Management of complex pain in children and adults with Ehlers Danlos Syndrome

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EDS Awareness 2017

Introduction

- Pain Medicine specialist with a special interest in complex pains in adults and children
- Training and Fellowship, Harvard Medical school in Pain Medicine
- Assistant Professor (Clinical) – Brown Medical School, Rhode Island, USA

Disclosure and disclaimer

- I have no actual or potential conflict of interest in relation to this presentation or program
- This presentation will discuss “off-label” uses of medications
- Discussions in this presentation are for a general information purposes only. Please discuss with your physician your own particular treatment. This presentation or discussion is NOT meant to take the place of your doctor.

New Terminology

Old	New
Ehlers-Danlos syndrome	the Ehlers-Danlos syndrome**s**
Hypermobility EDS	Hypermobile EDS
HEDS / VEDS / CEDS	hEDS / vEDS / cEDS
Joint Hypermobility Syndrome	Hypermobility Spectrum Disorders
Type 3, III, 4, 2, etc.	Please do not use numeral descriptors. It will now be Hypermobile, Classical, Vascular, etc. or hEDS, cEDS, vEDS, etc.

- Ehlers Danlos Syndrome (EDS) is not a disease

- It is a form of the human body

Connective tissue

- The human body is made up of different parts
- They are all connected to each other by connective tissue
- Joints, tendons, ligaments, bones, skin, internal organs are all made up of connective tissue

Find out what's broken

- It is crucial to understand the cause of the pain before deciding on treatment options.
- For example, pain in the shoulder joint can be from:
  - Dislocated shoulder joint,
  - Muscle spasms
  - Nerve or blood vessel impingement or damage
  - All of the above
- The treatment of each of these is different

Ehlers Danlos Syndromes

- Two important things to remember:

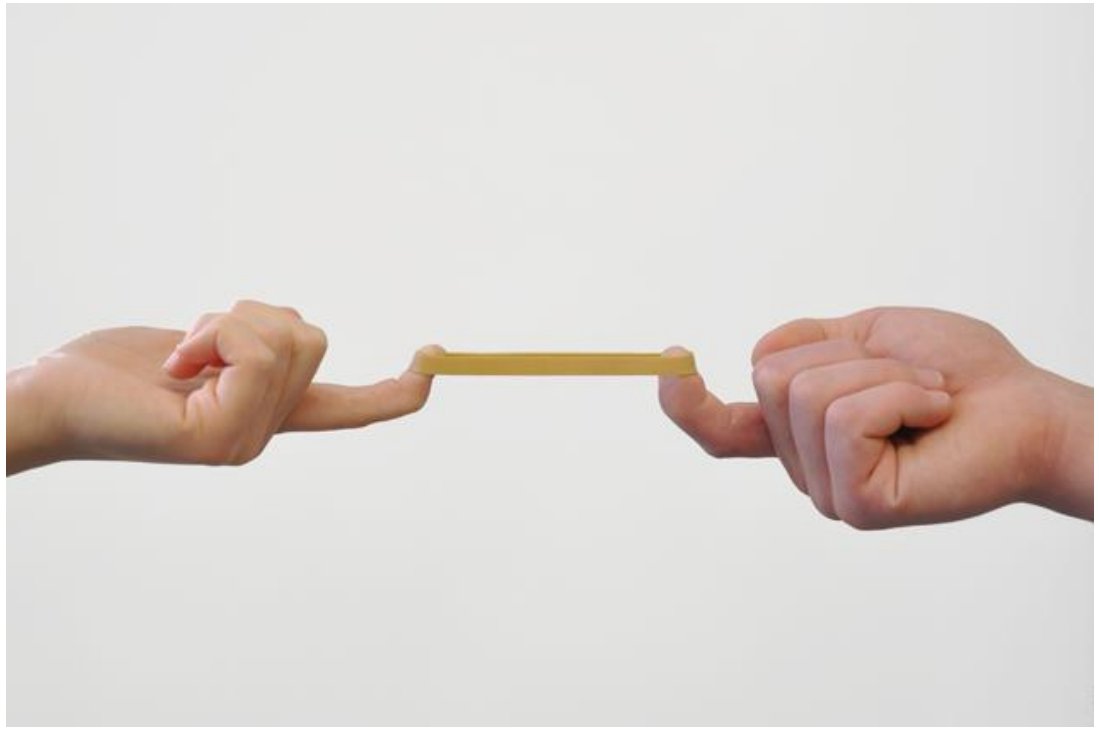
1. Weak connective tissue
2. Poor joint position sense (proprioception)

Connective tissue – non –Ehlers Danlos Syndromes

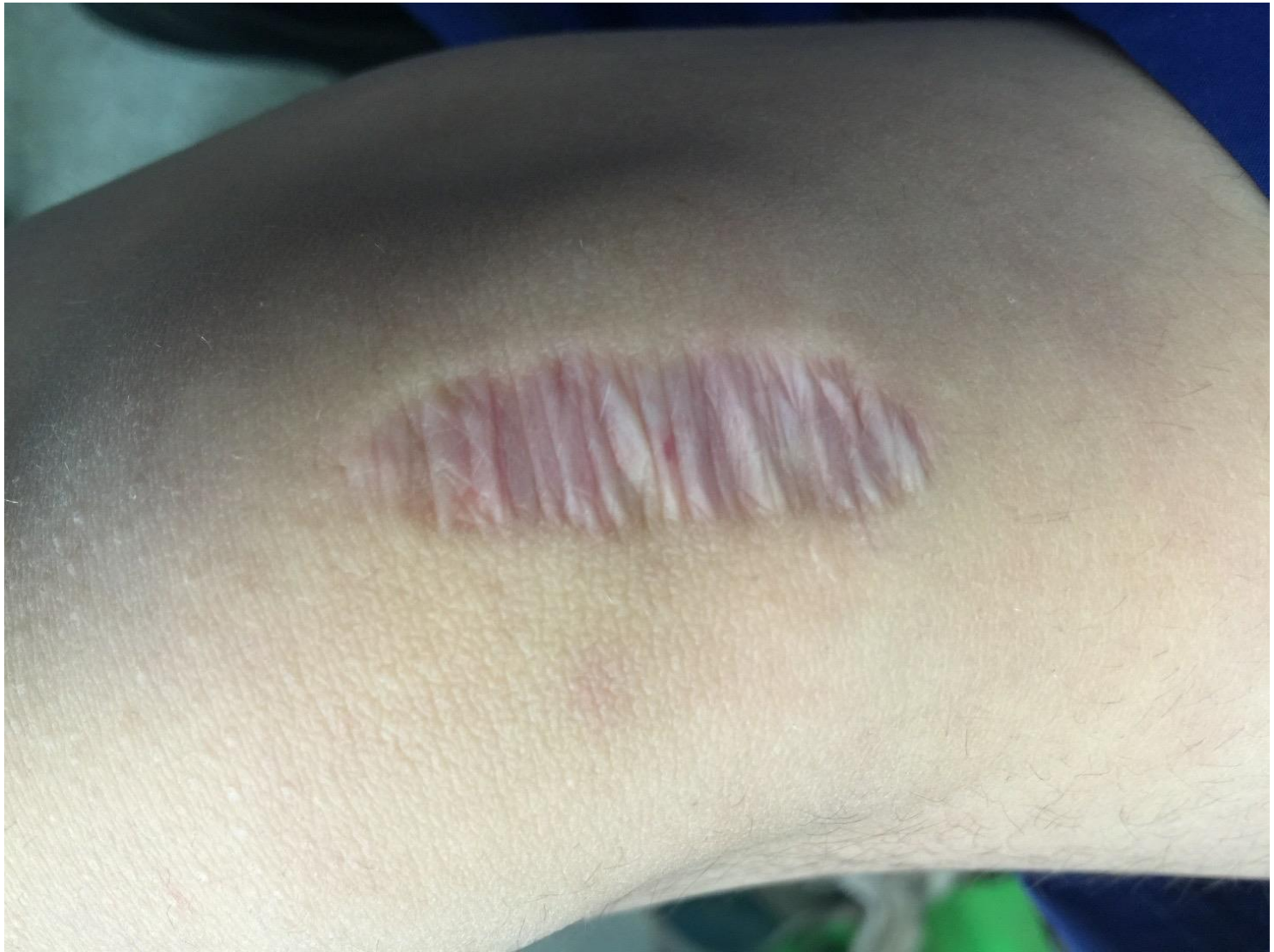
- Connective tissue is made of collagen
- The connective tissue is strong
- Does not stretch as much
- Does not break easily
- Heals well when broken

Connective tissue – Ehlers Danlos Syndromes

- Connective tissue is made of collagen
- The connective tissue is weak
- It stretches easily
- It breaks easily
- It does not heal well



Weak scar in EDS

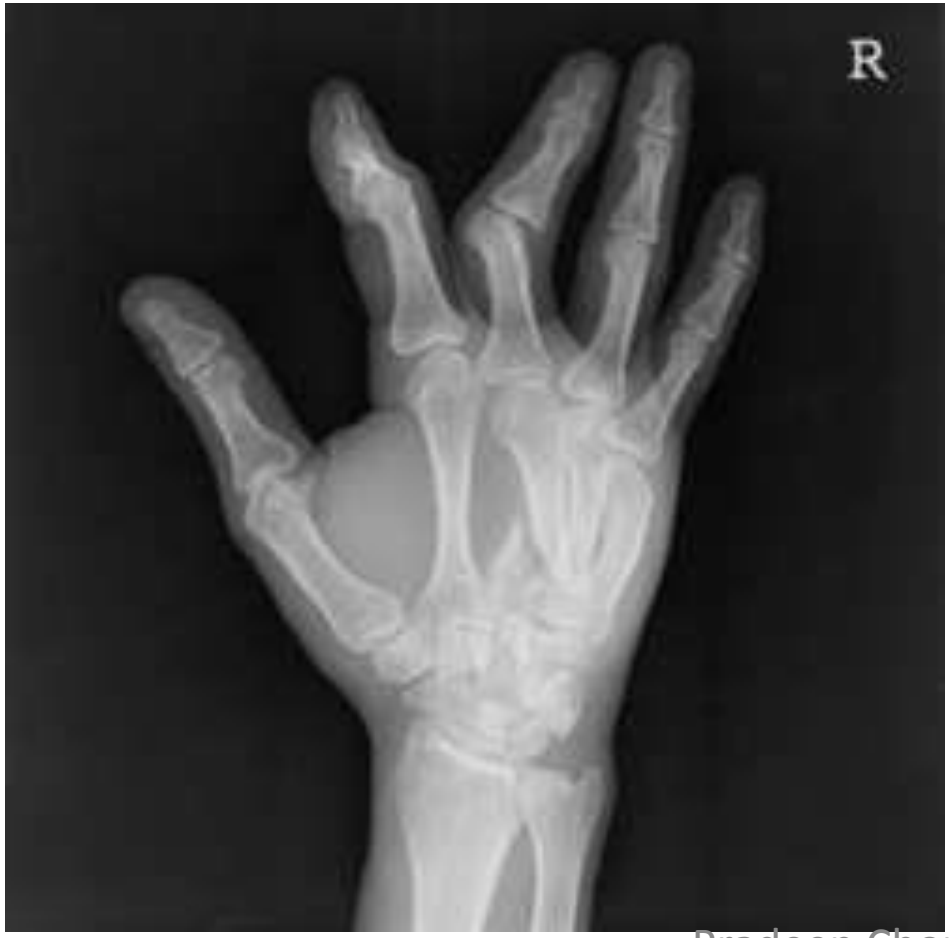


Types of tissue injury in EDS

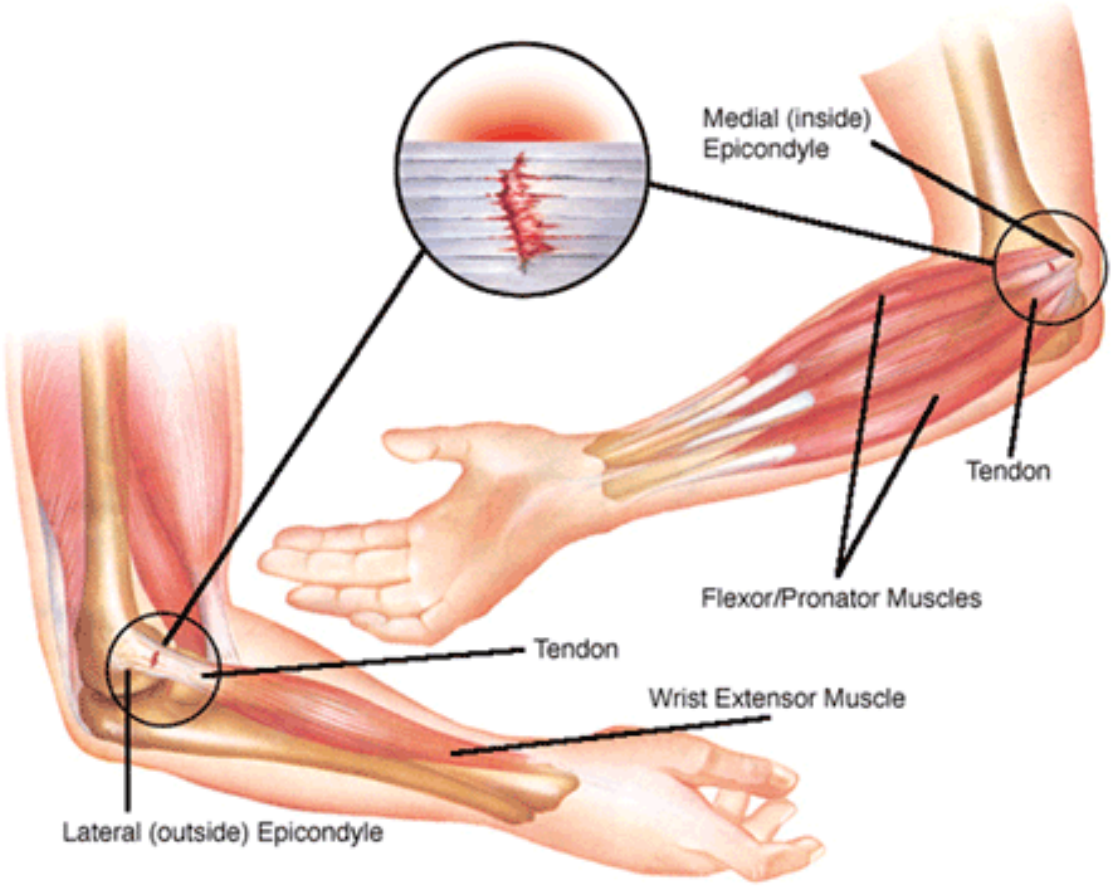
- Macro trauma – a large event or trauma resulting in injury. Dislocation or fracture

- Micro trauma – small repetitive traumas resulting in tissue breakdown. For example – overstretching muscles and ligaments.

Macro trauma



Micro trauma



Joint Position sense

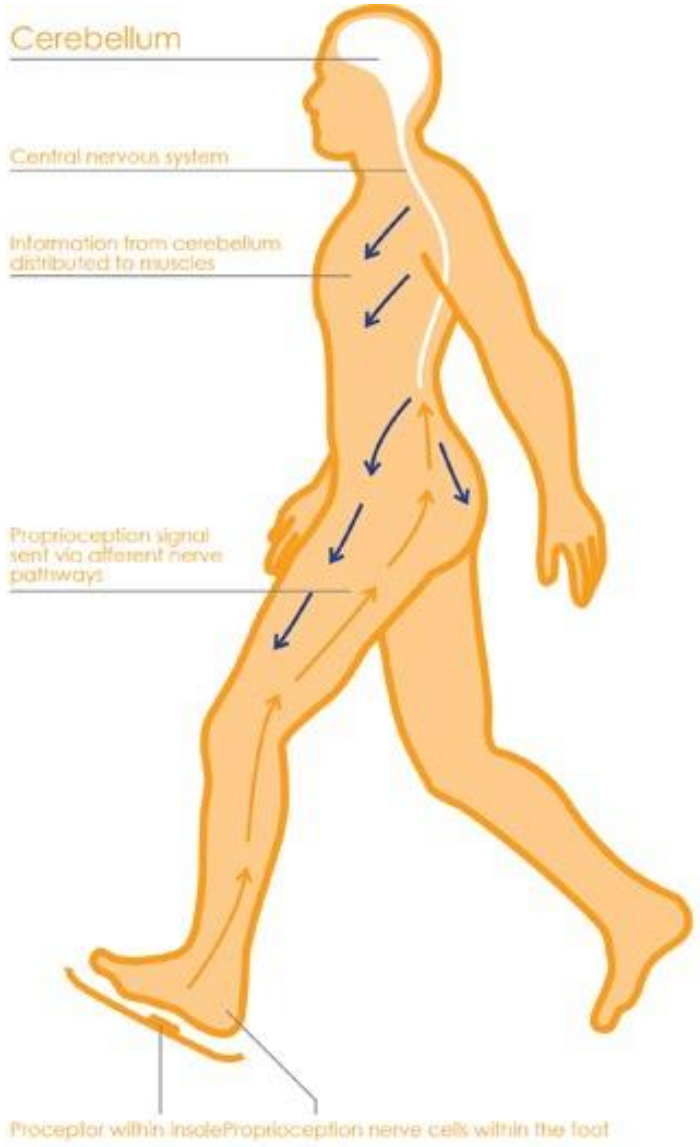
Proprioception

The body’s ability to sense movement of the joints and their position

Proprioception – Joint sense

- The brain constantly gets information from the joints as to the exact position of the limbs in space.
- It helps us walk, use our arms, maintain our posture without tipping over.
- Protects our joints from over extending and our muscles from over stretching
- EDS – poor proprioception. That is what makes them uncoordinated

Proprioception – Joint sense



Proprioception – Joint position sense

- With repetitive injury, wear and tear of joints, we start to lose proprioception
- This is seen with almost any condition that affects joints EDS, arthritis, athletics
- Patients tend to lose their balance easily
- When they lose balance, the body tends to counteract by straining other muscles.

Proprioception – Joint position sense

- With poor Joint Position sense (Proprioception) we do not use our muscles efficiently.
- This causes fatigue, tiredness and pain

Poor proprioception

Compression clothes

- The brain uses signals from the skin to understand the position of the joints and muscles.

- Wearing compression clothes helps the brain understand the position of the body parts, muscles

Compression garments

Proprioception exercises

- Juggling
- Balance board or wobble board
- Stork standing (stand on one leg)
- Stand up paddle board (SUP)
- Sitting on exercise ball
- Exercise in water – walking, treading but NO swimming

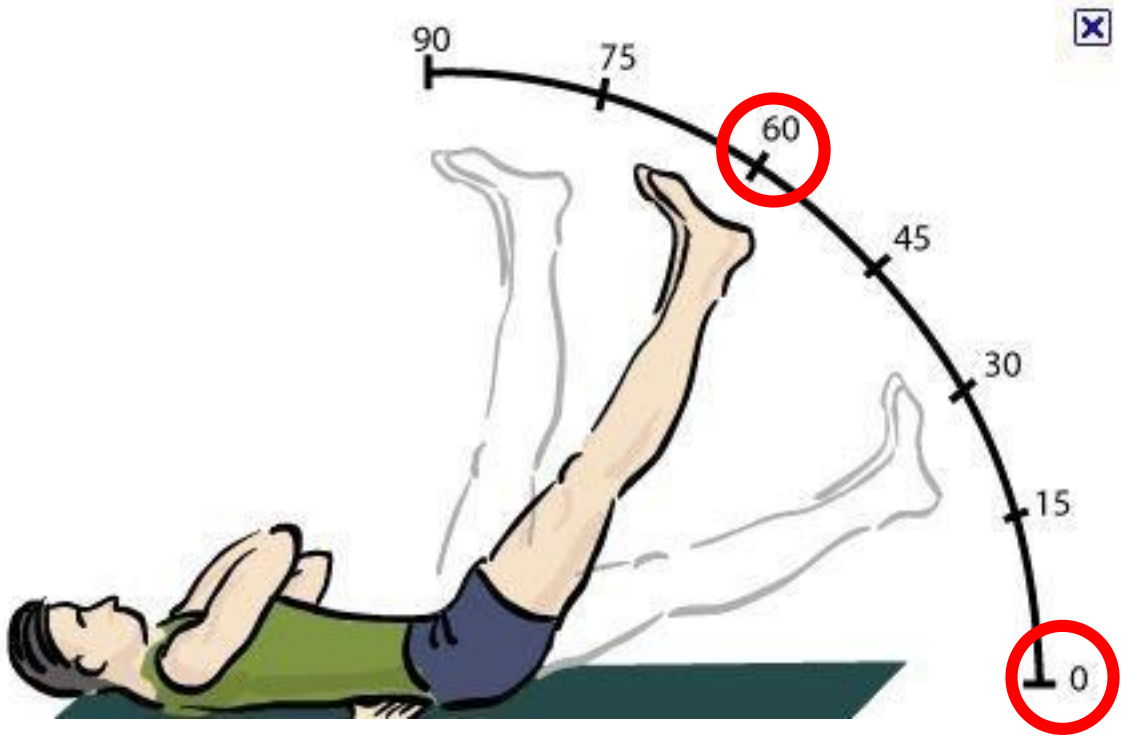
Proprioception exercises - Wobble board

Proprioception exercises - Stand up paddle board

Muscle strengthening exercises

- Avoid joint loading or joint stressing
- Start very low
- Progress slowly
- Focus on muscle strengthening
- Avoid extreme stretching

Keep limb movements within extreme range of motion



Exercise in water - walking

Avoid swimming – injury to shoulder and neck

Aquatic therapy

- Best form of exercise in EDS
- The contact of water with the skin helps the brain move your muscles more efficiently
- The water makes us weigh less which takes the load off the joints allowing us to exercise freely
- Avoid swimming – it strains the joints of the neck and shoulders.

The Feldenkrais Method

- It is a type of physiotherapy that helps repair impaired connections between the brain and the body
- Patients with EDS develop inefficient or strained habitual movement patterns
- The Feldenkrais Method teaches new patterns using gentle, slow, repeated movements.
- It uses slow repetition to teach correct and safe movements in EDS

The Feldenkrais Method

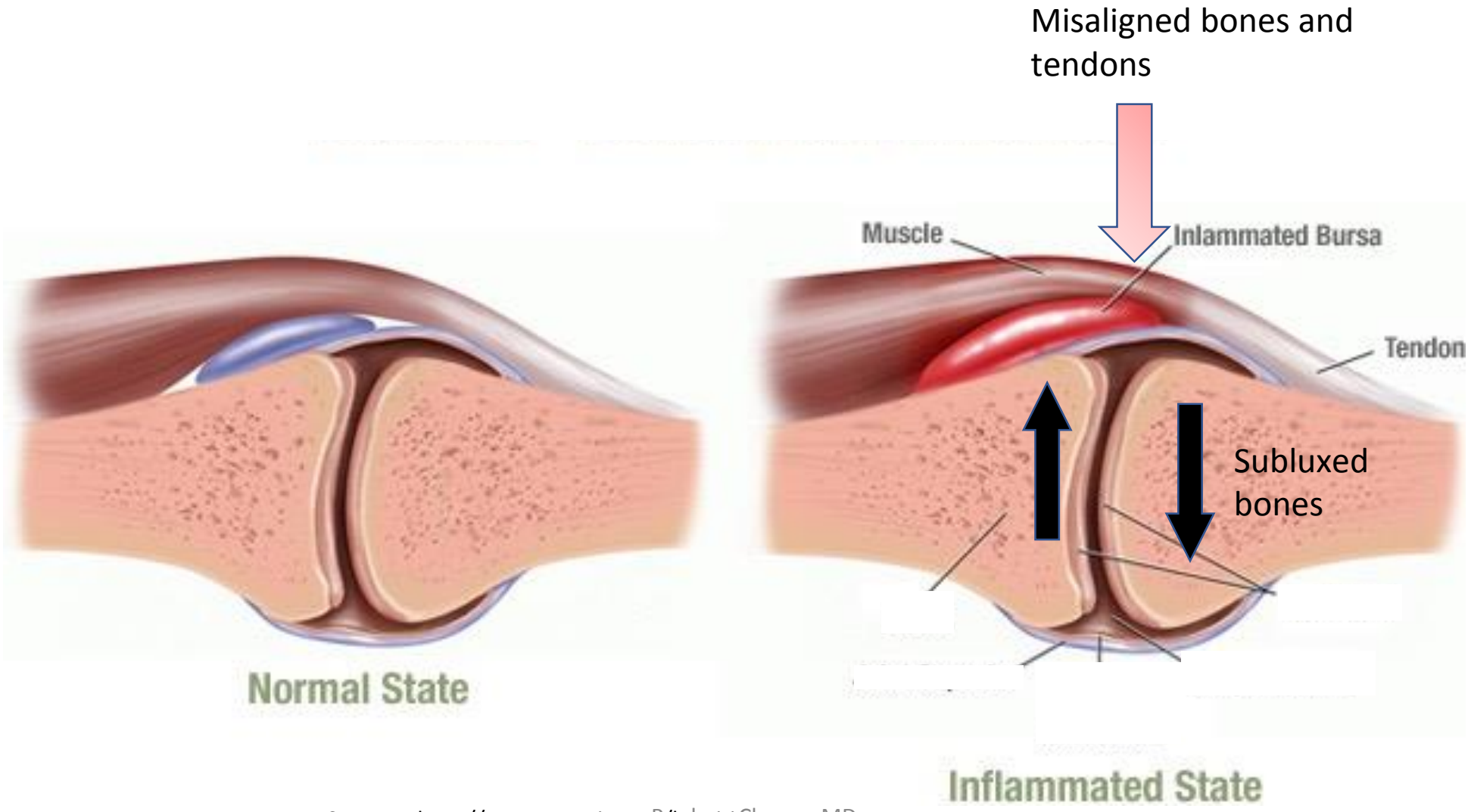
- It is based on principles of physics, biomechanics and an understanding of learning and human development.
- This method of exercise is excellent for improving proprioception in Ehlers Danlos Syndrome.
- Can be done sitting or lying down
- Each session consists of comfortable, easy movements within the limits of safety

The Feldenkrais Method

- http://www.feldenkrais.com

Tendonitis and bursitis

Tendonitis and bursitis in EDS



Courtesy http://www.ateevia.com/bursitis.aspx

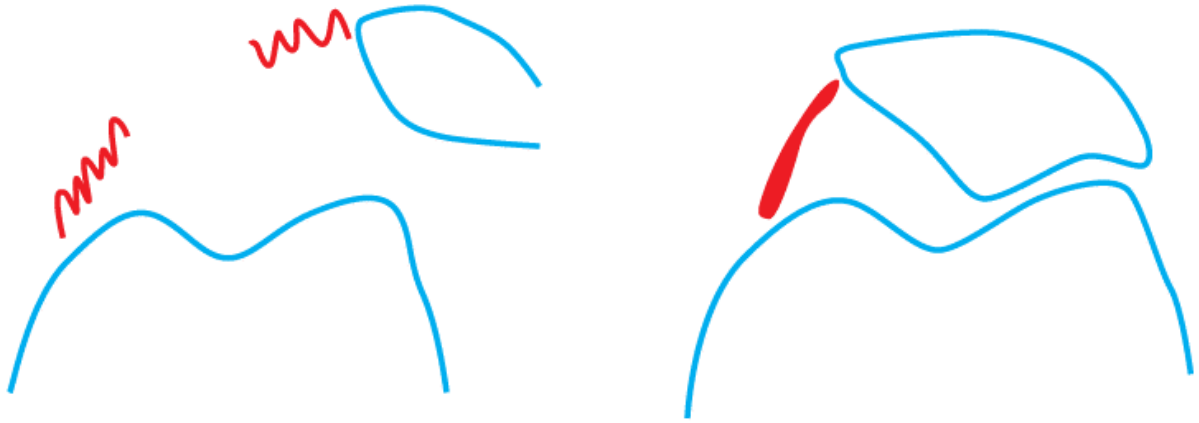
Tendonitis and bursitis in EDS

- Treatment lies in correcting the underlying problem –
  - correct bracing to align the joints
  - Correct posture (especially standing)
  - Avoid repetitive use of joint
  - Maintain proper balance

Subluxations and Dislocations

Pain in subluxation and Dislocations

- When a joint subluxes or dislocates, the pain is usually from muscle spasms around the joint.
- Pain from capsular stretch
- Not as much from the bones



Dislocation

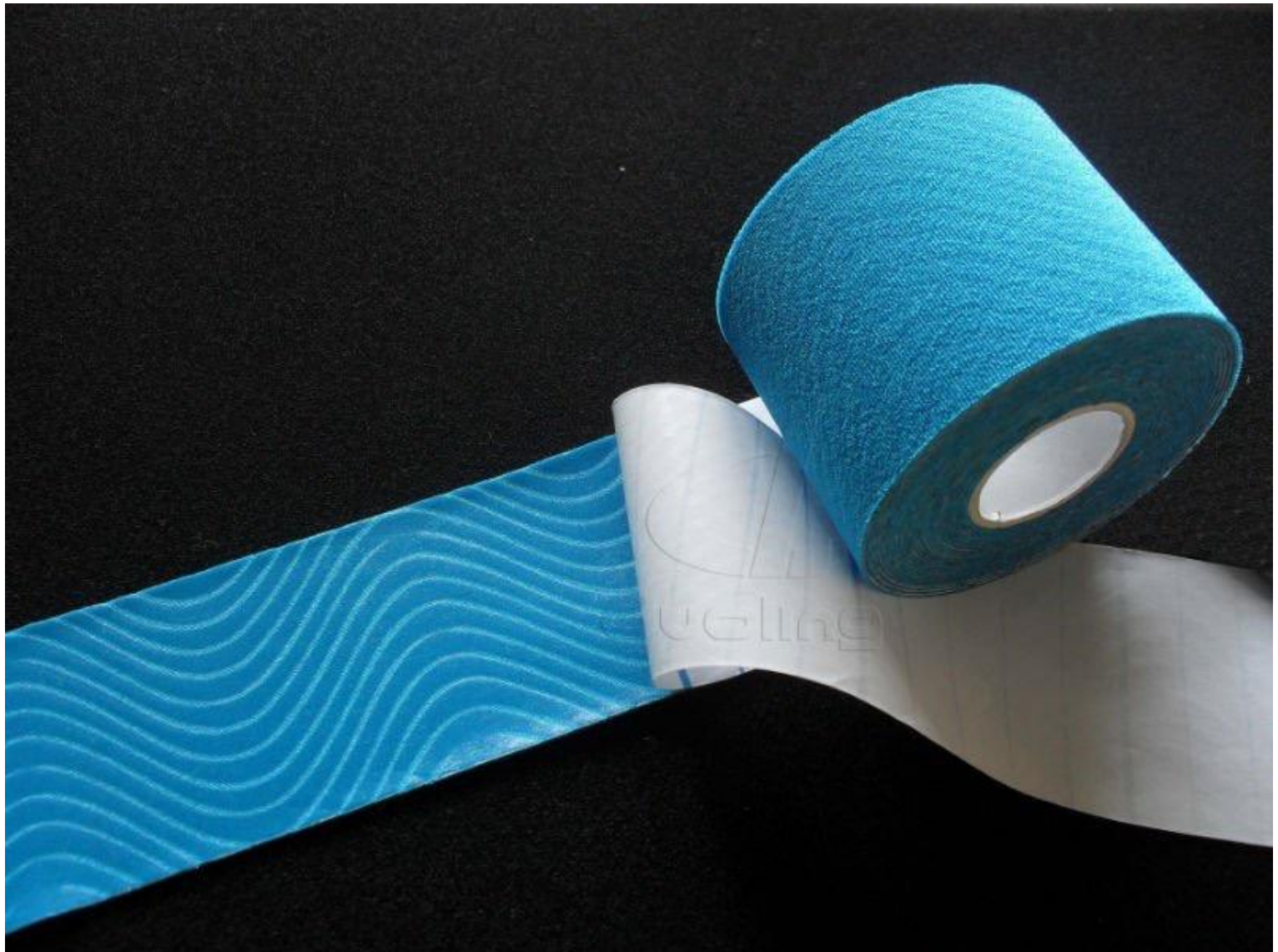
Subluxation

Neuromuscular taping (Kinesio™)

Kinesio™ taping - mechanism

- Mimics the superficial layer of skin – after 10 minutes you can not feel it
- Designed to stretch
- Porous – allows for drying easily. You can take a shower with it on
- The adhesive is applied in a wave like pattern to mimic the qualities of fingerprints.

Finger print pattern



Kinesio™ taping - mechanism

- The tape stimulates the sensors in the skin as we move – improves proprioception

- Helps reduce swelling

Kinesio™ taping - uses

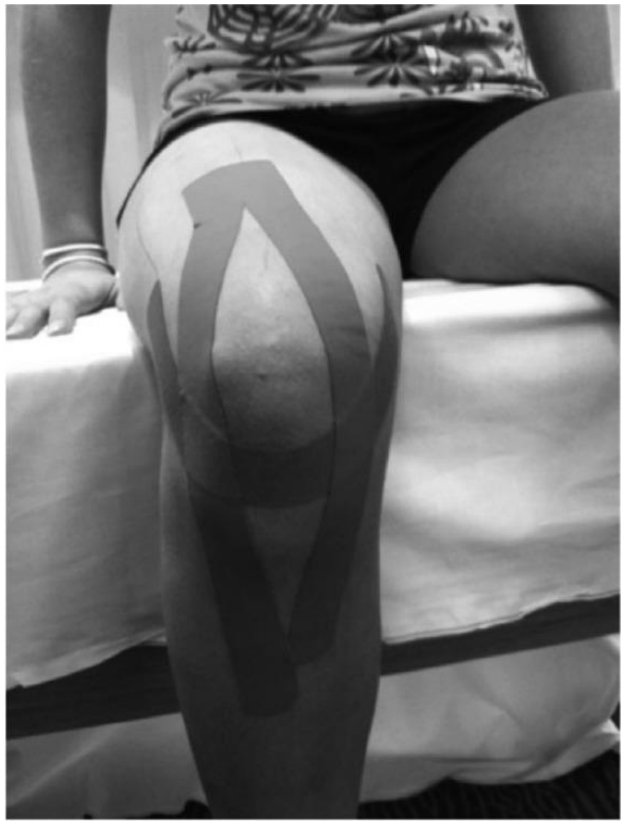
- Reduces pain
- Improves Proprioception
- Relaxes muscles
- Stabilizes joints
- Supports weak joints
- Reduces swelling

Kinesio taping helpful for

- Neck
- Upper back
- Lower back – SI joints, muscles
- Wrist
- Shoulders
- Knees
- Ankles and feet

Kinesio taping – EDS knee

- A combination of two strips of 25 cm in length and 2.5cm in width along the collateral ligament (sides of the knee) using 50% tape tension applied distally (furthest) to proximal, a horizontal tape below the patella 25 cm in length and 2.5 cm in width applied with 25% tension and lastly a Y tape 30 cm in length and 5cm in width cut with 5cm in initial base applied laterally to the patella with no tape tension.



Ther Adv Musculoskelet Dis. 2015 Feb; 7(1): 3–10. doi: 10.1177/1759720X14564561 PMCID: PMC4314299 The effects of neuromuscular taping on gait walking strategy in a patient with joint hypermobility syndrome/Ehlers–Danlos syndrome hypermobility type Filippo Camerota, Manuela Galli, Veronica Cimolin,corresponding author Claudia Celletti, Andrea Ancillao, David Blow, and Giorgio Albertini Author information

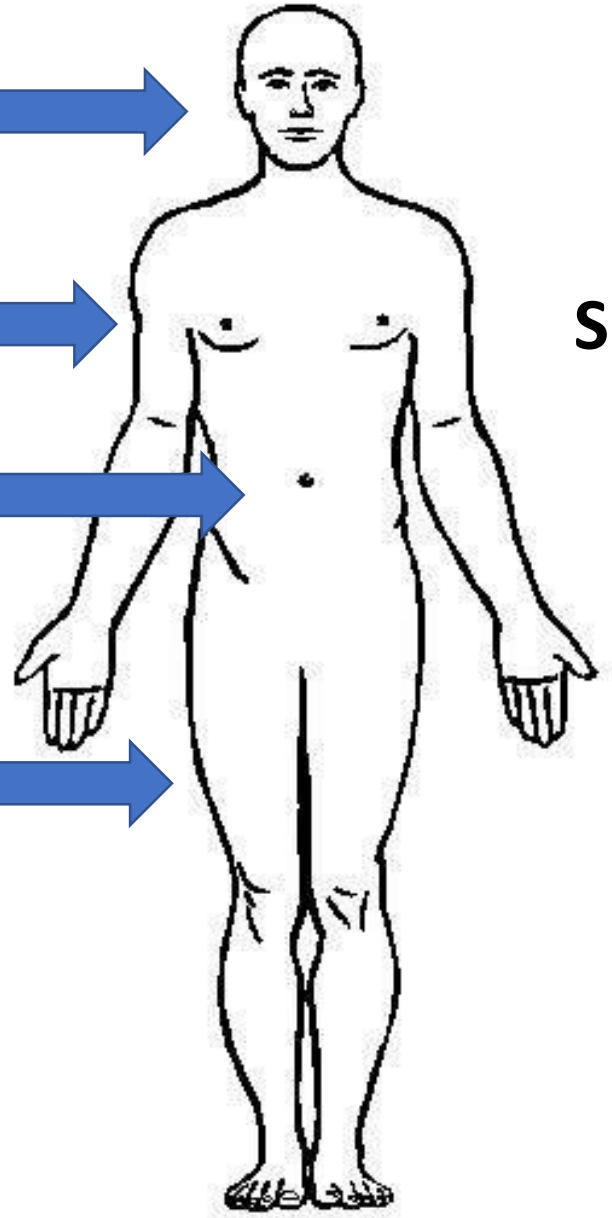
Pain in EDS by body regions

Head and neck

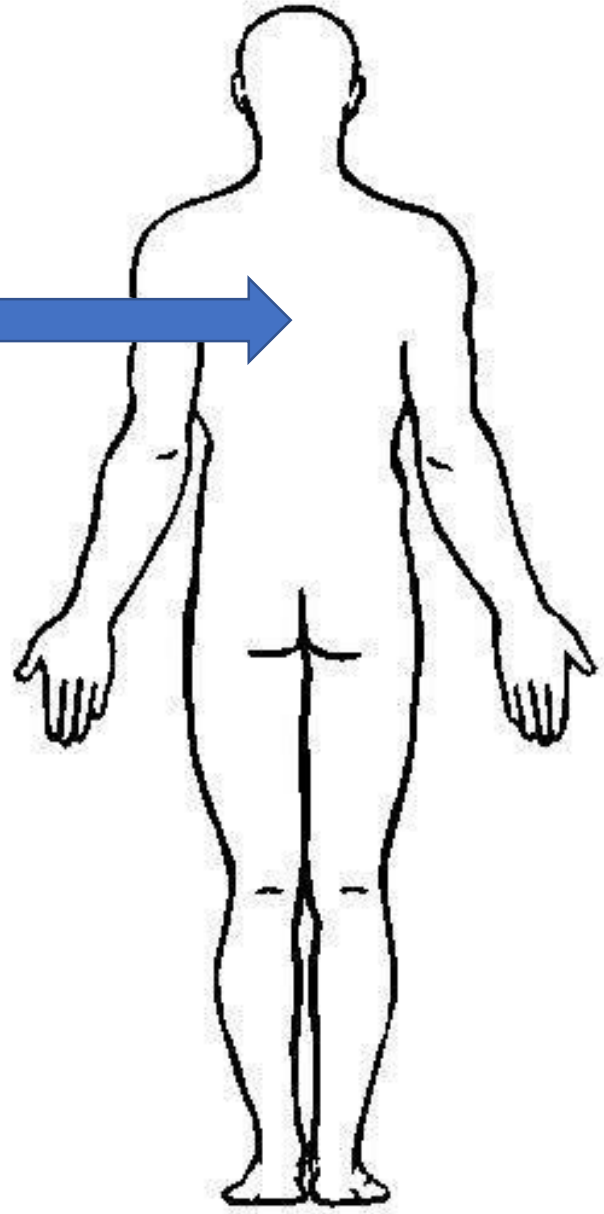
Shoulder and arms

Abdomen

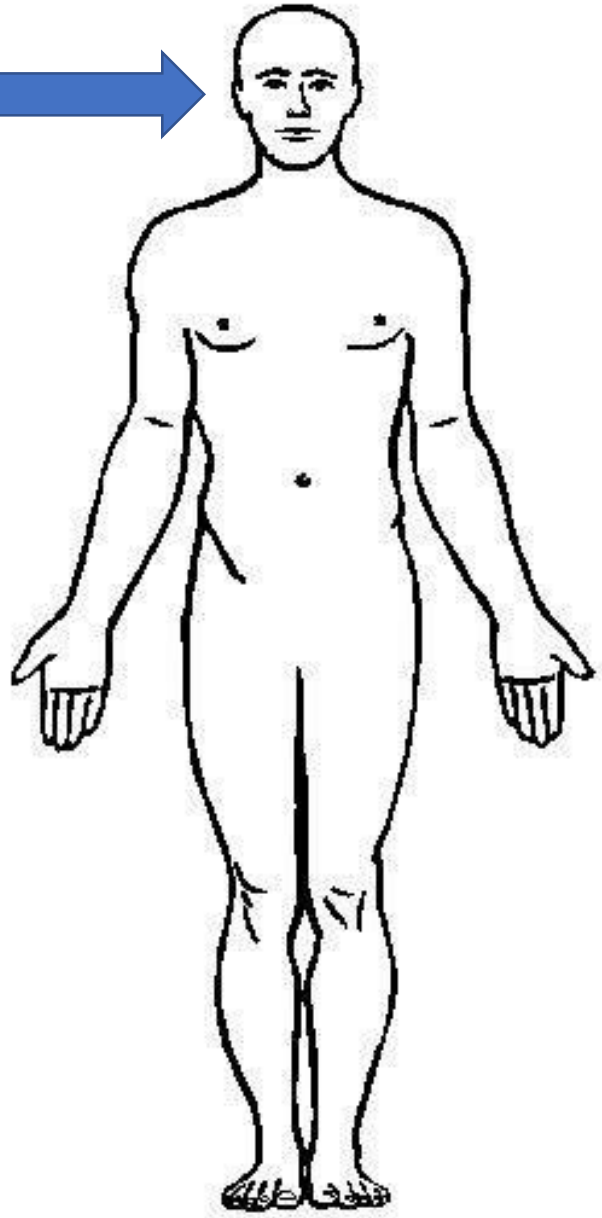
Legs



Spine



Head and neck



Common causes of headaches

1. Chiari malformation
2. Cervicogenic Headaches – from muscles
3. Temporo Mandibular joint dysfunction (Craniofacial pain)
4. Vision – blurry
5. POTS / Dysautonomia
6. Tethered Cord syndrome (TCF)
7. Spontaneous CSF (Cerebrospinal) leak
8. Cranio Cervical Instability (Instability of the neck and head)
9. Idiopathic Intracranial Hypertension

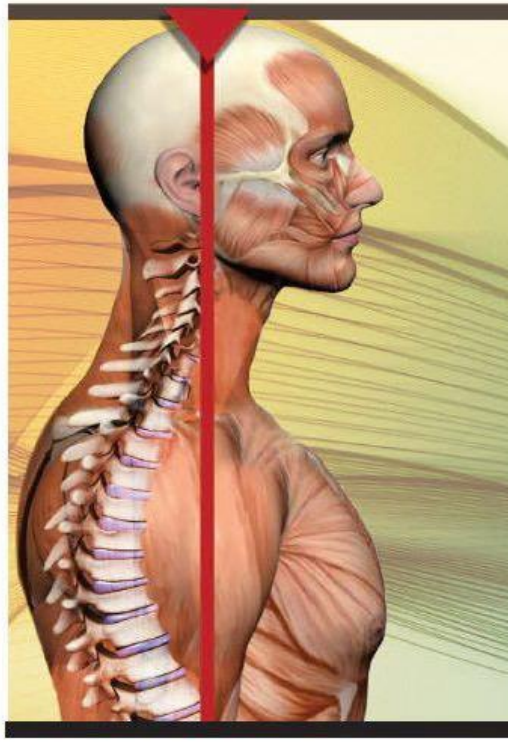
Neck pain and headaches

- A common cause of neck pain is posture
- Chin poking forward position
- Correction is easy.
- Before looking at other reasons, correct this first
- If there are other reasons like cervical instability, Chiari malformation etc – these need to be addressed

How Heavy is Your Head?

