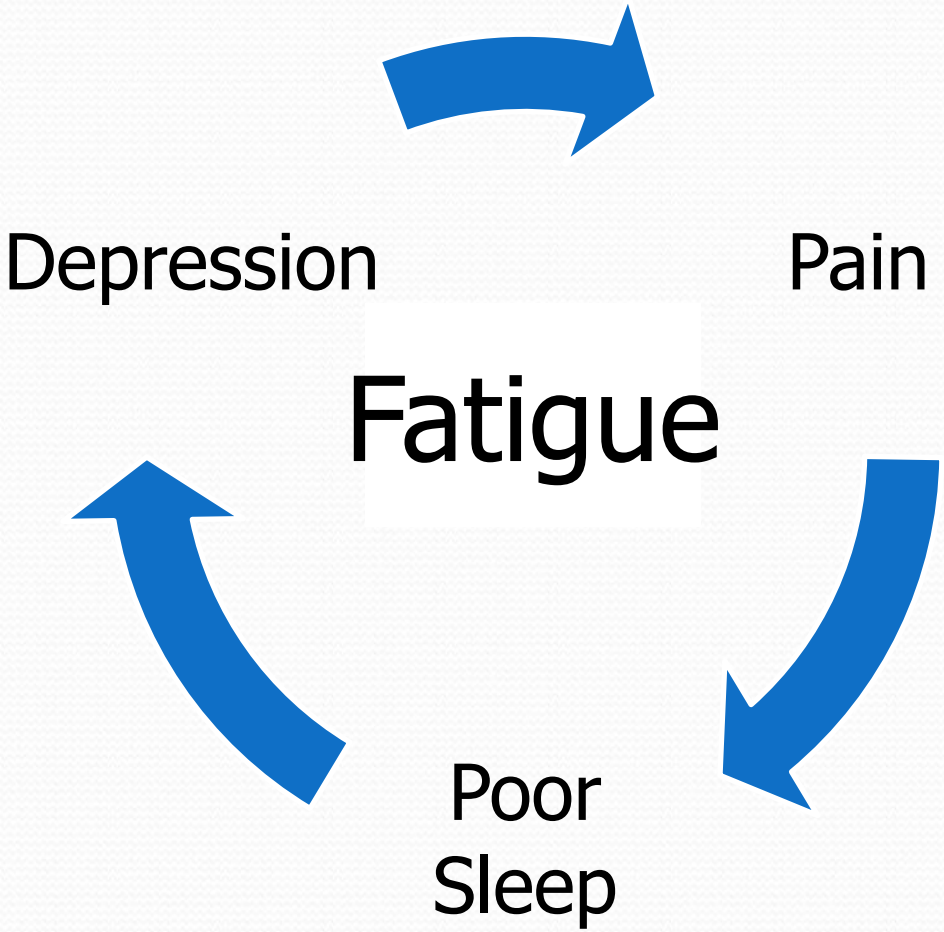
Designing a Comprehensive Treatment Program

- What are the goals of treatment?
  - Pain relief
  - Improvement in daily function, ability to do tasks
  - Just "feeling better"
- Are there limitations to treatment options?
  - Financial—no insurance or limited insurance coverage
  - Geographical, e.g. can't get to doctor's office or physical therapy regularly
  - Concomitant medical problems or medications
  - Patient reluctant/refuses to consider certain treatments

Remember:

Individual symptoms and systems are **parts of the whole**, so that one treatment might affect more than one system or might affect another treatment

