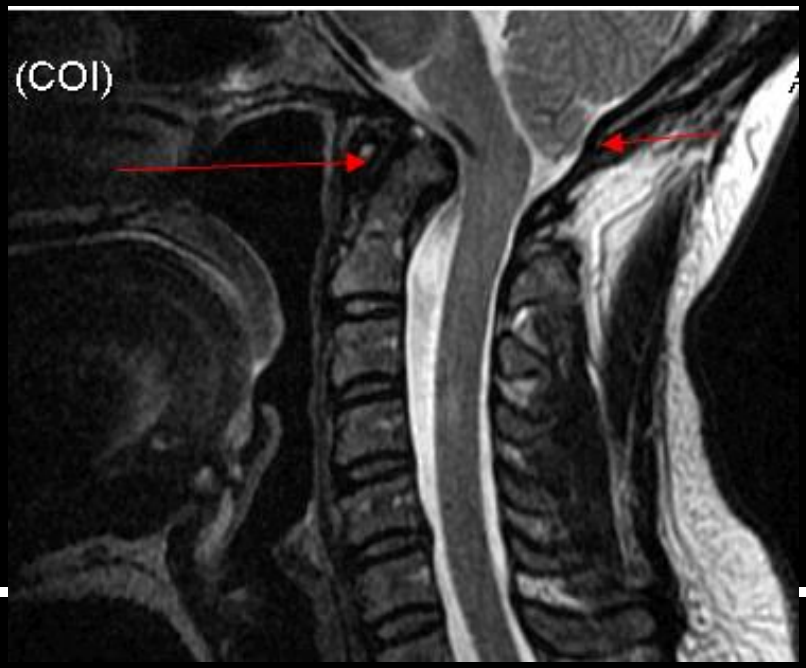
Neurosurgical Management of Hereditary Hypermobility Connective Tissue Disorders



Fraser C. Henderson Sr, MD

EDNF, Baltimore, August 14th, 2015

EDS

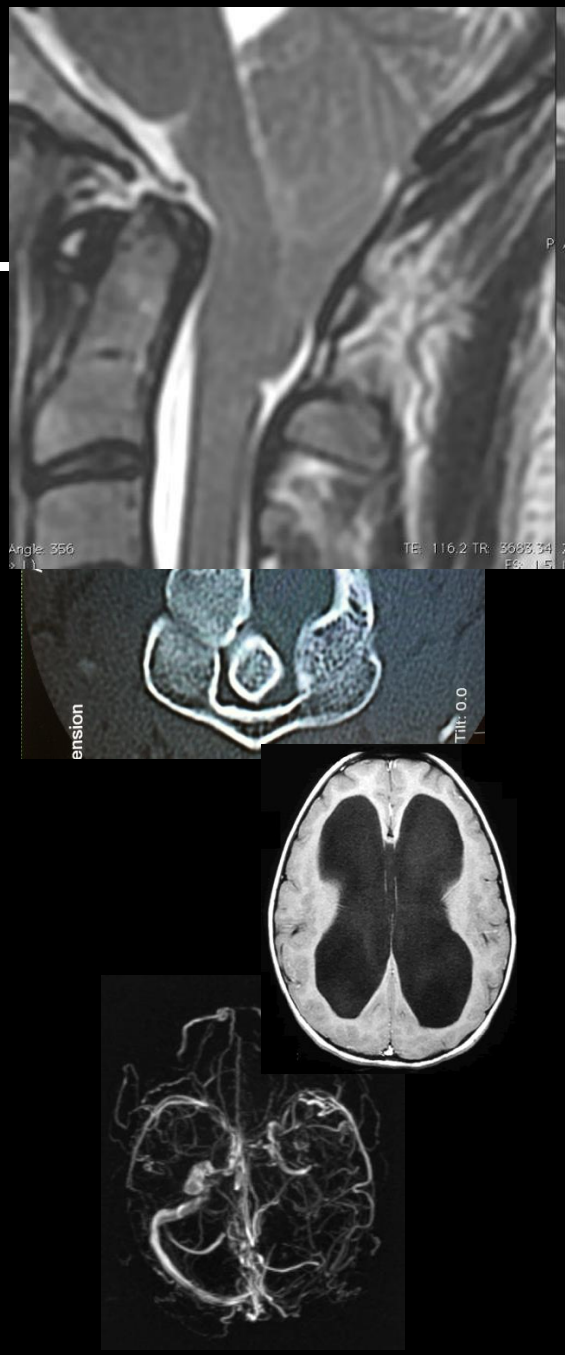
- Complex neurological syndromes
- Chronic ,severe pain
- Minimal radiological findings
- Multiple systemic dysfunction
- multiplicity of overlapping syndromes

Goals

- Lax ligaments result in abnormal bending cranio-cervical junction and spine with the result of stretching and deformation of CNS
- EDS may present with a variety of neurosurgical issues
- Neurobiology
- Outcome of 2 studies of craniospinal fusion for craniocervical instability
- Other neurological conditions associated with EDS

Causes of Headache in EDS

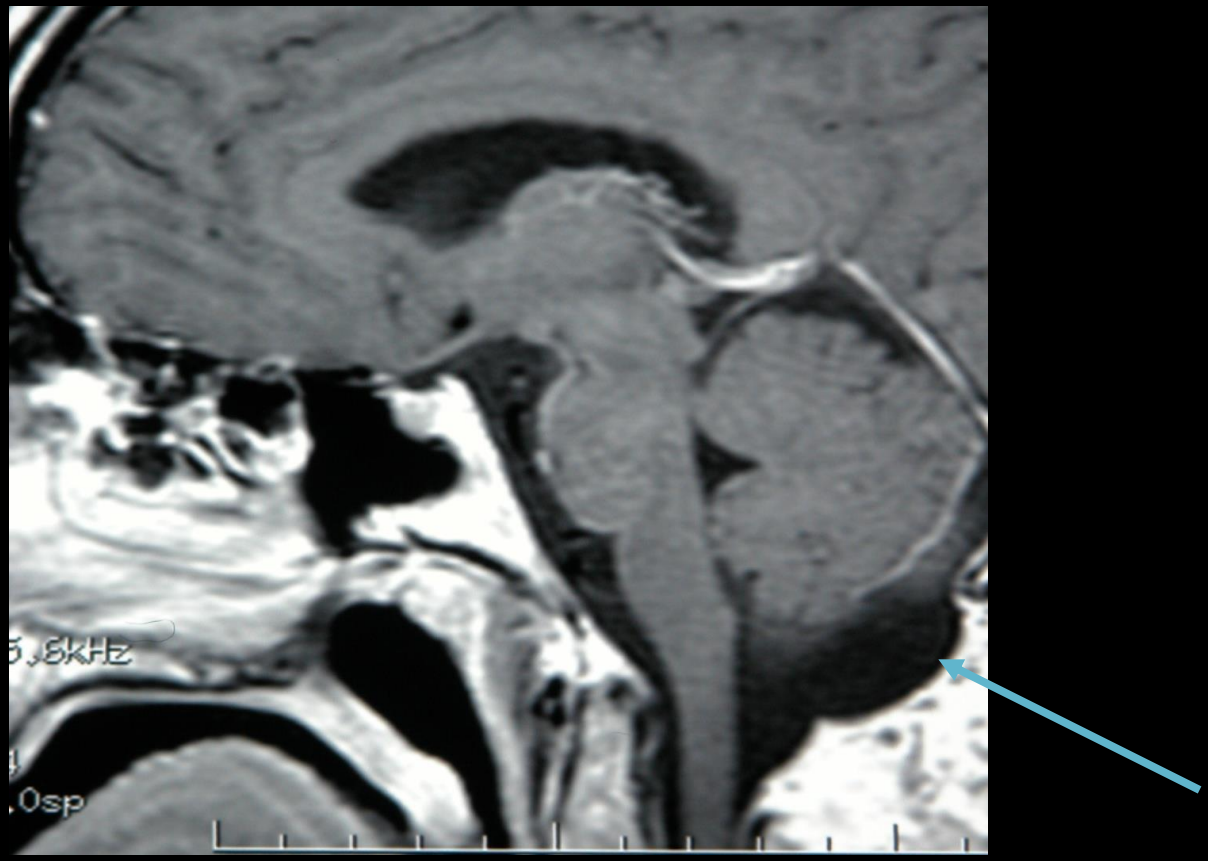
- Chiari Malformation
- Atlanto-axial or cervical instability
- TMJ Syndrome
- Occipital neuralgia
- Thrombosis, hypercoagulability
- Hughes Syndrome , migranous TIAs
- Pseudotumor cerebri
- Orthostatic intolerance
- Limbic encephalopathy, NeuroBehcet's
- Tethered cord syndrome
- Mast Cell release Disorder
- neck muscle spasm thoracic imbalance
- Cranio-vertebral instability (floppy head)



Chiari I Malformation

0.1- 1 % of population

Treatment of Chiari malformation



EDS causes craniocervical instability

- 12.7% of all Chiari patients have connective tissue disorder
- most EDS patients with Chiari malformation have CCI

Milhorat TM, et al. 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, 200

EDS

Clumsiness, poor coordination ….the relatively high rate of dyslexia and dyspraxia suggests possibility of CNS involvement in this condition.