Wie schwer ist dein Kopf?

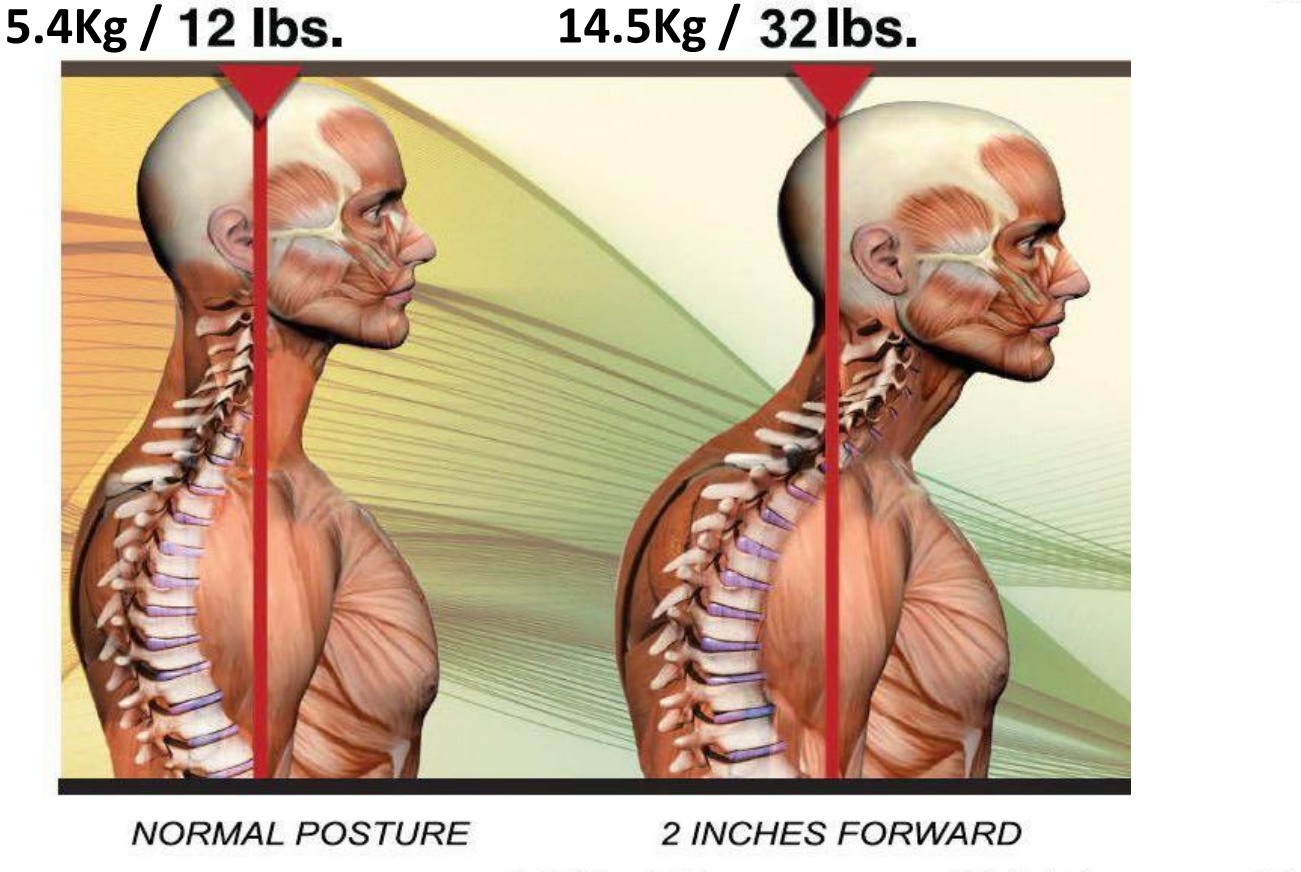
5.4Kg / 12 lbs.



NORMAL POSTURE

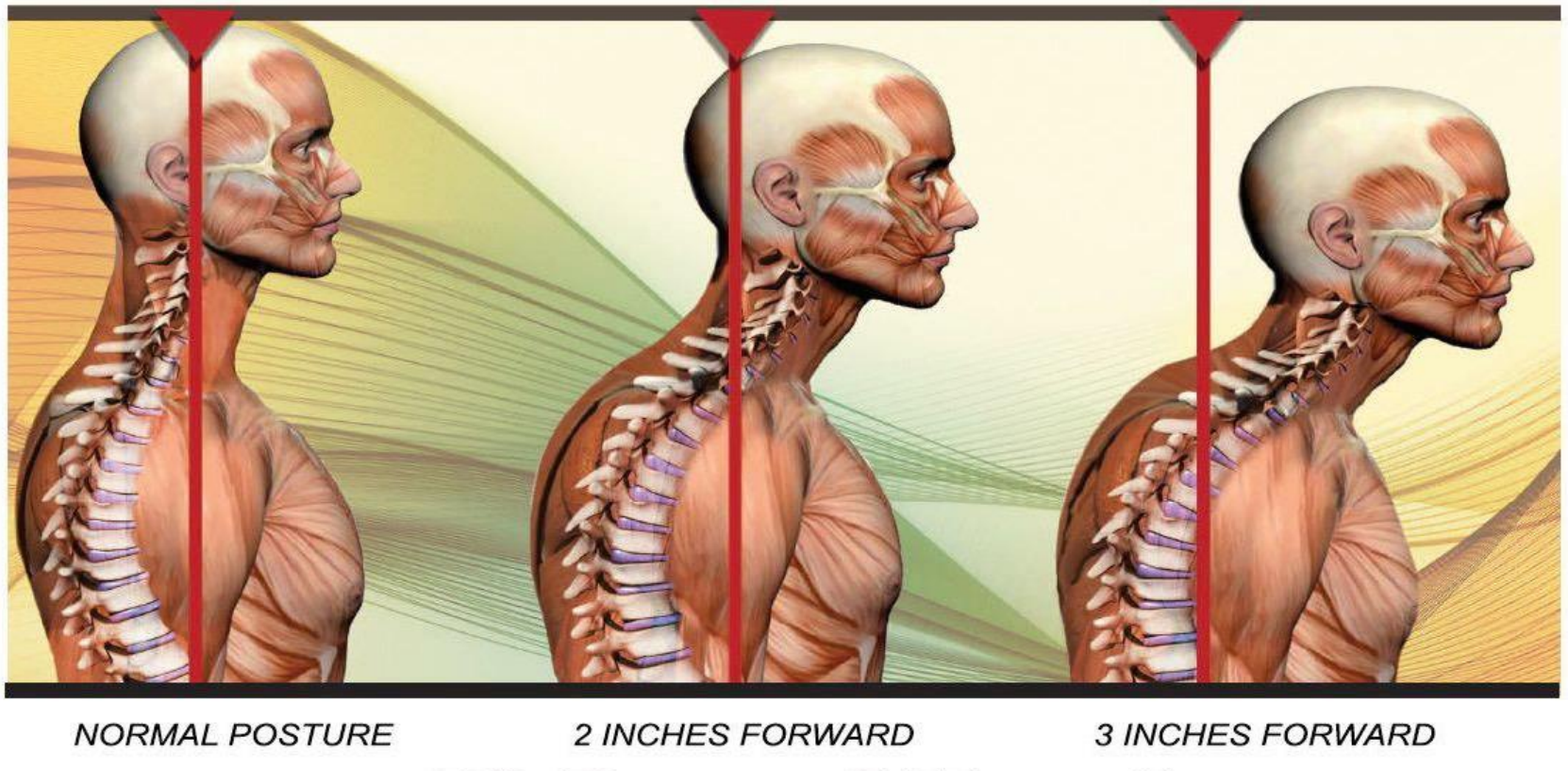
Wie schwer ist dein Kopf?

How Heavy is Your Head?



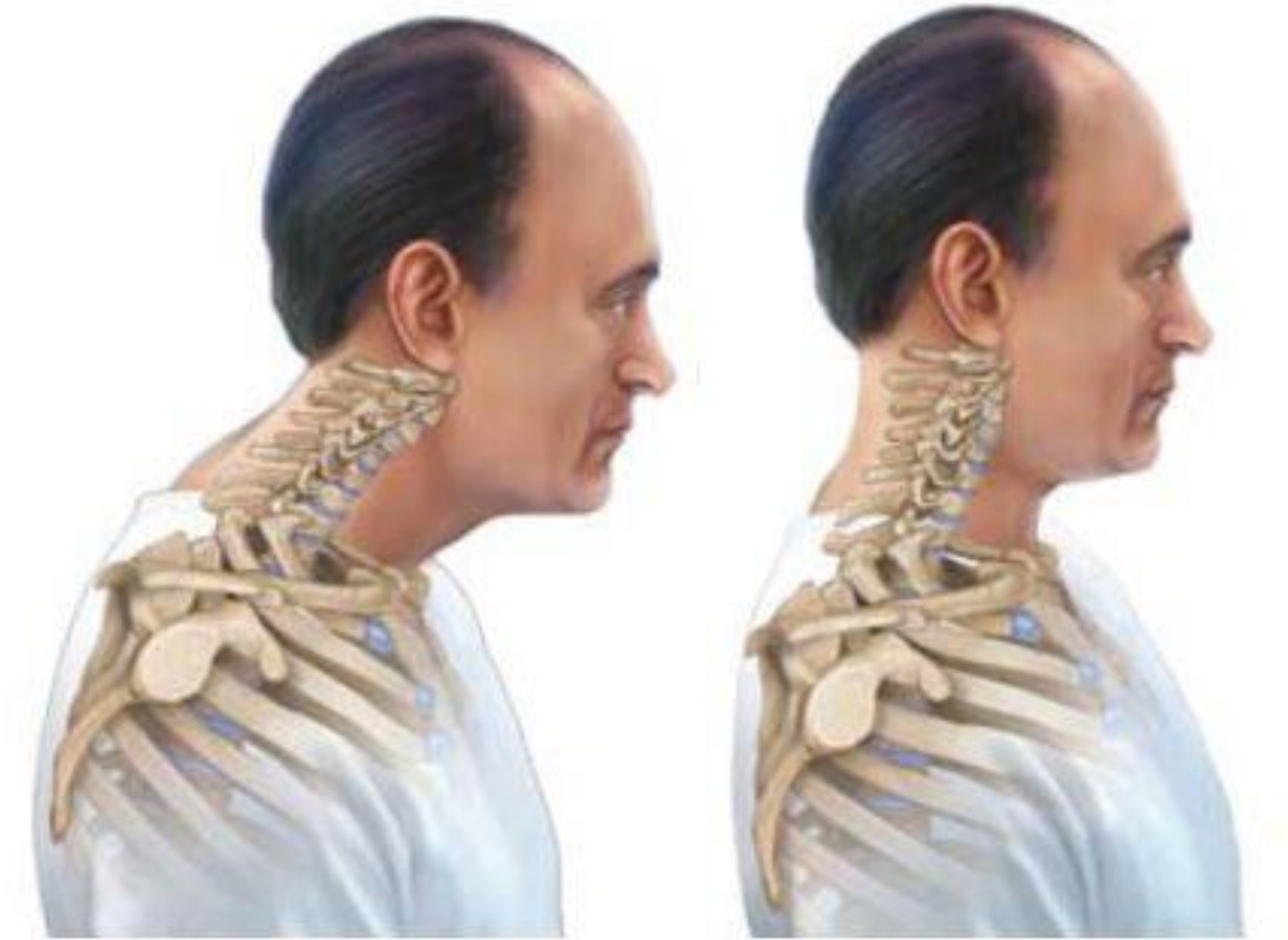
5 cm forward

5.4Kg / 12 lbs. **14.5 Kg / 32 lbs.** **19 Kg / 42 lbs.**



5 cm forward

7.6 cm forward



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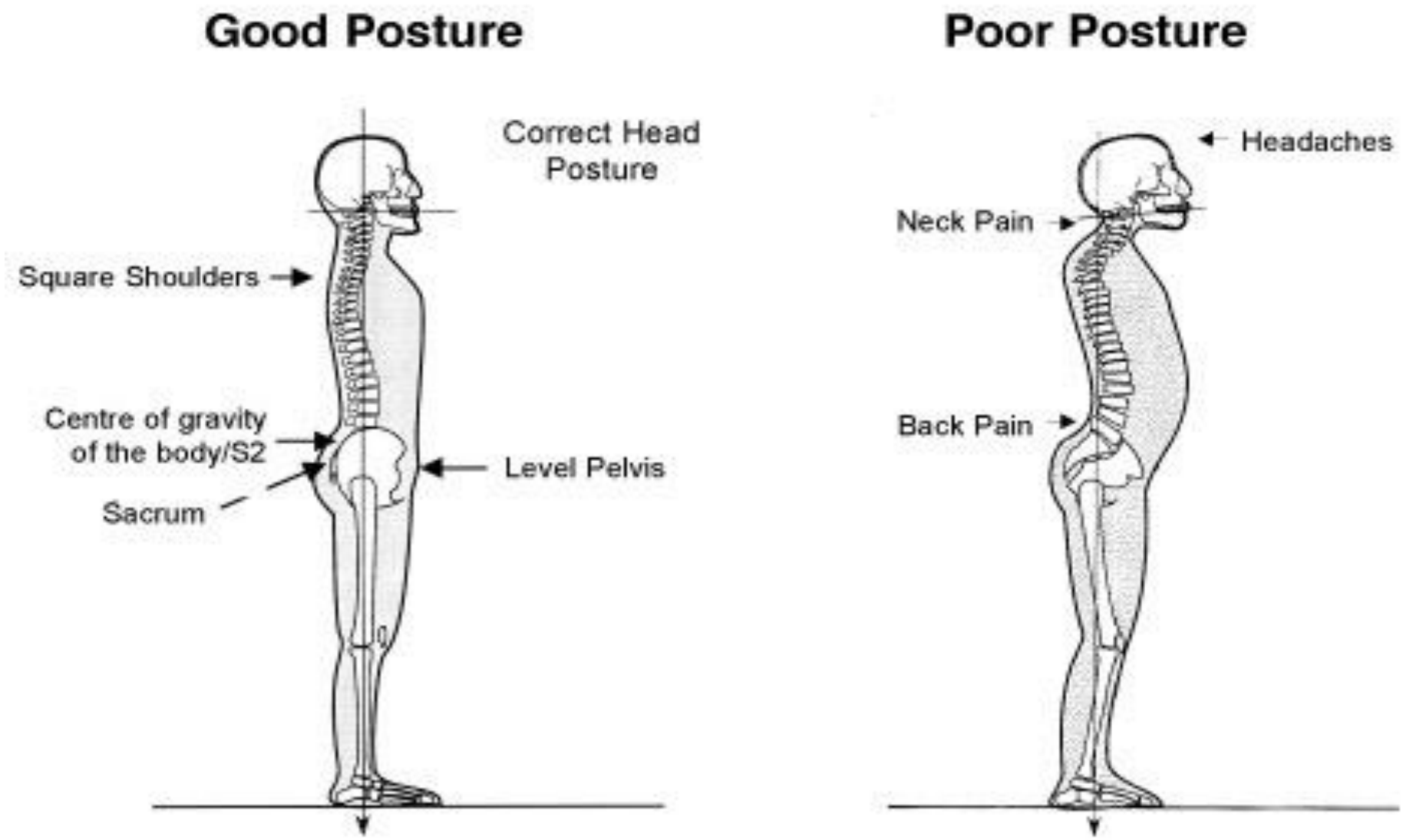
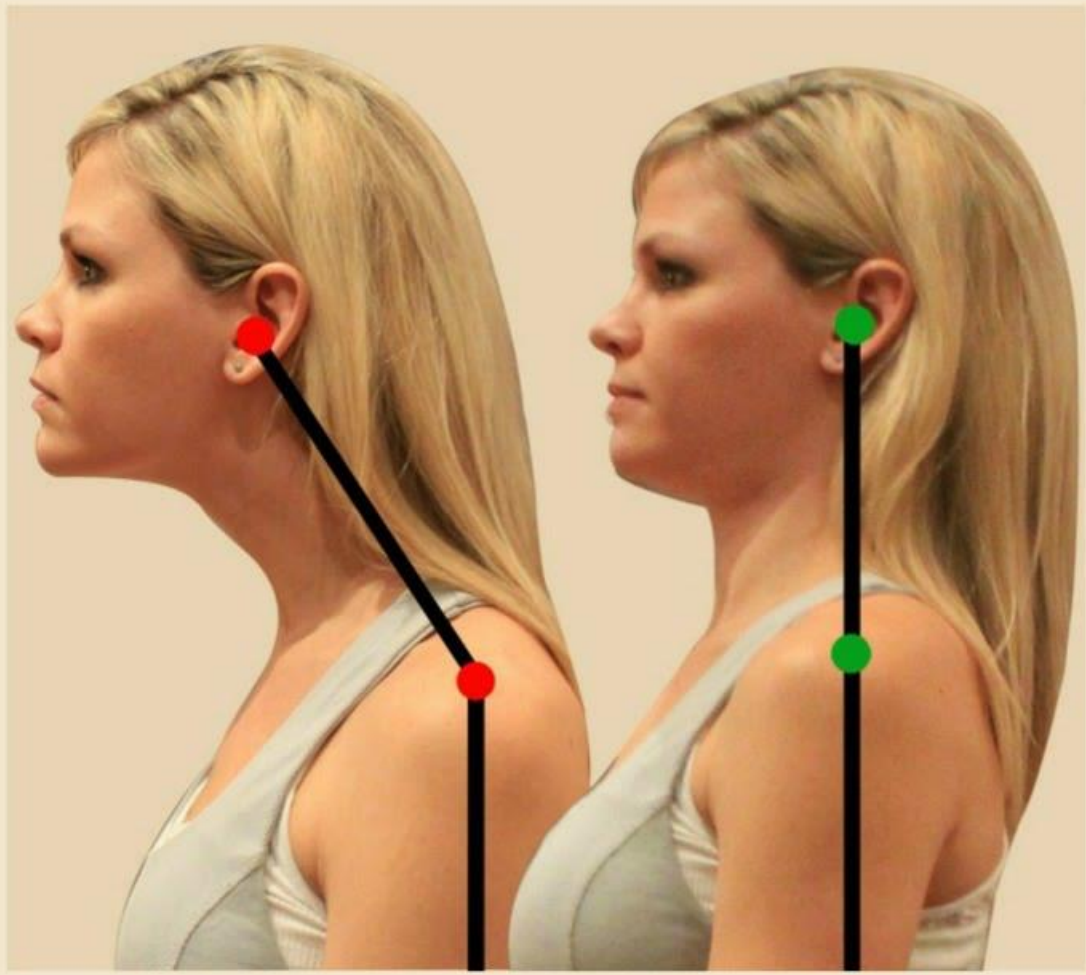
Pain from a poor posture



Common reasons for poor posture in EDS

- Vision – Blurry vision. Usually intermittent
- Postural Orthostatic Intolerance (POTS)
- Laxity of spinal ligaments
- Instability of the head on the neck (Cranio Cervical instability)



Managing neck pain and headaches from poor posture

- Place index finger in front of chin and push back head gently till ears are in line with shoulders
- Large monitor
- Post it note on monitor to remind you
- Vision correction
- Manage POTS

Lift the phone, don't drop your head!

Migraines

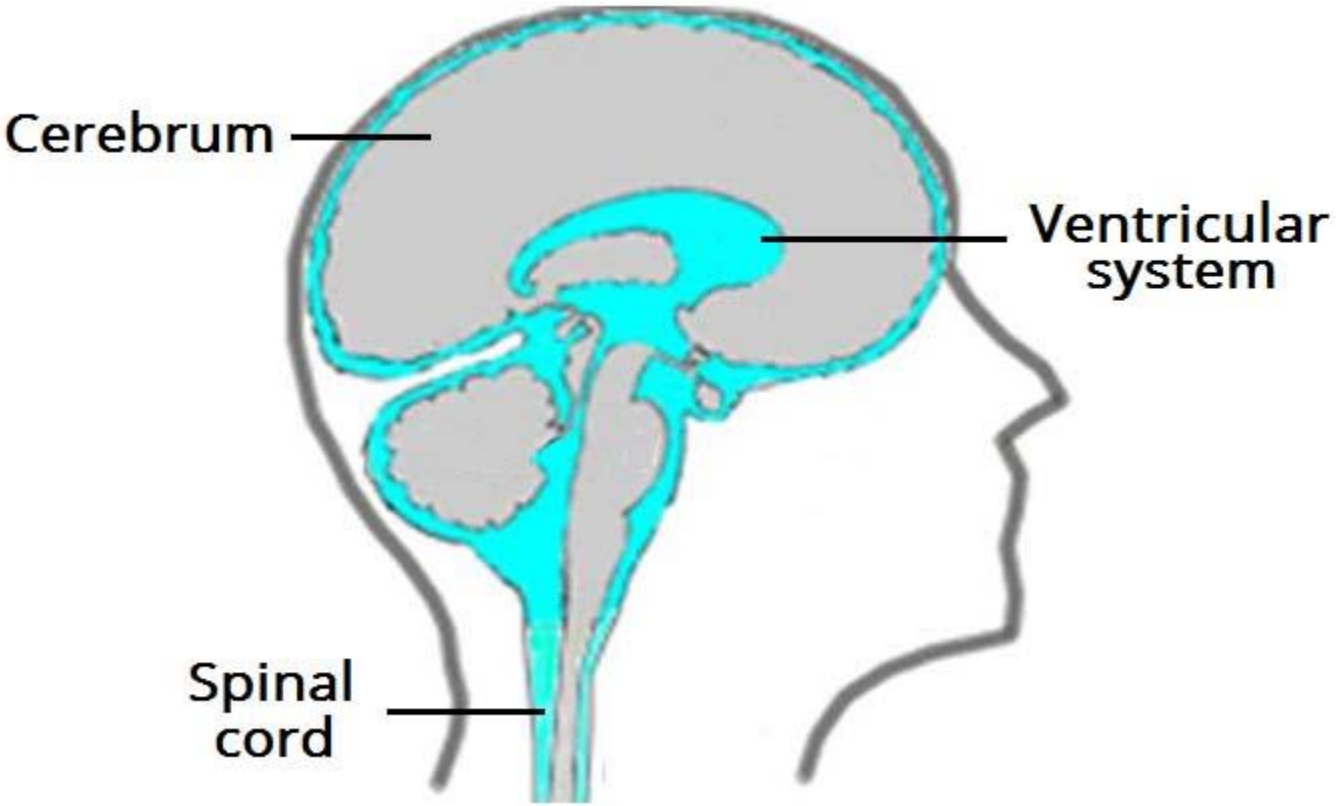
- Common in EDS
- Connection between EDS, MCAS, POTS, Dysautonomia
- Patent foramen ovale (a kind of hole in the heart)
- Strong link between diet and migraines.
- Good treatments for migraine.

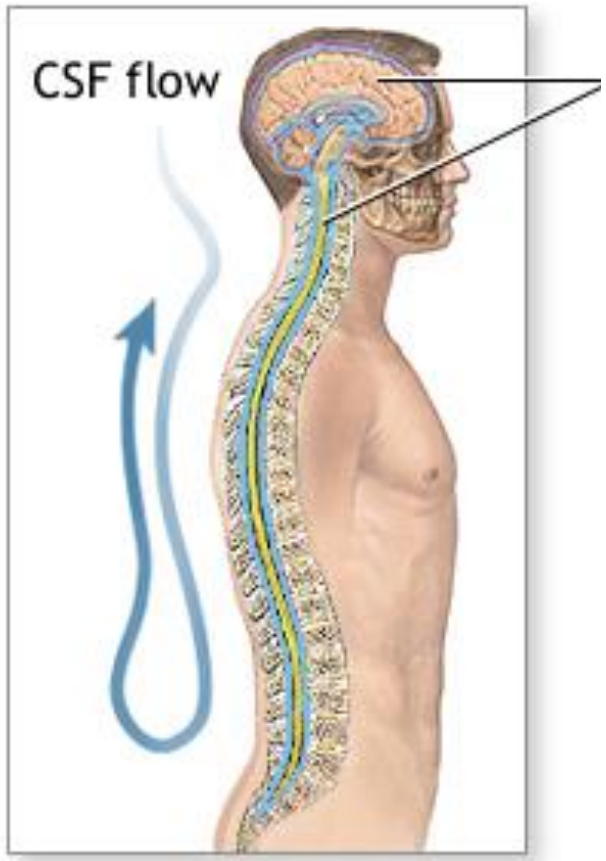
http://www.drtomaroexceptionaldentistry.com/headaches.html

Headaches – Idiopathic Intracranial Hypertension (IIH)

- Also known as pseudotumor cerebri
- Raised pressure inside the head
- Visual disturbances
- Photophobia (sensitivity to light)
- Ringing in the ears (tinnitus)
- Maybe because of narrowing of blood flow (venous sinus stenosis)
- Diagnosis: spinal tap, eye exam, MR venography
- Treatment: weight loss, medicines to decrease CSF, VP shunt, stent

Spontaneous CSF leak





Upper back pain

Upper back pain in EDS

- Usually poor posture
- Shoulder instability
- Rib subluxation
- Repetitive Strain Injury – doing a repetitive task with hands or arms (typing, vacuuming)
- In women, it can be the weight of the breast tissue dragging the upper torso forward and the muscles of the upper back attempting to stabilize the torso

Upper back pain in women with EDS

- Sports bra with:
- racer back (cross straps).
- Wide straps.
- Front closure
- Proper fitting – recommend getting it done professionally.
- May have to consider reduction mammoplasty (Breast reducion) in severe intractable upper back pain

High Racer back – Posture bra

Compression garments to improve proprioception

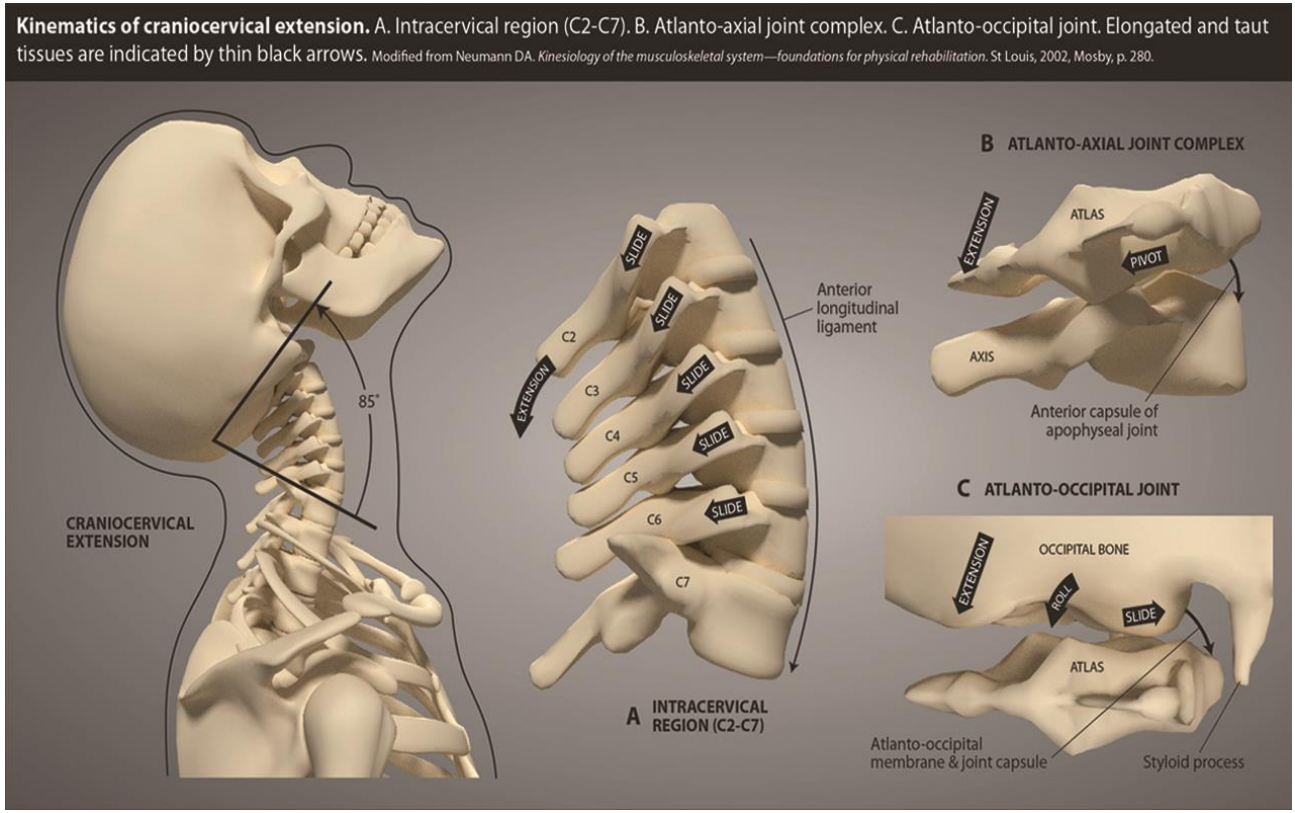
Neck

Cervical spine (Neck) issues in EDS

- Cranio Cervical Instability
- C1-C2 instability
- Lower Cervical kyphosis
- Cervical disc degeneration (commonly at C4-C5 and C5-C6)
- Chiari malformation

Cranio Cervical instability in EDS

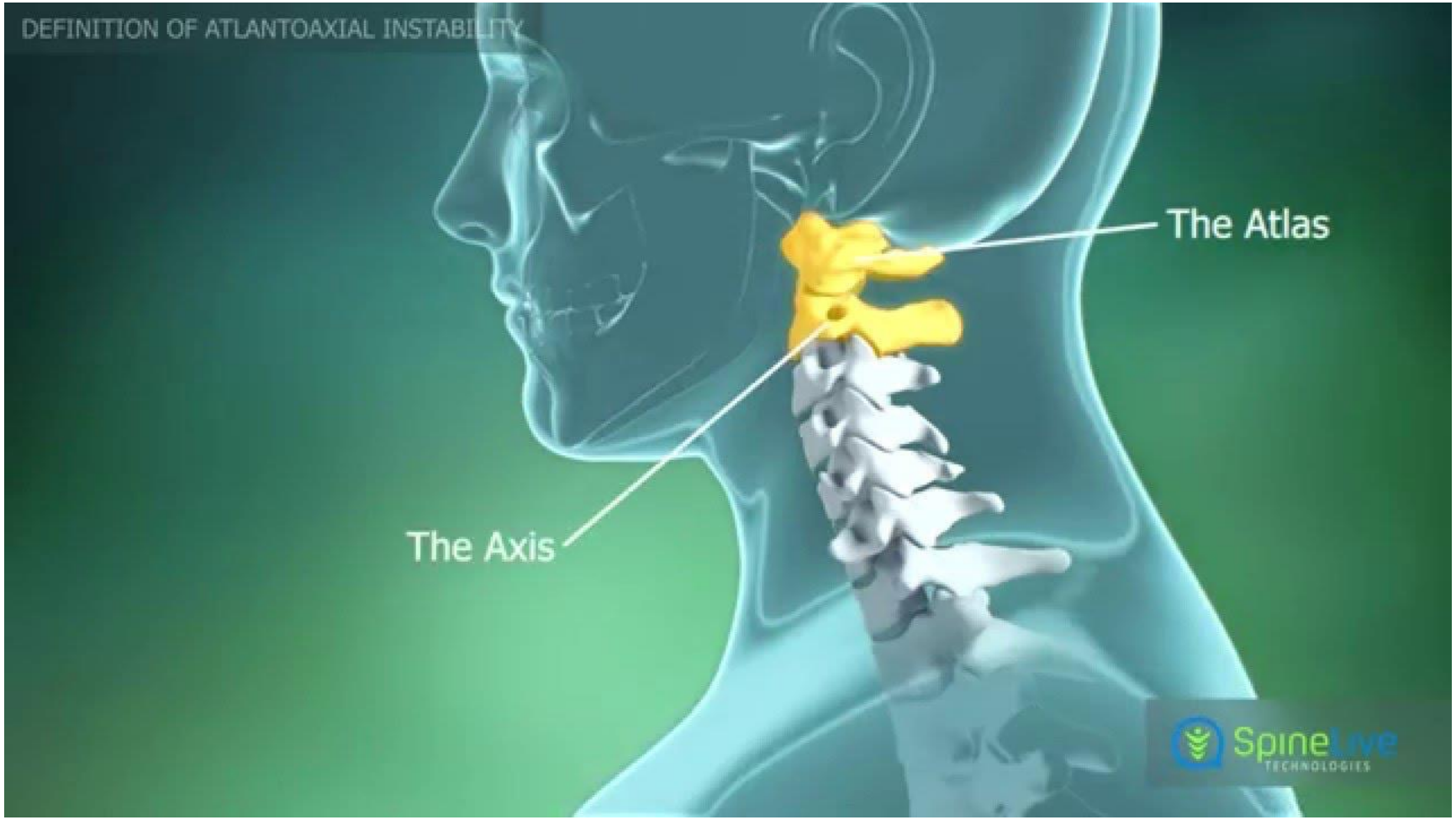
- The neck is stabilized by ligaments
- Laxity of the ligaments causes the joints in the neck to move more
- Excessive movement of the joints in the neck causes cranio cervical instability



Cranio Cervical instability (CCI) – Upper cervical (neck) – CO to C2

- Neck pain / stiffness
- Headaches
- Dizziness
- Paresthesia to face
- Fatigue
- Poor sleep
- Tinnitus (ringing in ears)
- Nausea
- Poor vision
- Anxiety
- Lightheaded
- Poor balance
- Difficulty swallowing

Atlanto Axial instability



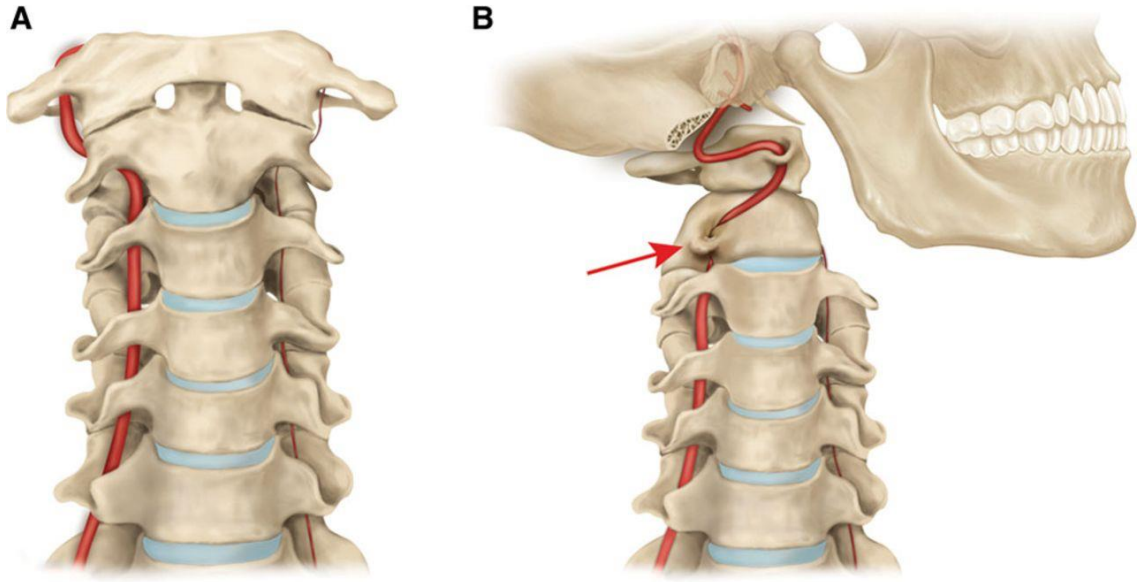
https://www.youtube.com/watch?v=4swxqxpW0Oc

Atlanto Axial instability (AAI)

- 50% of patients with Rheumatoid arthritis have AAI
- Also common in Marfan's syndrome
- It is one of the most mobile joints in the body (allow for the head to move in all sorts of angles)
- In EDS – ligament laxity (transverse and alar ligaments)
- As the C1 rotates over C2 to 35 degrees – the vertebral artery on the opposite side gets kinked
- At 45 degrees the opposite vertebral artery is completely occluded

Vertebral artery compression with rotation

- Tinnitus (38%)
- Fainting (24%)
- Blurred vision (19%)
- Headaches
- Difficulty swallowing
- Symptoms improve with neck brace
- Rotational MRI of neck



Stroke July 2013, Volume 44, Issue 7

Atlanto Axial instability

- Neck brace
- Physical therapy to strengthen neck muscles
- Avoid activities that provoke exacerbation
- Surgical fusion if all else fails.