Ideally, try to choose treatments that might improve multiple problems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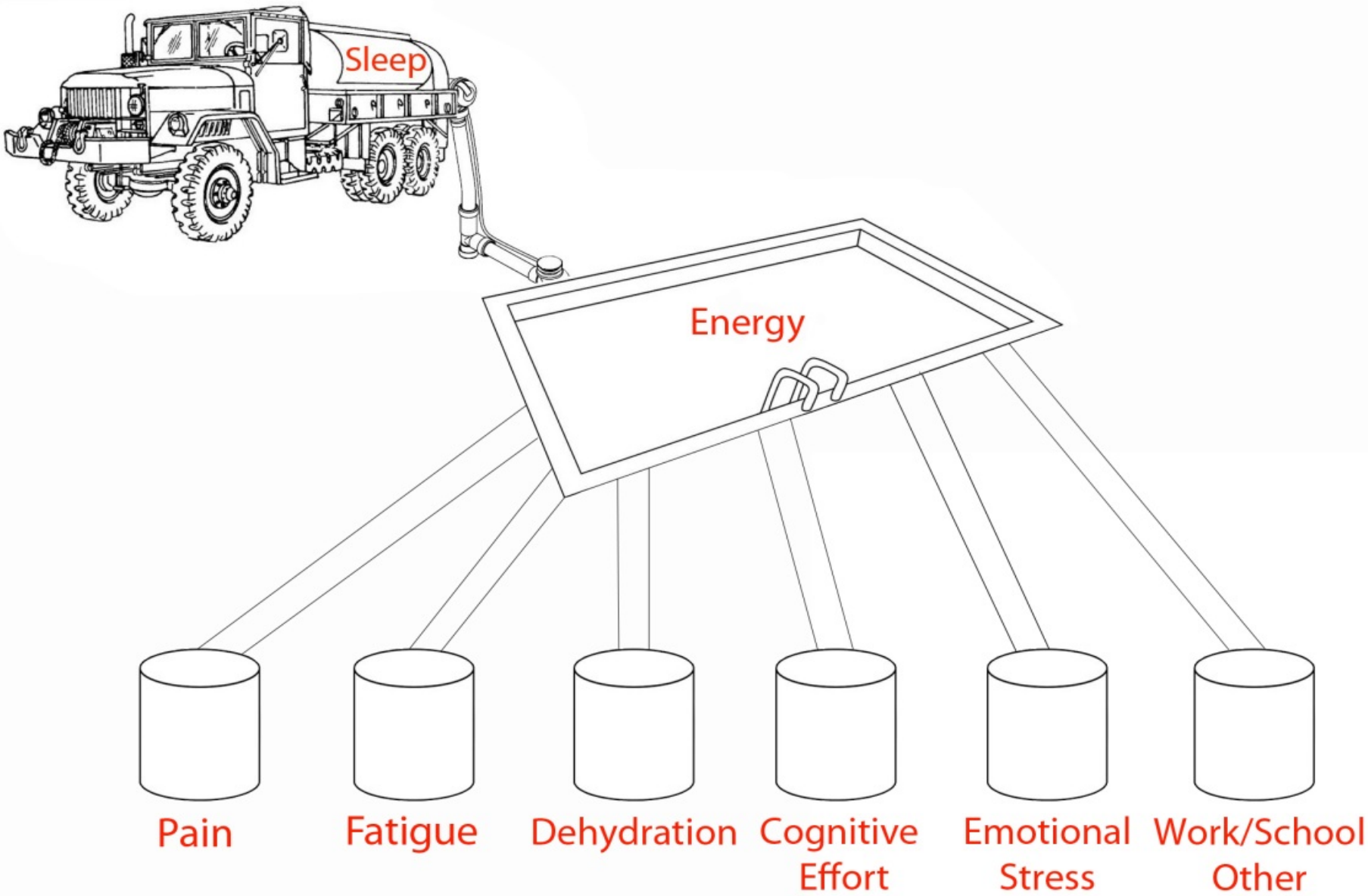

Sleep
Energy
Pain
Fatigue
Dehydration
Cognitive Effort
Emotional Stress
Work/School Other

Designing a Treatment Program—It's Not All About Medication

- Adjust Daily Activities, including exercise, rest, sleep, diet, salt and fluid intake
- Non-pharmacologic treatments for pain, depression, sleep, and fatigue