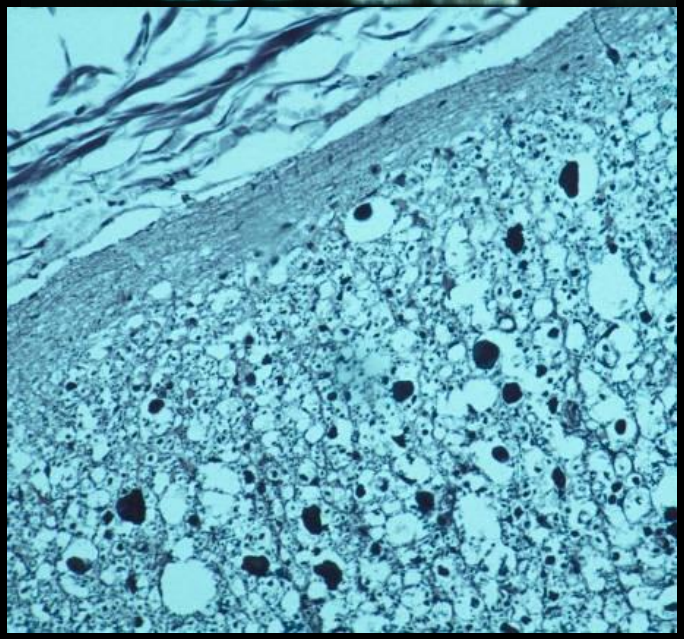
N. Adib, K. Davies, R. Grahame, P. Woo and K. J. N. Adib, and K. J. Murray1

Rheumatology 2005;44:744–750 Joint hypermobility syndrome in childhood

How does ligamentous laxity result in neurological changes ?

- The neurobiology of stretch injury

Ligamentous laxity results in deformation of the nervous system



Annals of the Rheumatic Diseases 1993; **52:** 629–637

EXTENDED REPORTS

Neuropathology of the brainstem and spinal cord in end stage rheumatoid arthritis: implications for treatment

Fraser C Henderson, Jennian F Geddes, H Alan Crockard

Abstract

***Objective*—To study the detailed histopathological changes in the brainstem and spinal cord in nine patients with severe end stage rheumatoid arthritis, all with clinical myelopathy and craniocervical compression.**

***Methods*—At necropsy the sites of bony pathology were related exactly to cord segments and histological changes, and correlated with clinical and radiological findings.**

***Results*—Cranial nerve and brainstem pathology was rare. In addition to the obvious craniocervical compression, there were widespread subaxial changes in the spinal cord. Pathology was localised primarily to the dorsal white matter and there was no evidence of vasculitis or ischaemic changes.**

***Conclusions*—Myelopathy in rheumatoid arthritis is probably caused by the effects of compression, stretch, and movement, not ischaemia. The additional subaxial compression may be an important component in the clinical picture, and may explain why craniocervical decompression alone may not alleviate neurological signs.**

(*Ann Rheum Dis* 1993; **52:** 629–637)

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Accepted for publication
20 May 1993

Rheumatoid arthritis is a systemic disease affecting the cervical spine in 16–88% of patients.[1–6] Progressive subluxation is common,[7–9] associated with increasing compression of the spinal cord and brain stem,[5 10–15] and may cause clinical myelopathy and even sudden death.[3 16 17] Despite these clinical effects, the pathophysiology and histopathology of cord and brain stem injury due to this type of compression are poorly understood, and there are only two studies available in which changes in the cord are described in any detail.[4 18] As part of our wider study of cervical myelopathy in over 250 patients with rheumatoid arthritis we performed a detailed histopathological study of the spinal cord and brain stem in nine patients, and compared the findings with clinical and radiological features.

Methods

This study includes nine patients with seropositive rheumatoid arthritis (eight women, one man) from our ongoing prospective study, who underwent necropsy at the National Hospitals for Neurology and Neurosurgery between 1987 and 1991. All patients were evaluated by rheumatologists, a neurosurgeon (HAC), two neuroradiologists, a physiotherapist, and a research nurse. The clinical assessment included a full neurological examination and a detailed questionnaire about neurological symptoms. In addition, all patients were graded according to Ranawat *et al*[19] and Steinbrocker *et al.*[20] The radiological assessment included plain lateral films of the cervical spine and high definition computed myelotomography with multiplanar reformatting.[21] All operations were carried out by or under the direction of the same surgeon (HAC). Necropsies were performed by or under the supervision of the same neuropathologist (JFG). The necropsy technique used to remove the foramen magnum and cervical spine with the cord and medulla intact has been described previously.[22]

Multiple transverse blocks of the cord were taken, and sections stained with haematoxylin and eosin, luxol fast blue, Woelche, Heidenhain, and modified Bielchowsky stains. Reticulin, Nissl, van Gieson, periodic acid-Schiff, and glial fibrillary acidic protein (Dako; 1:400) stains were performed on selected blocks.

Pre-operative results

CLINICAL FINDINGS

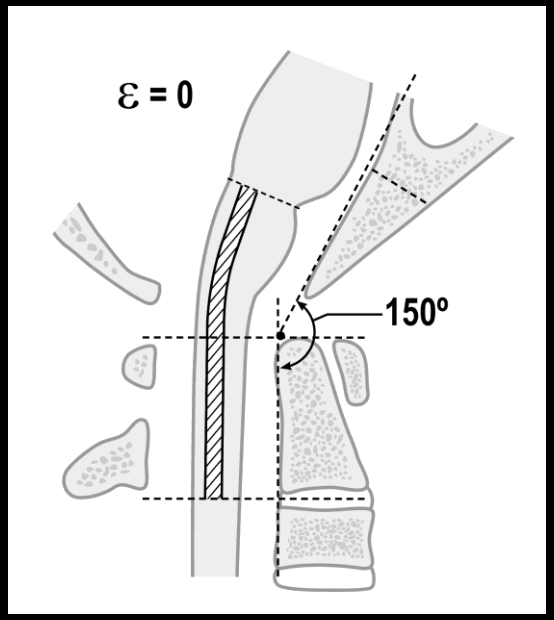
The table gives a summary of the principal clinical details.

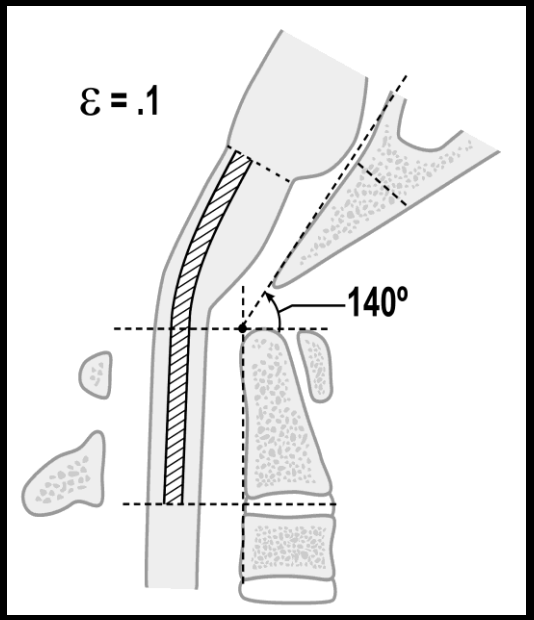
The nine patients presented in this study were all white with longstanding seropositive rheumatoid arthritis, aged 47–72 years (average age 60 years, median age 64 years). The only man in the study was the youngest patient.

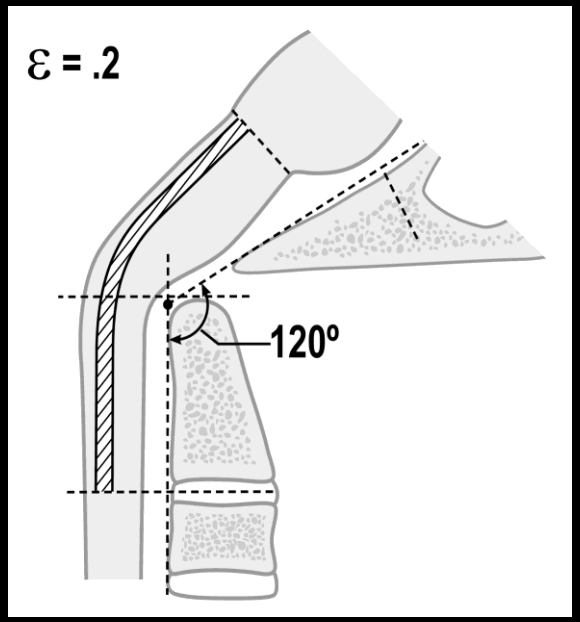
All patients had been treated with steroids during the course of the disease, three with gold and one with the addition of azathioprine. One other patient had azathioprine without gold.