Cranio Cervical Instability

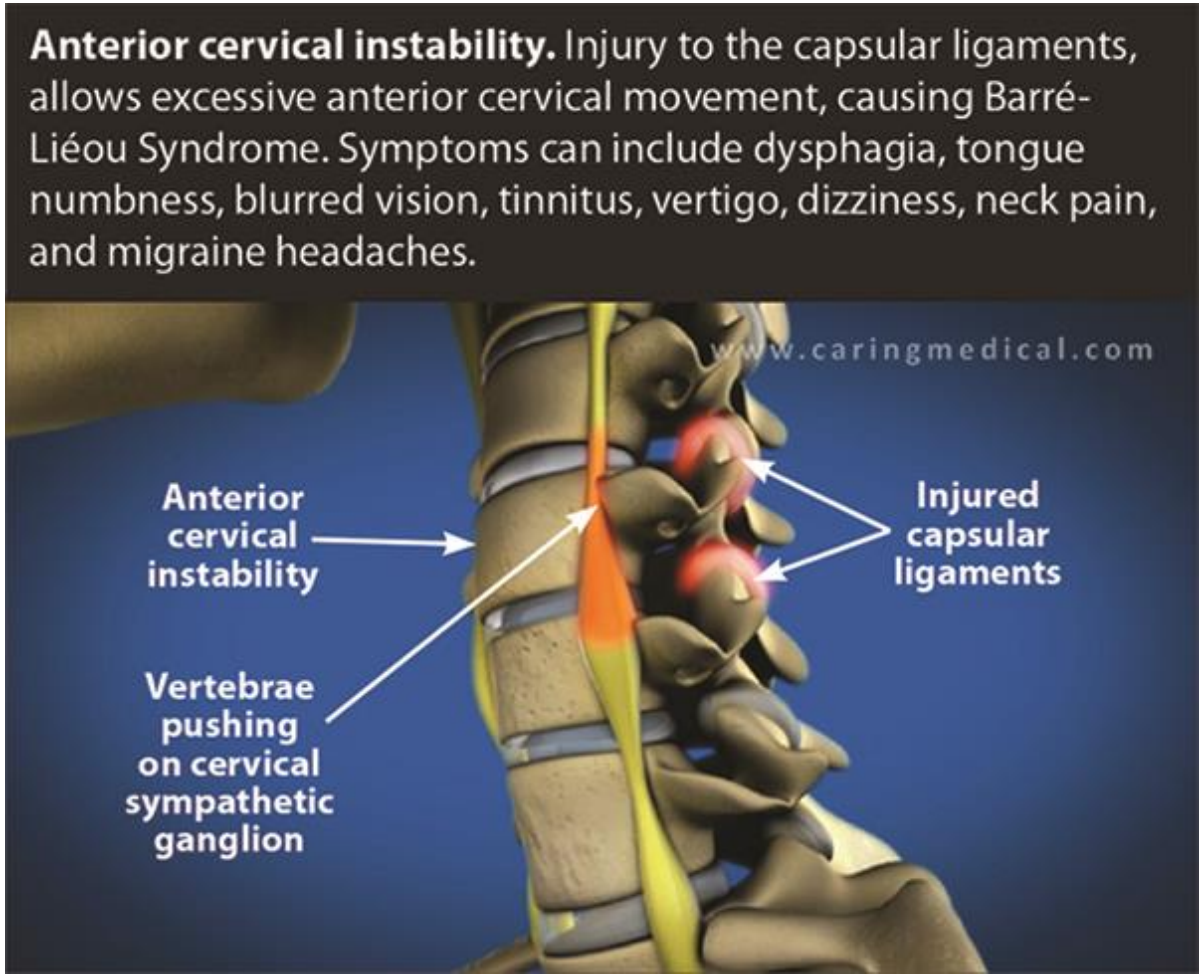
- The ligaments from the skull to the spine are incompetent
- Laxity of the ligaments causes nerve injury
- There is deformation of the brain stem (lower end of the brain) and the spinal cord
- Blood flow is altered
- CSF flow is altered
- Basilar invagination or ventral brainstem compression

Cranio Cervical instability (CCI) – Lower cervical (neck) – C3 to C7

- Muscle spasms
- Crepitation (cracking sensation)
- Neck pain
- Tingling and numbness in fingers

Barrie – Lieou syndrome

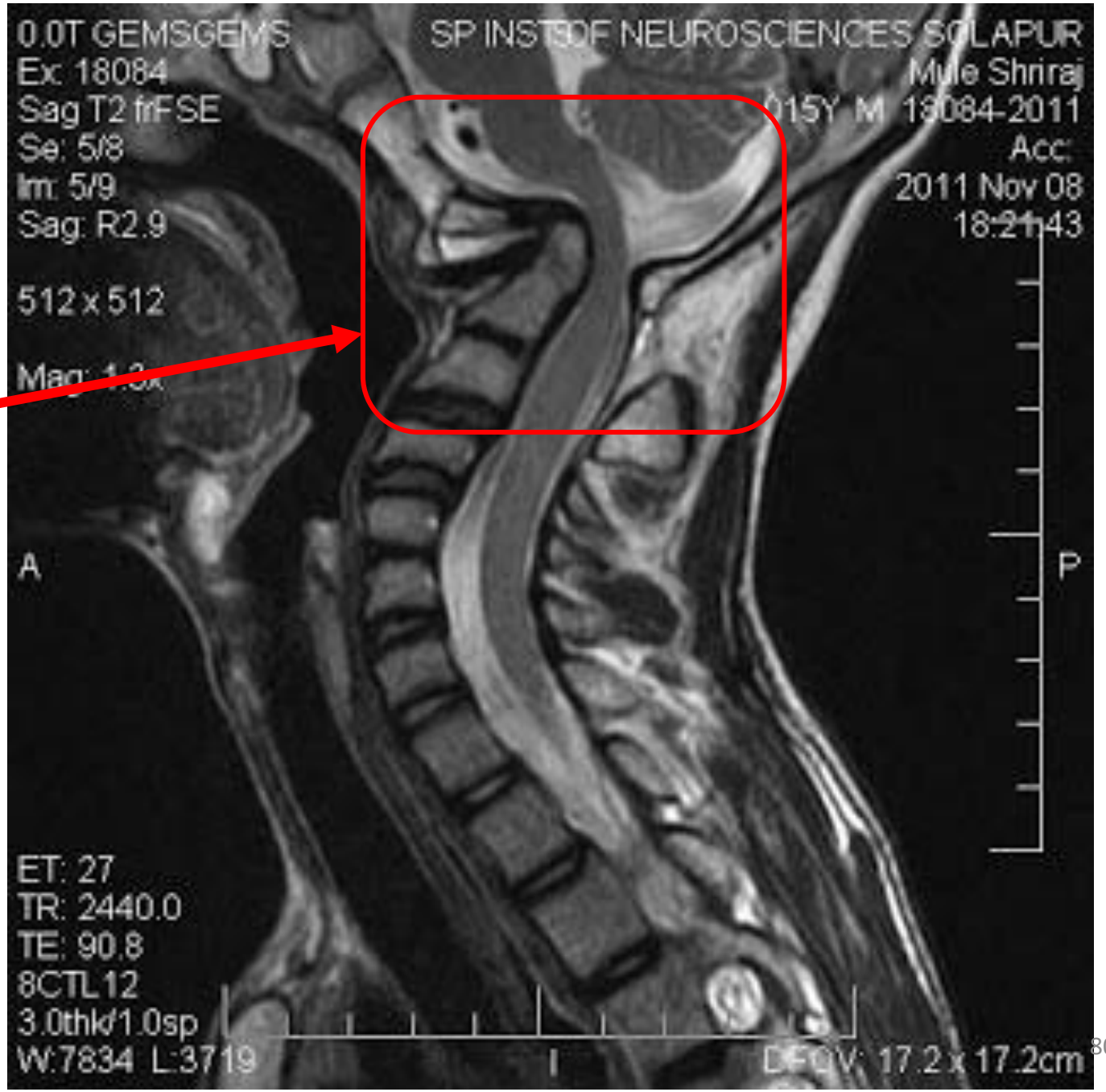
- Cervical instability pushing on the autonomic nerves
- Difficulty swallowing
- Tongue numbness
- Blurred vision
- Tinnitus
- Dizziness
- Neck pain
- Headaches



Ross Hauser, MD, Caring Medical

Basilar Invagination

- C2 pressing against the brain stem causing a narrowing of the foramen magnum



http://www.neuroradiologycases.com/2012/01/basilar-impression-bi.html

Basilar Invagination

- Symptoms are more apparent when the head is bent backwards
- Weakness of arms and legs
- Tingling in arms and legs
- Altered vision, hearing
- Neck pain
- Confusion
- Difficulty swallowing or talking
- Breathing problems

Imaging for Cranio Cervical Instability

- Need functional imaging technology
- Static pictures are not helpful
- Functional computerized tomography (fCT scan)
    - **Flexion.**
    - **Rotate neck left 90 degrees.**
    - **Rotate neck right 90 degrees.**
- Functional MRI (fMRI)
- Digital motion x-ray (DMX)

Cranio Cervical instability in EDS – MRI scan findings

- These measurements have to specifically asked for when getting an MRI.

1. Clivo-axial angle (normal 145 to 160 degrees)
2. Harris Measurement (instability if > 12mm(
3. Grabb, Mapstone and Oakes measurement (> 9mm suggests high risk of ventral brainstem compression)

Cranio Cervical Instability - management

- Mild to moderate:
  - Neck muscles strengthening exercises
  - Hard cervical collar (Vista Aspen collar)
  - Prolotherapy – Hackett-Hemwell prolotherapy

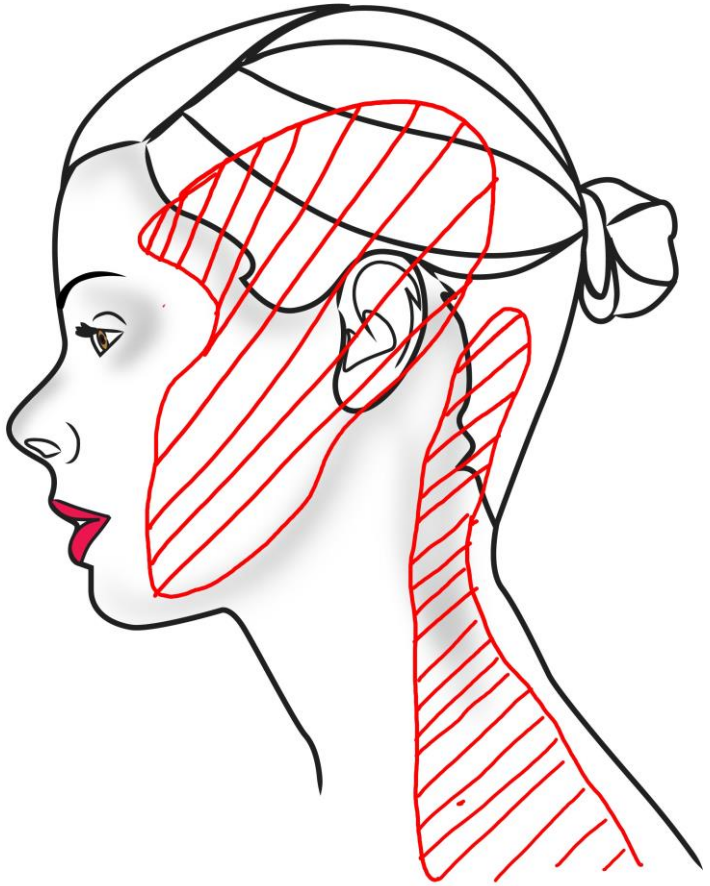
- Severe Instability:
  - Surgical fusion

TMJ Pain

Temporo Mandibular Joint Dysfunction

https://www.google.com/search?q=headaches+from+tmj&source=lnms&tbm=isch&sa=X&sqi=2&ved=0ahUKEwja_6mZ8aPTAhXD4iYKHclFB90Q_AUICCgD&biw=1025&bih=460#imgdii=auZ5m7XkpfECaM:&imgrc=cKJWId5mZ9OeNM:

Temporo-Mandibular joint pain



TMJ Pain

- Very closely related to neck issues
- Clicking noises
- Clenching, grinding
- Pain with chewing
- Difficulty opening mouth wide (eating an apple)
- Jaw locking up

Temporo-mandibular joint dysfunction (TMJ)

- Present in 70%
- Treatment: avoid excessive mouth opening, caution when yawning,
- orthodontist specializing in TMJ
- Avoid over the counter mouth guards

Dental issues in Ehlers Danlos Syndromes

- Teeth: weak and thin enamel, prone to cavities
- Gums: periodontal gum weakness, gingivitis, easy bleeding, delayed healing after surgery, tissue breakdown after surgery (tooth extraction), gum recession and pocketing
- Poor tooth stability, crowding of teeth
- Local anesthetic may not work or onset will be delayed

Chiari Malformation

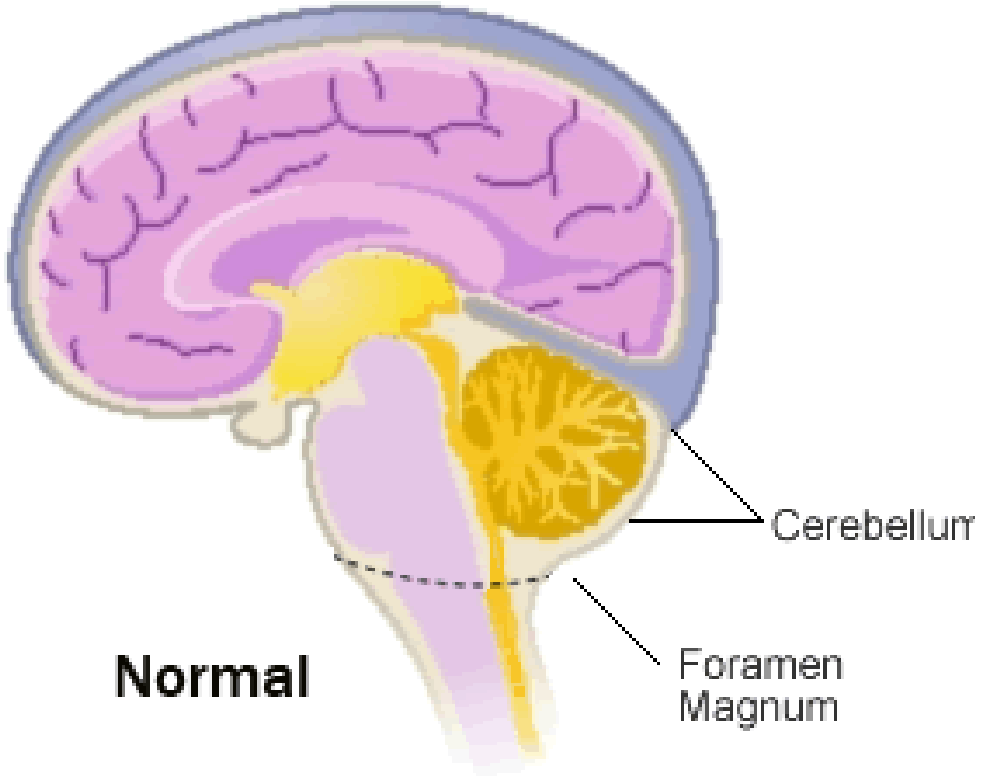
Symptoms of Chiari Malformation

- Neck pain
- Balance problems
- Numbness or paresthesia's to arms or legs
- Dizziness
- Difficulty swallowing
- Poor Hand co-ordination
- Ringing or buzzing in the ears
- Hearing loss
- Nausea, vomiting
- Headaches made worse by coughing or straining
- Pressure headaches in the back of the head (suboccipital)
- Muscle weakness
- Vision problems

Complex Chiari

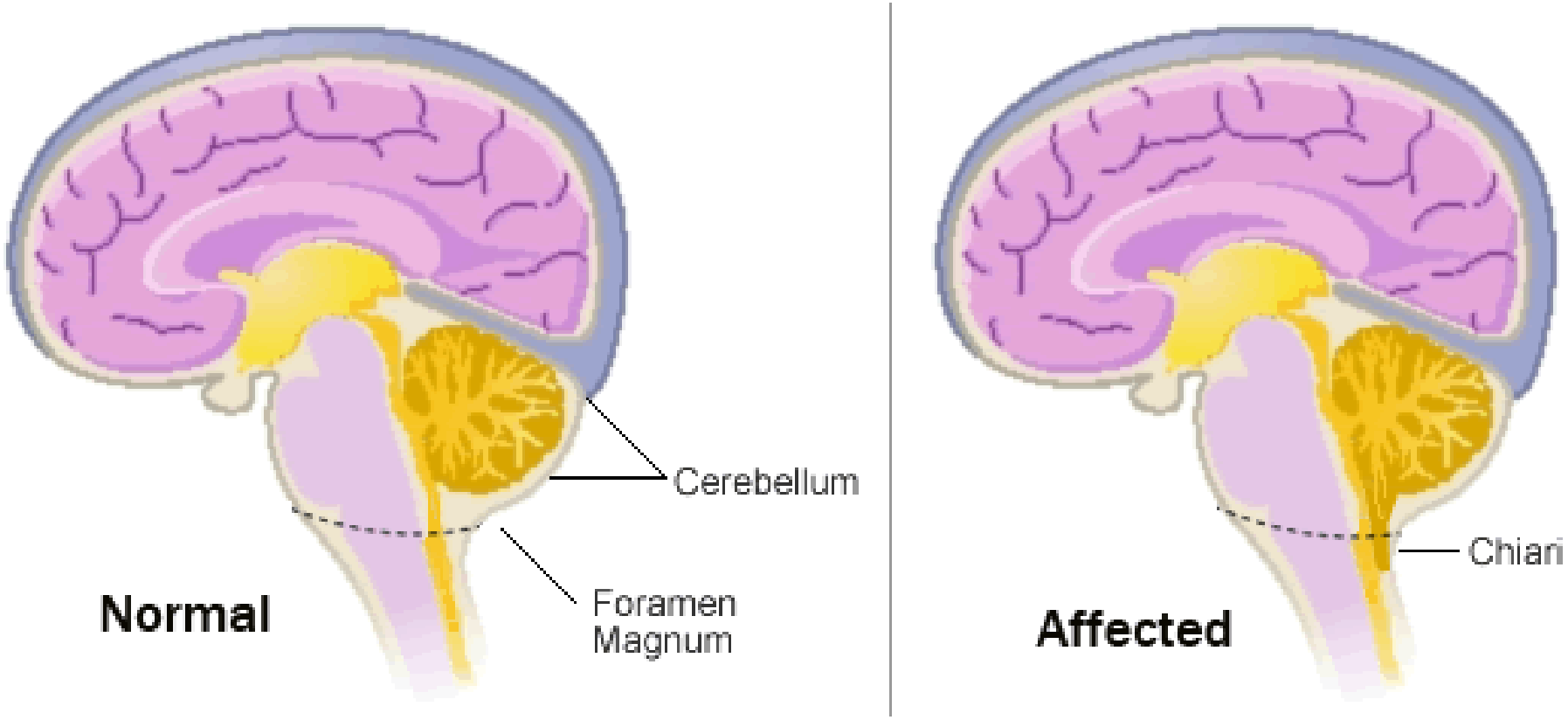
- Sleep apnea
- Dysautonomia /POTS
- Associated with cranio-cervical instability or basilar invagination

Chiari malformation



http://www.craniofacial.vcu.edu/conditions/chiari.html

Chiari malformation



http://www.craniofacial.vcu.edu/conditions/chiari.html

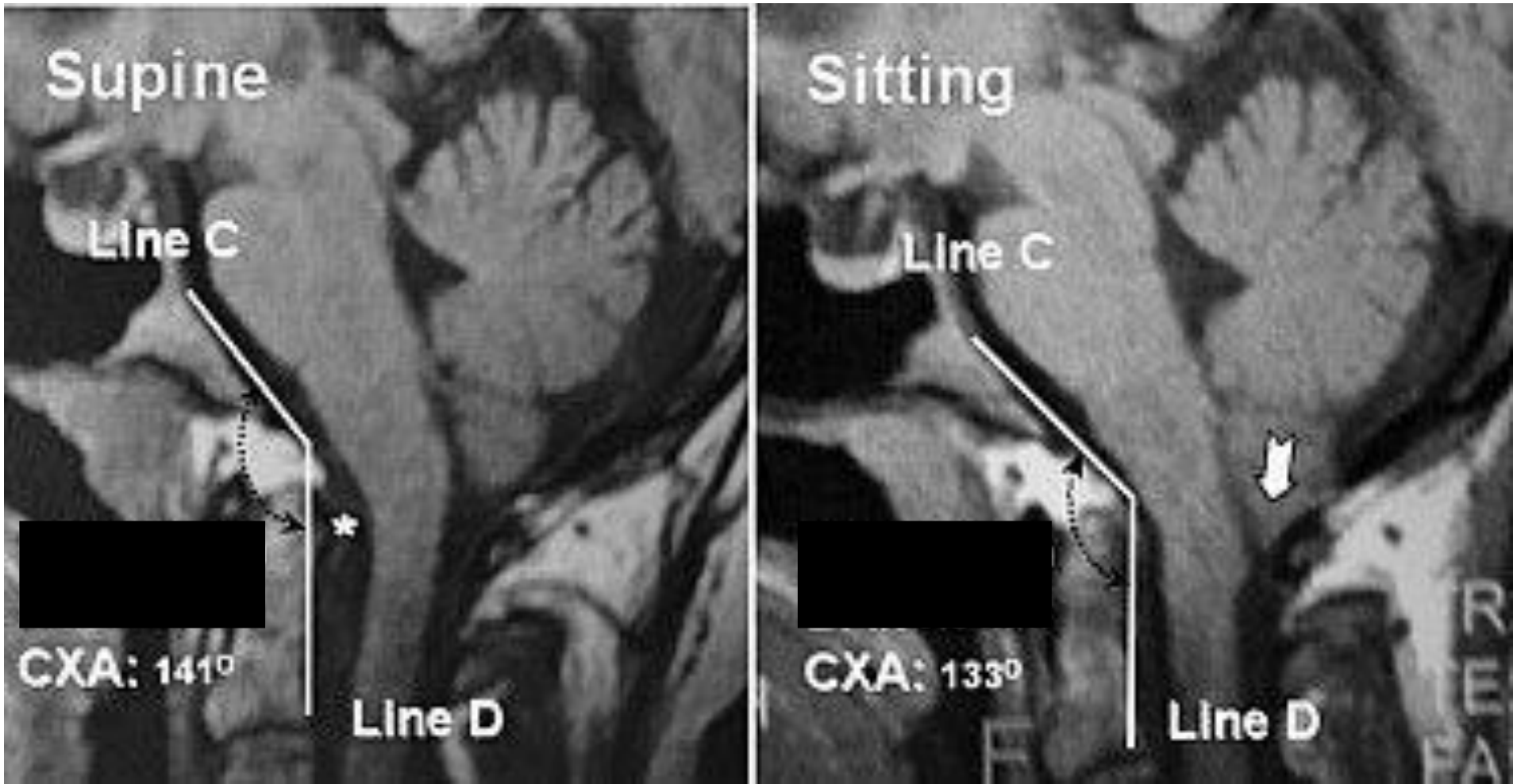
Chiari Malformation and EDS

- Higher incidence of Chiari in EDS
- Cranial settling (loose ligaments)
- Posterior gliding of condyles
- Reduction of the clivus-axis angles, clivus atlas angle, atlas-axis angle.

Thomas H. Milhorat, M.D.,1 Paolo A. Bolognese, M.D.,1 Misao Nishikawa, M.D.,1 Nazli B. Mcdonnell, M.D., Ph.D.,2 And Clair A. Francomano, M.D.3 Syndrome of occipitoatlantoaxial hypermobility, cranial settling, and Chiari malformation Type I in patients with hereditary disorders of connective tissue. J Neurosurg Spine 7:601–609, 2007

Cranial Settling in EDS- Deformative stresses on the brain stem, lower cranial nerves, spinal cord

Clivo-axial angle normal 140^0



MRI for Chiari Malformation in EDS

- MRI in upright position – Important
- These measurements have to specifically asked for when getting an MRI.

1. Clivo-axial angle (normal 145 to 160 degrees)
2. Harris Measurement (instability if > 12mm(
3. Grabb, Mapstone and Oakes measurement (> 9mm suggests high risk of ventral brainstem compression)

Pain in the back

Spinal Instability

- The spine is made up of multiple joints – held together by ligaments and muscles.

- Spinal instability with reflex muscle spasms may happen at any level

Spinal Instability

- Thoracic spine – subluxations where the ribs meet the spine (costo—vertebral joints)
- Lumbar spine – subluxations of the facet joints.
- Sacroiliac joint pain (SI Joint) – maybe more from uneven posture or pain from joints in the legs
- Kyphosis (spine poking backwards), scoliosis (spine sideways)
- Maybe a symptom of Tethered Cord syndrome

Spinal pain

- If the pain is from the joints in the spine – postural correction, compression garments, muscle strengthening

- Steroid injections not very helpful but can be used in very select cases

Brace for lumbar and Sacroiliac joint

Tethered Cord Syndrome

Clinical symptoms

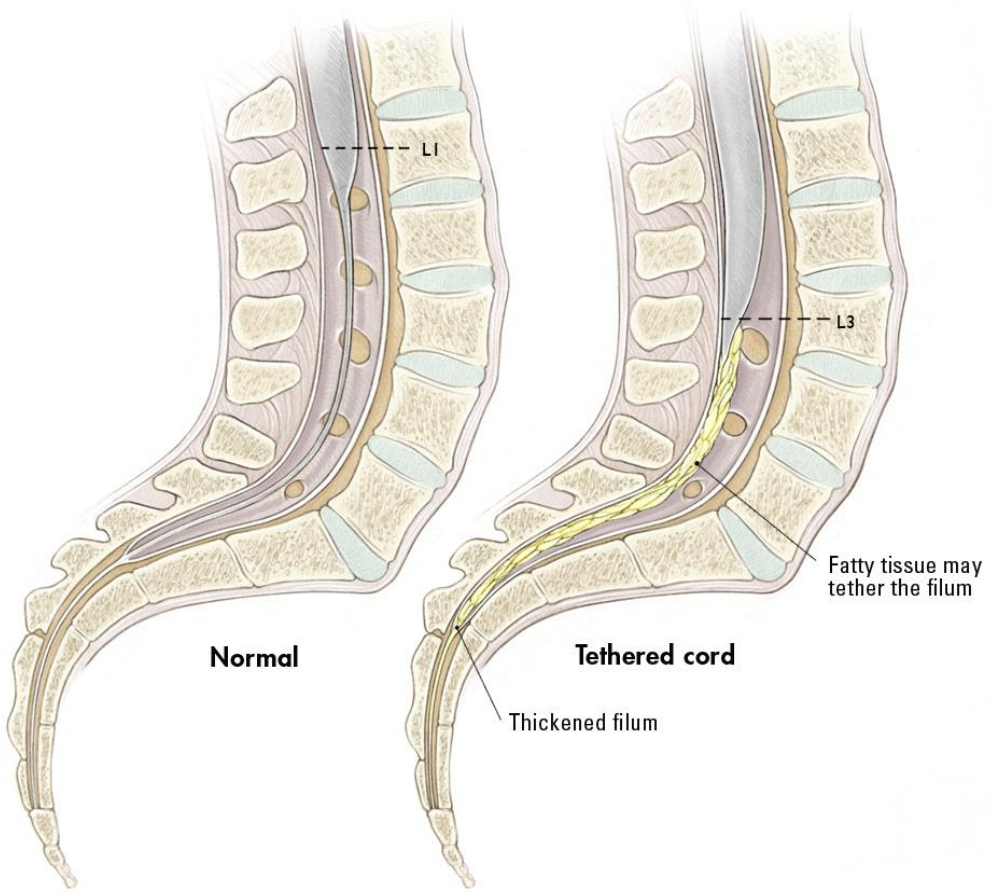
- Low back pain
- Neurogenic bladder
- Leg weakness and sensory loss
- Musculoskeletal abnormalities

Tethered Cord syndrome and EDS

- Tethered cord syndrome present in 14% of patients with Chiari Malformation
- Tethered cord syndrome present in 63% of patients with low lying cerebellar tonsils (i.e. these people did not quiet meet the criteria for Chiari)

- That means 77% of patients with EDS and Chiari symptoms may have Tethered Cord.

Tethered Cord Syndrome (TCS)



http://javid1985.hubpages.com/hub/Tethered-Spinal-Cord-Syndrome-What-You-Need-To-Know

Tethered Cord syndrome

- Aching, burning pain in low back, legs and feet.
- Weakness in legs
- Legs – heaviness, stiffness, tightness, cramps
- Tingling or numbness in pelvic area or legs
- Decreased sensation in the area between the legs
- History of toe walking

Tethered Cord Syndrome and EDS

- Check for Tethered cord if diagnosed with Chiari Malformation and vice versa
- Bladder problems:
- Urinary hesitancy
- Increased (decreased) frequency,
- Urgency
- Sense of incomplete emptying of the bladder
- Nocturia – going often at night
- Irregular stream
- More than 3 urinary tract infections in a year
- Incontinence

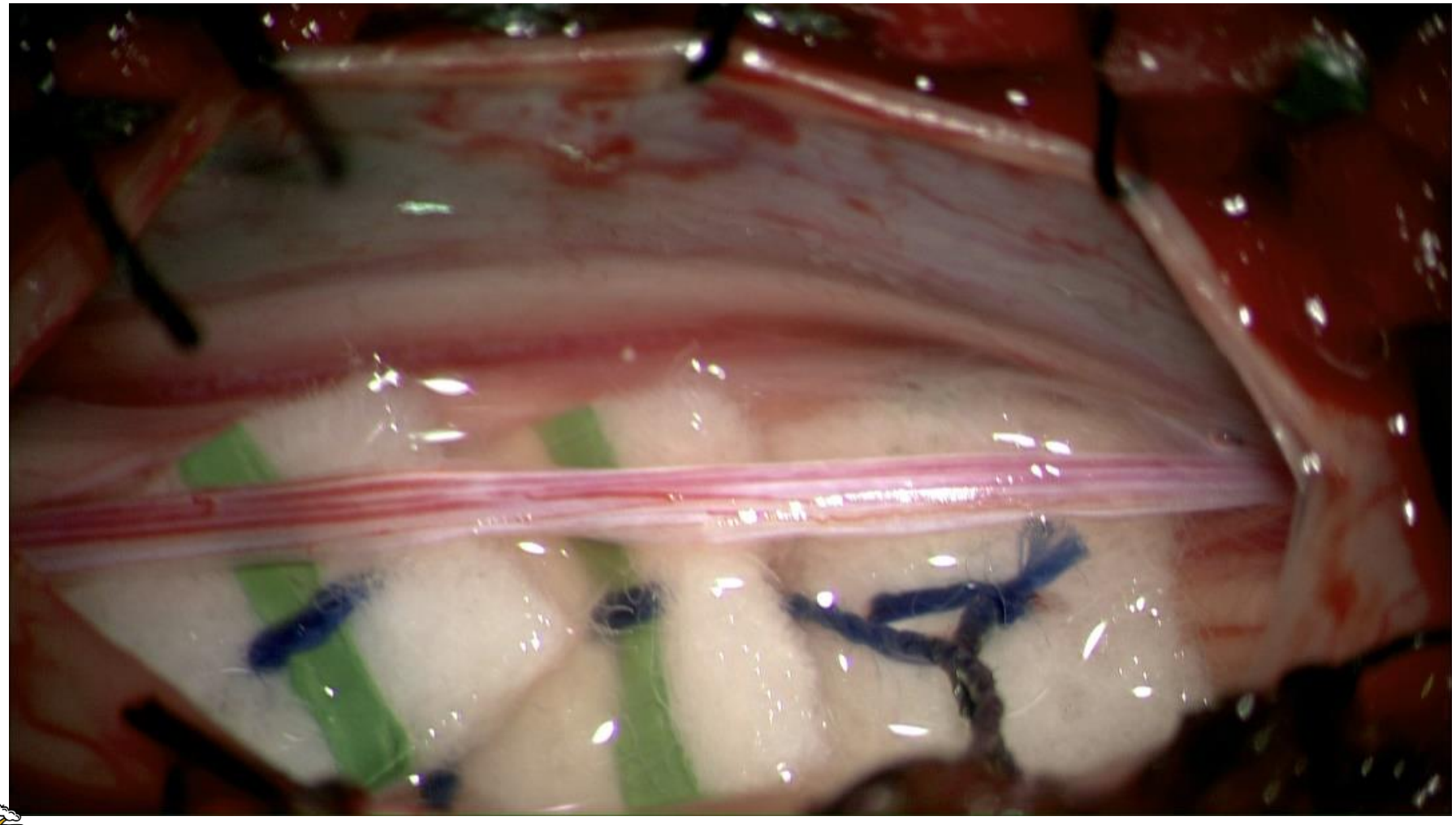
Tethered Cord Syndrome and EDS

- Weakness to legs with normal arm strength
- Scoliosis, kyphosis
- Ankle and foot deformities
- Ankle pronation
- Flat feet

Tethered Cord Syndrome and EDS

- MRI is NOT a useful tool for diagnosing TCS
- MRI may be done to rule out other problems
- Diagnosis is based on clinical history and examination
- A urodynamic study maybe helpful in case of urinary symptoms / neurogenic bladder

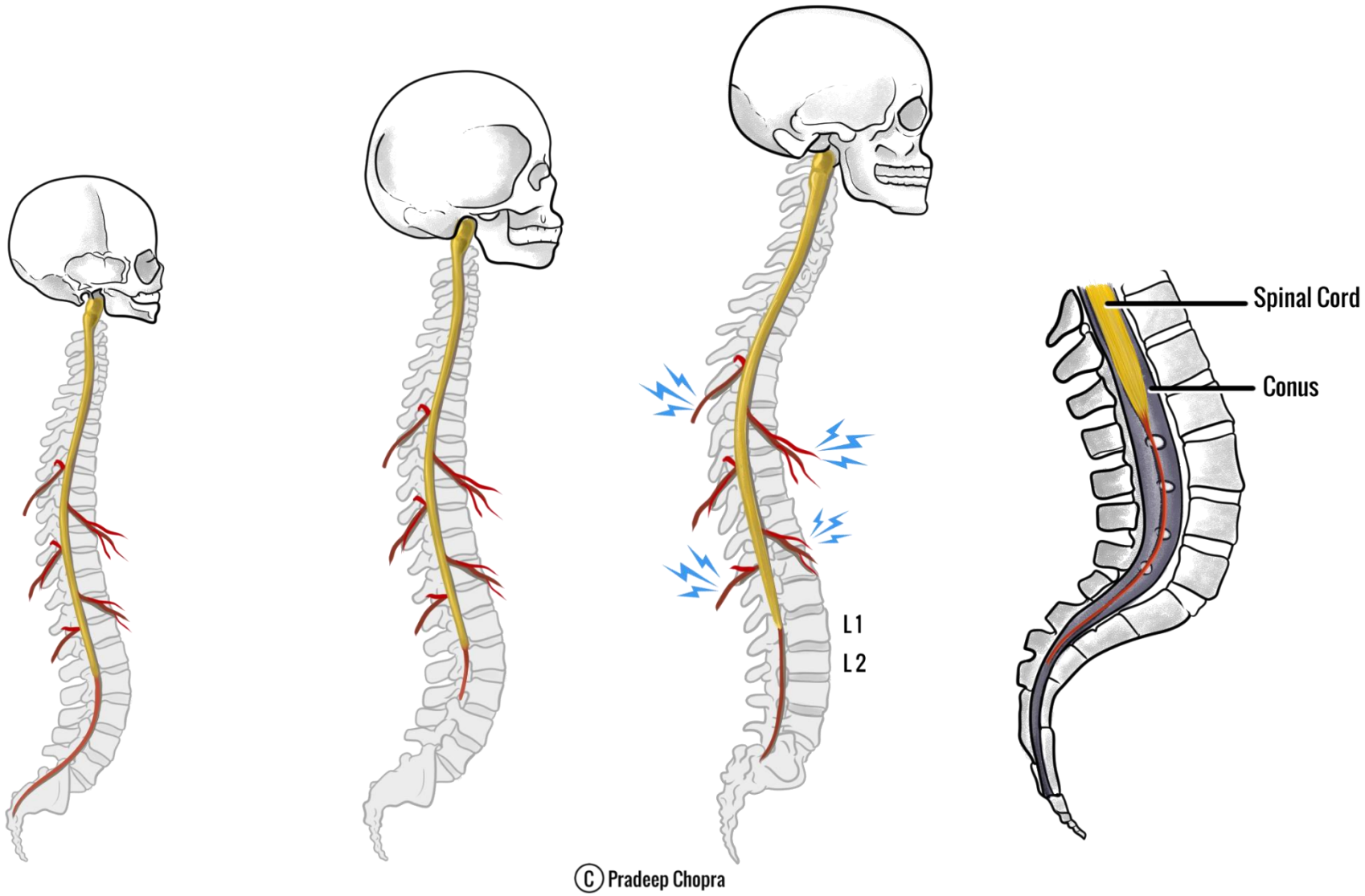
Intraop finding in TCS



BROWN Courtesy P Klinge, MD

Tethered Cord Syndrome (TCS)

- The spinal cord hangs freely in the spine, it slides up and down in a sheath (much like a sword in a sheath)
- In TCS the lower end is tethered to the bottom of the spine
- As we grow taller, the spinal cord gets stretched.


L1
L2
Spinal Cord
Conus
© Pradeep Chopra

Neurogenic bladder

- Increased frequency
- Urgency
- Sense of incomplete evacuation of bladder
- Incontinence to urine
- More than 3 urinary tract infections in a year

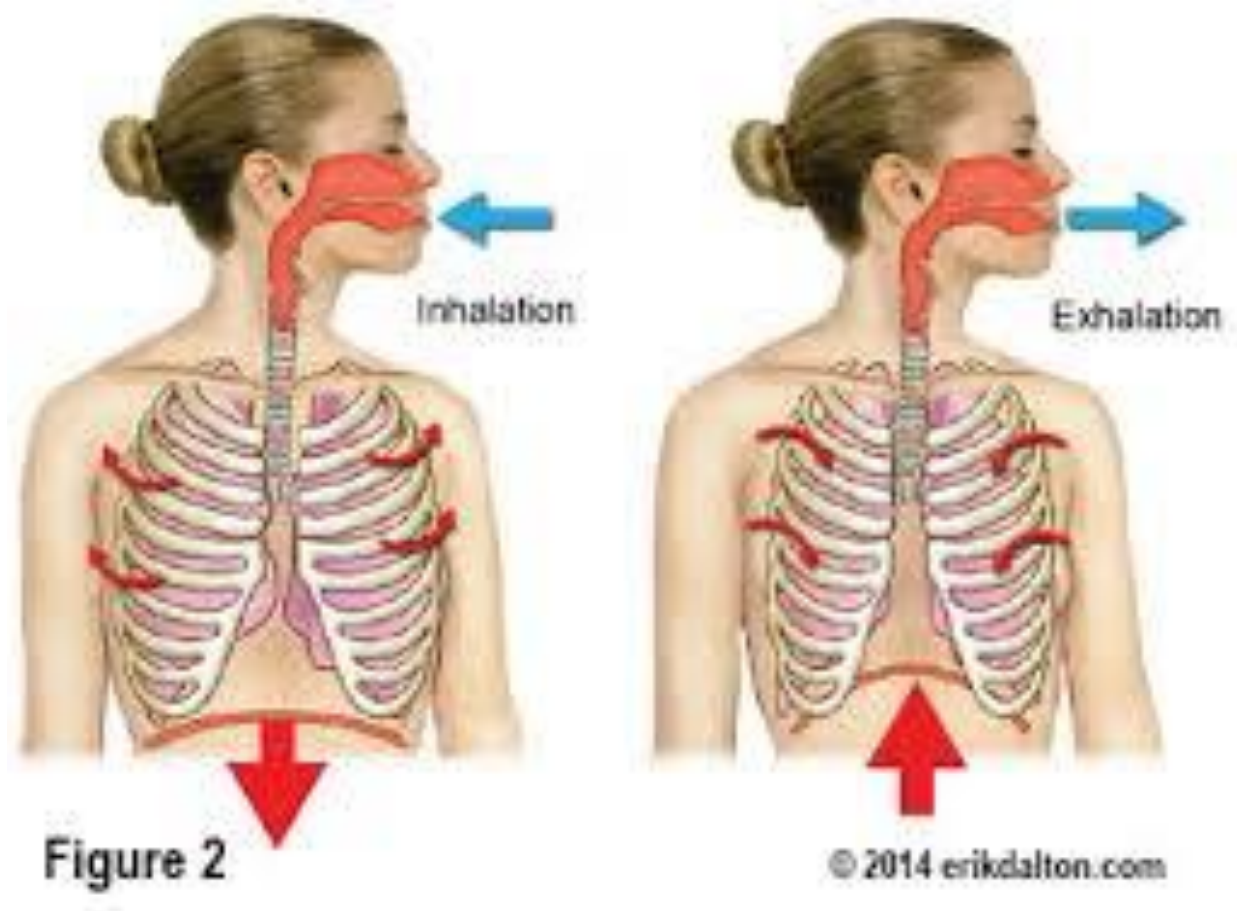
Tethered Cord Syndrome and EDS

- MRI is NOT a useful tool for diagnosing TCS
- Diagnosis is based on clinical history and examination
- A urodynamic study maybe helpful

Breathing in EDS

Breathing and rib pain

- Patients with EDS often complain of not being able to take a breath in or difficulty breathing
- Pain from ribs
- All the tests for heart and lungs are normal.
- Each rib has 3 joints in the back
- The diaphragm is an important muscle for breathing



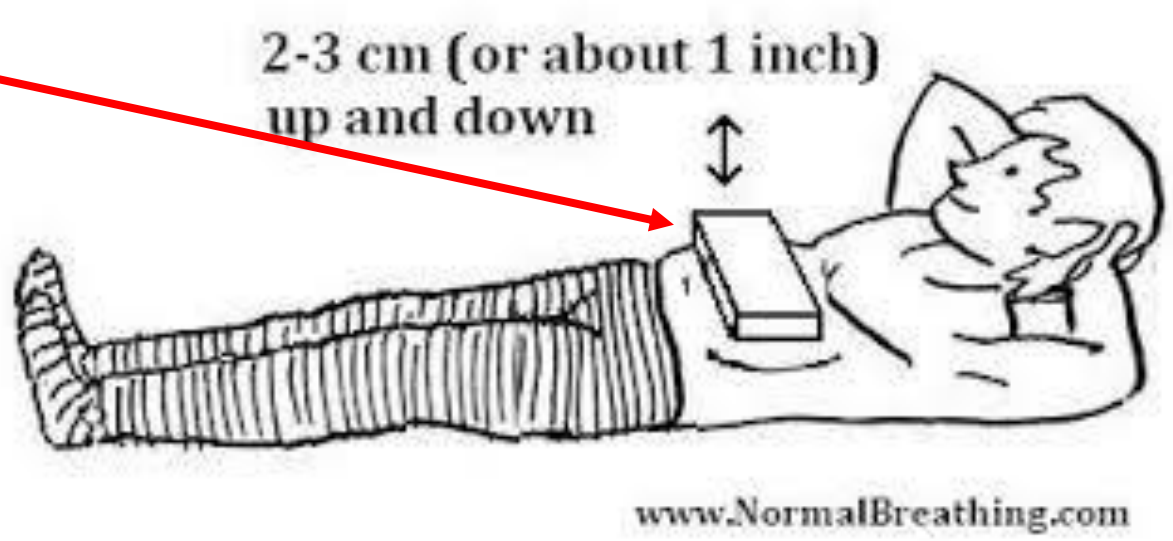
http://thecompleteherbalguide.com/entries/back-pain/breathing-and-back-pain/

Breathing and rib pain

- Loss of proprioception from the ribs, muscles of breathing and diaphragm gives a feeling of not having taken a full breath in or full breath out
- Similar to the uncoordinated movement of the rest of the joints in the body
- Some of the muscles of breathing are also part of the lower back

- Book or sand bag should be over the belly button

- Lie on your back
- Breathe in and breathe out for 20 minutes a day



http://www.normalbreathing.com/

Diaphragm release exercise

- Lie on your stomach on the floor
- Place a 1.5 inch rubber ball under your belly button
- Just lie comfortably in this position for 20 minutes.
- If you get uncomfortable before a minute, use a smaller ball.