Non-Pharmacologic Treatments for Pain

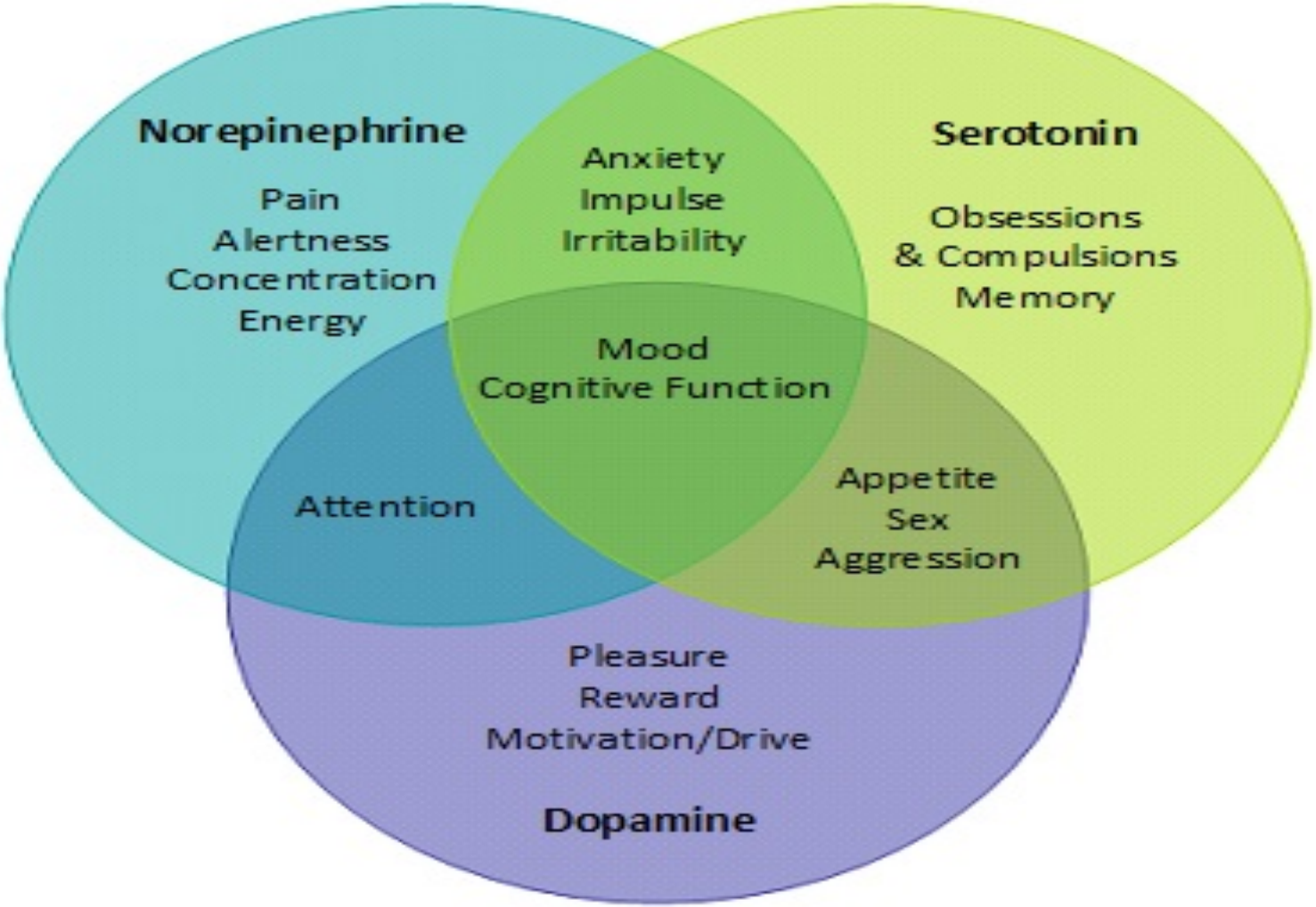
- Exercise
- Physical therapy
- Massage
- Acupuncture
- Dry needling
- TENS, etc.

Pain Medications

- Anti-inflammatories, e.g. prednisone and NSAID's: Ibuprofen, Naproxen, Celebrex™, etc.
- Acetaminophen and Tramadol
- Muscle relaxants
- Cymbalta™, Savella™, amitryptiline
- Neurontin™, Lyrica™
- Narcotics, short- and long-acting, patches
- Topicals, e.g. Lidoderm™, Flector™, Voltaren Gel™, Pennsaid™, compounded combinations

Non-Pharmacologic Measures to Reduce Depression, Anxiety, Stress

- Improving Psychological Supports and "Outlook," "Empowerment"
- Stress Management, both reducing external stresses and modifying the way the body responds to stress
- Relaxation techniques, e.g. deep breathing, meditation, yoga, Tai Chi, etc.
- Counseling/psychotherapy, Hypnotherapy, EEG Neurofeedback, EMDR, etc. CBT, Mindfulness-based stress reduction



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Medications for Depression

- Serotonin (SSRI's): Prozac, Paxil, Zoloft, Celexa, Lexapro
- Serotonin/Norepinephrine (SNRI's) : Effexor, Cymbalta, Fetzima
- Dopamine: Wellbutrin
- Other: Remeron
- "Augmenting": Abilify, Seroquel, Lamictal,T3
- NOT Benzodiazepines (Valium, Xanax, Ativan, Klonopin, etc.)

Non-Pharmacologic Measures to Improve Sleep

- Good sleep hygiene
- Comfortable mattress
- Dark and quiet room
- Treat Apnea, limb movements only if significant
- Get rid of disruptive bed partners!