kyphotic CXA causes deformation and stretch of the brainstem

Prof Alfred Breig



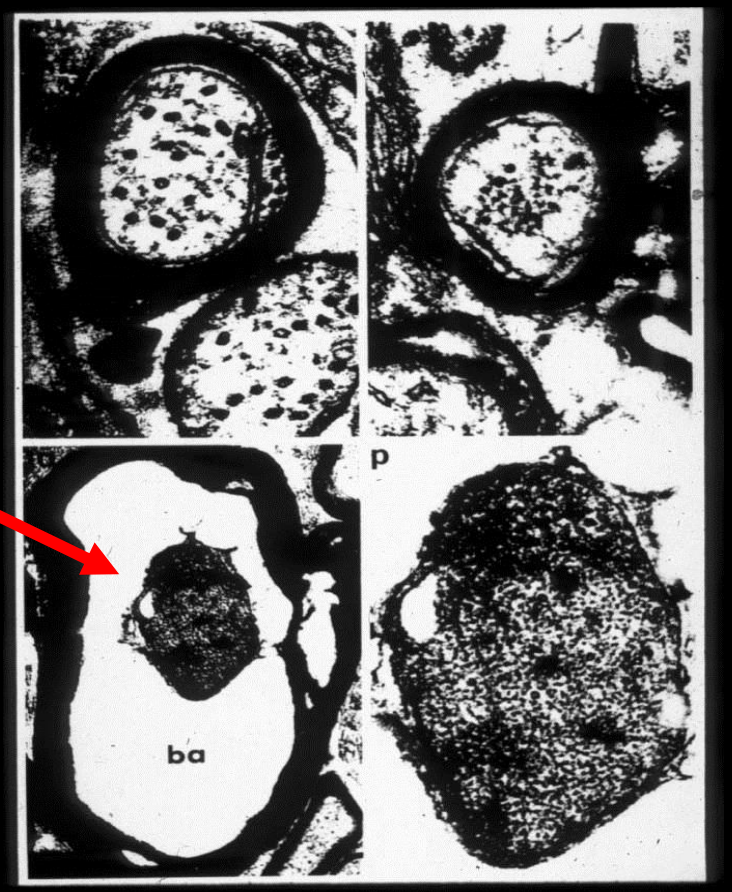




Henderson et al, Surg Neurol Internat, 2010

Stretching Neurons

- Clumping and loss of neurofilaments and microtubules

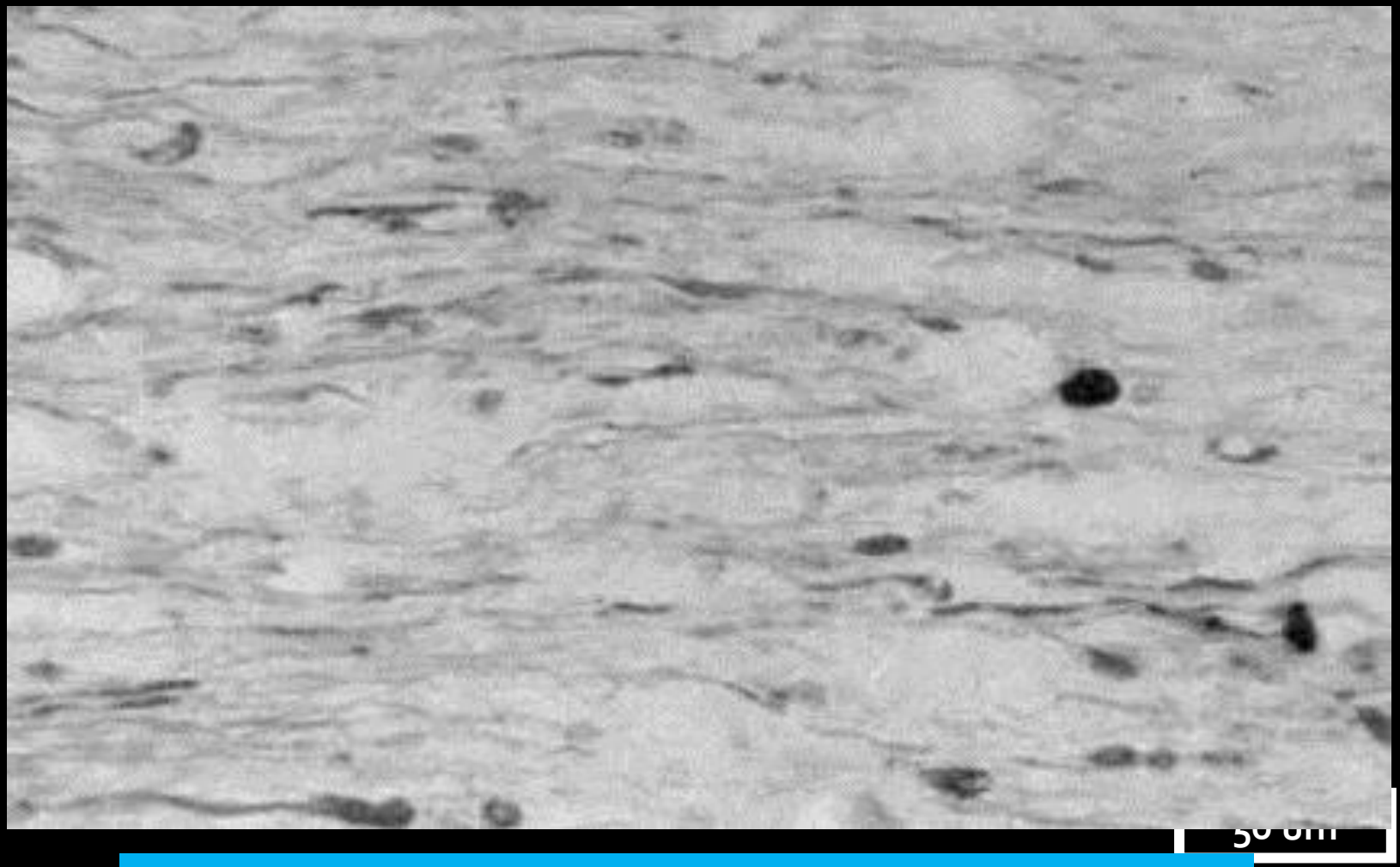


Povlishok, Brain Path,1995

Maxwell, J Neurotrama,2002

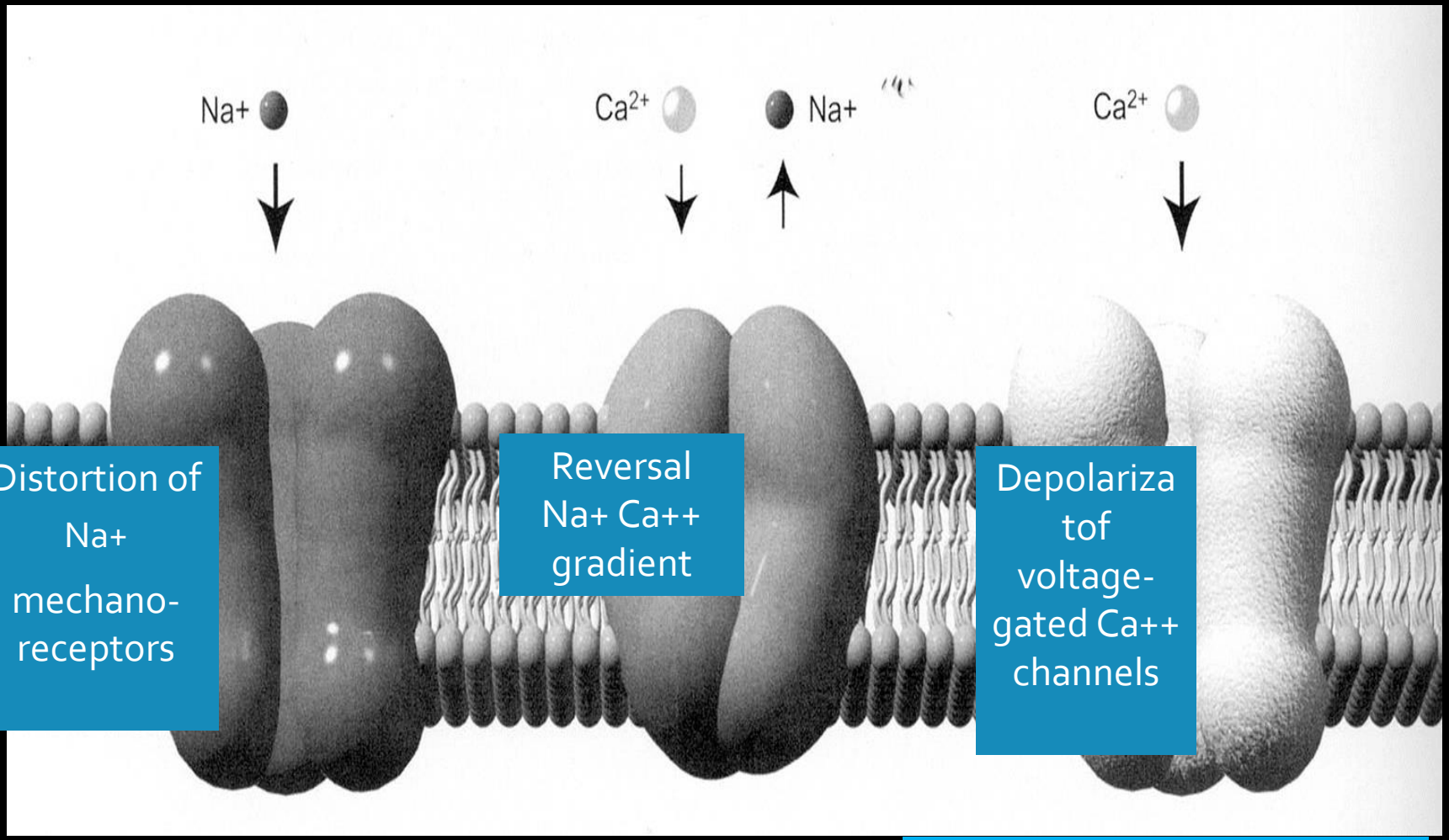
Jafari J Neurocytol,1997

Mouse optic nerve stretched 2mm (**ε = .2**)