Chest wall pain and rib subluxations

- Ribs form joints in the back
- Rib subluxations happen with uncoordinated breathing (remember poor proprioception), and poor posture
- Singing (high and low notes), wind instrument like a flute or recorder
- May help with chest muscle and rib pain and strengthening lower back

Pelvic pain

Pelvic pain in EDS

- Dysmenorrhea (painful menstrual periods)
- Dyspareunia (painful intercourse)
- Sacroiliac joint dysfunction

Pelvic pain in EDS - Dysmenorrhea (painful menstrual periods)

- Birth control to stop periods – may help with joint laxity also
- NSAID’s (ibuprofen, naproxyn)

Pelvic pain in EDS - Interstitial cystitis (bladder pain)

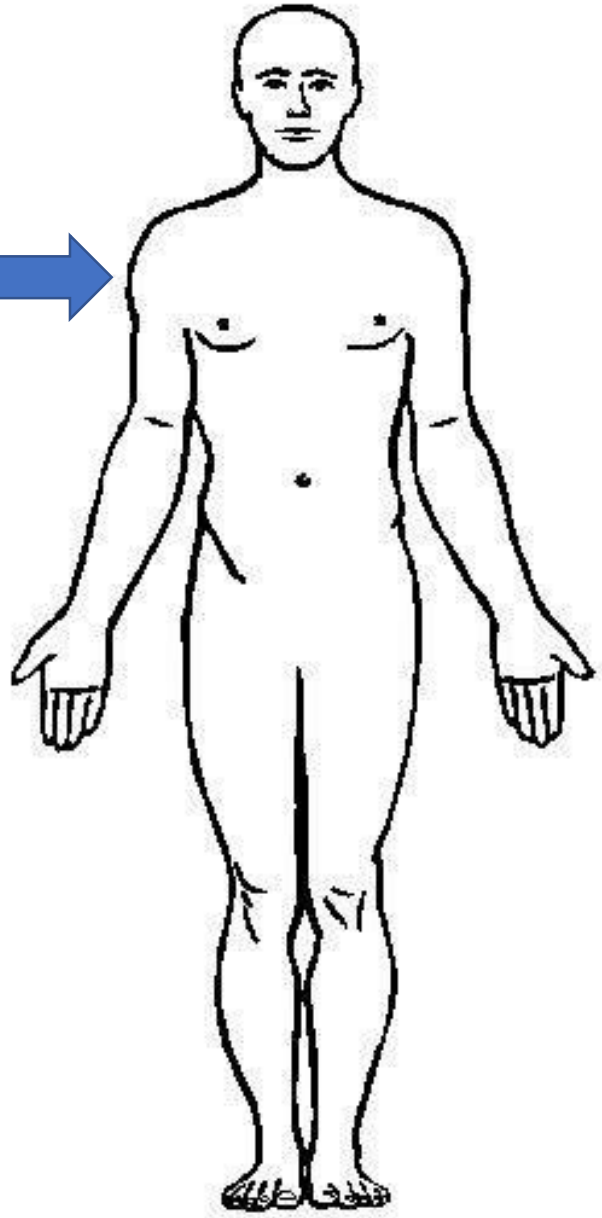
- Maybe part of Mast Cell Activation syndrome
- Cromolyn or Ketotifen
- Palmitoyl ethanolamide (PEA) (www.vitalitus.com)

Pelvic pain in EDS - Dyspareunia (painful intercourse)

- Maybe part of Mast Cell Activation syndrome or EDS
- Hyaluronic acid locally (try Amazon)

Pain in the arms in EDS

Shoulder and arms



Pain in arms

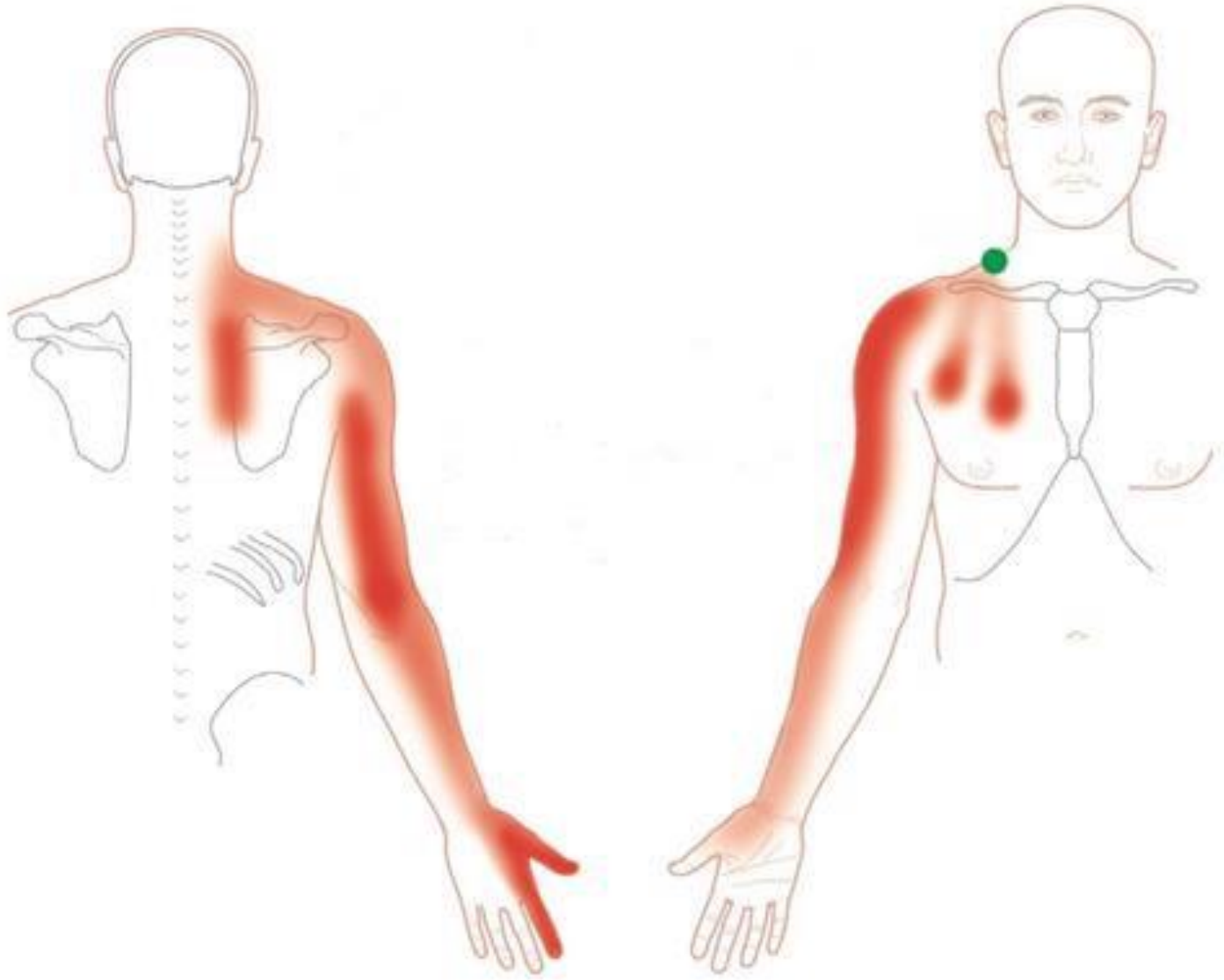
- Shoulder joint subluxations, dislocation
- Thoracic outlet syndrome
- Elbows: Tendonitis, bursitis, hyperextension
- Wrist and fingers: subluxations, muscle pain, tendonitis

Shoulder pain

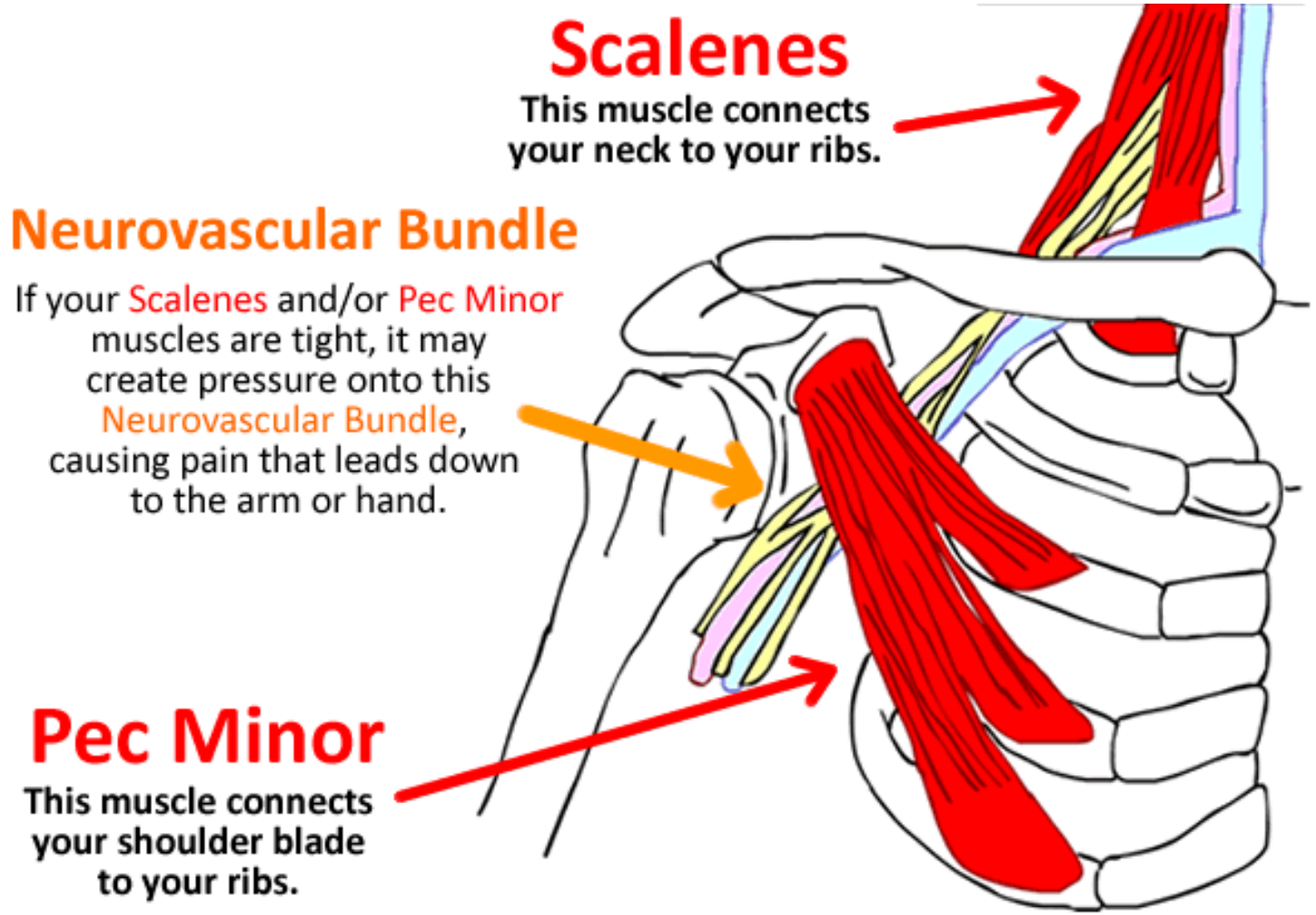
- Laxity of the shoulder joint causes the muscles (rotator cuff) around the shoulder to spasm

- Thoracic Outlet syndrome.

Pain patterns in Thoracic Outlet syndrome



Thoracic Outlet Syndrome

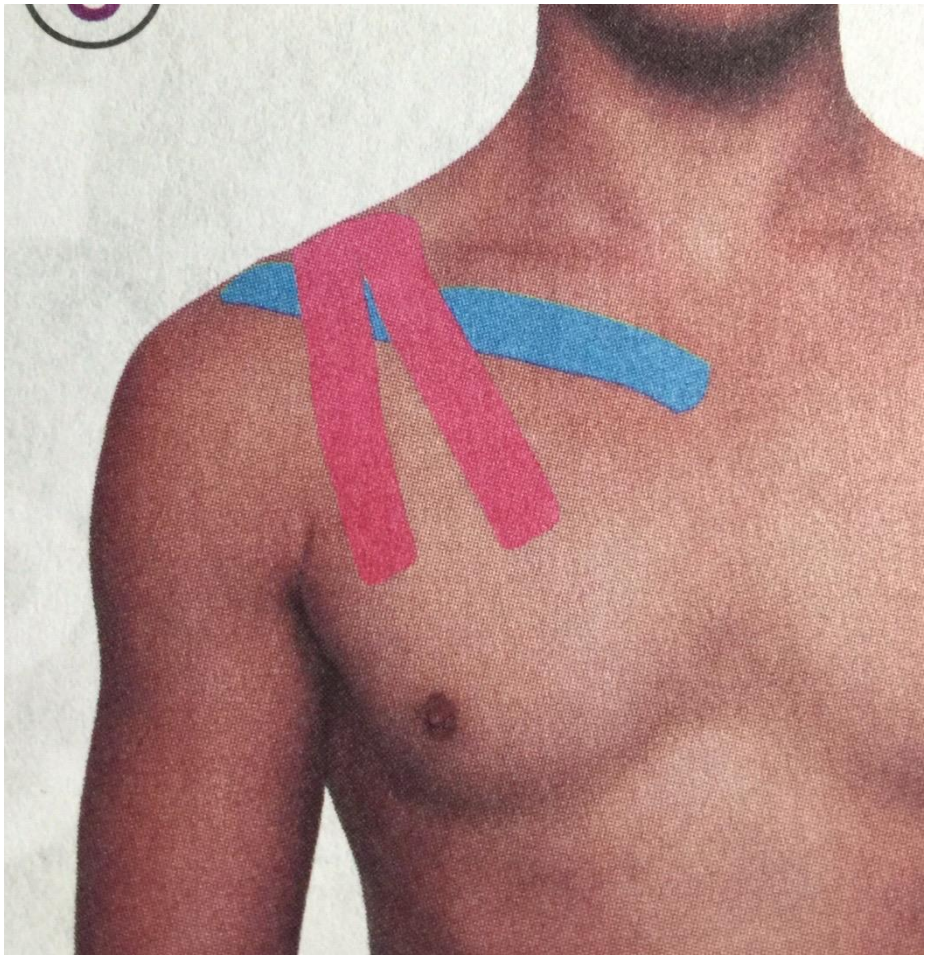


www.sgergo.com

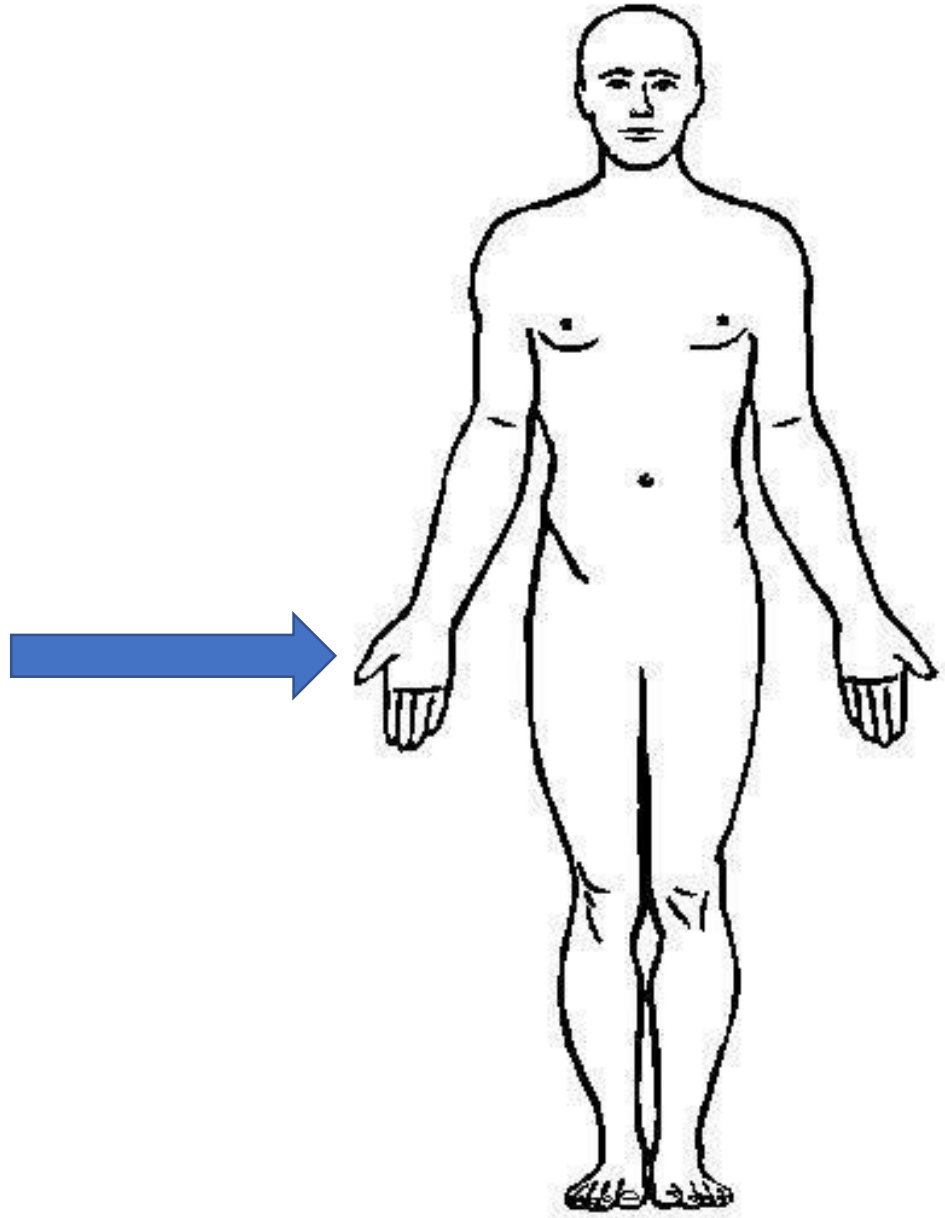
Thoracic Outlet Syndrome

- Physical therapy
- Kinesio taping
- Botox injections
- Surgical correction

Kineseo Taping for shoulder joint pain



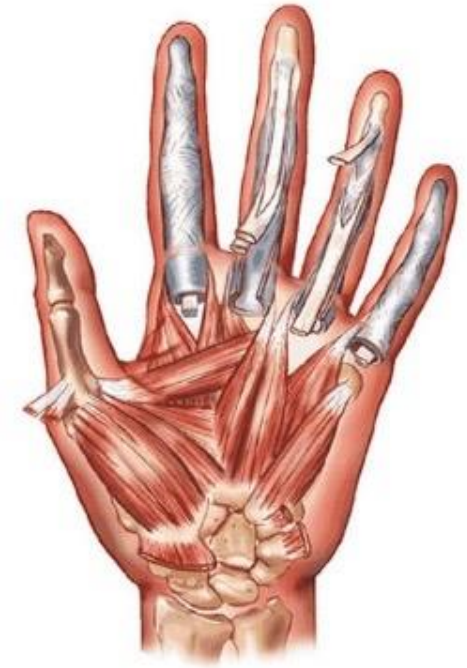
Hand and wrists



Muscles of the hand

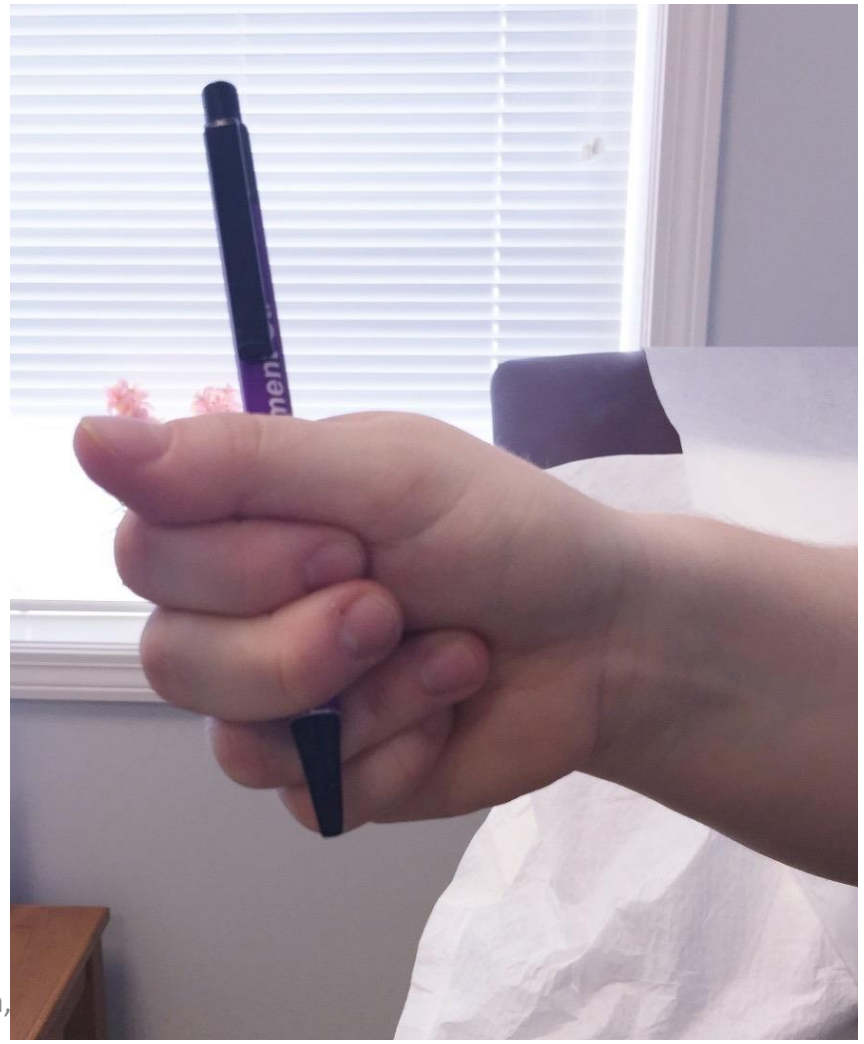
- In EDS, patients tend to grip objects tightly to compensate for poor proprioception

- Small intrinsic muscles of the hand fatigue easily



The EDS way of holding a pen

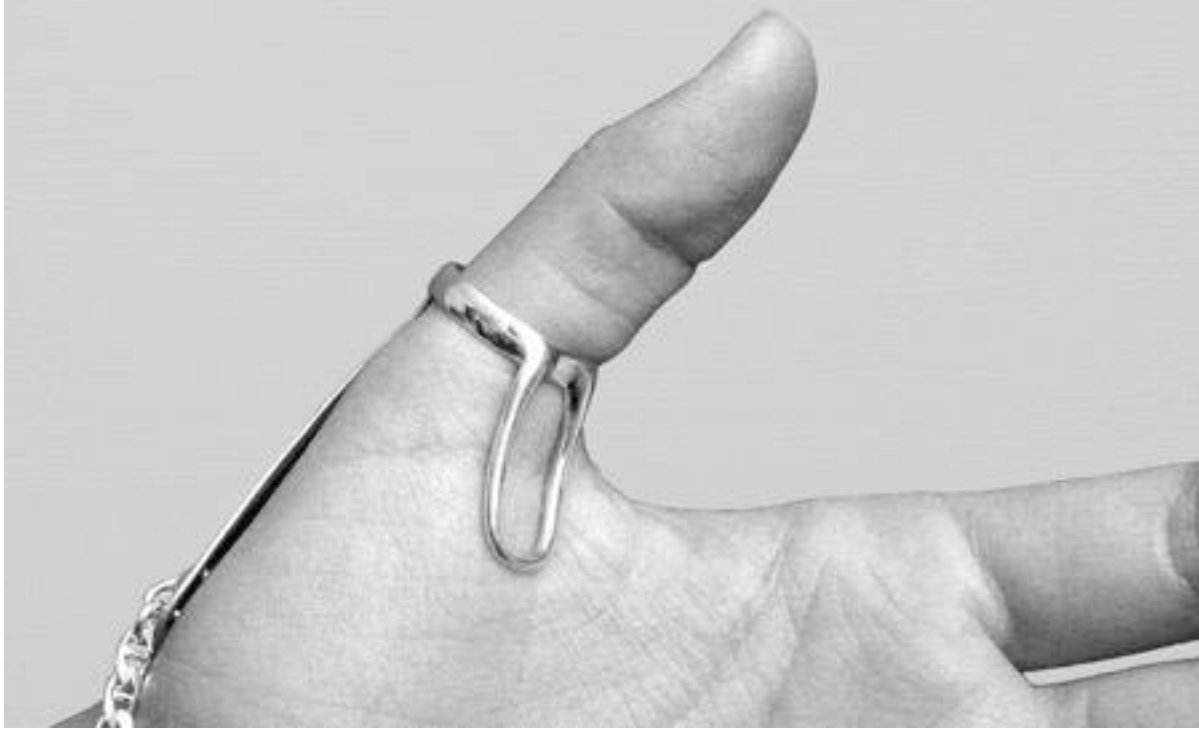
- Poor proprioception makes patients grip a pen with as many fingers as possible
- They hold the pen very tight and press down hard on paper (poor haptic feedback)
- Puts abnormal pressure on the muscles and joints of the hand and wrist

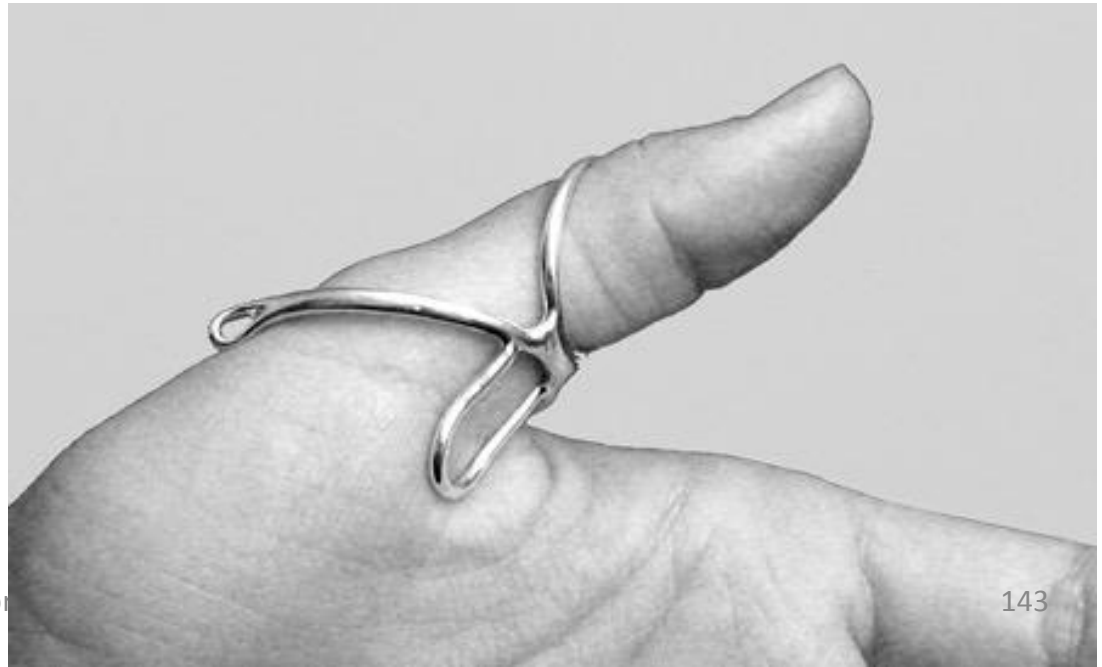


- Dense foam padding (Ableware®) or wrap a foam padded tape – for pens, tooth brush, forks, knives

- Compression half finger gloves
- Brace for unstable joints

Splints for fingers





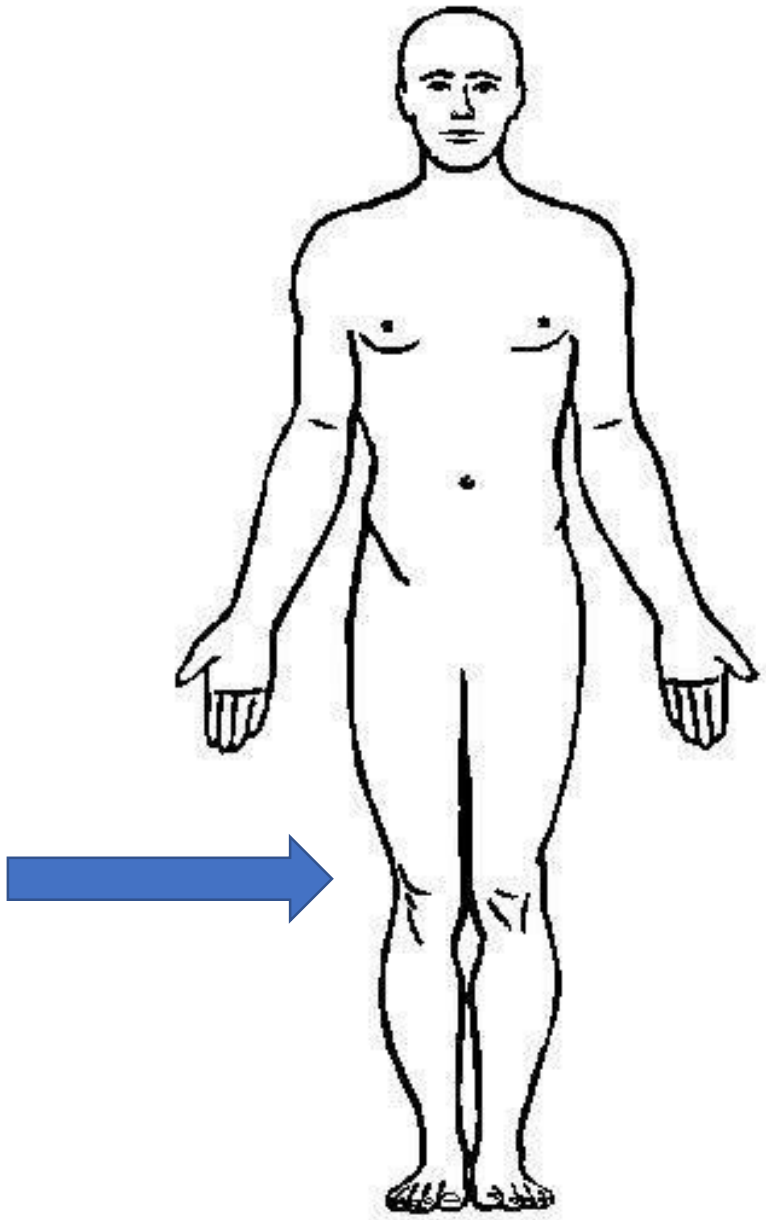
Splinting and braces in general

- Braces maintain joint in neutral position
- Avoid hyper – extension
- Braces help with joint position awareness (proprioception)
- Start using them gradually
- Gradually decrease their use as you gain strength
- Kinesio taping is a good option

Do braces make your muscles weaker?

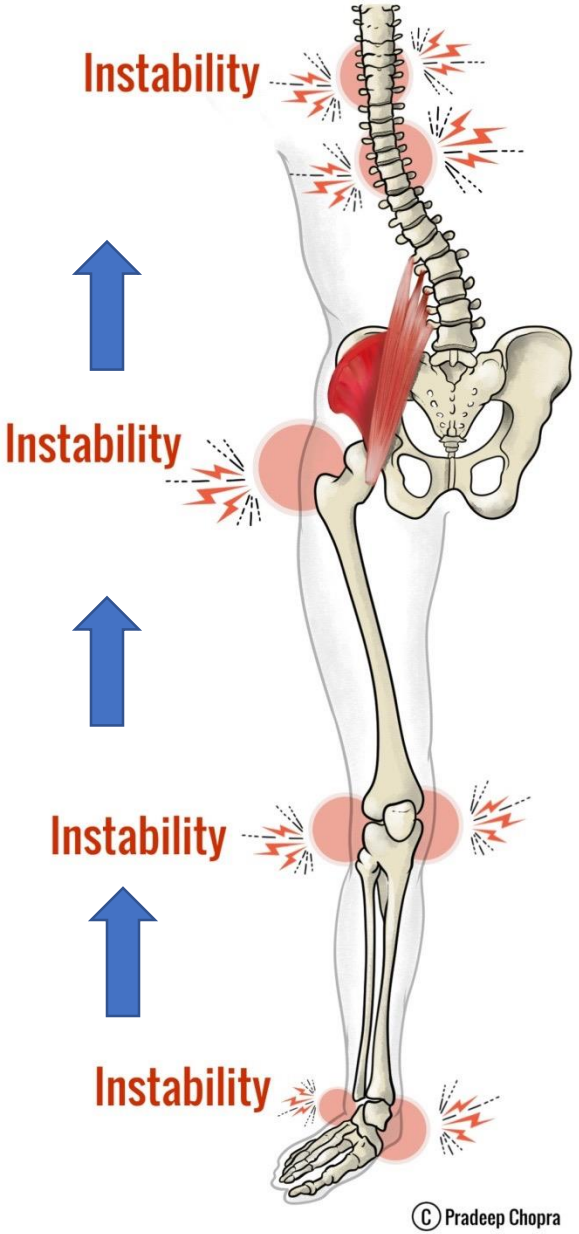
- **NO**
- It’s a common misconception
- No brace is tight enough to stop muscles from moving
- In fact, braces stabilize joints so your muscles can move the joints more efficiently.