Medications for Poor Sleep in Chronic Pain States

- Most Patients will require a medication "regimen"
  - Multiple medications with complementary effects usually needed
  - Finding the right combination can be a frustrating trial and error process

Medications for Non-Restorative Sleep

- Beta blockers (to reduce arousals)
- Trazodone, amitryptiline, doxepin (to increase deep sleep)
- Analgesics
- Muscle relaxants
- Benzodiazepines (lorazepam,diazepam,etc.)
- Neurontin™, Lyrica™
- Clonidine (to reduce arousals)
- Alpha blockers (to reduce intensity of dreams)
- Melatonin, Rozerem™
- "Sleeping Pills" (Ambien™, Lunesta™, Sonata™)

Measures to Reduce Fatigue

- Get adequate rest
- Don't "push through" fatigue!
- Exercise—however limited!
- Careful Use of Stimulants: Provigil™/Nuvigil™; Ritalin™, etc; Caffeine, Sudafed™
- Wellbutrin™, Cymbalta™, Effexor™, Fetzima™/Savella™, Strattera™
- Nutrient, hormone replacement/supplementation, e.g.:
  - Vitamin D, Vitamin B12, Magnesium
  - Hormonal contraception, thyroid, DHEA/testosterone
- Treatments to improve circulation/autonomic function
  - Fludrocortisone, midodrine
  - Adequate salt and fluid