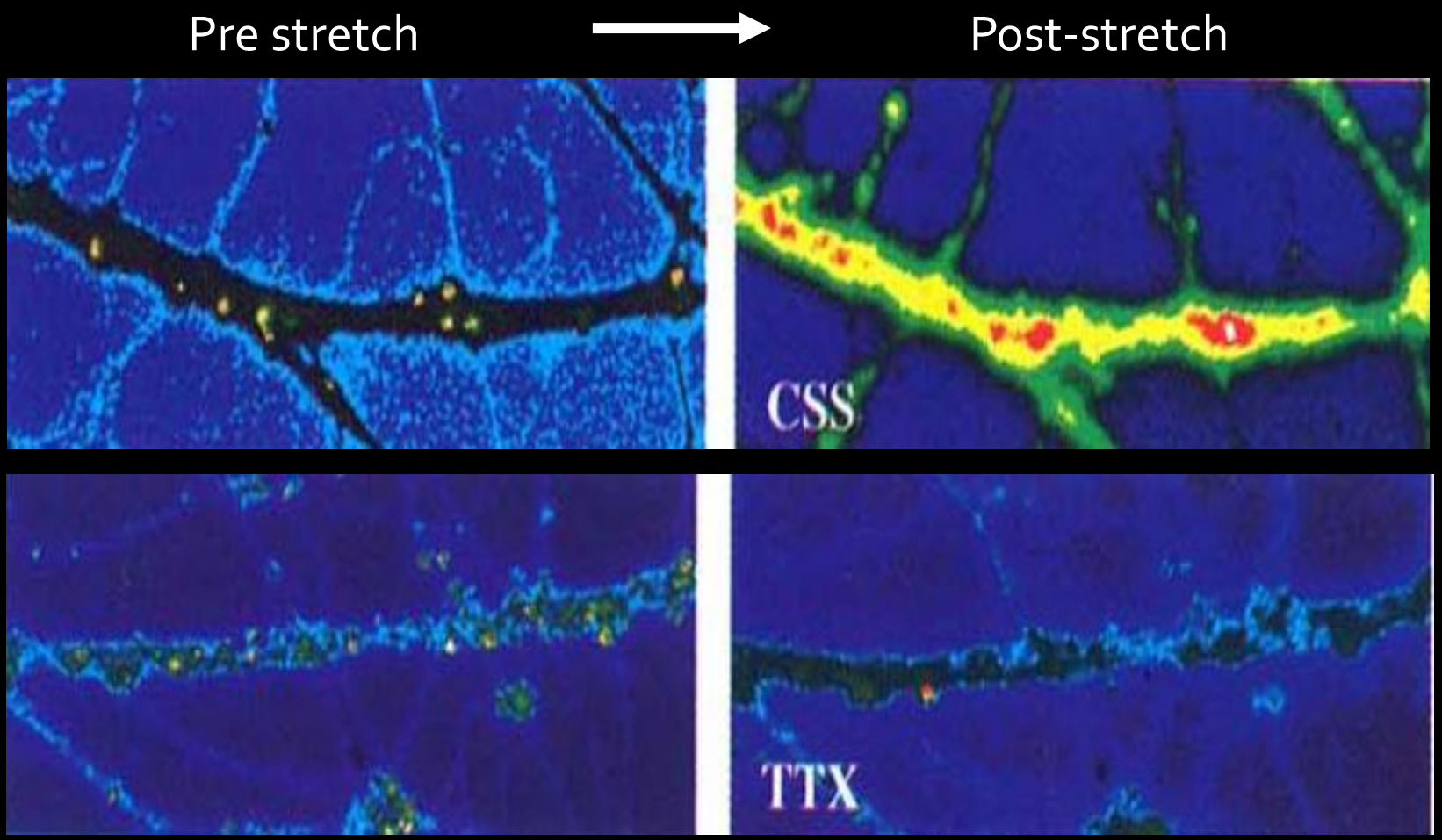
Saatman KE **J Cereb Blood Flow Metab.** 23(1):34-42, 2003

Calcium influx after stretch injury



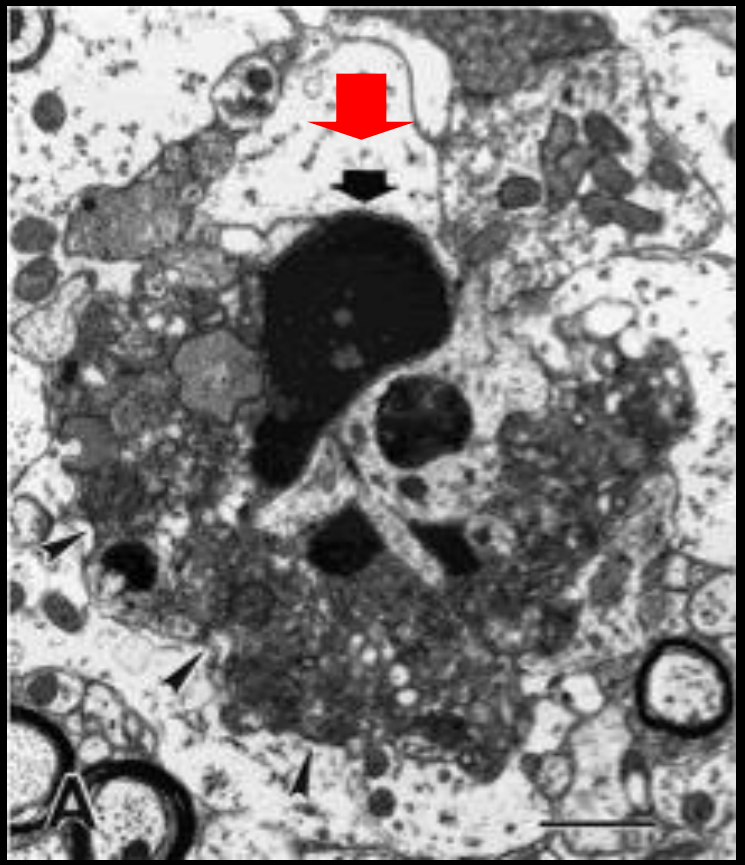
Wolf et al, J Neurosci 2001

Calcium influx after stretch injury, blocked by TTX



Wolf, Sties, Lizard, Smith, J Neurosci 2001

Stretching is an epigenetic stimulus

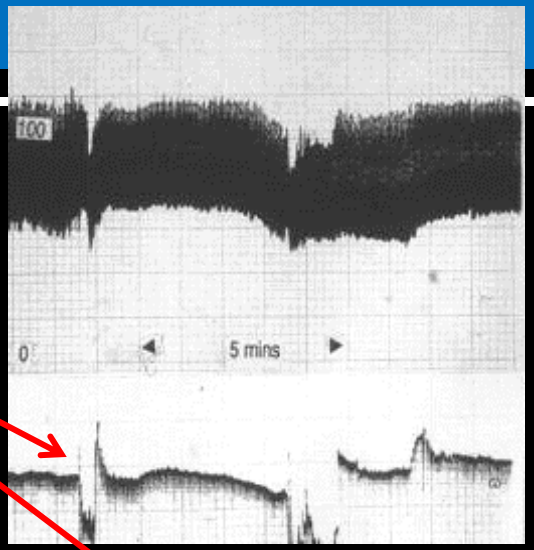


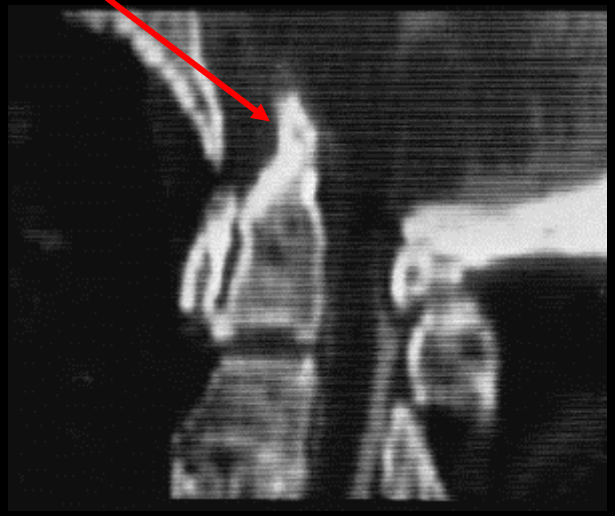
Arundine M et. al. J Neuroscience. 2004, 24(37): 8106-8123)

- Secondary injury
- Up-regulation of NMDA receptors
- Vulnerability to nitrous oxide and reactive oxygen species
- Mitochondrial dysfunction and DNA fragmentation
- Programmed cell death (apoptosis)

Sleep apnea results from dynamic compression

- Basilar invagination causes sleep apnea
- Reduction and stabilization in pts with RA resulted in resolution of sleep apnea, in all cases





Howard,Henderson et al. Ann Rheum Dis,1993
Menezes,J NSGY,1985

Ann Rheum Dis. 1994 February; 53(2): 134–136.
PMCID: PMC1005266

Respiratory abnormalities due to craniovertebral junction compression in rheumatoid disease.