Legs and knees

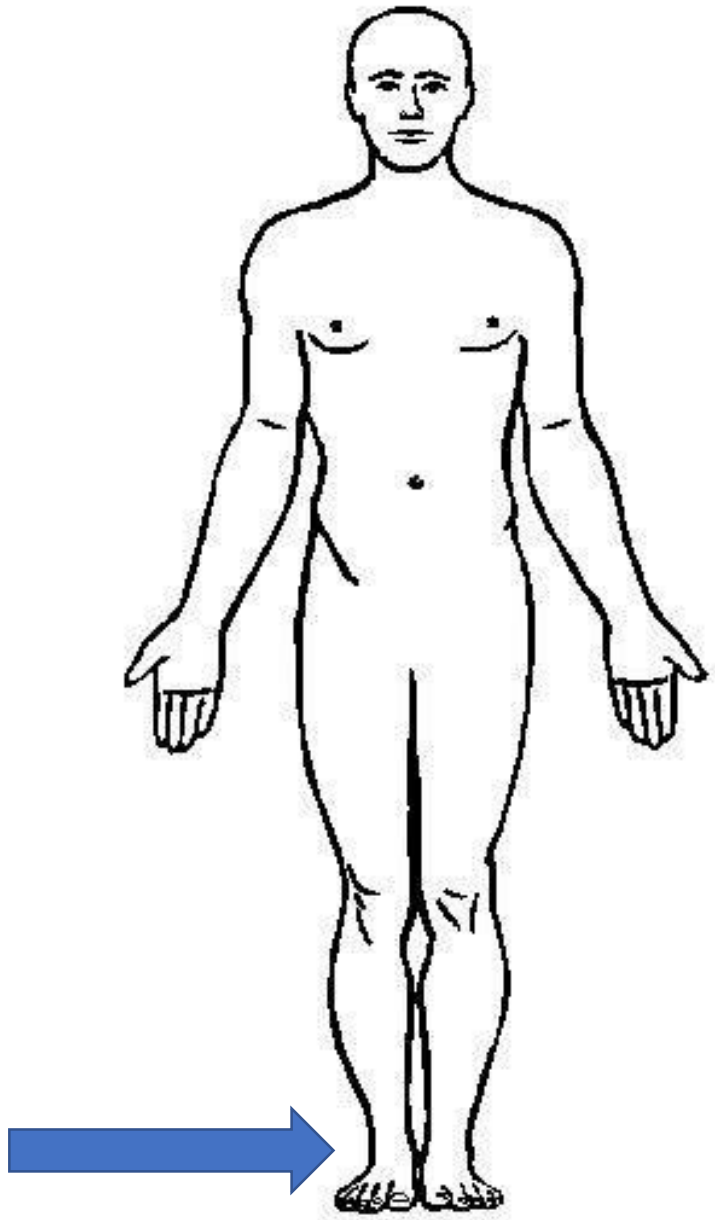


Pain in lower half of the body

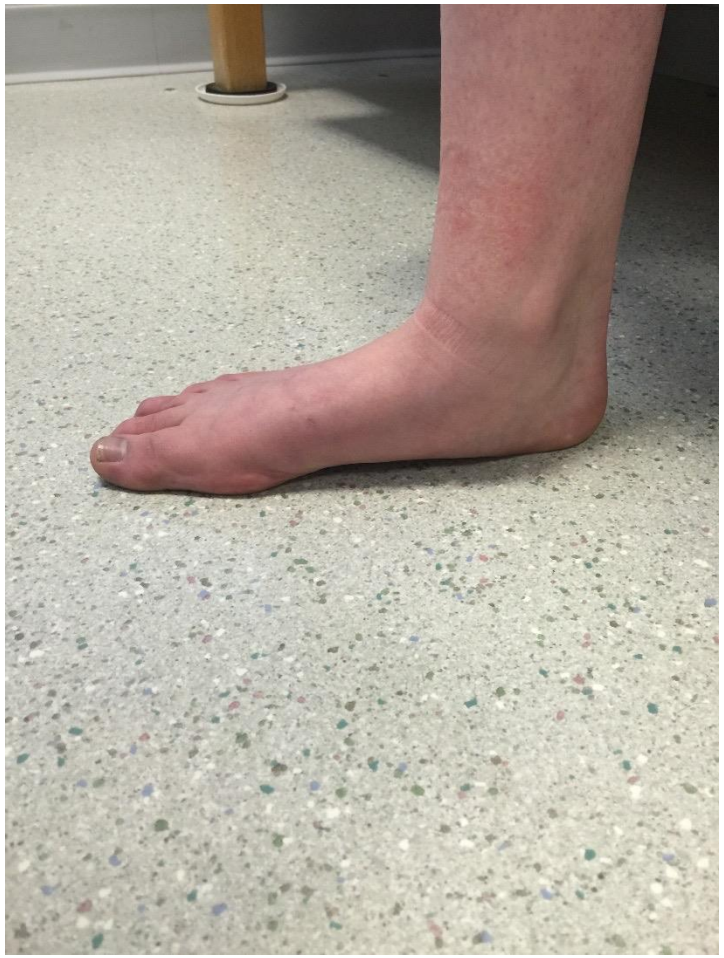
- If the feet and ankles are unstable, they make
- The knees even more unstable, which then
- Makes the hips unstable, which then
- Throws the pelvis and spine off

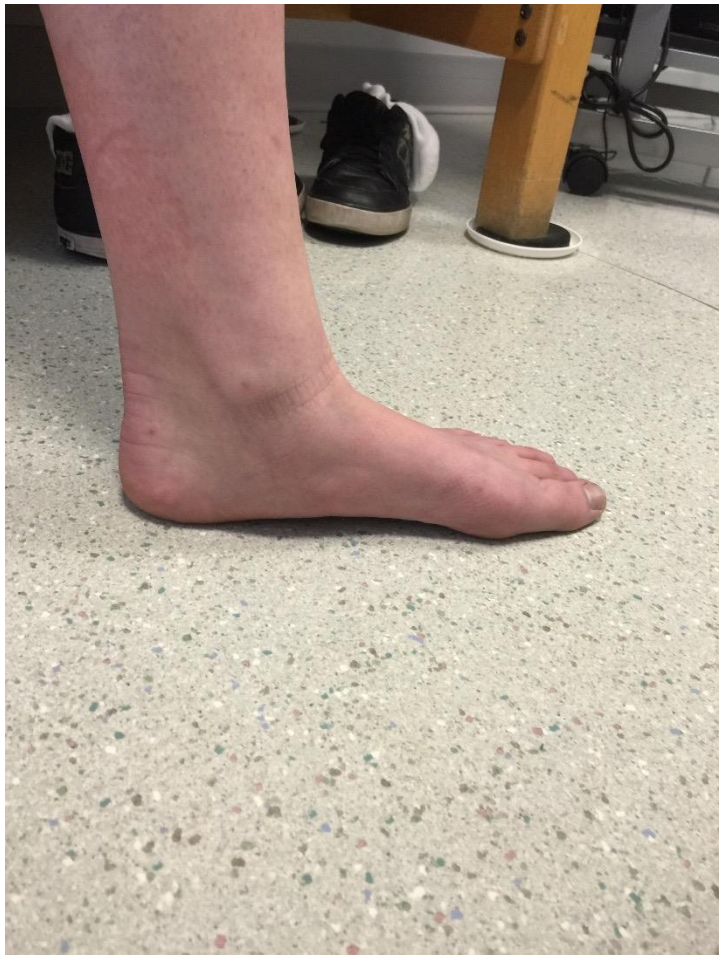

Instability
Instability
Instability
Instability
© Pradeep Chopra

Ankles and feet

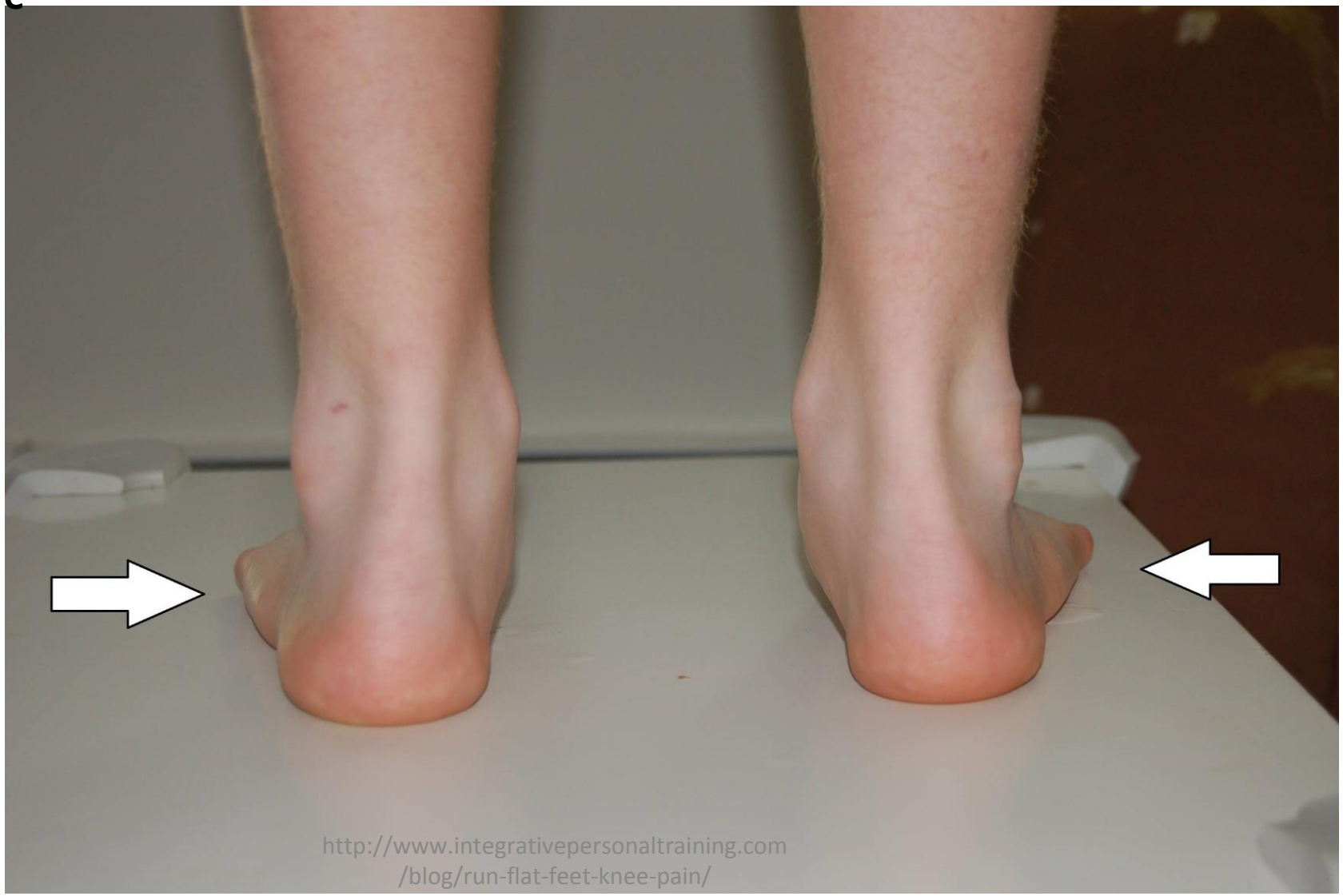


Flexible flat feet – predominantly in the forefoot

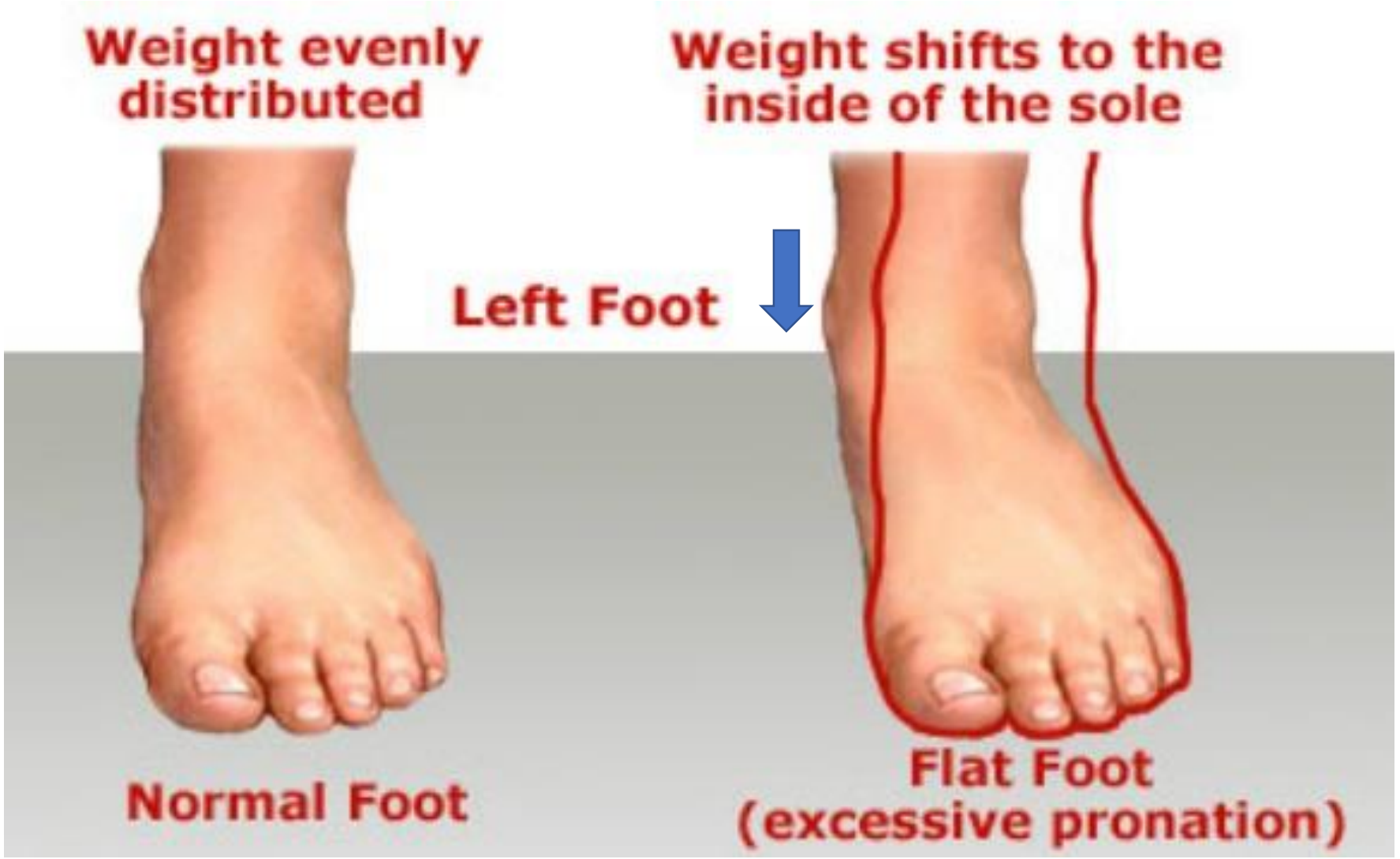




Over-Pronation ankles usually associated with flat feet



http://www.integrativepersonaltraining.com/blog/run-flat-feet-knee-pain/


Weight evenly distributed
Weight shifts to the inside of the sole
Left Foot
Normal Foot
Flat Foot
(excessive pronation)

The feet in EDS

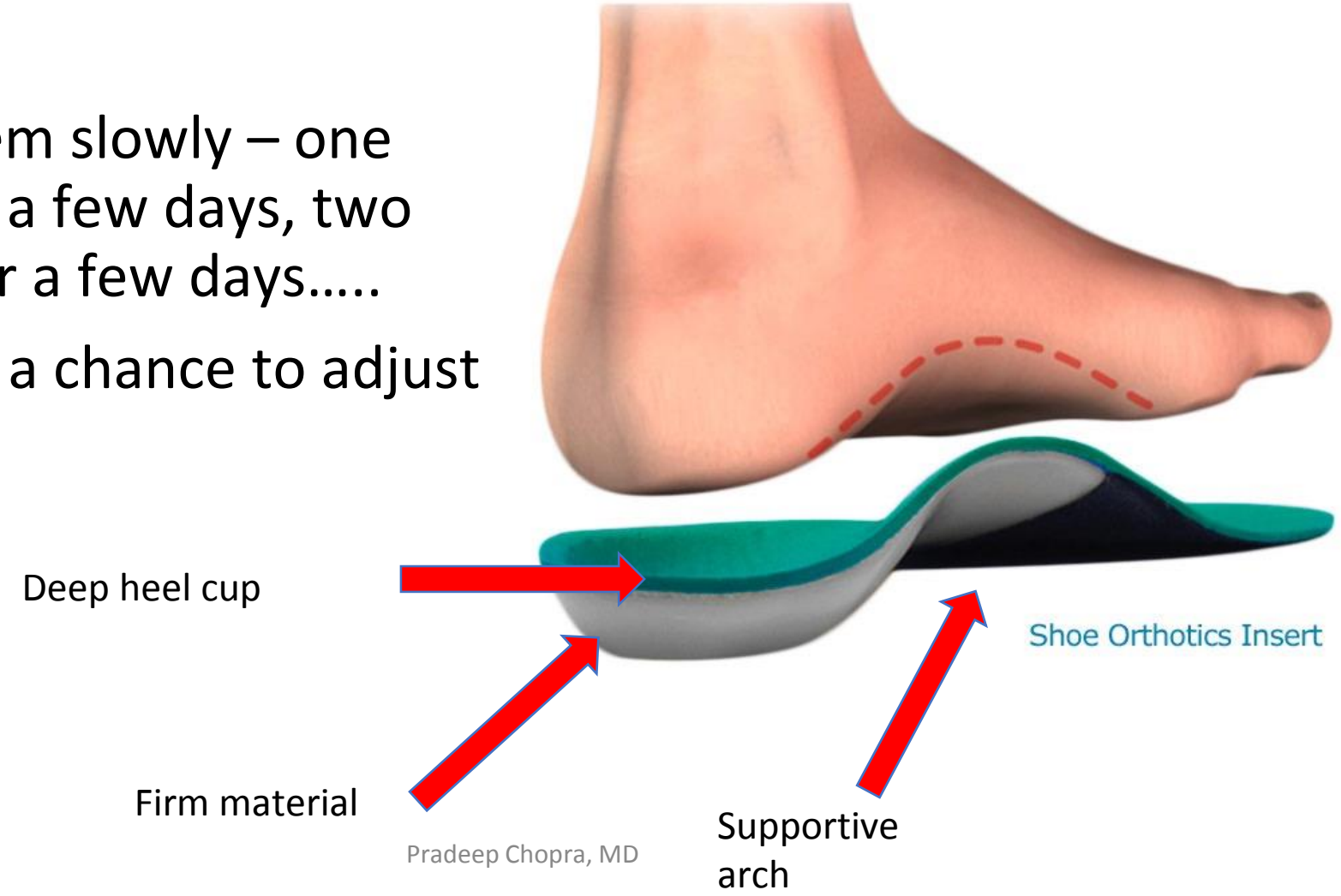
- Barefoot walking, where safe and comfortable – helps with conditioning of muscles under natural loads
- Repeated rising on tip toes – strengthens the muscles in foot and with proprioception
- Ankle raises by lifting heel (not leaning forward)
- Descend in a slow controlled way

Footwear - shoes

- Extremely important to wear proper footwear
- Help with unstable ankles, hypermobile feet
- Cushioned mid sole
- Good, strong heel counter provides stability
- Fastenings should be over the mid-sole for better support
- Sneakers !!

Orthotics

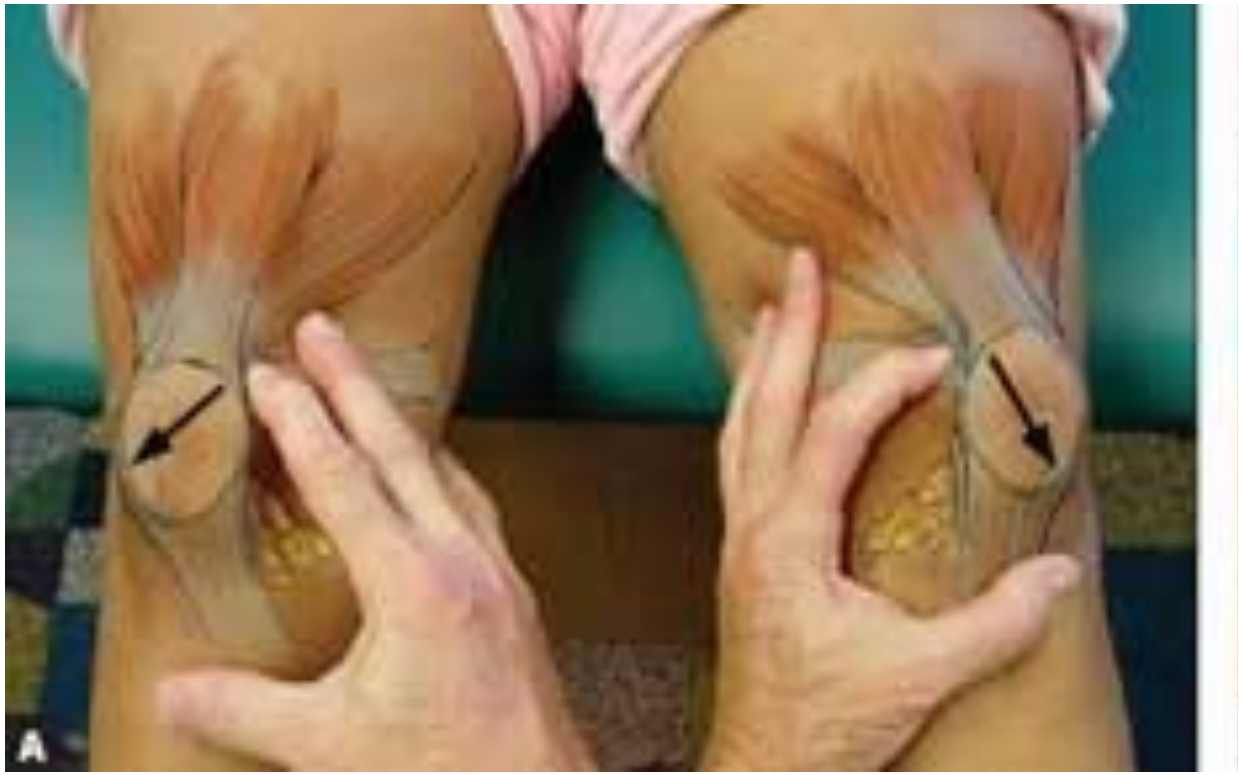
- orthotics
- Start using them slowly – one hour a day for a few days, two hours a day for a few days…..
- Give your feet a chance to adjust



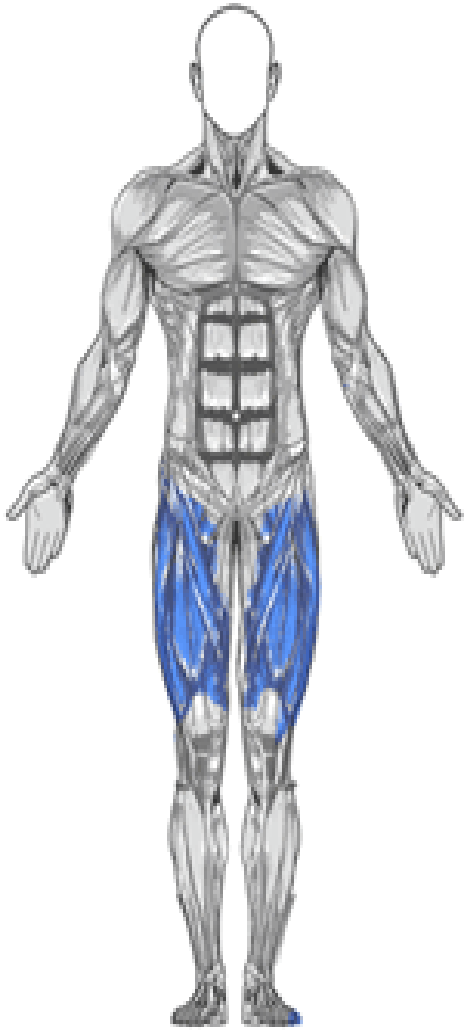
Ankle brace to stabilize the ankle joint

Knees

Patella is stabilized muscles of the thigh



- A hypermobile patella can make the knee unstable
- It causes pain in the muscles that support the patella



http://www.mygeofit.com/member/Front-Thigh-(Quadricep)-Exercises.html

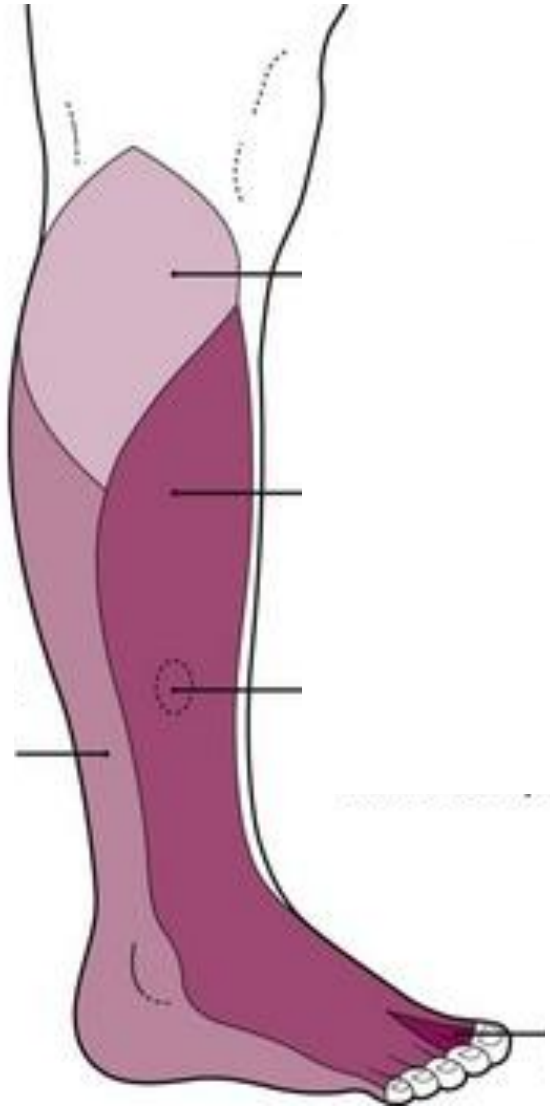
Treatment options for knee pain in EDS

- Stabilize the feet and ankles, first
- Strengthen muscles around the knee
- Knee brace
  - Two straps above knee
  - Two straps below knee
  - Patella stabilizer
  - Metal strut to prevent hyperextension

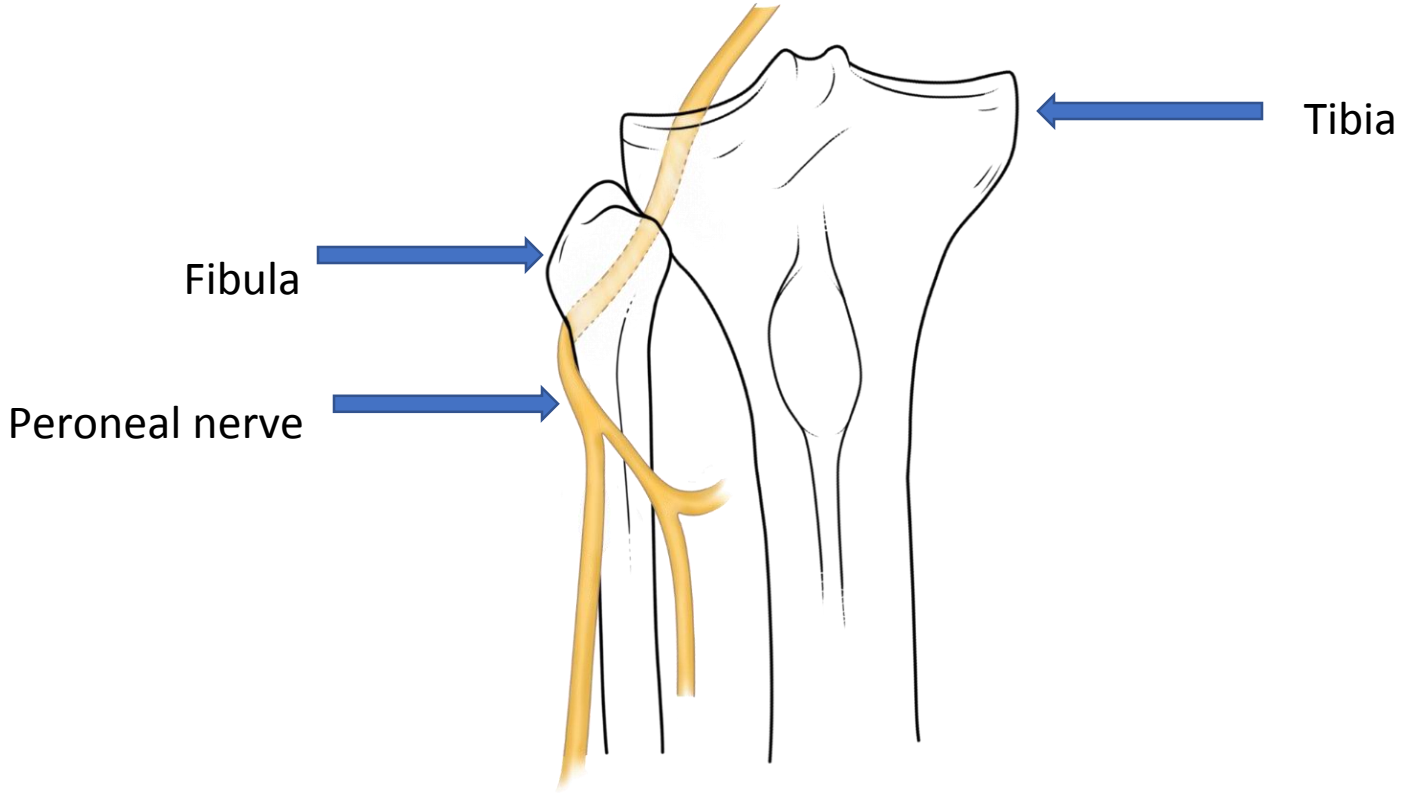
A missed cause of leg pain – the proximal tibio fibular joint

Knee pain – often missed cause

- Site of pain from the proximal Tibiofibular joint
- It can inflame the peroneal nerve which causes pain down the side of the leg and even foot drop



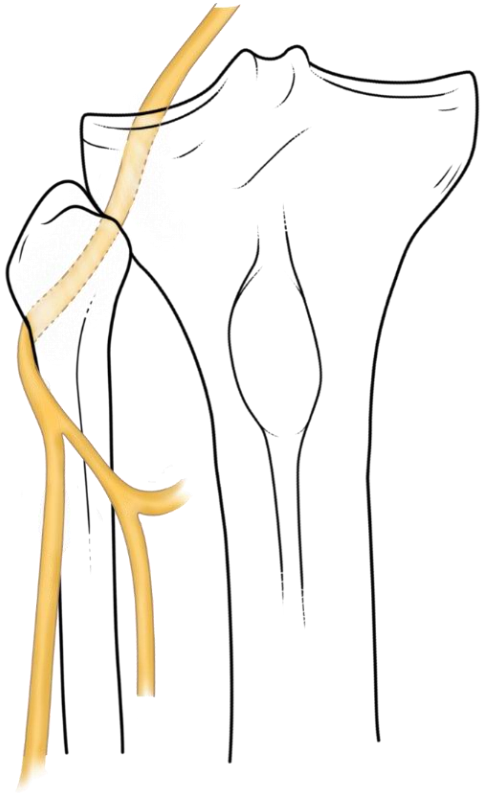
Proximal Tibio-Fibular joint

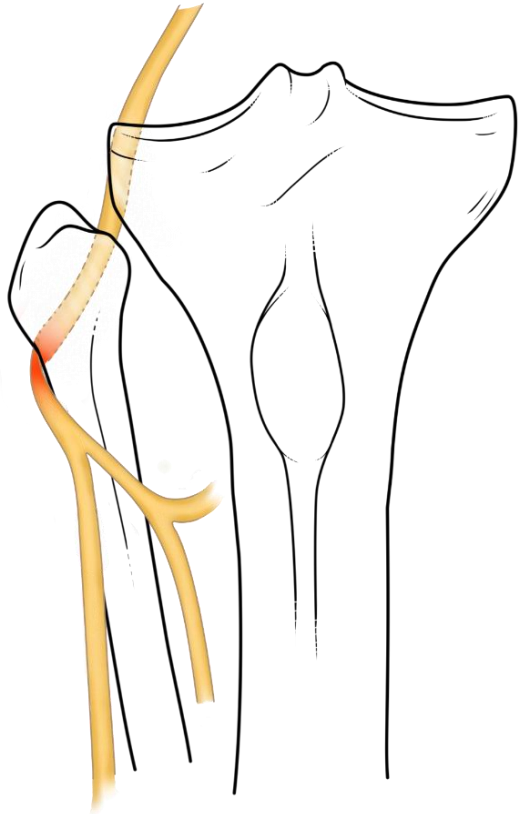


Knee pain – often missed cause of pain in the leg

- The proximal tibio-fibular (PTF) joint is on the outside of the knee.
- Like all joints it is prone to subluxations or arthritis.
- A subluxing PTF joint affects the Peroneal nerve, which affects the side of the leg and causes pain in the leg and foot drop

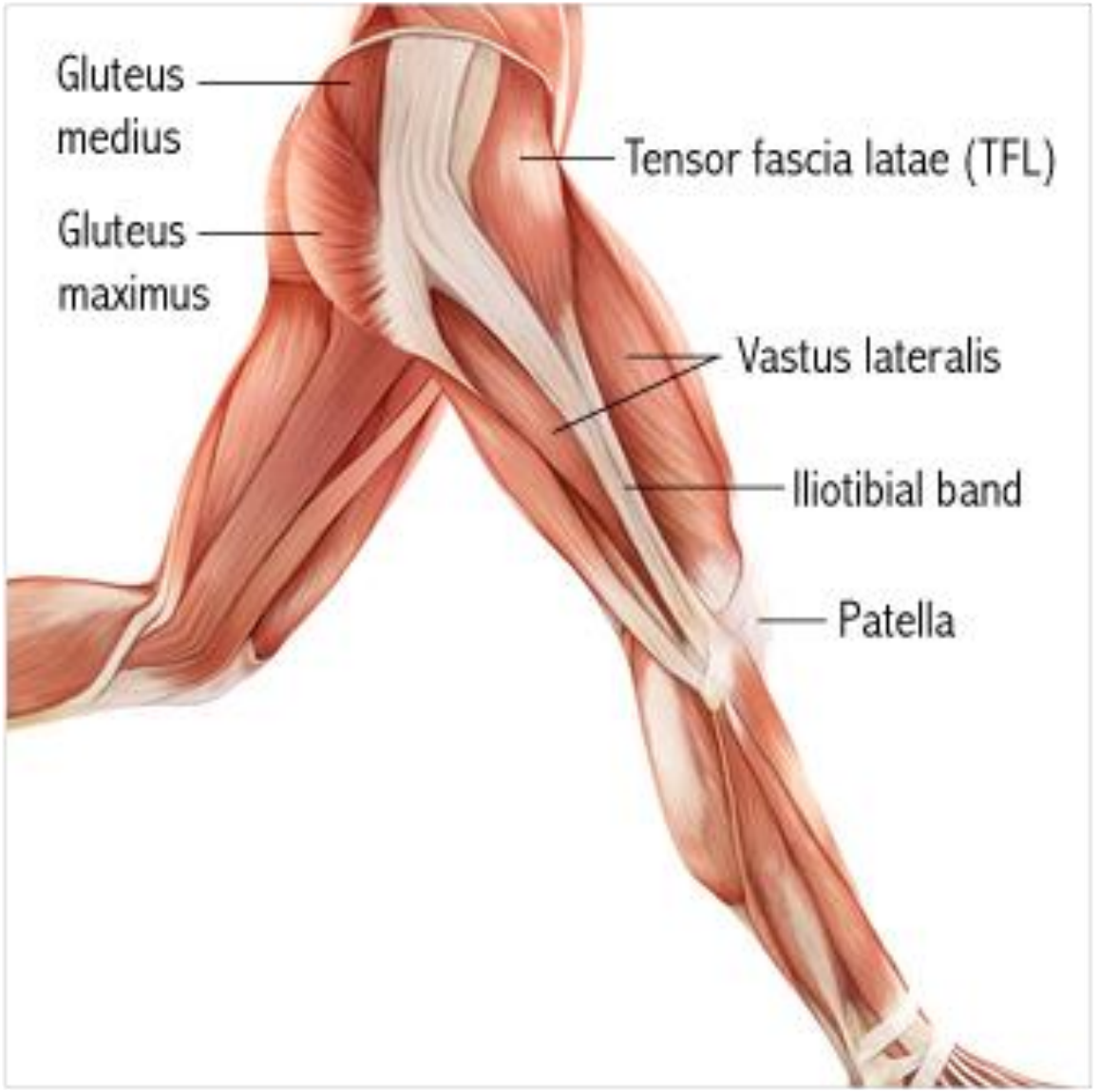
Proximal Tibio-Fibular joint





Ilio Tibila band (Fascia Lata Fascitis)

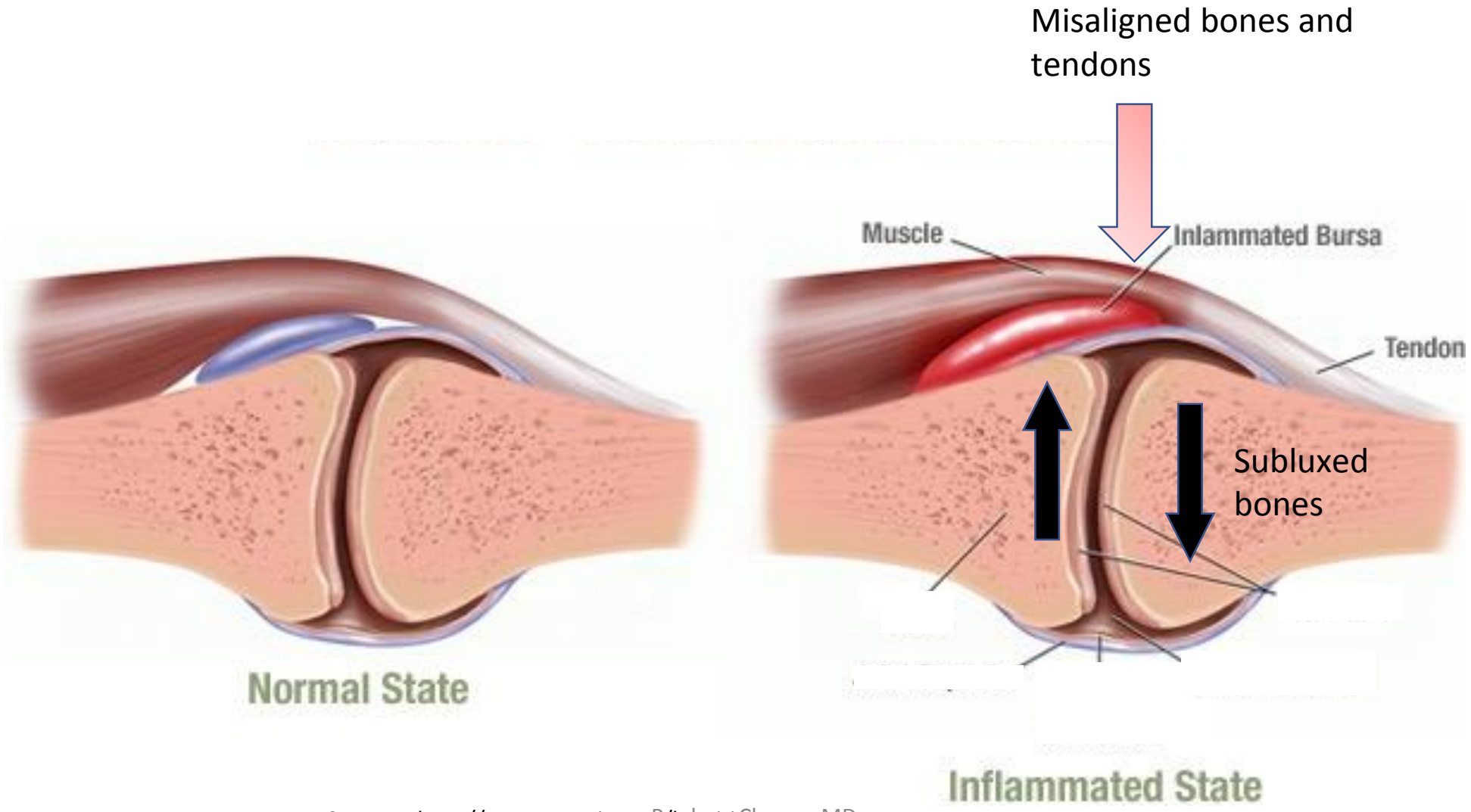
- Pain on the side of the thigh up to the knee
- It is usually because of an unstable knee or hip joint
- The IT band is tightened in subluxation of the PTF and hypermobile patella
- Treat the knee or hip problem
- Stretching the IT band may not help



Trochanteric Bursitis

- Pain on the side of the hip
- Worse with lying on that side
- Getting up from a chair after being seated for a while.
- The problem may be because of an unstable hip or knee

Tendonitis and bursitis in EDS



Courtesy http://www.ateevia.com/bursitis.aspx

Abdominal Pain in EDS

Abdominal Pain in EDS

- Very high incidence
- Gastroparesis
- Laxity of the intestines
- Prolapse of internal organs
- Hernias

Abdominal pain

- Mast Cell Activation syndrome is a very common cause of GI motility issues.
- The intestines are controlled by the same autonomic nervous system that is responsible for Dysautonomia.
- GI motility may be either slow or fast
- Acid reflux – part of EDS and also because of MCAS

Constipation

- May be ‘rectal evacuatory dysfuntion’.
- Squatty potty
- Patients with EDS having gastrointestinal issues are often labelled as having “Functional GI disorder”.
- In the true sense Functional GI disorders are not psychological BUT very often gastroenterologists who don’t quite understand EDS use the term to imply the abdominal pain is psychological

Gastrointestinal system (GI system) and Chronic pain

- In chronic pain the diversity of bacteria is less (normally, approximately 1000 different types of bacteria)
- This causes GI inflammation, the lining of the intestines is damaged, and increased production of pro-inflammatory cytokines
- TLR4 receptor activity is increased. This has been associated with inflammation.
- TLR4 is one of the receptors where LDN works.

3-84

Erin R. Reichenberger a, Guillermo M. Alexander b, Marielle J. Perreault b, Jacob A. Russell c,
Robert J. Schwartzman b, Uri Hershberg a,1, Gail Rosen. Establishing a relationship between bacteria in the human gut and Complex Regional Pain Syndrome. Brain, Behavior, and Immunity 29 (2013) 62–69

Gastrointestinal system (GI system) and CRPS

- Are we destroying our ’friendly’ bacteria with our artificial foods, preservatives, chemicals, antibiotics?
- SIBO – Small Intestine Bacterial Overgrowth – talk to Gastroenterologist
- The test for SIBO is a breath test and can be done at home

Manjula | 4 Color Fig(s): F1-2 | 02/4/16 | 11:14 | Art: XAA-D-15-00144

Identification and Treatment of New Inflammatory Triggers for Complex Regional Pain Syndrome: Small Intestinal Bacterial Overgrowth and Obstructive Sleep Apnea

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Complex regional pain syndrome (CRPS) is evoked by conditions that may be associated with local and/or systemic inflammation. We present a case of long-standing CRPS in a patient with Ehlers-Danlos syndrome in which prolonged remission was attained by directing therapy toward concomitant small intestinal bacterial overgrowth, obstructive sleep apnea, and potential increased microglia activity. We theorize that cytokine production produced by small intestinal bacterial overgrowth and obstructive sleep apnea may act as stimuli for ongoing CRPS symptoms. CRPS may also benefit from the properties of low-dose naltrexone that blocks microglia Toll-like receptors and induces production of endorphins that regulate and reduce inflammation. (A&A Case Reports. 2015;XXX:00–00.)

Complex regional pain syndrome (CRPS), formally known as reflex sympathetic dystrophy, is a neuropathic pain disorder that may fail to respond to current therapy including a variety of medications, nerve blocks, and ketamine infusions.[1,2] The incidence of CRPS is uncertain because there are few epidemiological studies. In a Mayo Clinic study, the rate was 5.46 per 100,000 person-years compared with a 6-fold larger study in the Netherlands where the rate was 26.2 per 100,000 person-years.[3,4] A marked female predominance was noted in each study. A familial occurrence of CRPS has been described.[5] The natural history of CRPS varies widely. The Mayo Clinic reported that 56 of the 74 patients with CRPS for 1 month to 5 years had complete remission after various treatments. Spontaneous remission was observed when the initial symptoms were mild.[3] By way of comparison, there were no remissions in 656 Drexel University patients who had CRPS for 1 to 46 years.[6] Pain had only modest improvement with their treatments. No spontaneous remissions occurred in 102 Dutch database patients who had CRPS for 2.1 to 10.8 years.[7] Progressive disease was reported in 16%, and permanent disability was present in 31% of the Dutch patients.