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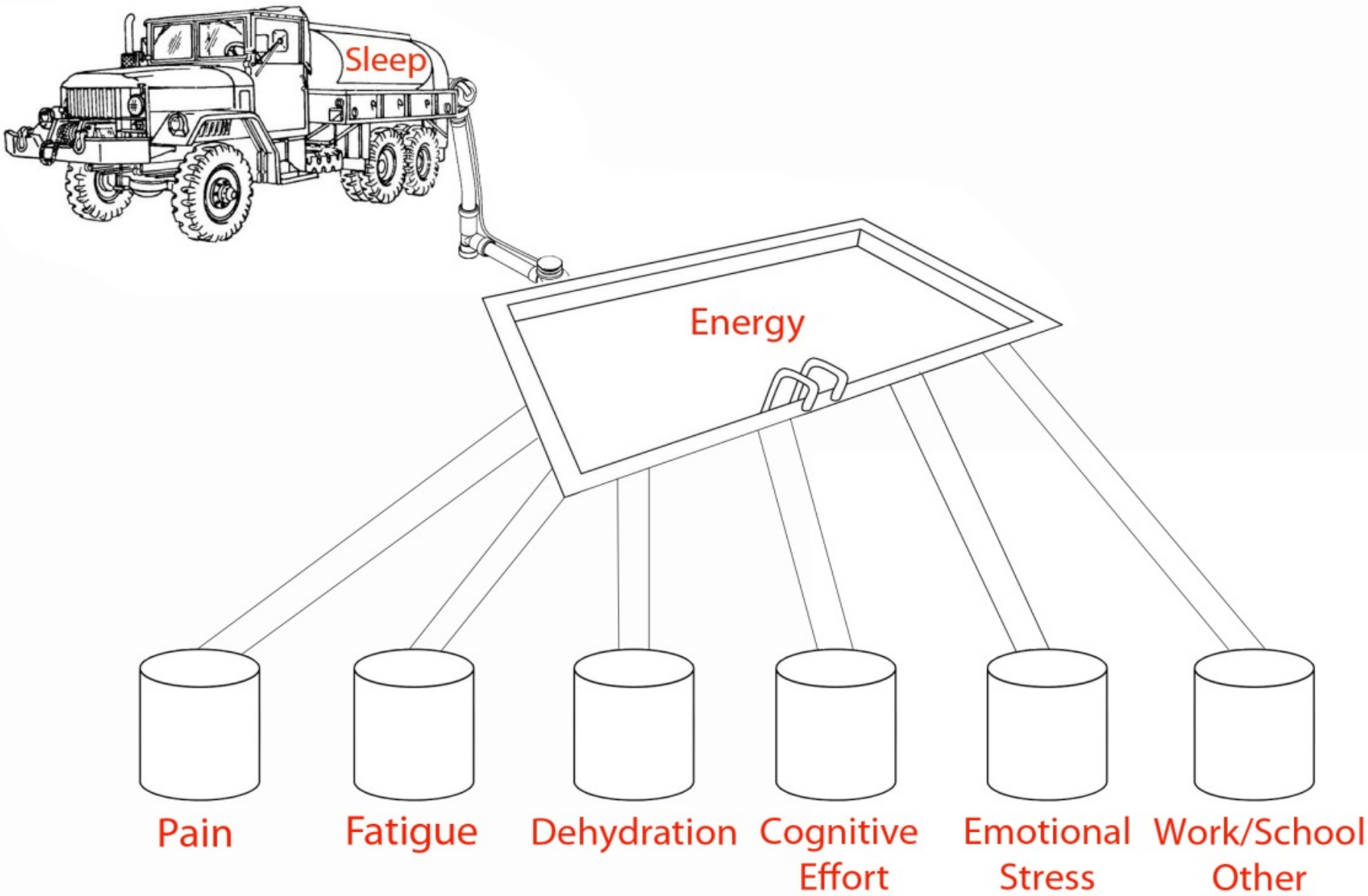
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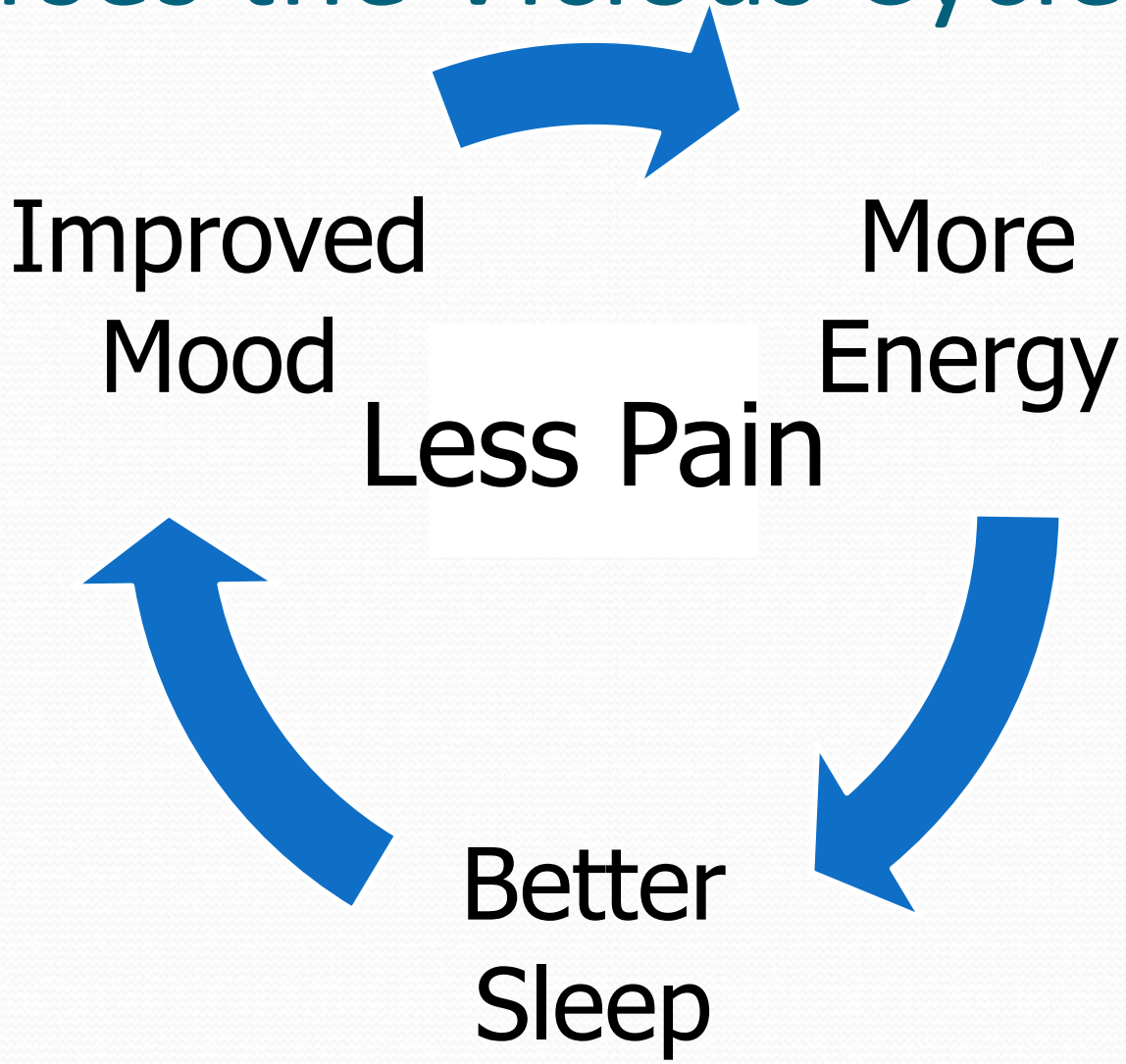
Reverses the Vicious Cycle



- Now, as pain is reduced depression, fatigue, and sleep improve.
- As depression gets better, pain, sleep and fatigue improve.
- As sleep improves, fatigue, depression, and pain are lessened.
- As fatigue improves, patients feel better, do more, and sleep better.
- The vicious cycle of pain, fatigue, poor sleep, and depression is reversed, and this.....

Is How You Get Better!

Rest Break