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Harris Unit, National Hospital for Neurology and Neurosurgery, Queen Square, London, United Kingdom.

Abstract

OBJECTIVE--To assess the extent and severity of respiratory insufficiency associated with severe rheumatoid atlantoaxial dislocation and its relation to compression of the neuraxis. METHODS--Twelve patients with severe atlantoaxial dislocation due to rheumatoid disease were studied. Detailed clinical, CT myelography and respiratory assessment including nocturnal oximetry, were performed on all patients

Mechanical forces modulate gene expression and biochemical composition , directly effecting neurons, making them more sensitive and more vulnerable to injury.

This injury arising may underlie many of the neurological deficits that we observe in “floppy head syndromes”

Stretch-Associated Injury in Cervical Spondylotic Myelopathy: New Concept and Review

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Accepted, January 24, 2005.

THE SIMPLE PATHOANATOMIC concept that a narrowed spinal canal causes compression of the enclosed cord, leading to local tissue ischemia, injury, and neurological impairment, fails to explain the entire spectrum of clinical findings observed in cervical spondylotic myelopathy. A growing body of evidence indicates that spondylotic narrowing of the spinal canal and abnormal or excessive motion of the cervical spine results in increased strain and shear forces that cause localized axonal injury within the spinal cord.

During normal motion, significant axial strains occur in the cervical spinal cord. At the cervicothoracic junction, where flexion is greatest, the spinal cord stretches 24% of its length. This causes local spinal cord strain. In the presence of pathological displacement, strain can exceed the material properties of the spinal cord and cause transient or permanent neurological injury.

Stretch-associated injury is now widely accepted as the principal etiological factor of myelopathy in experimental models of neural injury, tethered cord syndrome, and diffuse axonal injury. Axonal injury reproducibly occurs at sites of maximal tensile loading in a well-defined sequence of intracellular events: myelin stretch injury, altered axolemmal permeability, calcium entry, cytoskeletal collapse, compaction of neurofilaments and microtubules, disruption of anterograde axonal transport, accumulation of organelles, axon retraction bulb formation, and secondary axotomy. Stretch and shear forces generated within the spinal cord seem to be important factors in the pathogenesis of cervical spondylotic myelopathy.

KEY WORDS: Apoptosis, Axon spheroids, Cervical spondylotic myelopathy, Focal axonal injury, Shear, Spinal cord stretch, Strain

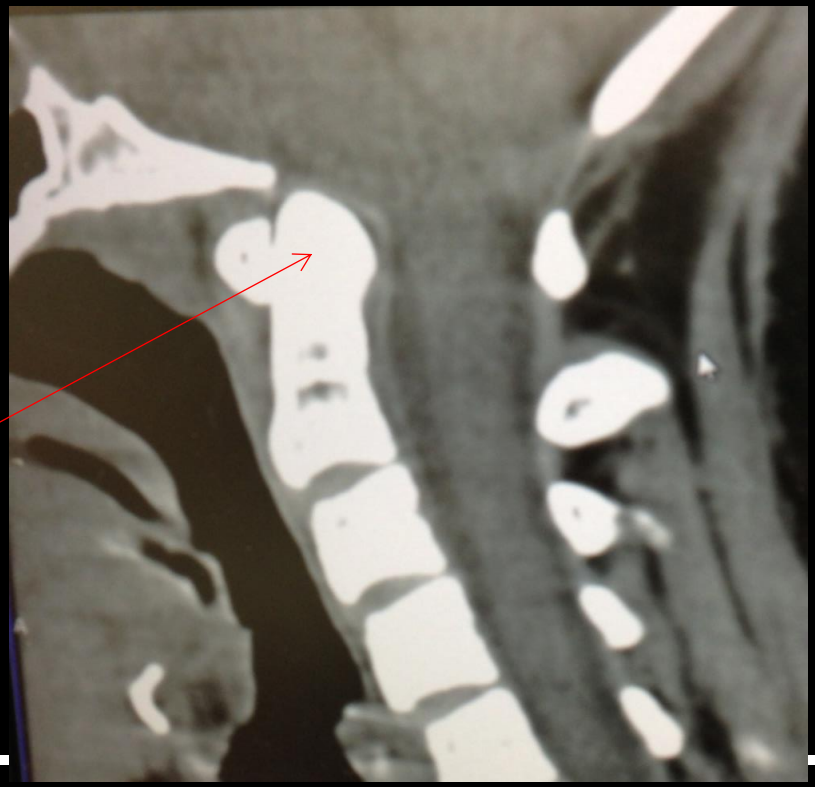
Neurosurgery 56:1001–1012, 2005 DOI: 10.1227/01.NEU.0000156518.38370.2C www.neurosurgery-online.com

Cervical spondylotic myelopathy (CSM) is a well-described clinical syndrome that may evolve from a combination of etiological mechanisms. The strong association between a narrowed, spondylotic cervical spinal canal and the development of CSM has previously led to the formulation of a relatively simple pathoanatomic concept that a narrowed spinal canal causes compression of the enclosed cord, leading to local tissue ischemia, injury, and neurological impairment. However, this simple mechanism fails to explain the entire spectrum of clinical findings

ical studies of cervical mobility in patients with CSM, 2) histopathological studies of spinal cord tissue from CSM patients, and 3) biomechanical studies that have led to an improved understanding of the material properties and biomechanical behavior of spinal cord tissue under various physiological and pathological conditions. A growing body of evidence indicates that spondylotic narrowing of the spinal canal results in increased strain and shear forces, and that these pathological forces cause both widespread and localized axonal injury within the spinal cord. The term strain

Henderson et al, Neurosurgery: May 2005 - Volume 56 - Issue 5 - pp 1101-1113

What are the tools that we use to predict deformative stress?



The Consensus Statement

Chiari Syringomyelia Foundation Multi-disciplinary Colloquium for Craniocervical Hypermobility San Francisco, October 19th, 2013

University College ,London, GB
General Hospital of Chinese People's Armed Police Forces, Beijing, China
Johns Hopkins
Cleveland Clinic
UCLA
Tufts
Medical University of South Carolina
Georgetown University
University of Washington/ Seattle Children's Hospital
University of Utah Health Care
Moriguchi -Ikuno MemorIal Hospital, Japan
North Shore University Hospital
The Canine Chiari Institute
Greater Baltimore Medical Center
University of Maryland
Doctor's Hospital, Maryland
Advocate Children's Hospital, Chicago

Deformation of the brainstem may manifest as the

Cervical Medullary Syndrome

- Headache, suboccipital or neck pain
- Diplopia , decreased or blurred vision
- Dizziness, vertigo, imbalance
- tinnitus or decreased hearing
- Dysautonomia, POTS, syncope or pre-syncope
- Dysarthria, dysphagia,choking
- Altered breathing and sleep architecture
- Weakness, clumsiness, spasticity,
- Altered sensation, paresthesia, dysesthesia
- Gait changes, urinary urgency or frequency

The Consensus Statement

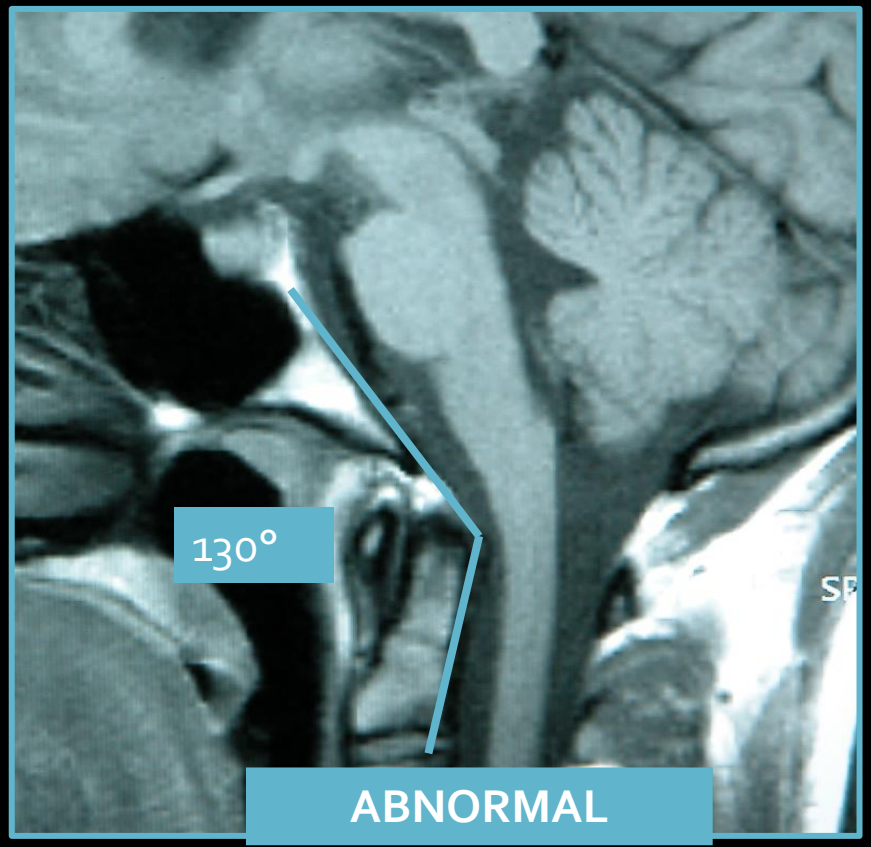
Chiari Syringomyelia Foundation Multi-disciplinary Colloquium for Craniocervical Hypermobility Francisco, October 19th, 2013