Pathophysiologic consequences of cytokine release, microglia activation, central sensitization, and autonomic nervous system dysfunction result in regional pain along with vasomotor, motor/trophic, and sudomotor/edema dysfunction.[1,2,8,9] Microglia cells are an integral part of the anatomic framework of the nervous system with attachments to astrocytes.[10] They act as neuromodulators, which alter central nervous cell and spinal sensory neuron excitability. Various syndromes marked by hyperalgesia including fibromyalgia and CRPS may be mediated by microglia cell activation as a consequence of proinflammatory cytokines.[11,12] Events known to trigger the onset of CRPS include bone fractures, sprains, trauma (injections, nerve injury, surgery, burns, and frostbite), nerve injury, infection, pregnancy, myocardial infarction, and stroke.[1,2] Some of these triggers may be associated with local and/or systemic inflammation.[13–17] In stroke-associated CRPS, inflammation from the stroke has been theorized as one of several possible pathophysiologic mechanisms.[17]

In light of the complex pathophysiology of CRPS and that no single therapy is completely effective, it is desirable to consider all theories. We theorize that cytokine release by various triggering events and disorders could initiate CRPS through the activation of microglia via inflammation. We also propose that underlying unrecognized chronic inflammatory conditions may allow CRPS to persist. Parkitny et al.[18] performed a systematic and meta-analysis review of the role of inflammation in acute and chronic CRPS. In the former, serum interleukin-8 and tumor necrosis factors were increased. In the latter, there were many inflamma-

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Leonard B. Weinstock has served on the Speakers bureau for Salix: Relistor (methylnaltrexone) for constipation and Xifaxan (rifaximin) for irritable bowel syndrome. He is a coauthor for a manuscript and was PI on a study of

Pradeep Chopra, MD

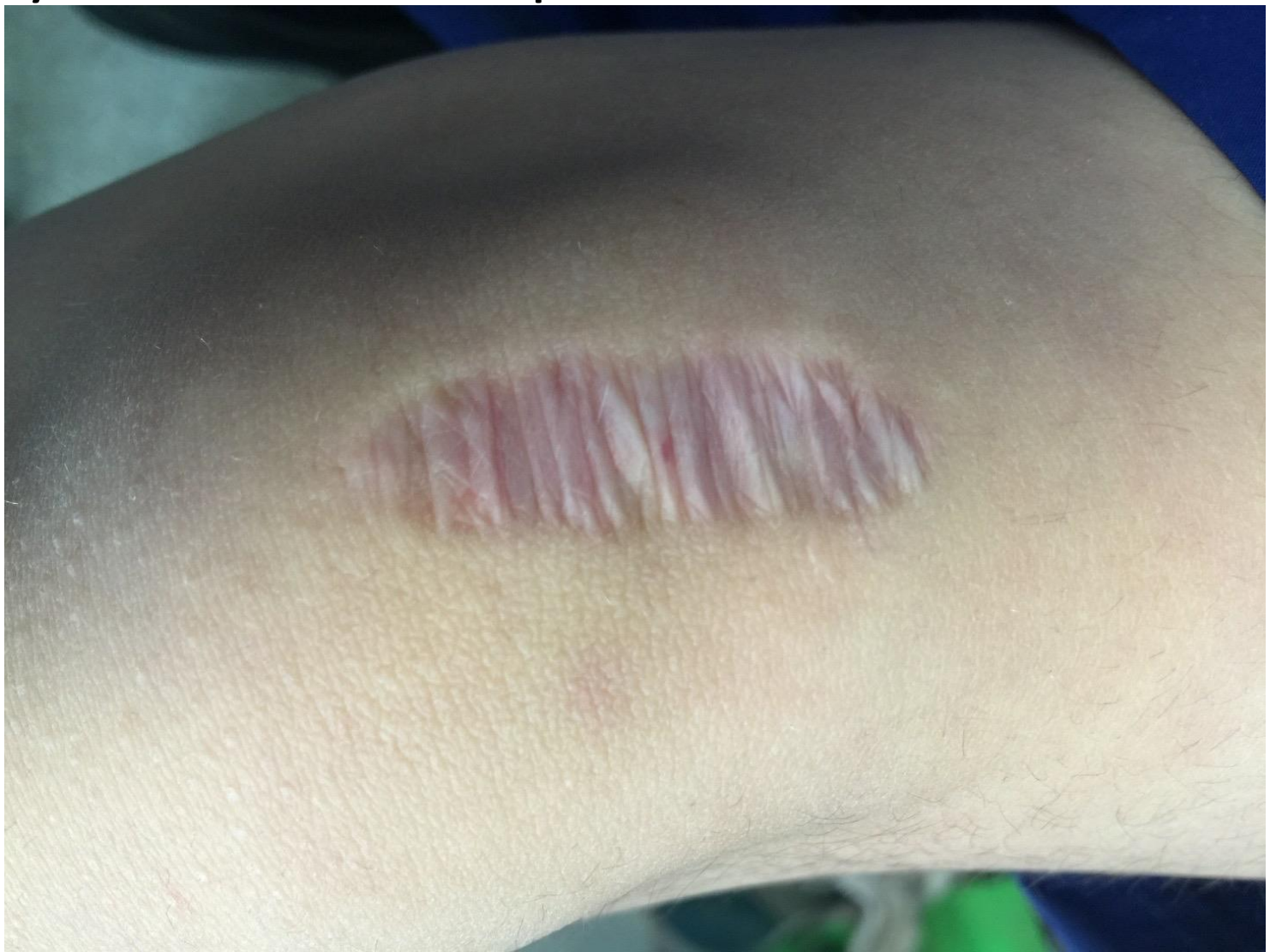
Diet

- Low FODMAP diet – Fructose, Oligosaccharides, Disaccharides, Momoamines, Polyols
- Gluten free
- Cromolyn oral

Caution

- Antibiotics of the fluoroquinolone such as cipro may cause tendonitis and tendon rupture.

Surgery in EDS done to help with pain, actually makes the pain worse.



Behavioral

- Conversion disorder (CD) – less than 1% (1)
- Munchausen by Proxy (MBP) – 0.5/100,000 (2)
- EDS – 1% to 10%
- The diagnosis of CD or MBP are often made by providers with little training in Psychiatry and vice versa most psychiatrists have no training in pain conditions.

1 Marsden CD. Hysteria: a neurologist's view. Psychol Med. 1986;16:277–88
2. R J McClure, P M Davis, S R Meadow, and J R Siber. Epidemiology of Munchausen syndrome by proxy, non-accidental poisoning, and non-accidental suffocation. Arch Dis Child. 1996 Jul; 75(1): 57–61.

Behavioral

- To diagnose a child with Conversion disorder or Munchausen by Proxy without a dedicated multidisciplinary team approach and without concrete evidence is extremely harmful to the patient.

- To label an adult with pain as being psychological is severely harmful. It closes all doors to correct treatment.

Dysautonomia / POTS (Postural Orthostatic Tachycardia Syndrome)

Postural Orthostatic Tachycardia syndrome (POTS) - Symptoms

- Fainting, dizziness
- Heart racing (Palpitations)
- Fatigue
- Headaches
- Cold hands and feet
- Poor concentration “brain fog”
- Feeling of constant anxiety

POTS - Postural Orthostatic Tachycardia syndrome - diagnosis

- Increase in heart rate by 30 beats/min within 10 minutes of standing
- heart rate of 120 beats / min within the first 10 minutes of standing
- No significant change in blood pressure
- Syncope or almost syncope (fainting)
- In children an increase of 40 beats/minute

POTS - tests

- Orthostatics – Measure blood pressure and heart rate while lying down, standing up for 10 minutes - preferred
- Tilt table test

Diagnosis of POTS

5 mins

120/80

70

Standing Immediately

118/78

110

Standing for 10 minutes

122/80

105

Increase in heart rate by 40 beats/minute with very little change in blood pressure

Treatment of POTS

- Increase oral salts
- Increase oral electrolyte fluids
- Compression tights up to thighs.
- Abdominal binder (wear swim suit 1 size smaller)
- Cardiology consult for Dysautonomia/POTS.

POTS - Postural Orthostatic Tachycardia syndrome

Consult Dysautonomia International for more information and high salt diet recipes.

http://www.dysautonomiainternational.org/

- The constant feeling of dizziness makes patients feel unstable
- The laxity of the joints makes the muscles tighten reflexly
- This constant use of muscles worsens their pain and fatigue

Anxiety in EDS

- Patients with EDS and POTS (Dysautonomia) are often over diagnosed to have anxiety
- Symptoms of undiagnosed palpitations, fatigue, dizziness, chronic pain are attributed to ‘anxiety’.
- In most cases its simply Dysautonomia – malfunction of the autonomic system.

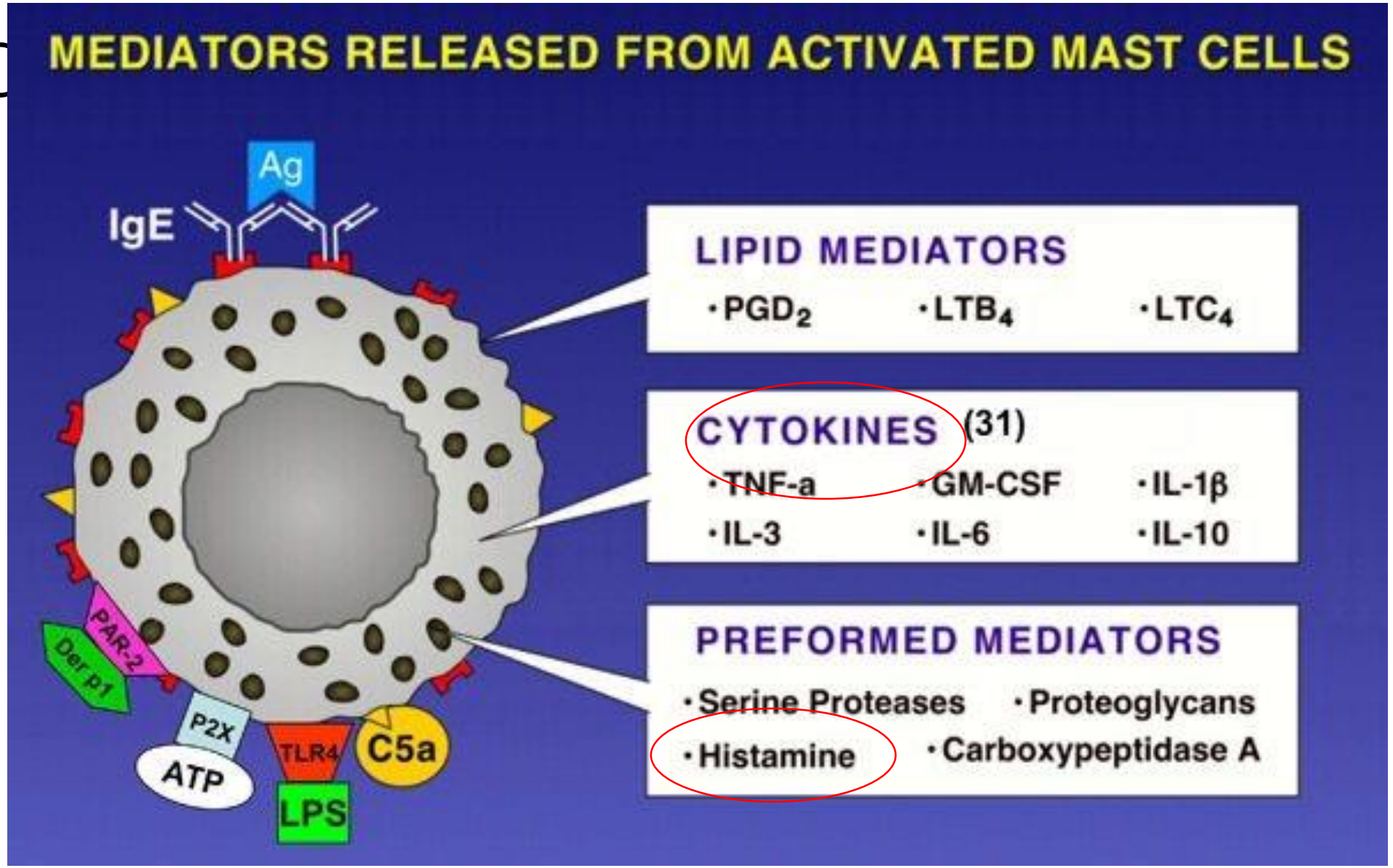
Mast Cell Activation Syndrome

MCAS

Mast cells

- Cells in blood
- Normally present in blood
- Contain histamine, cytokines and a bunch of other chemicals
- Involved in allergy, wound healing and protection against infection

MC



Courtesy Ann Maitland, MD

EDS, POTS and MCAS

A New Disease Cluster: Mast Cell Activation Syndrome, Postural Orthostatic Tachycardia Syndrome, and Ehlers-Danlos Syndrome

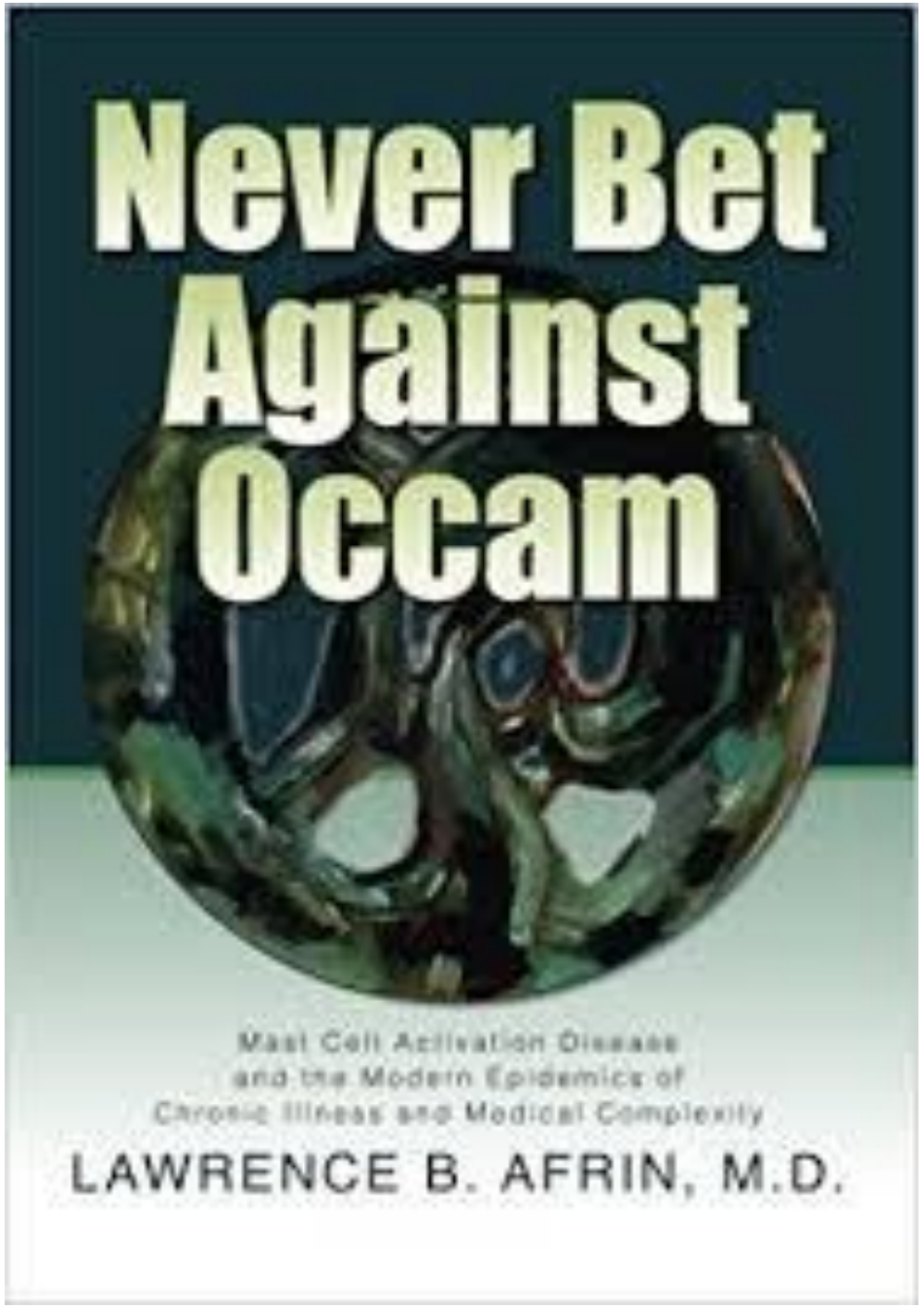
Cheung, Ingrid, Vadas, Peter

Journal of Allergy and Clinical Immunology , Volume 135 , Issue 2 , AB65, February 2015

Mast Cell Activation Syndrome (MCAS)

- MCAS is a large, prevalent collection of illnesses resulting from mast cells which are inappropriately activated but are NOT significantly proliferated (different from Mastocytosis).

Lawrence B Afrin, MD. The Presentation, Diagnosis And Treatment Of Mast Cell Activation Syndrome - review article. Current Allergy & Clinical Immunology 2014 September Vol 27 No.3


Never Bet Against Occam
Mast Cell Activation Disease
and the Modern Epidemics of
Chronic Illness and Medical Complexity
LAWRENCE B. AFRIN, M.D.

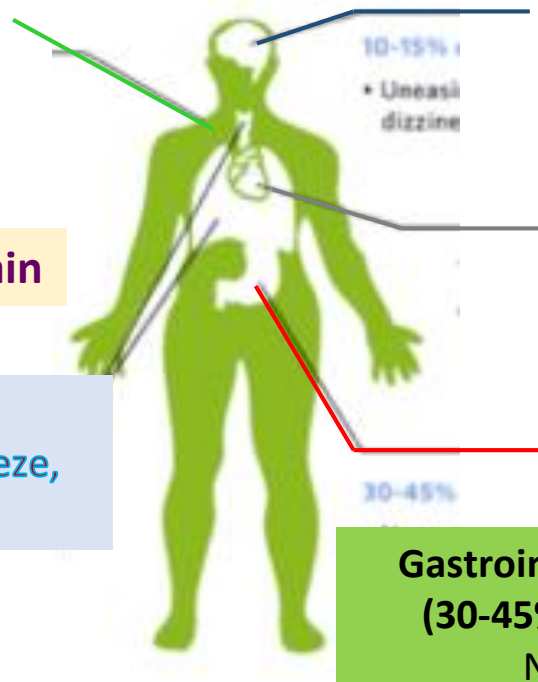
Mast Cell Activation Syndrome (MCAS)

- Unexplained skin flushing, unexplained hives
- Headaches
- Sweating
- Flushing after a hot shower
- Mental Fog
- Abdominal discomfort
- Diarrhea, constipation - alternating
- Dermatographism (write on skin)

Signs and Symptoms of Mast Cell Activation Disorders

Skin (80-90% reactions)
Hives, Itch, Rashes

Brain
(> 20% reactions)
Mental fog
Headache
Dizziness
Confusion



Heart, Blood Pressure (10-45 % reactions)
Fast Heart Rate,
Palpitations
Dizziness
Fainting

Joint and Muscle Pain

Airway (70% reactions)
Lungs = chest tightness, wheeze, can't take a deep breath

Gastrointestinal tract
(30-45% reactions)
Nausea
Cramping
Abdominal Pain
Vomiting
Diarrhea

Genito-Urinary tract
(>10% reactions)
Uterine Cramping,
frequent urination,

Mast cells

- Inappropriately activated
- MCAS may present as waxing-waning or persistent inflammatory condition
- Activated Mast cells release mediators including histamine and cytokines

Mast Cell Activation Syndrome - Labs

Evidence of an increase in a validated urinary or serum marker of mast cell activation:

1. Tryptase:
    1. levels are persistently >15 ng,
    2. an increase of tryptase greater than the patient's baseline during a symptomatic period on >2 occasions

2. Less specific but helpful markers are
    1. 24-hour urine histamine metabolites
    2. Prostaglandin D2 or its metabolite 11-b-prostaglandin F2.

3. Bone marrow biopsy

Diagnosis of MCAS

- Think of MCAS if you feel that the presentations is “unusual”, “odd”, “weird”, “bizarre”
- “allergies” to innocuous medications or “allergies” to unusually high number of things

Lawrence B Afrin, *MD* The presentation, diagnosis and treatment of mast cell activation syndrome, Current Allergy & Clinical Immunology 2014 September Vol 27 No.3

Management of Mast Cell Activation Syndrome (MCAS)

- Anti-histamine:
  - Diphenhydramine, cetirizine (H1 blockers)
  - Ranitidine, famotidine (H2 blockers)
- Cromolyn
- Ketotifen
- Montelukast
- Dietary changes

Management of Mast Cell Activation Syndrome (MCAS)

- Avoid triggers for Mast cell activation such as NSAIDs, alcohol, opioids and sudden temperature changes.
- Inactive ingredients (binding agents, preservatives) in pills may contribute to MCAS.
- Low histamine diet.
- Review and change possible hidden food sources and the possibility of accidental exposure to such foods.
- Some of the usual suspects for MCAS to avoid are:
  - Seasonings (except olive oil, salt).
  - All dairy.
  - Eggs.
  - Grains except quinoa and rice.
  - Avoid beef products but okay to take lamb, venison and poultry.

Management of Mast Cell Activation Syndrome (MCAS)

- Food and drug reactions are a common cause of unexplained hives and rashes. Some of the other causes of hives may be exposure to change in temperature (hot to cold), rubbing skin, physical exertion, pressure and direct exposure to sunlight.
- Other methods to avoid exacerbation maybe:
  - Use pollen guards in windows.
  - HEPA air filters, A/C.
  - Use a mask while dusting or vacuuming.
  - Avoid long baths or showers, rapid changes in temperature, wool, dust and cigarette smoke.
- May use nasal saline.

Mast Cell Activation Syndrome (MCAS)

- Temperature instability – hot / cold
- Multiple chemical sensitivities – food, drugs,
- Sensitivities to multiple drugs maybe due to fillers – changing to a different brand may help
- Dry eyes, difficulty focusing,
- Hair loss
- Bladder pain: Interstitial cystitis – inflammation of bladder

Symptoms of EDS,POTS, MCAS

Headaches, brain fog, dizzy

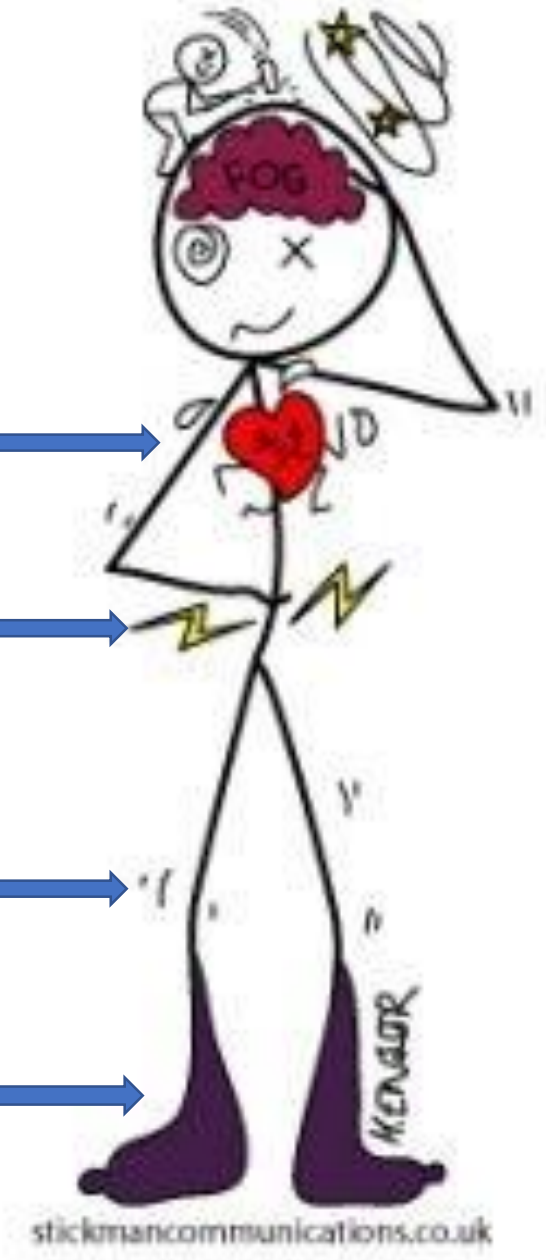
Blurry vision

Racing heart

Belly pain

Tremulousness

Dark discoloration of feet



Nerve pain

Complex Regional Pain Syndrome (CRPS) Neuropathic pain in EDS

Reflex Sympathetic Dystrophy (RSD)

Joan M. Stoler et al. Patients with Ehlers Danlos syndrome and CRPS: A possible association? Pain 123 (2006) 204–209

Lies Rombaut et al. Chronic pain in patients with the hypermobility type of Ehlers–Danlos syndrome: evidence for generalized hyperalgesia. Clin Rheumatol 2014 DOI 10.1007/s10067-014-2499-0

Family of Neuropathic pain such as CRPS and EDS

- Chronic widespread pain is common in EDS
- Part of this pain is neuropathic and Complex Regional Pain Syndrome (CRPS)

Joan M. Stoler et al. Patients with Ehlers Danlos syndrome and CRPS: A possible association? Pain 123 (2006) 204–209

Lies Rombaut et al. Chronic pain in patients with the hypermobility type of Ehlers–Danlos syndrome: evidence for generalized hyperalgesia. Clin Rheumatol 2014 DOI 10.1007/s10067-014-2499-0

Signs and Symptoms of CRPS

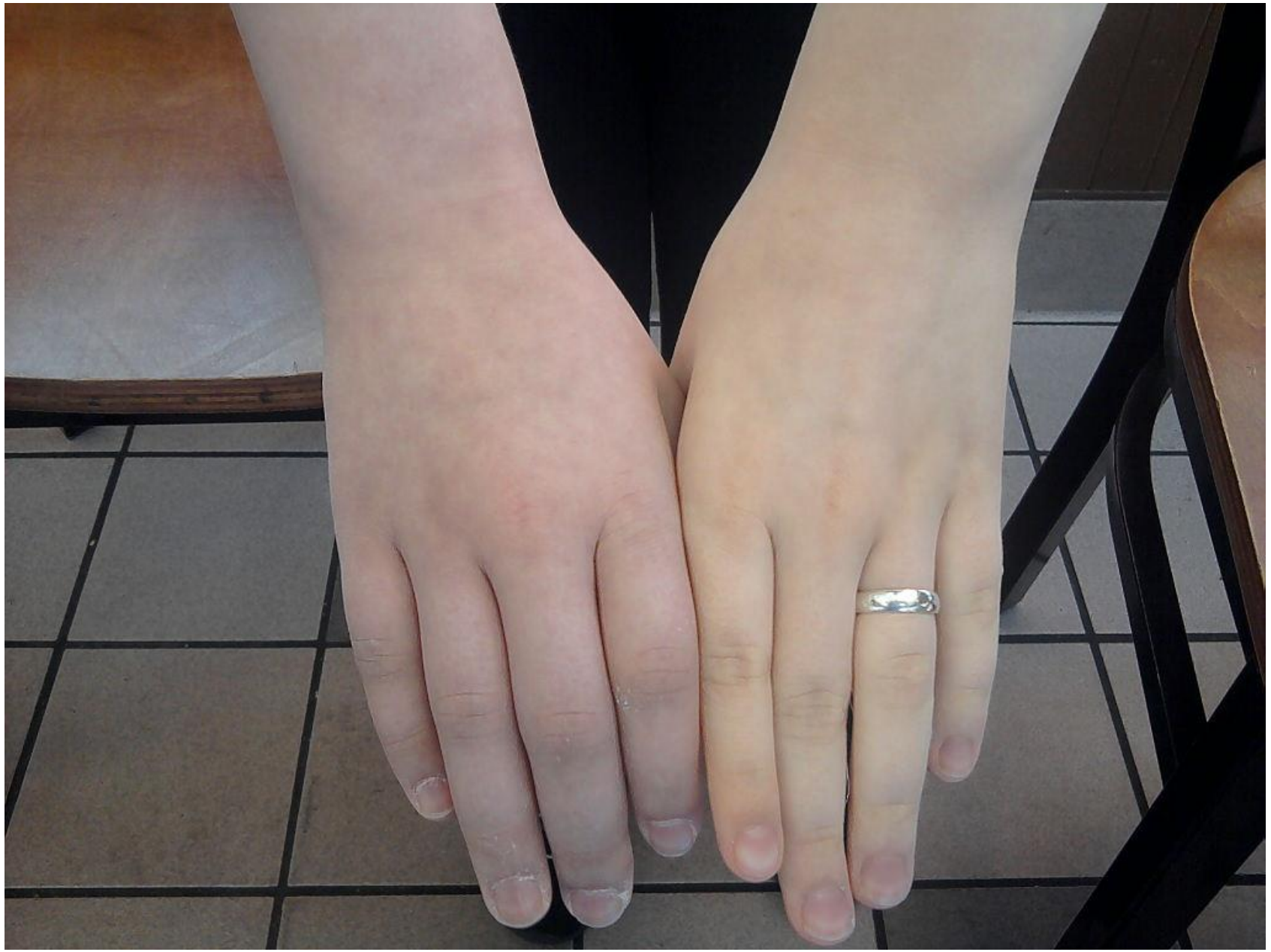
- Pain starts in one limb
- Constant pain, even at rest with intermittent exacerbations. Unexplained and diffuse
- Severe pain
- Temperature change, color change.
- Edema
- Area of pain larger than the primary injury
- Limited range of motion

Signs and Symptoms of CRPS 2

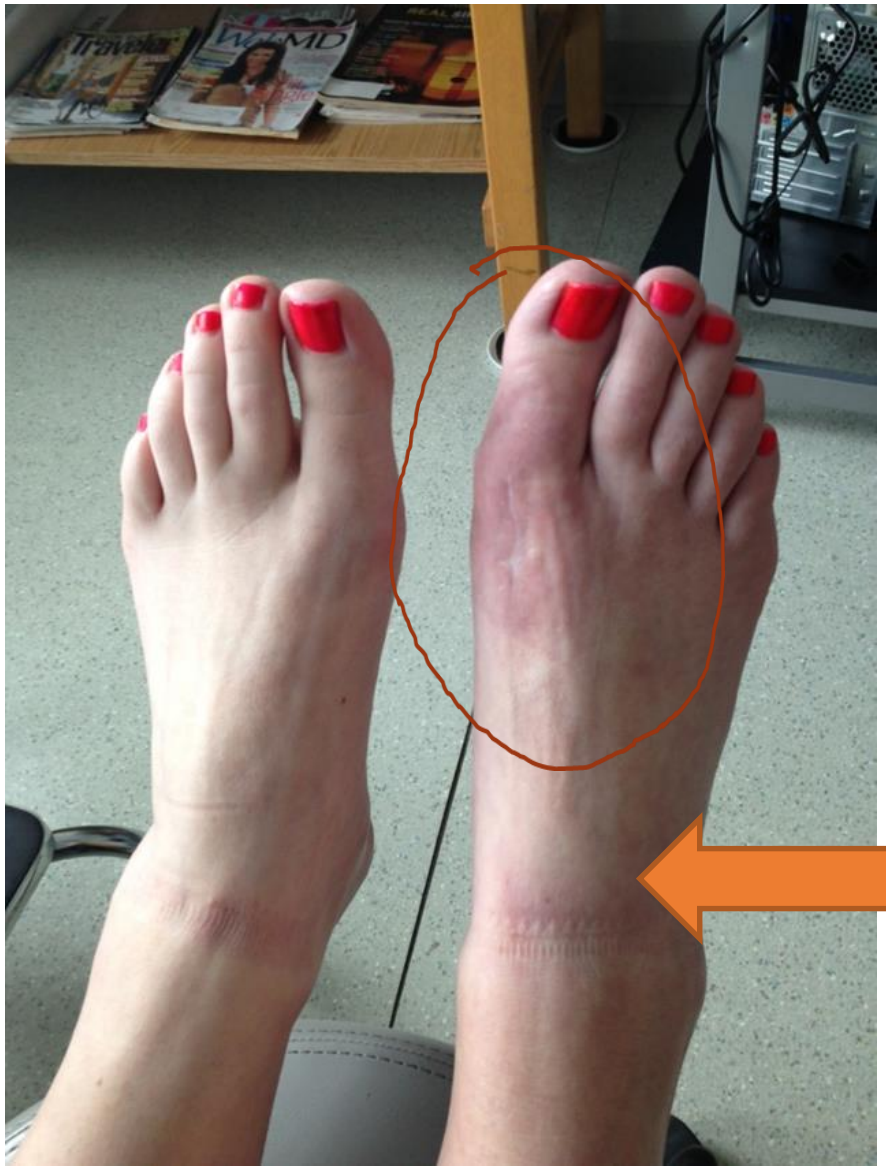
- Allodynia - pain on light touch
- Creepy, crawly sensation to touch - dysesthesia
- Nail growth changes (faster, distorted), hair growth changes (coarser, darker, rapid growth, hair falling), skin changes (atrophy of skin), skin lesions

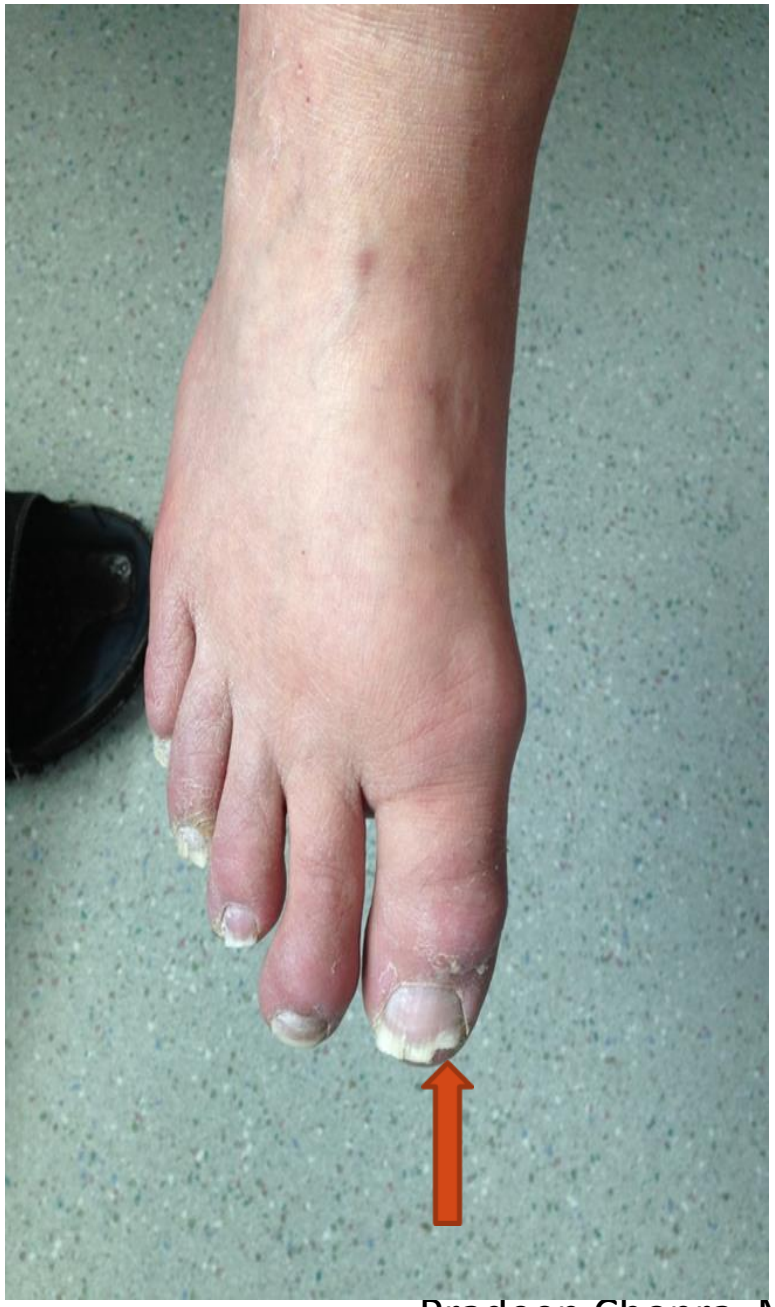
What Complex Regional Pain Syndrome is not…..

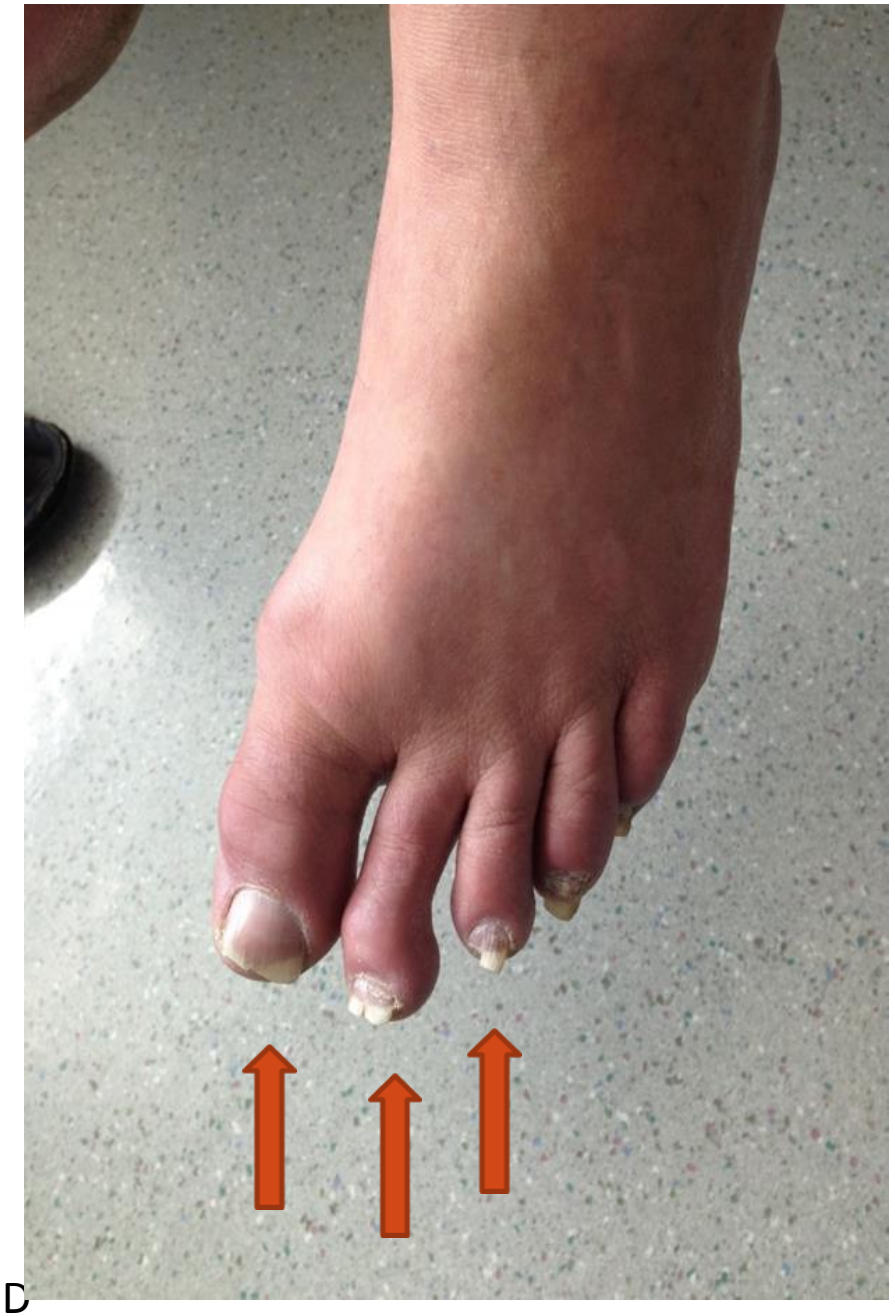
- There is no such thing as Amplified Pain Syndrome.
- It has been classified as the worst pain known to mankind – worse than amputation of a digit (McGill University)



Color, temperature and swelling







Fatigue in EDS

Fatigue

- Plenty of reasons for fatigue
- EDS
- POTS
- MCAS
- Drugs
- Pain
- Poor sleep

Fatigue in EDS

- Myopathy and axonal sensorimotor polyneuropathy (EMG with mixed myopathic and neurogenic) (1)
- They depend largely on their muscle tone to maintain posture at rest because of ligament laxity
- Non-restorative sleep
- Postural Orthostatic Tachycardia Syndrome
- MCAS
- ?secondary mitochondrial dysfunction

1. Voermans NC, van Alfen N, Pillen S, Lammens M, Schalkwijk J, Zwarts MJ, van Rooij IA, Hamel BCJ, van Engelen BG (2009) Neuromuscular involvement in various types of Ehlers–Danlos syndrome. Ann Neurol 65:687–697

Non Ehlers Danlos Syndrome

- Muscles – relaxed at rest and contract with activity
- Ligaments – tensed at rest, they support and stabilize the body

Ehlers Danlos Syndrome

- Muscles – They are tensed and constantly attempt to stabilize even at rest
- Ligaments – provide no tension and stability

Fatigue in EDS

- Stimulating the nervous system with amphetamine may not be the best choice
- Correct the underlying cause.
- Combination of ubiquinone and L-Carnitine
- Frequent breaks, do not push through fatigue
- Adequate hydration

Sample mixture of supplements for fatigue

Ubiquinone	**300mg PO QD**
Riboflavin (B_2)	100mg PO QD
Acetyl-L-Carnitine	416 mg PO QD
Thiamine (B_1)	300mg PO QD
Pyridoxine (B_6)	50mg PO QD
Cobalamin (B_{12})	50 mcg PO QD
Creatine	2g PO QD
Mannitol (filler)	1.834 g

Other treatments

- Oxygen
- Hormonal modulation
- Levodopa/carbidopa for muscle spasms
- EPSOM (Magnesium) salt bath
- Topical analgesics – predictable absorption

Oxygen supplementation

- Anecdotal experience
- Oxygen by non-rebreather mask 3 liters to 5 liters, 20minutes per day up to twice a day.
- May administer as needed for severe symptoms of fatigue or dizziness.