Radiological metrics to assess basilar invagination or craniospinal instability

- Clivo-axial angle
- Grabb-Mapstone-Oakes measurement
- Harris' measurement

The Consensus Statement
Chiari Syringomyelia Foundation Multi-disciplinary Colloquium Craniocervical Hypermobility Francisco, Oct 19th, 2013

Clivo-axial angle - surrogate measurement of basilar invagination and cervico-medulllary deformity



Chiari decompression failed if the CXA < 135º

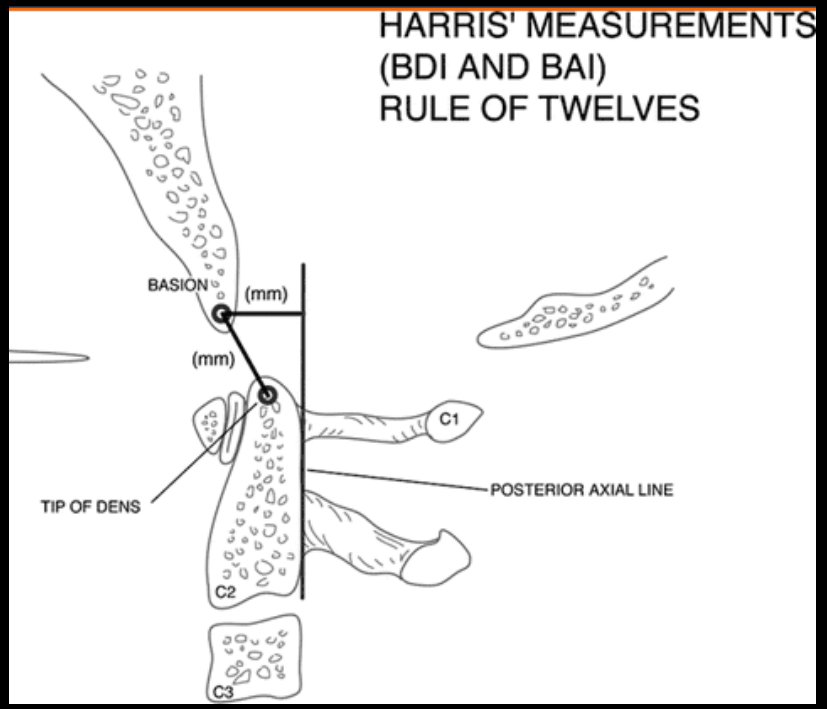
Kim, Rekate, Klopfenstein, Sonntag 2004

Chiari decompression failed to improve syringomyelia if CAA < 127º KUbota 2004

Grabb Oakes Measurement

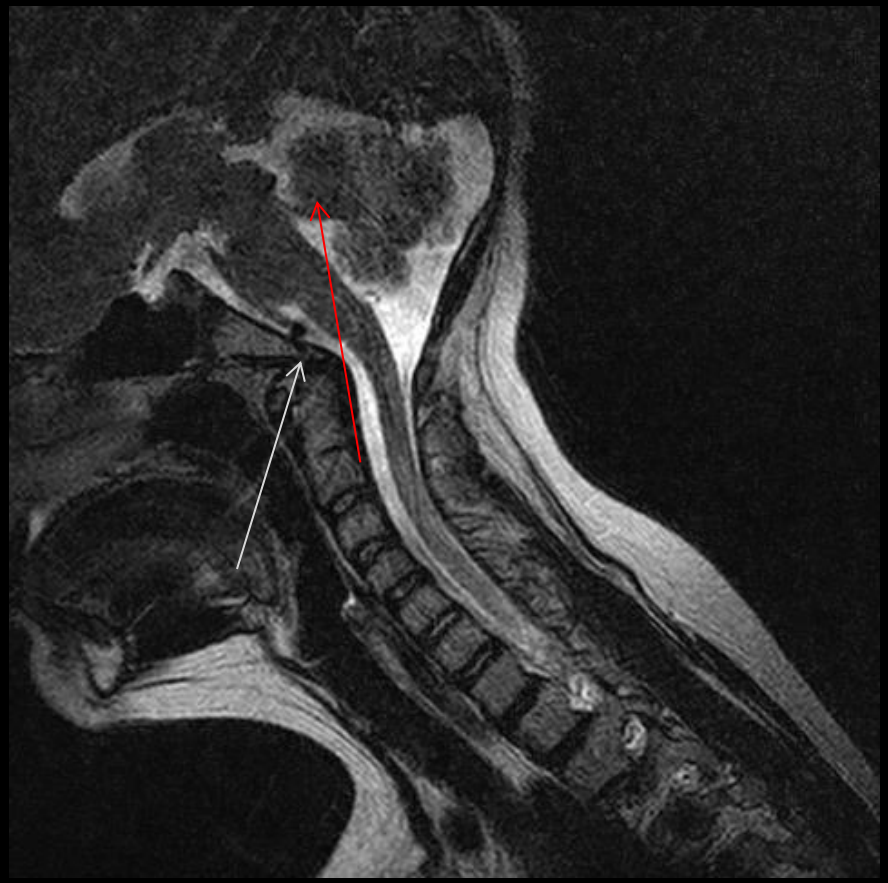
Harris Measurement

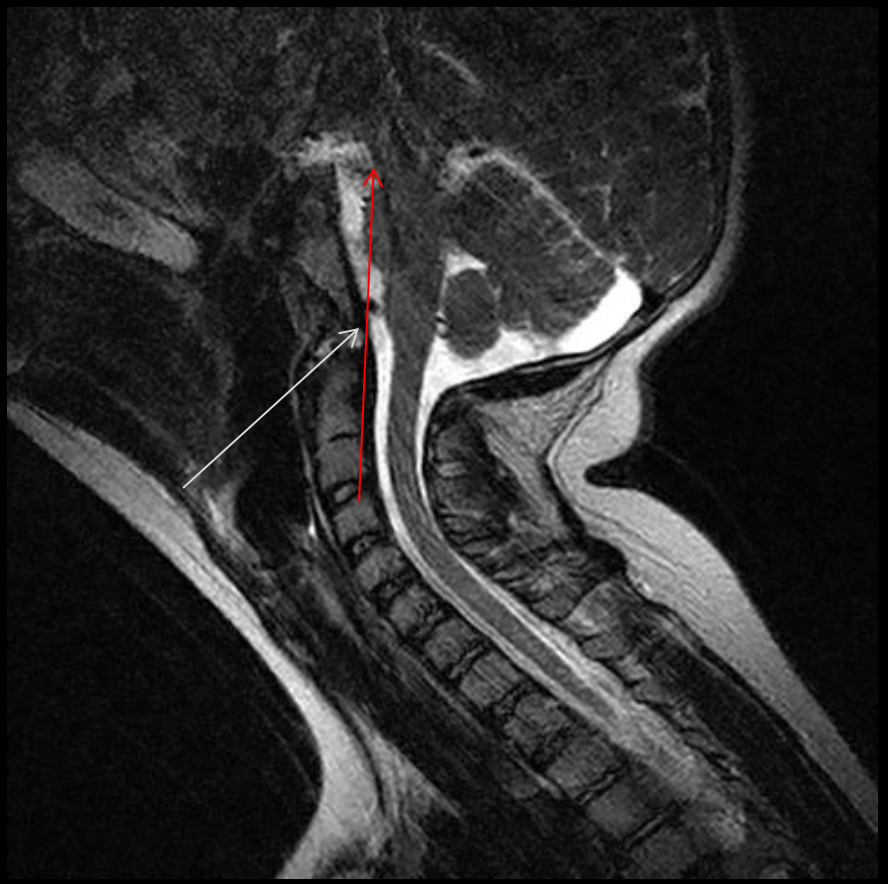
- Of 400 normal subjects, none had basion to PAL >12mm
- “In adults, the occipito-vertebral junction can be considered normal when both the basion axial interval and the basion dental interval are 12mm or less”



Harris JH, Carson GC, Wagner LK: Radiological diagnosis of traumatic Occipitovertebr4al Dissociation

Harris measurement measures distraction and pathological translation





How do we treat craniocervical instability ?