Levodopa-carbidopa

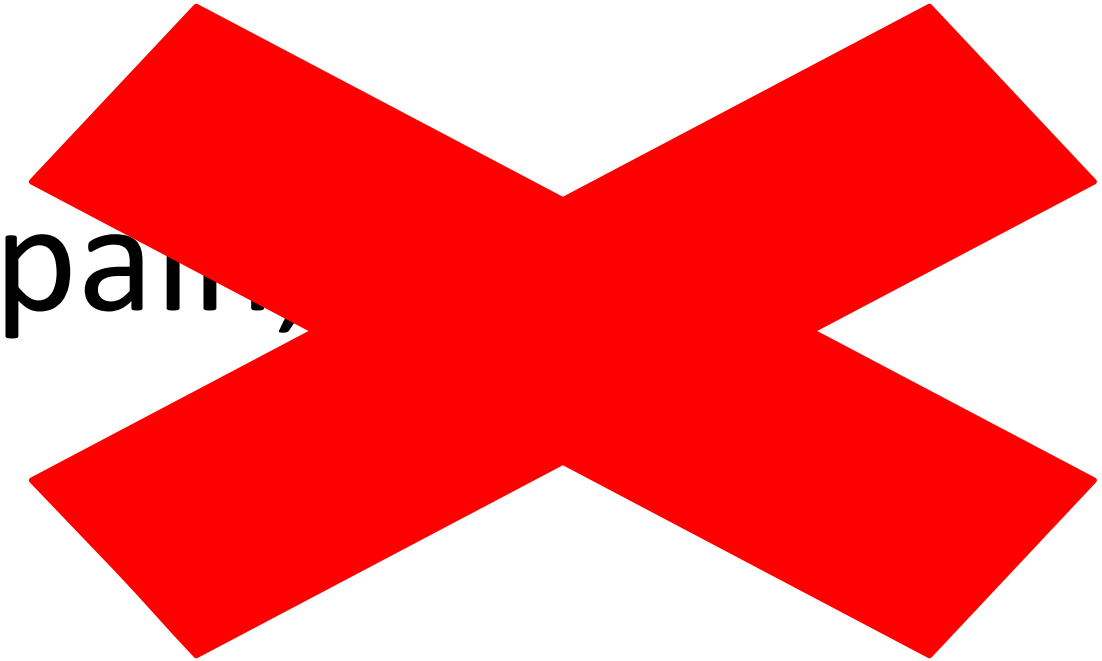
- Anecdotal experience
- Significant relief for muscle spasms and dystonia
- Low dose
- Sinemet ®

Poor concept of exercising in pain

- No pain, no gain

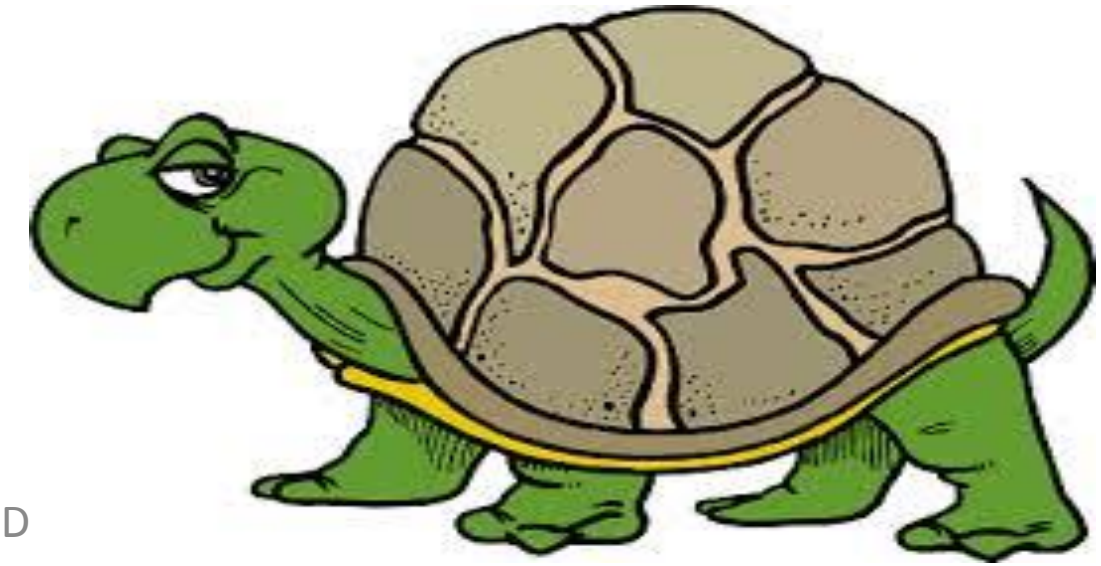
Poor concept of exercising in pain

- No pain



Starting treatment - medicines and exercise

Start low, go slow



Service Dogs - invaluable

- POTS – they can sense when their owner is having an episode of dizziness or seizure
- EDS and pain - they protect the limb from being injured or touched
- Helps boost confidence in their owners, making them more independent
- Help with balance, call for help, open doors, switch on lights, pull wheelchairs, anxiety,

Medicinal marijuana

- The human body has two types of receptors – CB1 and CB2
- CB1 receptors are found in the brain
- CB2 receptors are found in the rest of the body, immune cells and glia cells in the Central Nervous System
- Chemicals that cause inflammation in the peripheral parts of the body are modulated by cannabinoids. Hence, cannabis applied topically may be helpful

Medicinal Marijuana

- MM basically contains 2 substances – THC and CBD
- THC works on CB1 and is responsible for the cognitive effects
- CBD works on CB2 and is responsible for pain relief, helps autoimmune dysfunction.
- For MM to work, both THC and CBD have to be together, separating them is not as effective. This is called the Entourage effect.
- One can take MM with a higher concentration of CBD and lower concentration of THC – for pain
- Higher THC and lower CBD for sleep

Cannabis

- Cannabis can reduce the migration of inflammatory chemicals to the site of injury and into the brain.
- This is especially important because in immune dysfunction, migration of inflammatory cells into tissues and nervous system contributes to neuropathic pain

Medicinal Marijuana

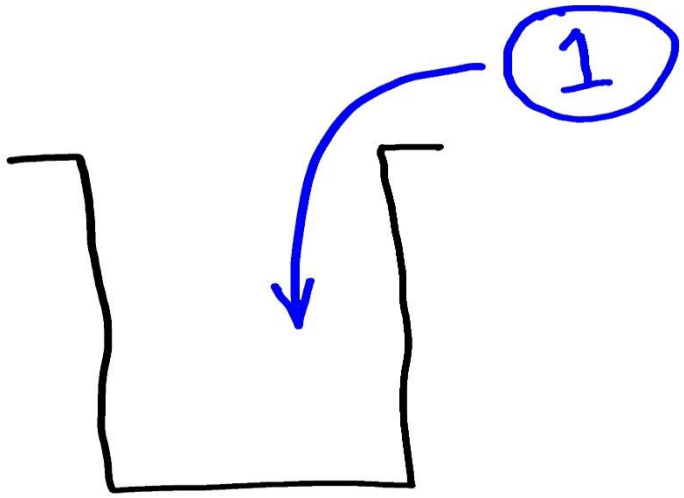
- Reasonable choice to try.
- Anecdotally – works well in patients with EDS
- Higher CBD levels and lower THC levels
- Vaporizing, edibles
- Topical over joints and muscles.
- Does not affect Mast Cell Activation Syndrome (MCAS) as much as NSAID’s and opioids

NC10 rule

Expectations from different therapies

3-111

NC 10 rule



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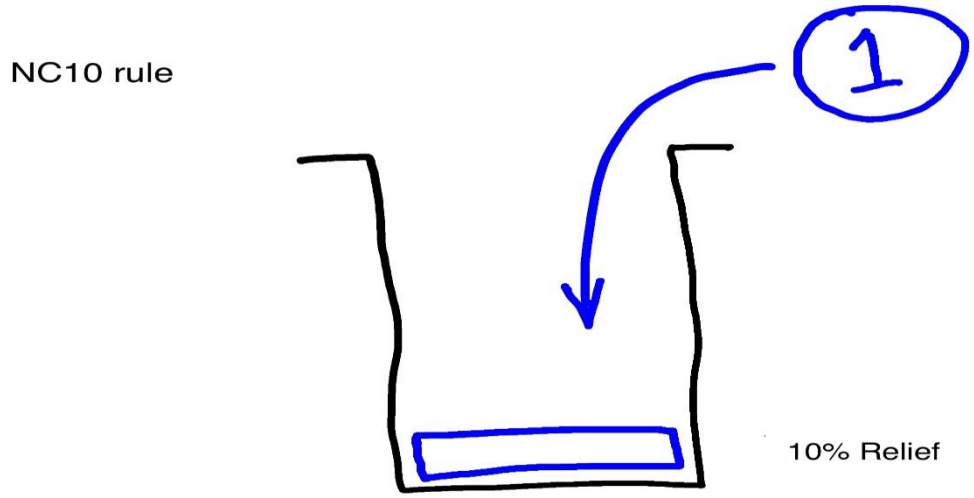
NC 10 rule



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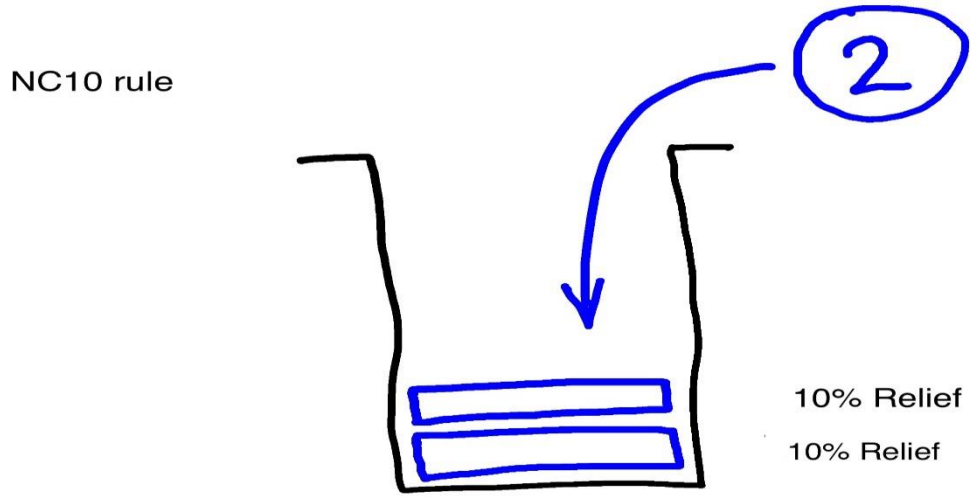
NC 10 rule



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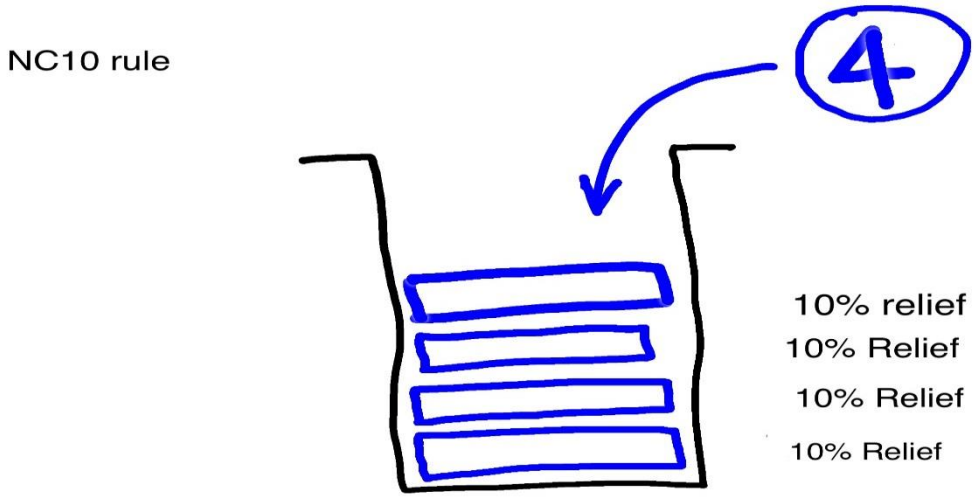
NC 10 rule



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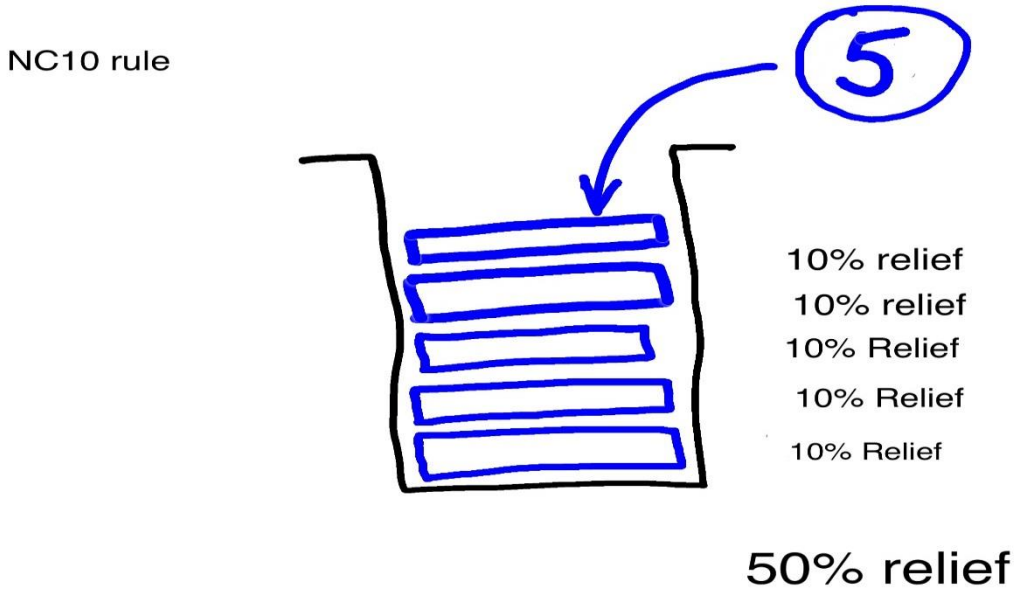
NC 10 rule



3-116

Low Dose Naltrexone

LDN

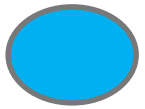
3-65

Low Dose Naltrexone (LDN)

- Competitive antagonist of opioid receptors
- Clinically used for 30 years for addiction
- Suppressive effects on the CNS glia, which….
- Attenuates production of pro-inflammatory cytokines and neurotoxic superoxides (chemicals that cause inflammation)

3-66

Low Dose Naltrexone (LDN)



- There are several theories as to how LDN may work.

1. Transiently blocks opioid receptor leading to positive feedback production of endorphins (Zagnon)
2. LDN increases production of OGF (opioid growth factor) as well as number of and density of OGF receptors by intermittently blocking the opiate receptor. Increased in OGF repairs tissue and healing.
3. Naltrexone blocks the effect of TLR4 (Toll Like receptors) which decreases glial cell activation

3-67

Low Dose Naltrexone (LDN)

- Dose can vary anywhere between 1.75mg to 4.5mg
- May cause insomnia, mild headaches initially.
- Patients report increased physical activity, flare ups not as acute, better tolerance to pain.
- Recommend a trial of at least 6 months
- To avoid all opioids or tramadol.

J Neuroimmune Pharmacol (2013) 8:470–476
DOI 10.1007/s11481-013-9451-y

PERSPECTIVE

Treatment of Complex Regional Pain Syndrome (CRPS) Using Low Dose Naltrexone (LDN)

Pradeep Chopra · Mark S. Cooper

Received: 7 November 2012 / Accepted: 4 March 2013 / Published online: 2 April 2013

Abstract Complex Regional Pain Syndrome (CRPS) is a neuropathic pain syndrome, which involves glial activation and central sensitization in the central nervous system. Here, we describe positive outcomes of two CRPS patients, after they were treated with low-dose naltrexone (a glial attenuator), in combination with other CRPS therapies. Prominent CRPS symptoms remitted in these two patients, including dystonic spasms and fixed dystonia (respectively), following treatment with low-dose naltrexone (LDN). LDN, which is known to antagonize the Toll-like Receptor 4 pathway and attenuate activated microglia, was utilized in these patients after conventional CRPS pharmacotherapy failed to suppress their recalcitrant CRPS symptoms.

Keywords Chronic pain · Complex regional pain syndrome · CRPS · Reflex sympathetic dystrophy · RSD · Neuropathic pain · Naltrexone · Fixed dystonia · Allodynia · Vasomotor · Ulceration · Dystonic spasms · Conversion disorder · Functional movement disorder · LDN

3-69

Introduction

Pradeep Chopra, MD

Complex Regional Pain Syndrome (CRPS), formerly known as Reflex Sympathetic Dystrophy (RSD) is a dysfunctions. One of the characteristic symptoms of this condition is that the pain is out of proportion to the initial injury. Diagnoses of CRPS are often delayed because it is under recognized (Binkley 2012). If effective treatments are given early enough in progression of the disease, there is reduced chance for the spread of regional pain, autonomic dysfunction, motor changes, and negative sensory symptoms, such as hypoalgesia (Marinus et al. 2011). As CRPS progresses, it becomes refractory to sympathetic nerve blocks, conventional analgesics, anticonvulsants and antidepressants.

During neuroimmune activation, TLR4 (Toll-Like Receptor 4) is upregulated in microglia, resident immune cells of the central nervous system (Watkins et al. 2009). After transection of the L5 spinal nerve in the rat, TLR4 expression is increased in spinal microglia. This correlates with the rodent developing neuropathic pain (Tanga et al. 2005). From a post-mortem analysis of a CRPS patient, activated microglia and astroglia in the central nervous system (CNS) have been implicated in the generation of CRPS symptoms (Del Valle et al. 2009).

Activation of TLR4 in both microglia and CNS neurons augments the production of pro-inflammatory cytokines via the NF-κB pathway (Milligan and Watkins 2009; Leow-Dyke et al. 2012). NF-kB is a multi-functional transcription

CENTRAL SENSITIZATION

Key concept to understanding all chronic pain

3-12

Central Sensitization

- A normal sensation (e.g. touch) produces an abnormal response (like pain) because the brain and spinal cord are sensitized

- Definition: Increase in the excitability of neurons within the central nervous system (CNS) so that normal inputs produce abnormal responses

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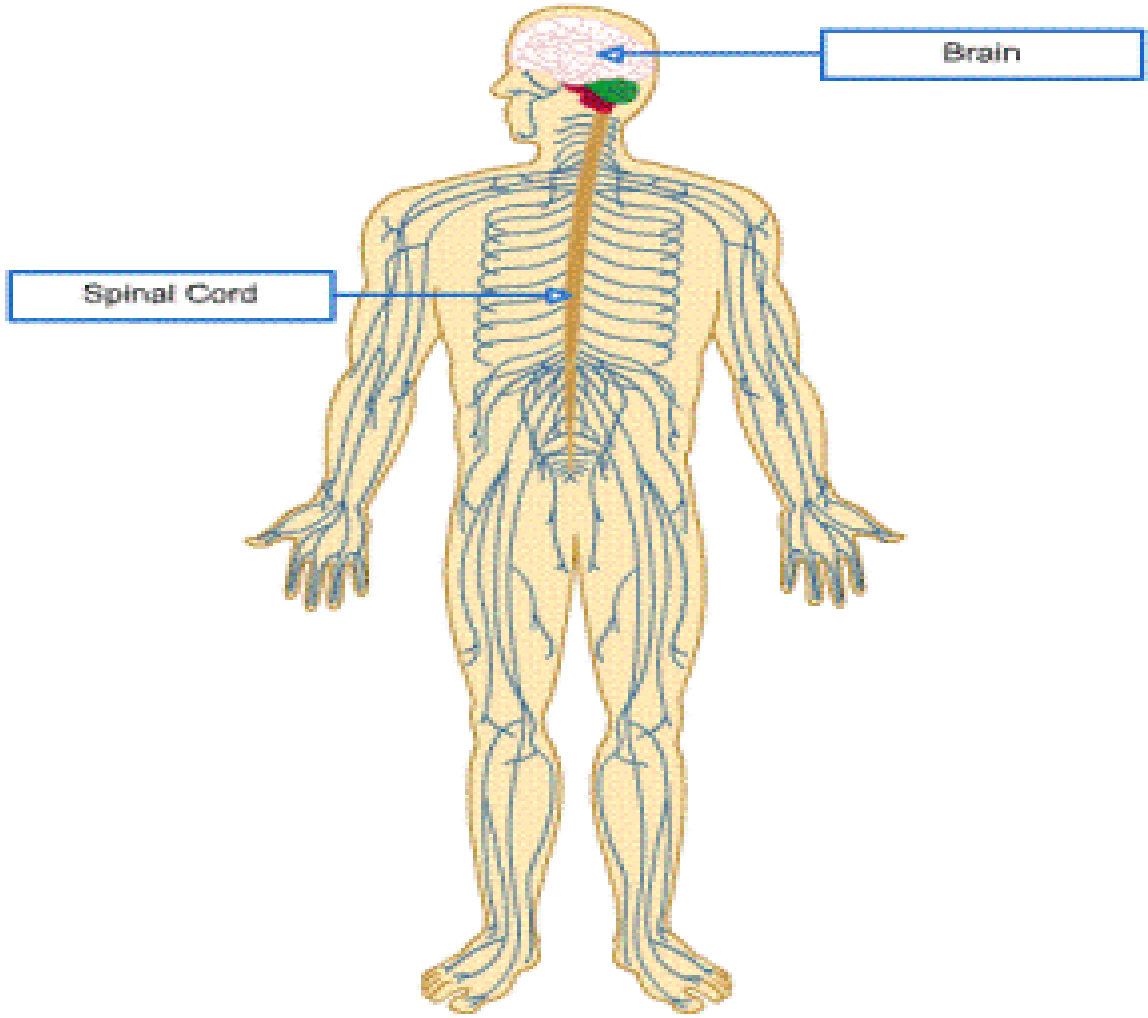
Central Nervous System

- The Central Nervous system (CNS) is made of 2 parts:

1. Brain
2. Spinal cord



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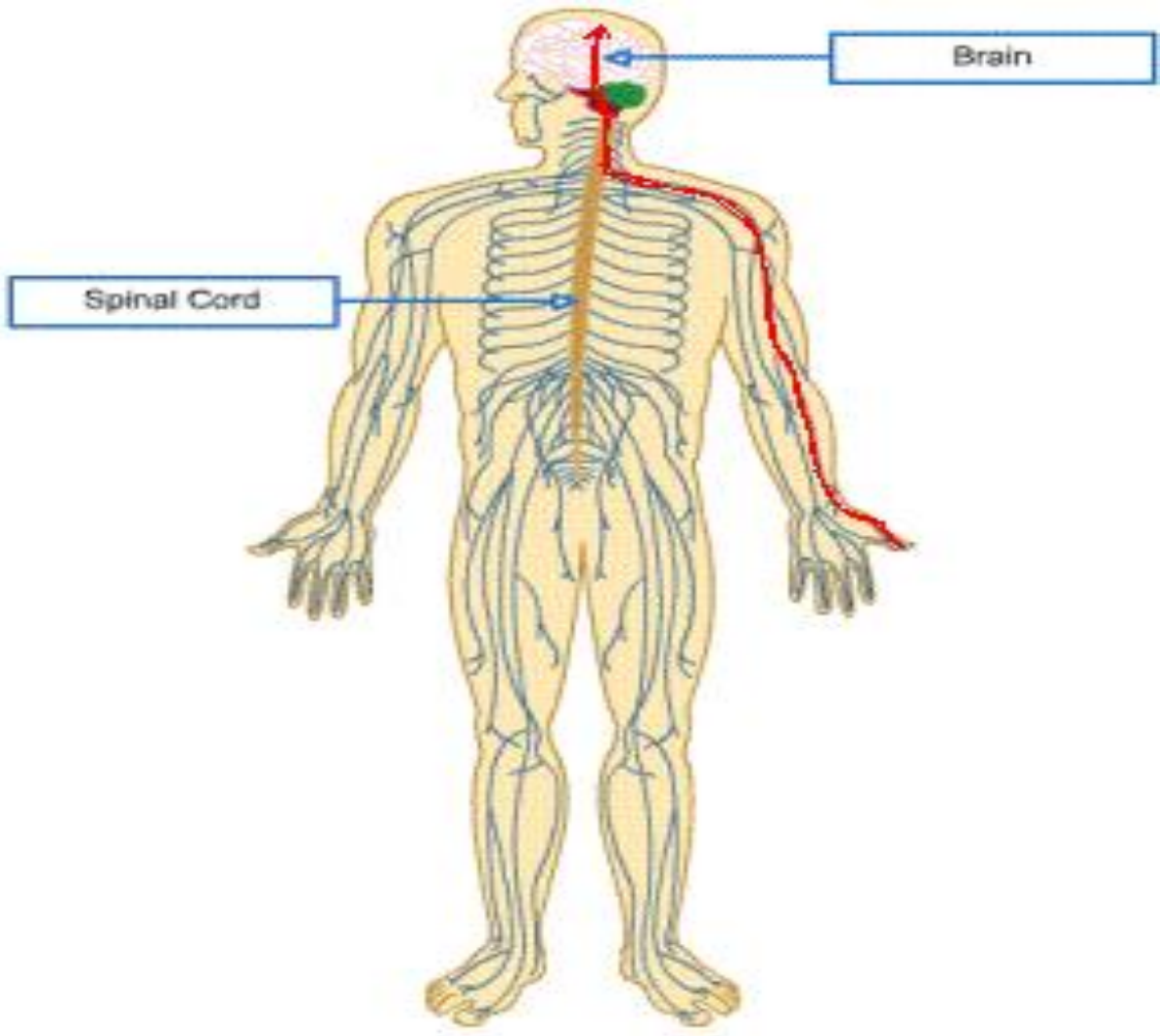
Normal pain

- Normally, an injury will cause pain and the signals are sent to the brain
- In the brain, the signal gets an emotional component and we sense pain



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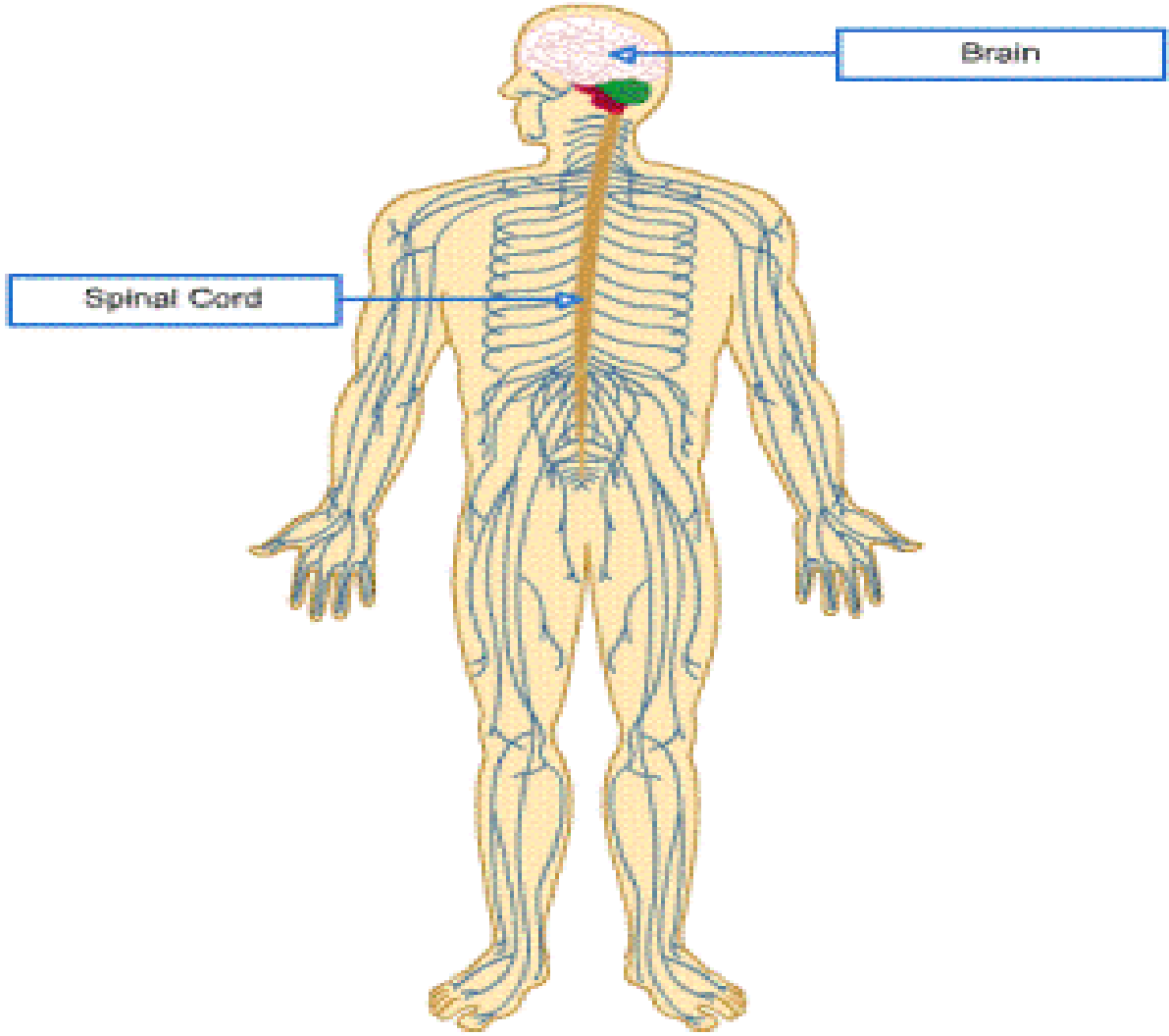
Normal pain

- Once the injury heals, the signals stop and everything returns to normal



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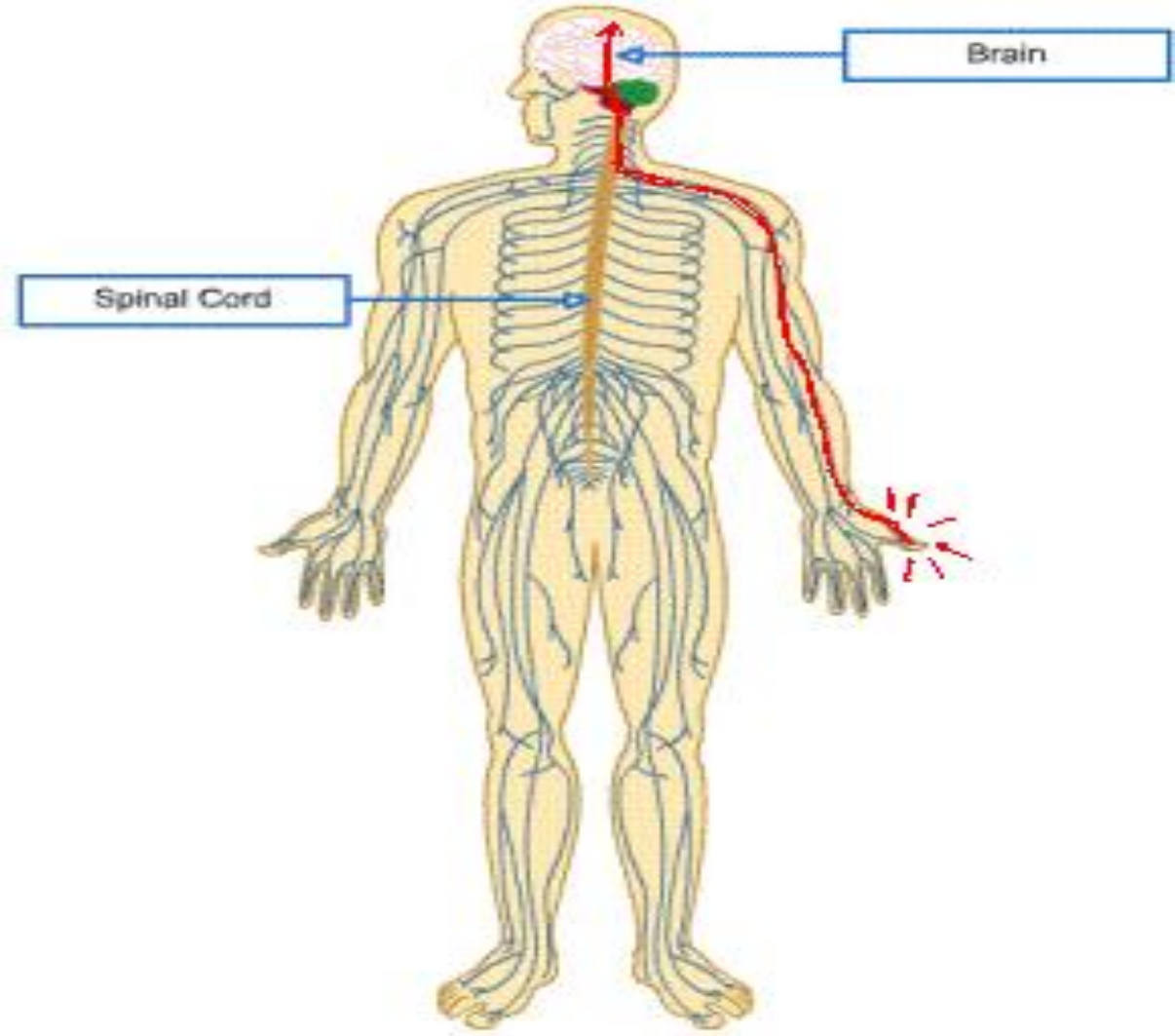
CRPS

- In CRPS, the pain signals continue even after the injury heals
- The brain also tries to send signals down to suppress the pain signals
- In CRPS, there is a constant barrage of pain signals travelling up and down



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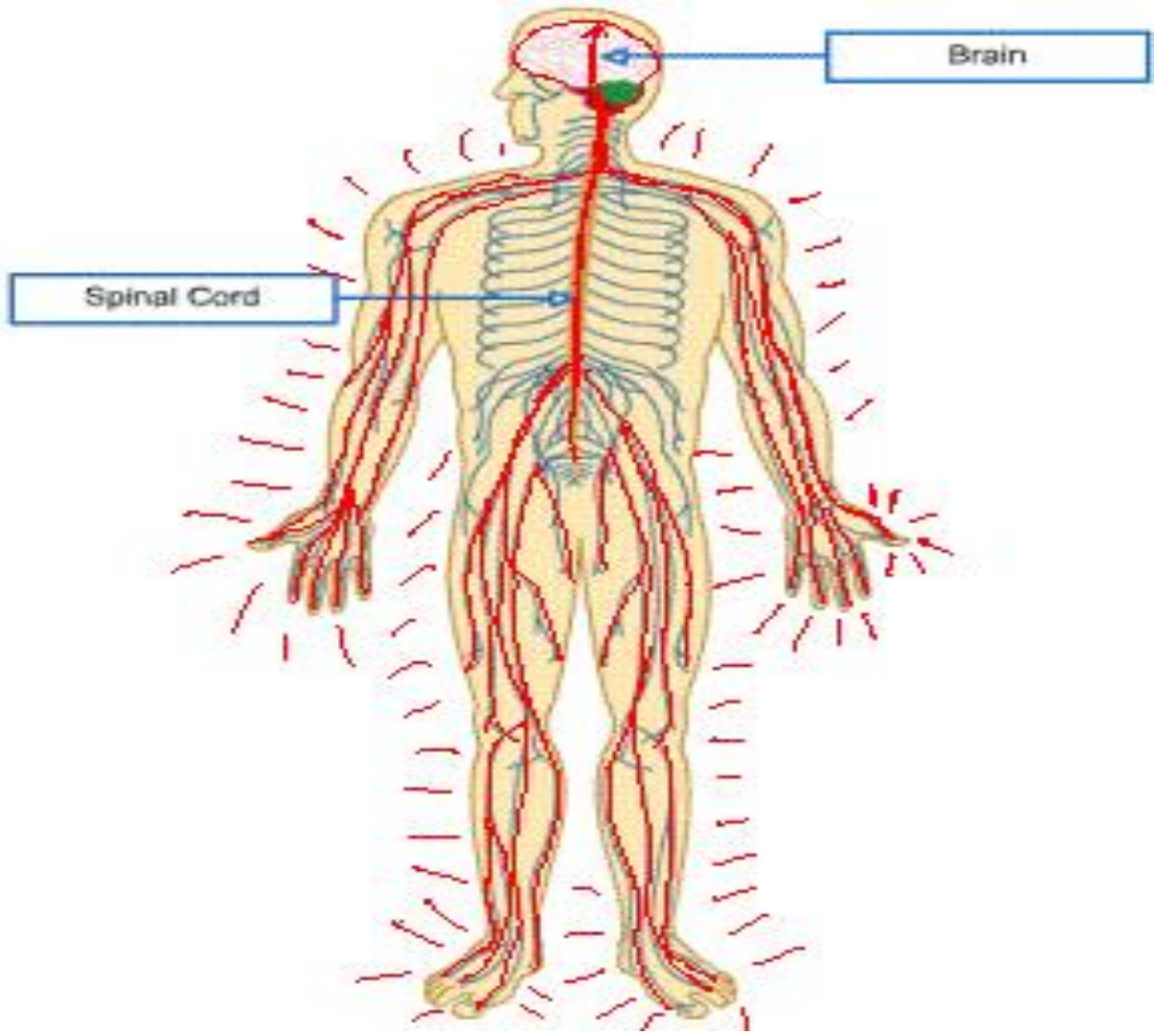
Central Sensitization

- The constant barrage of signals travelling up and down the brain and spinal cord makes the nervous system sensitive
- This is called Central Sensitization
- Hence, normal touch or a minor injury anywhere in the body, magnifies the pain greatly



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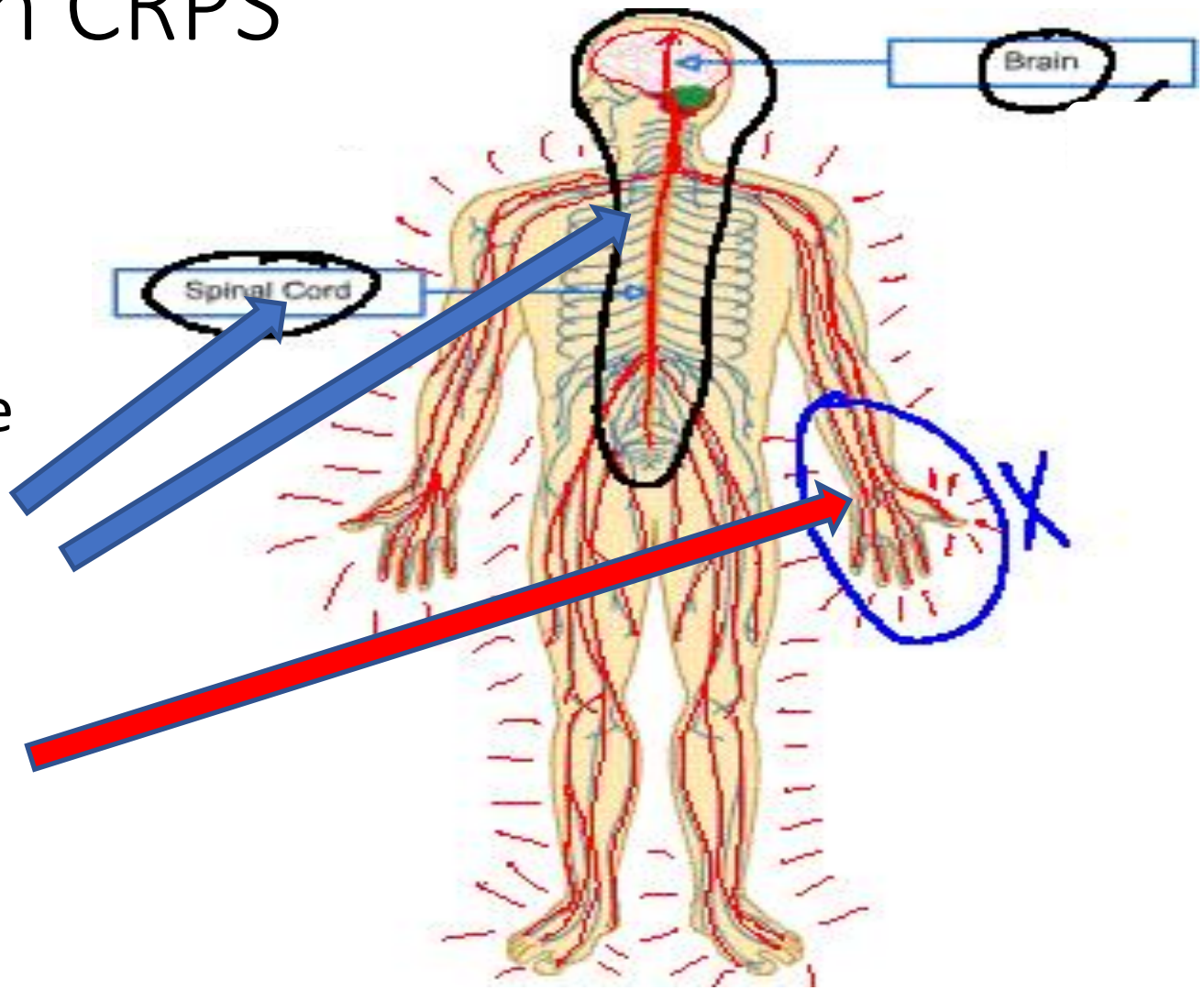
Central Sensitization in CRPS