Treatment of CCI

- Multidisciplinary, centralized
- Surgery = the last option, after a thorough medical vetting
- r/o other causes : co-morbid conditions, MS, dystrophy, mitochondrial disorders, vitamin deficiencies, Lymes etc
- brace, activity limitation
- physical therapy : isometrics, sagittal balance, core strengthening, cardio
- Pain management : preop , postoperative plan
- Psychiatric evaluation where indicated

Medical management

- MCAS: aspirin 325 mg po tid
  amitriptylline 25 mg po qhs
  quercetin 500 mg po bid
  zantac 150 mg twice daily
  zyrtec 10 mg daily
  valium 5 mg daily
  Singulair 10 mg daily
  cromolyn sodium I puff twice daily
- Nutritional replacement : B12,
  thiamine, pantothenate, vit D
- Hydrocortisone 5 mg twice daily

Medical Management

- POTS : propranolol 20 mg twice daily for tachycardia, improves sleep
  fludrocortisone- volume
  midodrine - vasoconstriction
  Nunn salt tablets
- Gastroparesis: pyridostigmine,
  lubiprostone,
  methyl-naltrexone
- Hypercoagulability: full evaluation,
  treatment with anticoagulants
- Pseudotumor cerebri : Diamox 250 mg twice daily

When arranging for clinical visit

- primary care physician must be involved for ongoing medical care - POTS, adrenal insufficiency, gastroparesis, mal-absorption issues, poor sleep architecture, dystonia
- Confirm EDS diagnosis with geneticist before seeing the surgeon
- complete diagnosis of active surgical problems will usually not be accomplished in the first appointment
- Plan on several Follow up visits

Precise diagnosis

- EDS is one of the most complex disorders in medicine
- If you are willing to risk your life on the operating table, then you will want the most precise diagnosis as to what is causing your most significant problem
- It takes 13 years to train a neurosurgeon
- much longer time for the neurosurgeon to develop the expertise to know when not to operate
- Very important to establish a relationship of mutual trust and confidence in your neurosurgeon, and this trust begins with a careful diagnostic process

Diagnostic evaluation

- Flexion extension MRI
  - reveals craniocervical instability
  - assess the clivo-axial angle
  - assess instability or deformity of the cervical spine
- CT Scan : rotation of the neck
  - to assess C1C2 subluxation
  - Scans may need to be repeated
- Diagnostic tests may take a long time- but the surgeon is trying to understand you and the problem
- If the surgeon is on the fence about surgery, he will need to trust you

Indications for Craniocervical fusion

- Severe headache or neck pain >7/10
- And cervical medullary syndrome
- And neurological deficits referable to craniocervical junction
- And radiological findings

- After non operative treatment has been maximized
- Appropriate response to neck brace
- Family support peri-operatively
- Local physician support

Headache

- > 7/10

After r/o

- subaxial segmental instability
- Pseudtotumor
- Tmj dysfnc
- Migraine
- MCAS
- Tethered cord
- Intracranial thrombosis

Typical brainstem symptoms

- Vertigo Headaches
- Balance problems
- Upper extremity numbness
- Dizziness
- Speech problems
- Neck pain
- Memory problems
- Upper extremity weakness
- Walking
- Fainting
- Hearing problems
- Swallowing/choking problems
- Lower extremity numbness
- Visual problems
- Numbness in back
- Syncopal episodes
- Photosensitivity , hyperacusis

Characteristic neurological deficits of CCI

- Tender C1C2
- Decreased gag reflex
- Hypoesthesia to pinprick
- Decreased vibratory sensation
- Hyperreflexia
- Dysdiadochokinesia
- Romberg
- Difficulty with heel to toe walking
- Abnormal gait
- Weakness
- Loss of abdominal reflex
- Babinski, Hoffman’s signs

The radiological metrics

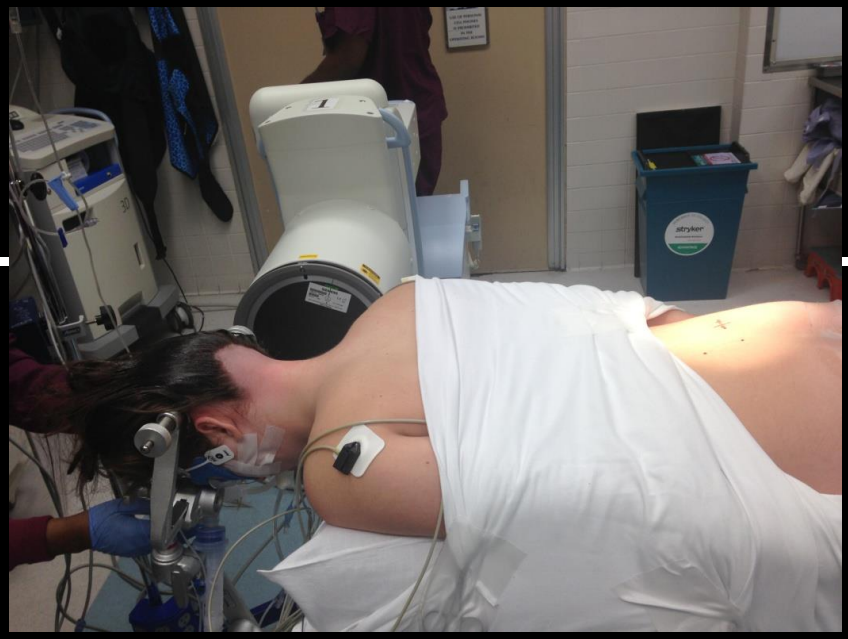
Basilar invagination,
or

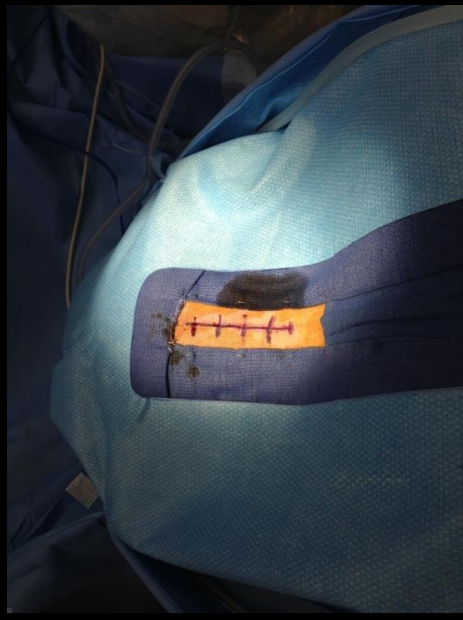
Two or more:

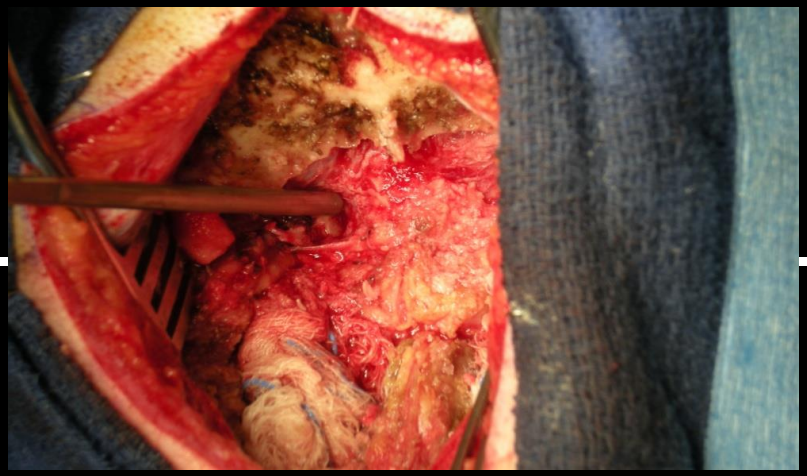
- kyphotic CXA <135 degrees
- Translation >4 mm by Harris
- VBC >9mm
- Chiari malformation, foramen magnum stenosis or crowding

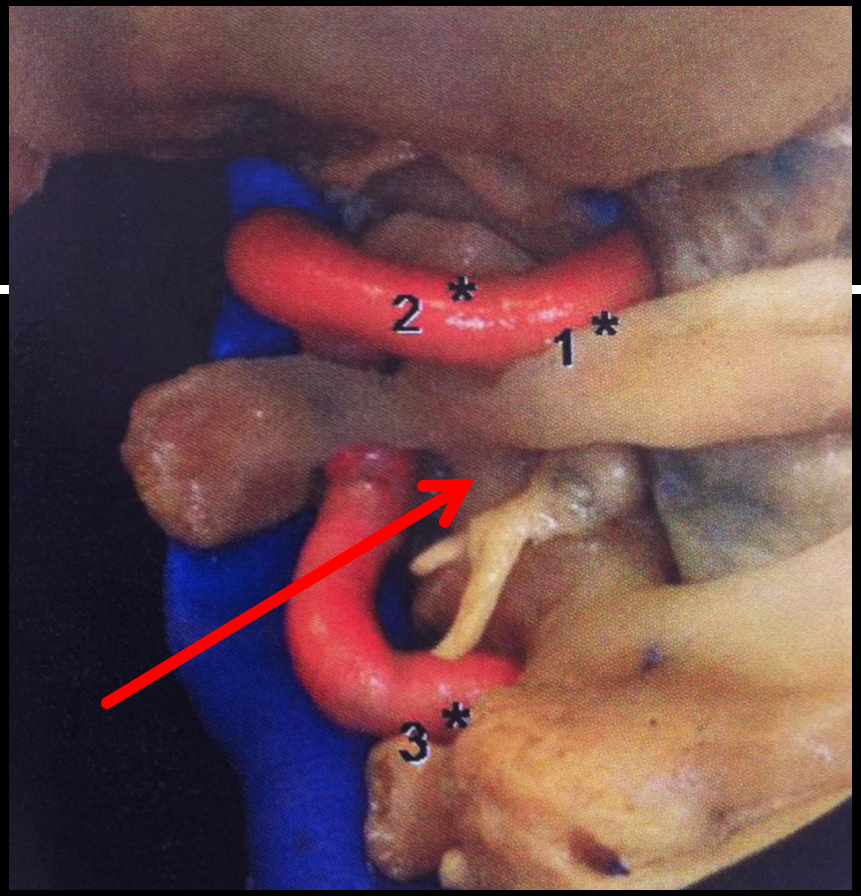
Operative Procedure

- Positioned prone in head holder Fluoro CT unit
- Brainstem and spinal somato-sensory evoked potentials
- Very careful and precise positioning of the cranio-cervical junction and cervical spine
- Gentle handling of soft tissue