- In CRPS (and other chronic pains), the problem lies in the Central Nervous system
- Any treatment for CRPS, should be to treat it at the level of the Central Nervous system
- Treating the pain at the periphery may not help and may even make the pain worse



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What really happens in CRPS /Central Sensitization

3-20

Central Sensitization

- Two things happen in Central Sensitization:
  1. Glial cells get activated
  2. NMDA receptors are activated

3-21

Central Sensitization: Activated Glial Cells

- Glial cells make up 70% of all the cells in our Central Nervous System
- Under normal circumstances, they remain dormant and are part of the nervous system's immune function

3-22

Milligan ED, Watkins LR (2009) Pathological and protective roles of glia in chronic pain. Nat Rev Neurosci 10:23–36 254

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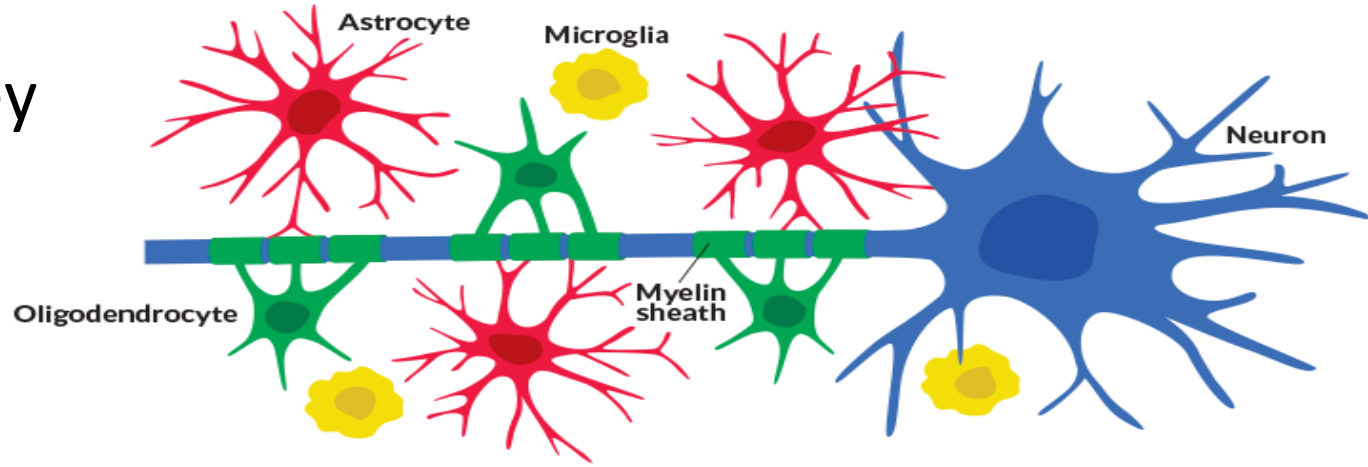

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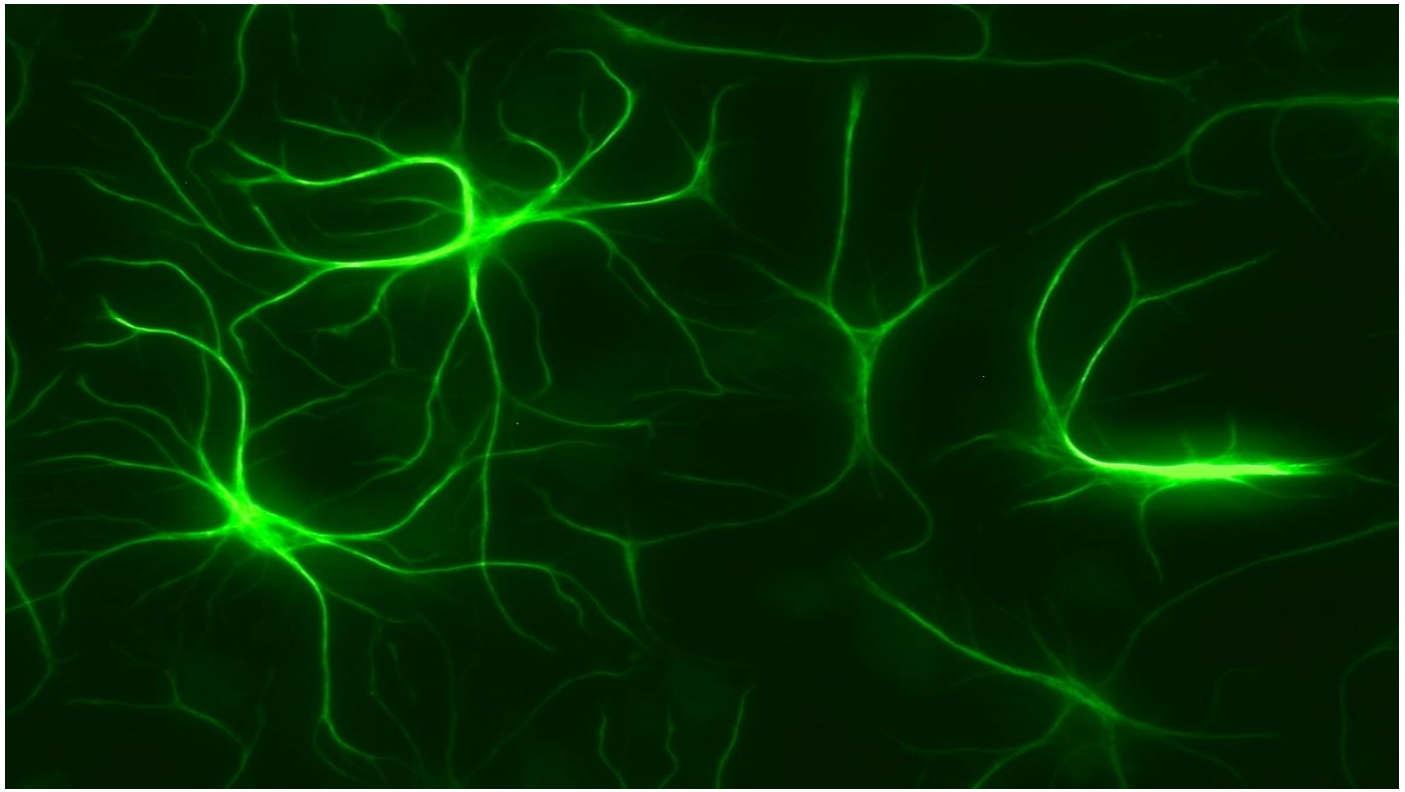
This is what glial cells look like



Courtesy Jarred Younger, PhD

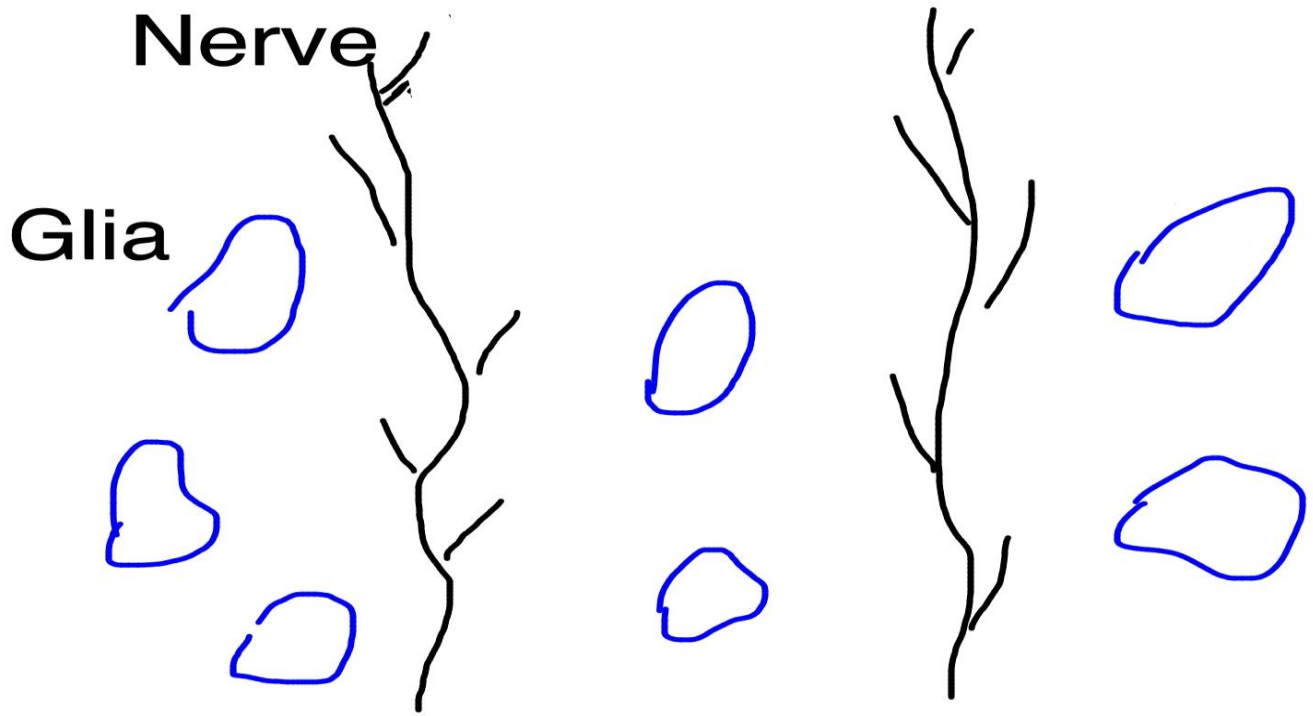
Sonja Paetau, University of Helsinki

Central Sensitization: Activated Glial Cells

- In CRPS these glial cells are activated.
- Activated glia release certain chemicals (Cytokines) that cause nerves to become inflamed
- Glial cells are an important link between the nervous system and the immune system and inflammation and pain

Milligan ED, Watkins LR (2009) Pathological and protective roles of glia in chronic pain. Nat Rev Neurosci 10:23–36

Glia and nerves under normal conditions



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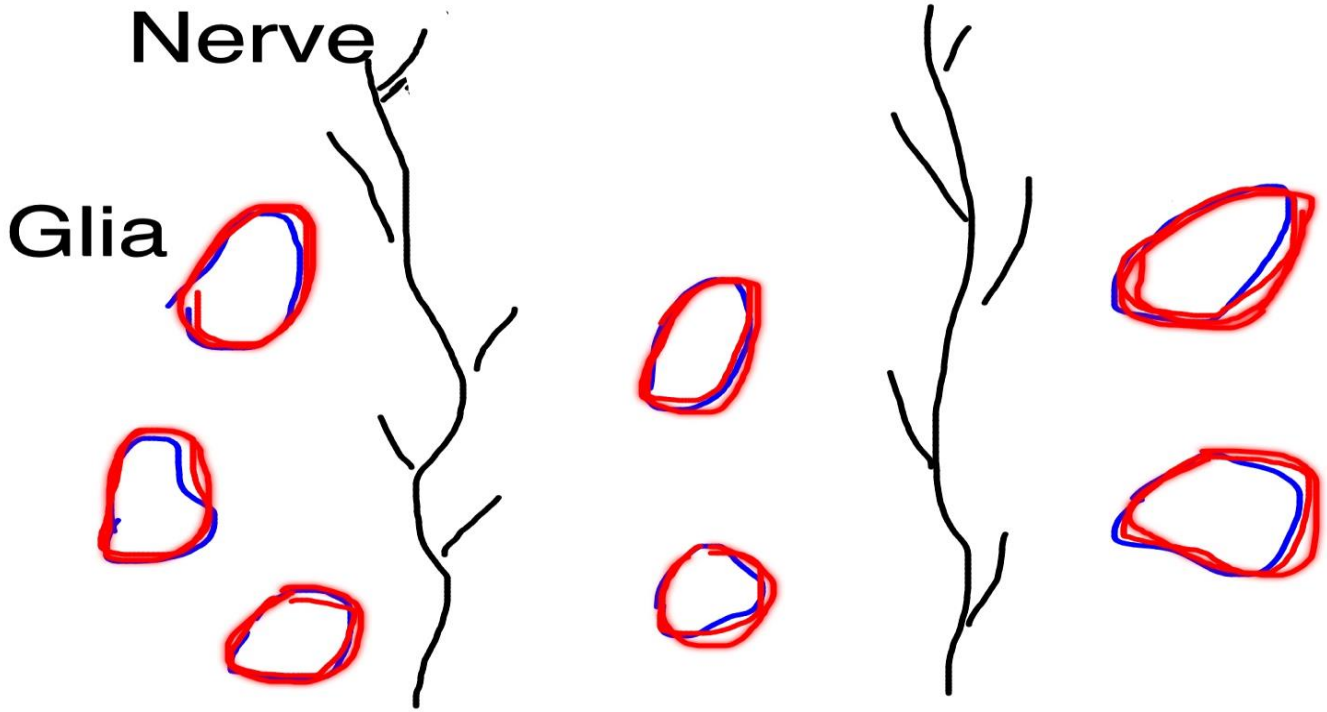
Activated Glia



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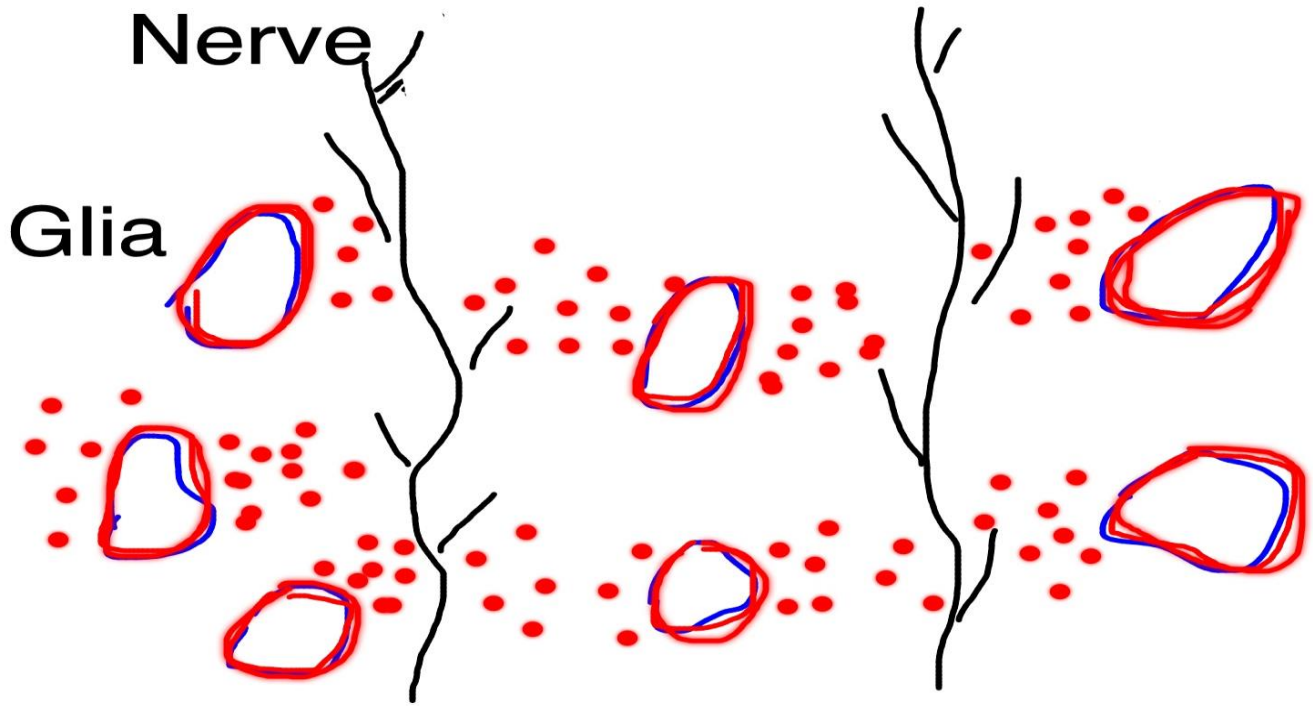
Chemicals released by activated Glia



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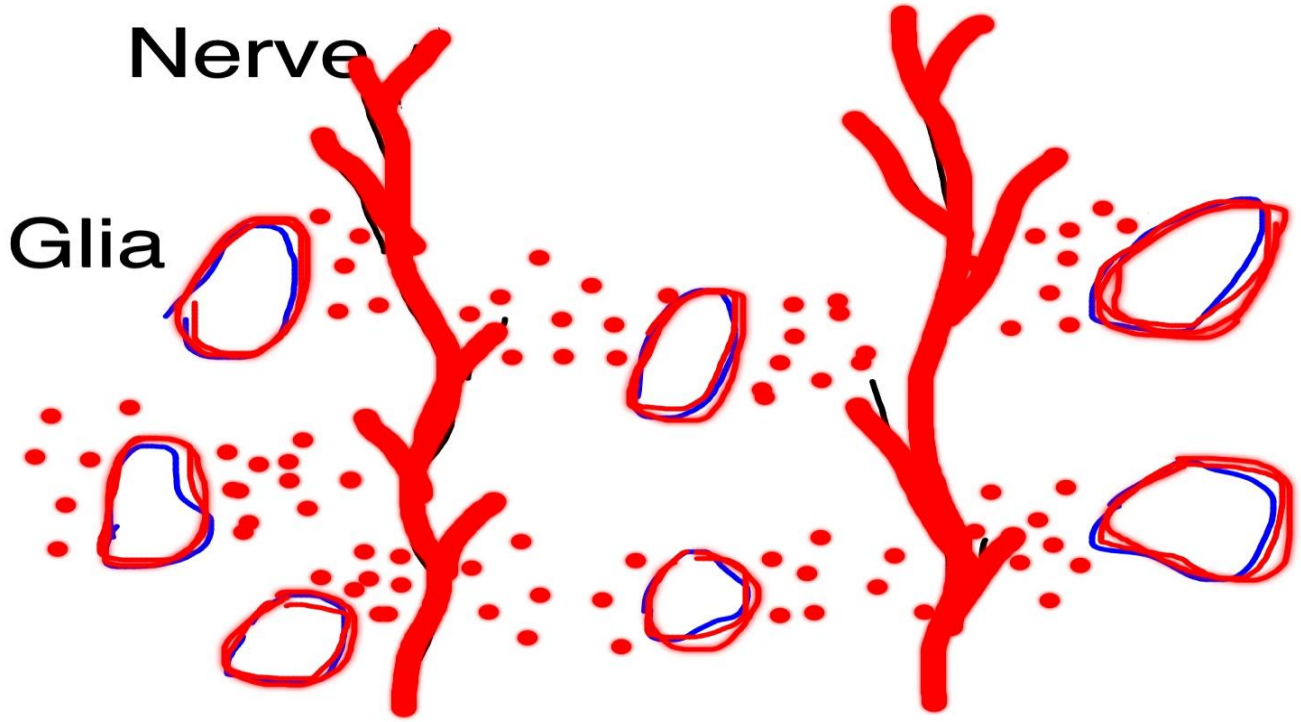
Nerve inflammation



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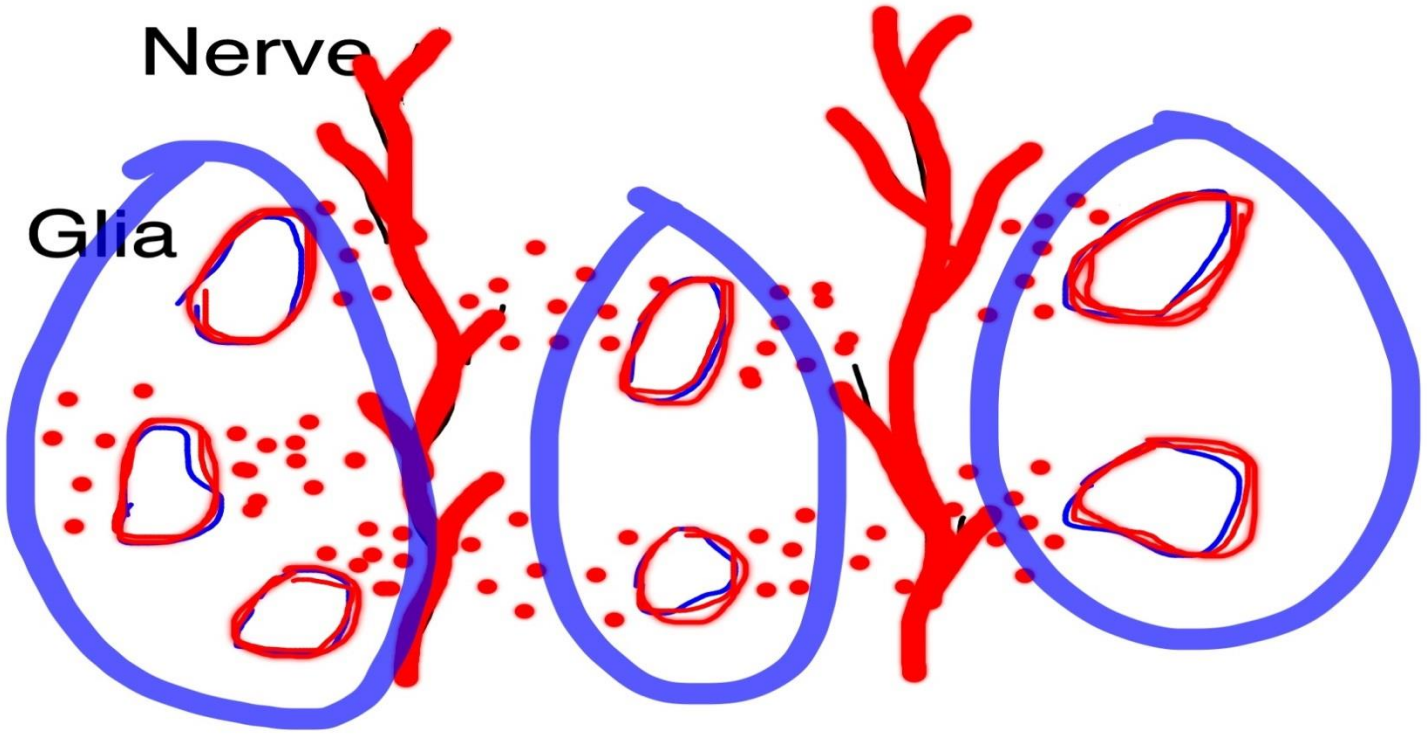
The problem is with the glia cells



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Graded Motor Imagery

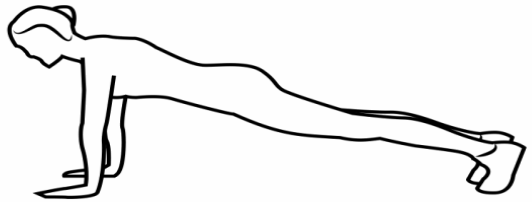
Stage 1: Left/Right discrimination – Graded Motor Imagery

- In CRPS, people often lose the ability to identify left or right images of their painful body parts.
- This ability is important for normal recovery from pain
- The good news is that the brain is plastic and changeable.
- The ‘Recognise’ app helps regain this ability

3-79

Stage 2: Explicit Motor Imagery - Graded Motor Imagery

- The process of thinking about moving without actually moving
- Imagined movement can actually be hard work if you are in pain.
- 25% of our brain is made of ‘mirror neurons’ – they start firing when you think of moving or even watch someone else move
- Imagining movements before actually moving you use the same neurons that you would use when you actually move



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www.gradedmotorimagery.com Neuro Orthopedic group, Australia

Stage 3: Mirror therapy- Graded Motor Imagery

- By hiding the affected limb behind a mirror, you can trick the brain into believing that the reflection of the normal hand is the affected limb.
- In your brain you are exercising the affected limb as you move the normal limb.

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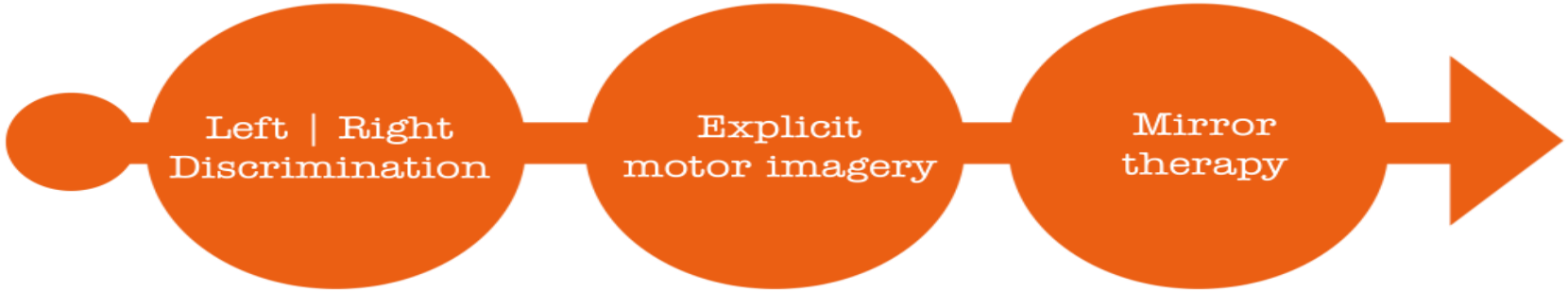
Three stages of Graded Motor Imagery delivered sequentially



- Left / right discrimination
- Explicit Motor imagery
- Mirror therapy
- www.gradedmotorimagery.com

3-82

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Pain receptor behavior

- When we take a drug for pain for a long time there is downregulation of the receptors, which means….
- The body's response to the drug is not as good.
- If we stop the drug for sometime, the receptors are upregulated, which means….
- Restarting the drug gets a better response at a lower dose.

3-117

Pain receptor behavior - drug rotation

- Ideally, a person could switch between drugs of a different class.
- For example, a patient on opioids for some months can take a ‘drug holiday’ for a few weeks to months.
- During this time, they can try medicinal marijuana (if legal) or ketamine (sublingual) or NSAID’s
- After some time restart opioids at a lower dose.

3-118

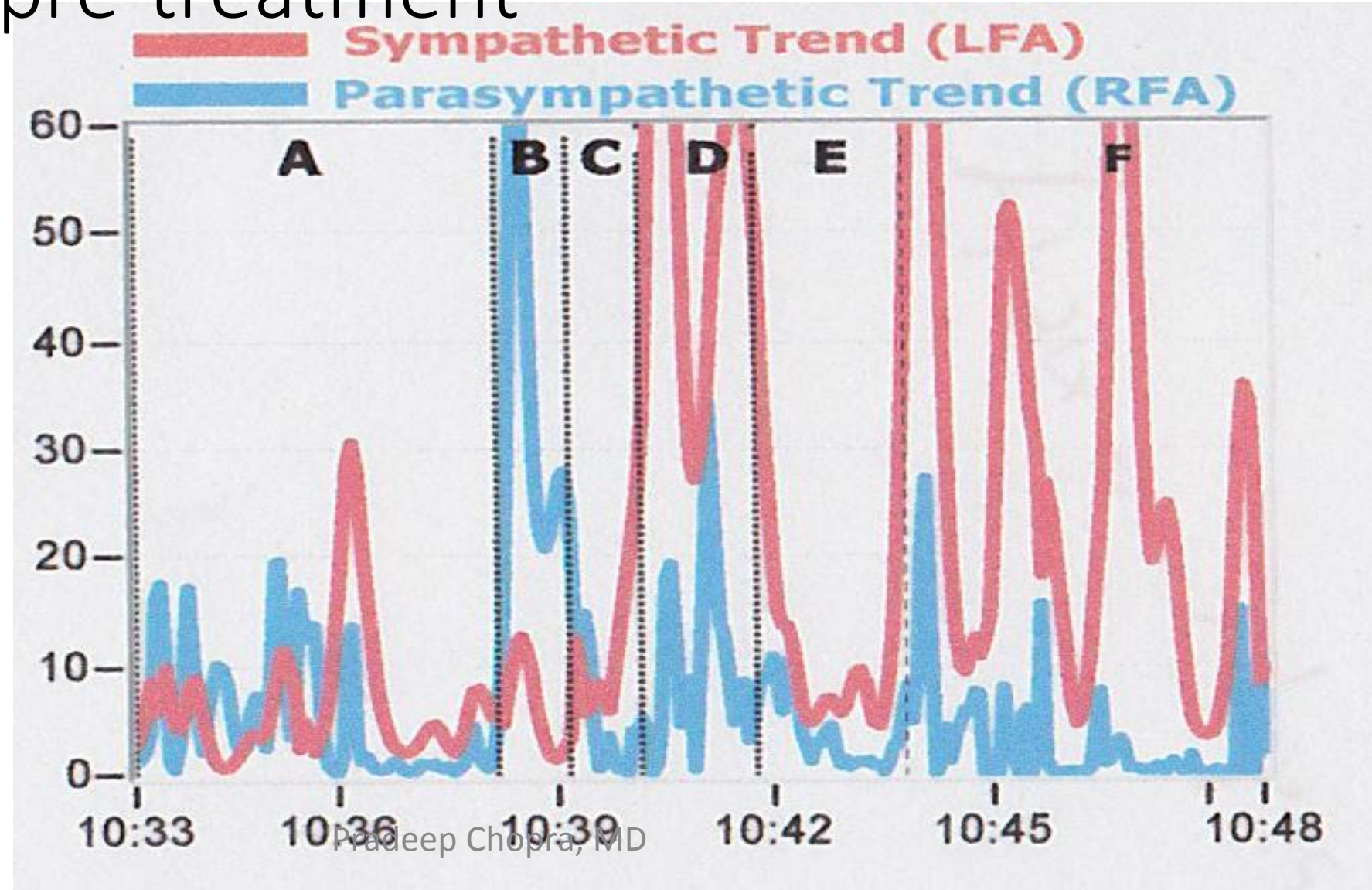
Sleep and EDS

Sleep and EDS

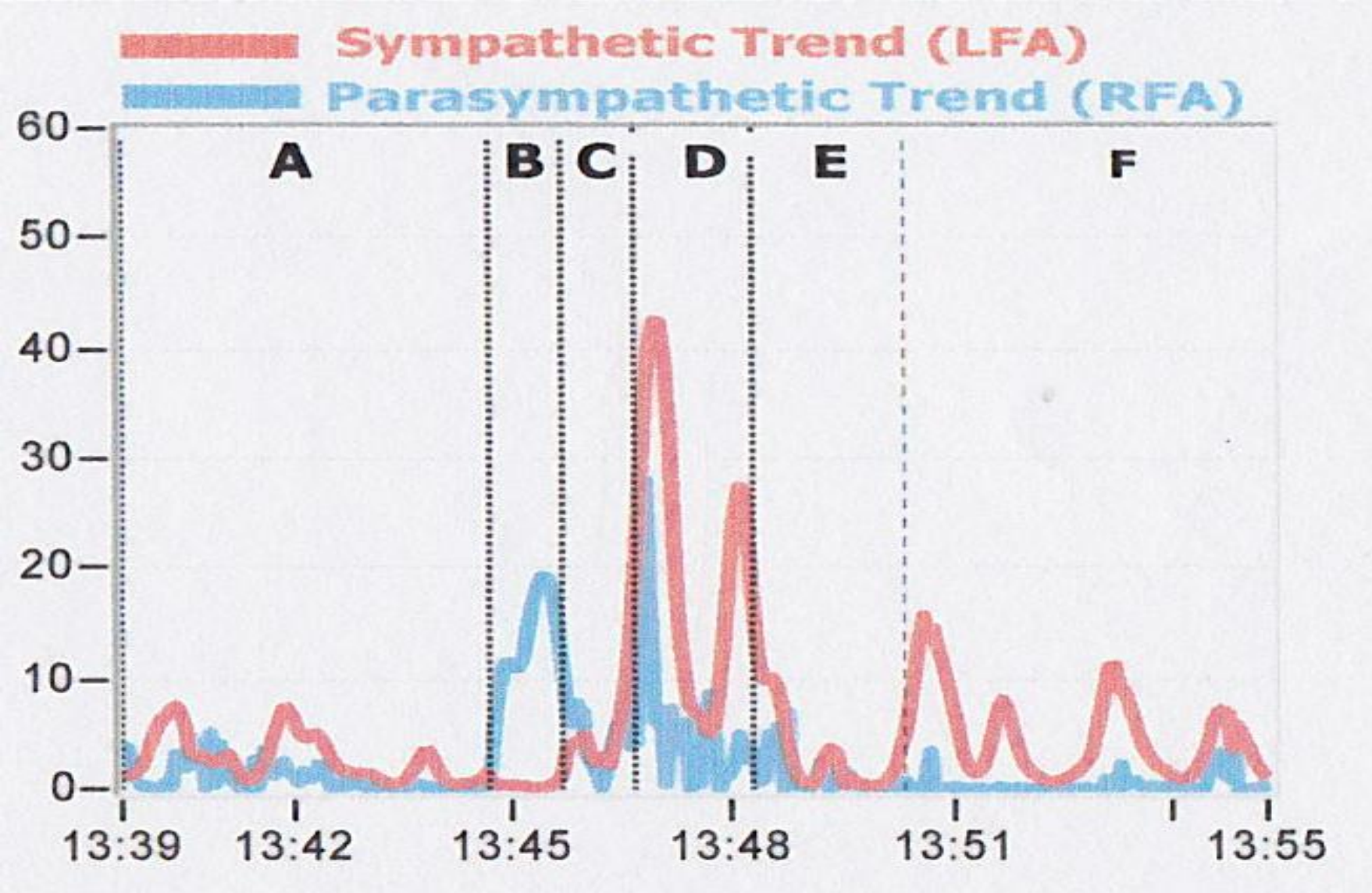
- Pain keeps them awake
- If they fall asleep they continue to produce adrenaline (because of Dysautonomia/POTS) they have light, dream-filled sleep
- Increased number of sleep disrupting ‘arousals’
- Wake up unrefreshed – Non-restorative sleep.

Courtesy Alan Pocinki, MD

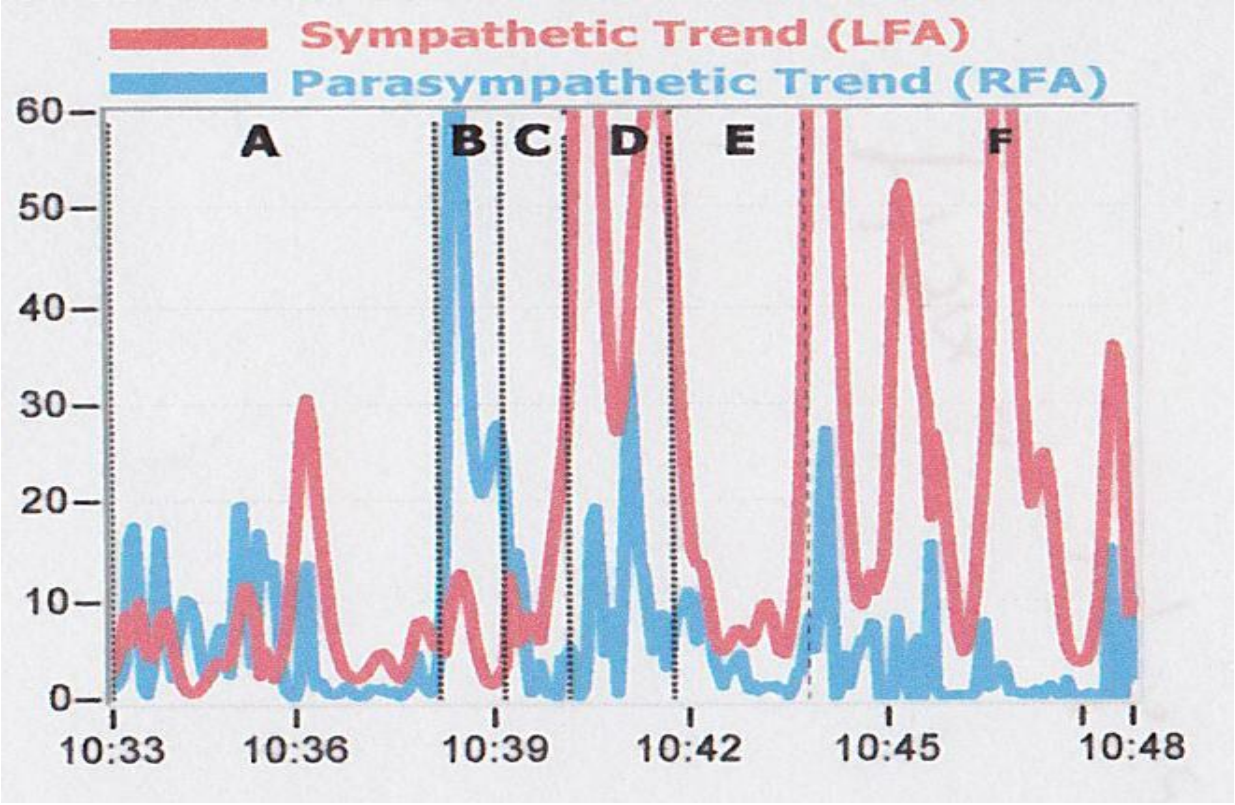
Brain activity during sleep – non-restorative sleep pre-treatment

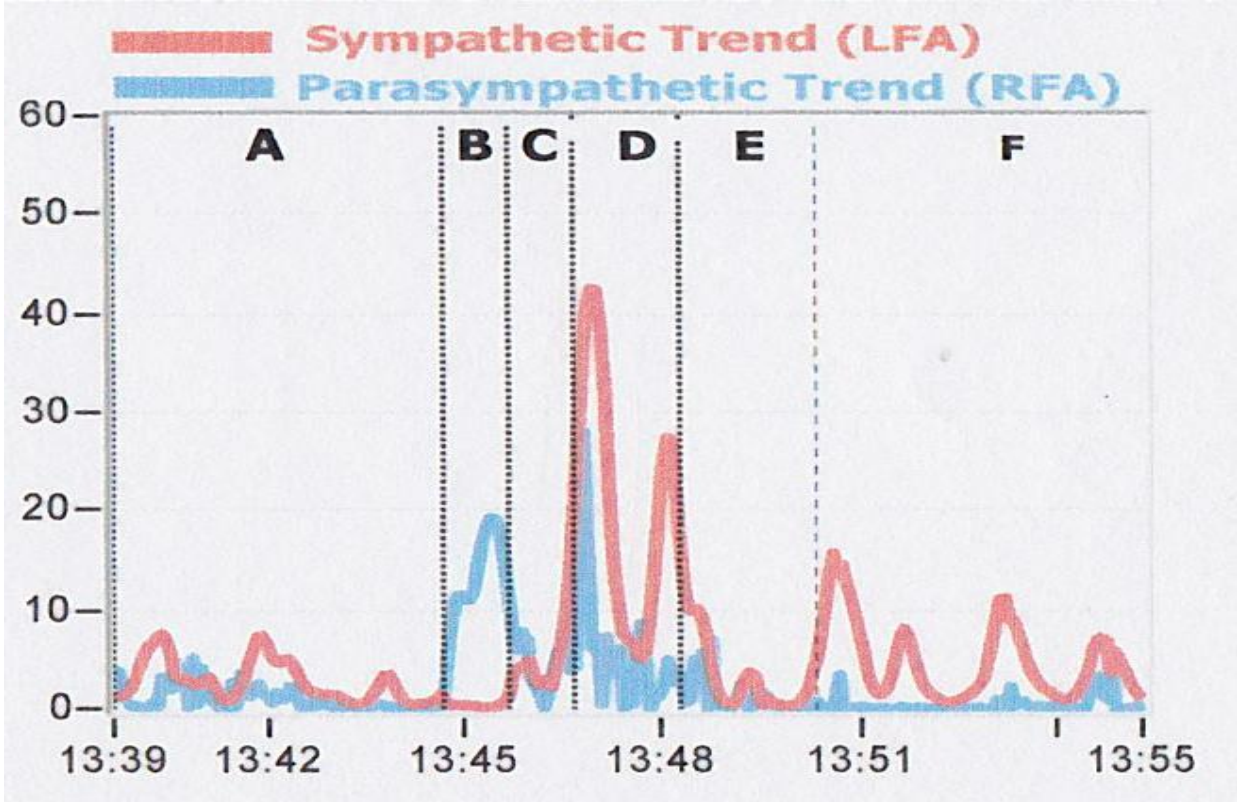


Brain activity during sleep – after beta blocker



Non-restorative sleep





Courtesy Alan Pocinki, MD

Non-restorative sleep

- Good sleep hygiene – comfortable mattress, dark and quite room, no digital lights
- Beta blockers – propranolol
- Alpha blockers – clonidine, guanfacine
- Pain medicines

Connecting the dots…..

- Fatigue (EDS, POTS, MCAS)
- Diffuse pain (EDS, POTS, MCAS)
- Headaches (EDS, POTS, MCAS, TCS, CM)
- Joint pain (EDS, TCS)
- Dizziness (POTS, CM)
- Poor balance (EDS, POTS, TCS, CM)
- GI issues (MCAS, EDS)
- Feeling anxious (POTS, MCAS)

Thank you

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