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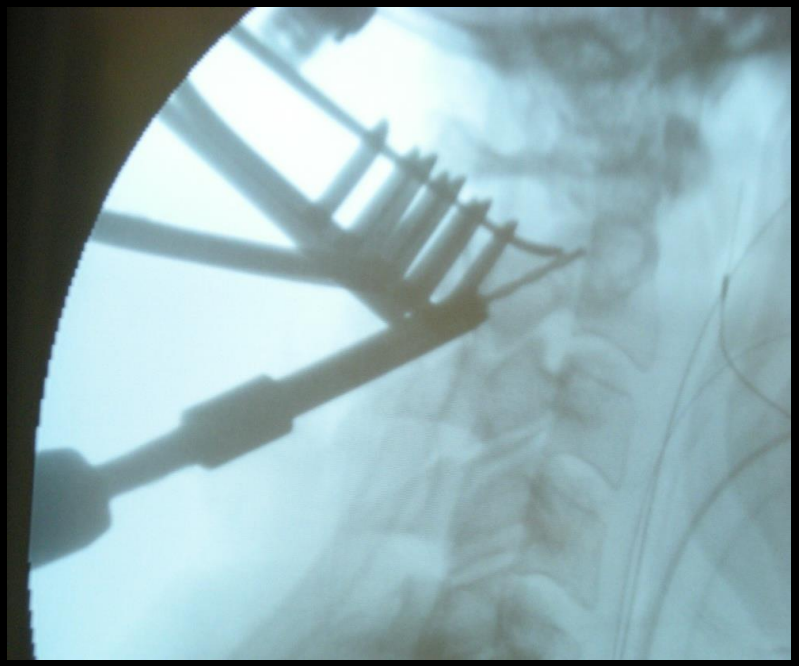
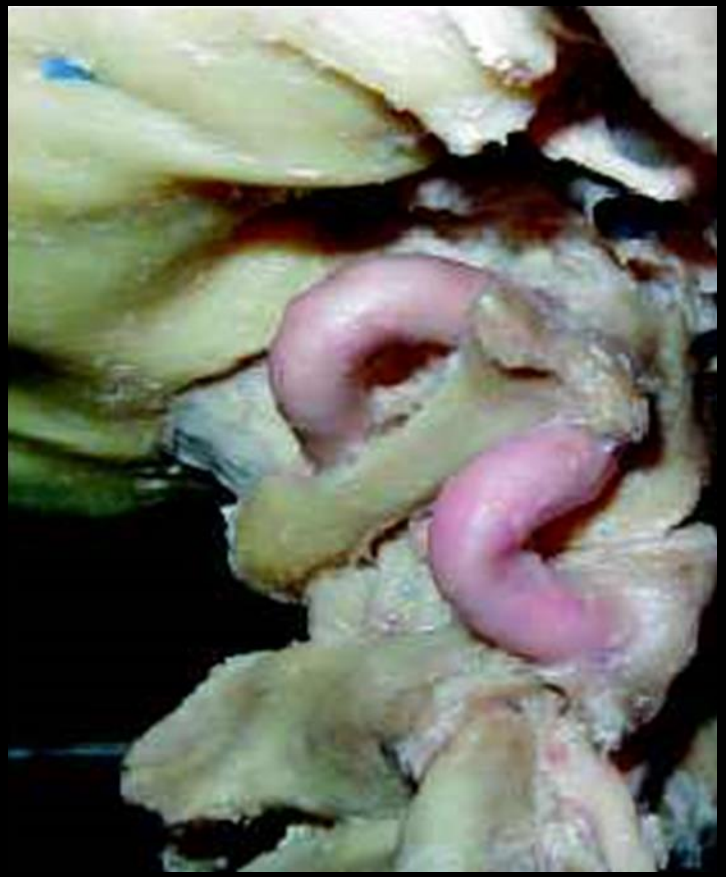
3 *



pitfall : vertebral artery injury

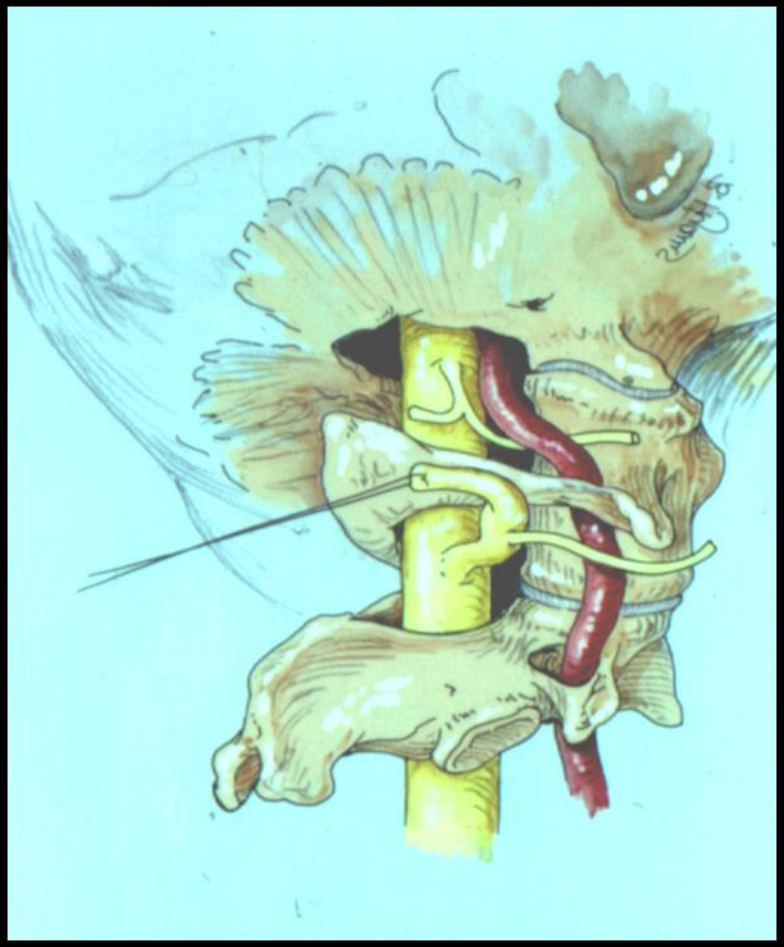
- 10% PICA extracranial origination
- 2 % vertebral artery passing beneath the posterior arch proatlantal variant
- 10% muscular branch wide dissection may result in loss of collateral flow from occipital artery
- risk of VA injury 2cm from midline, wherein the VA lying postero-lateral to the ring of C1



Pitfall: arterial injury

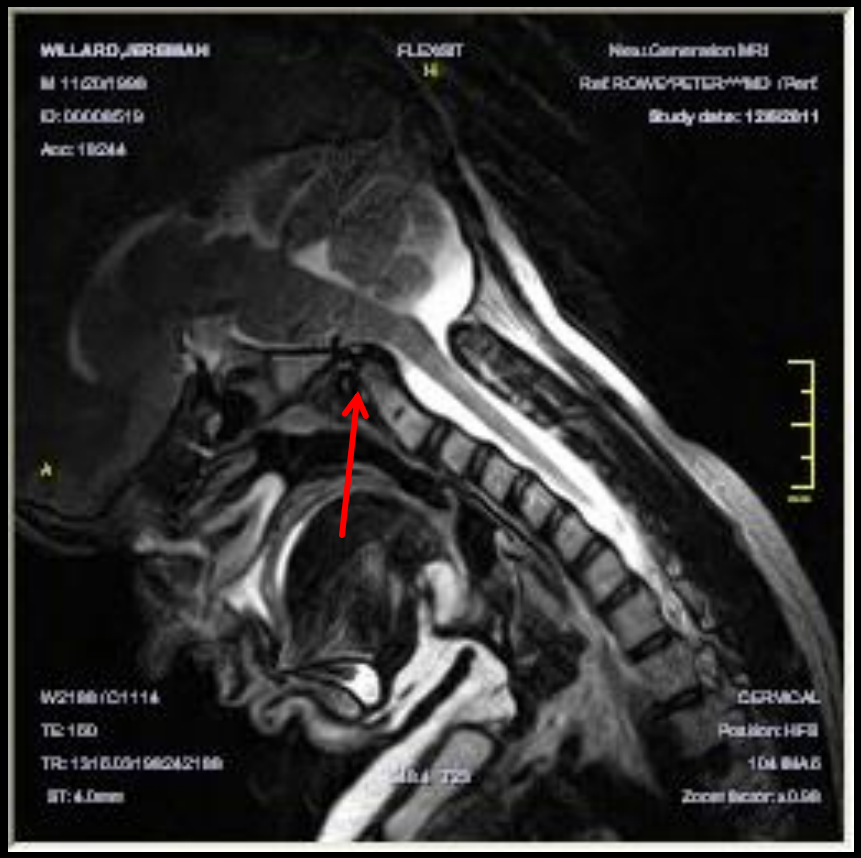
- 10% patients at risk for VA injury
- Mandel Spine ,2000
- EDS HAVE Small pedicles
- Most EDS have medially placed VA

Pitfall: injury to occipital nerve



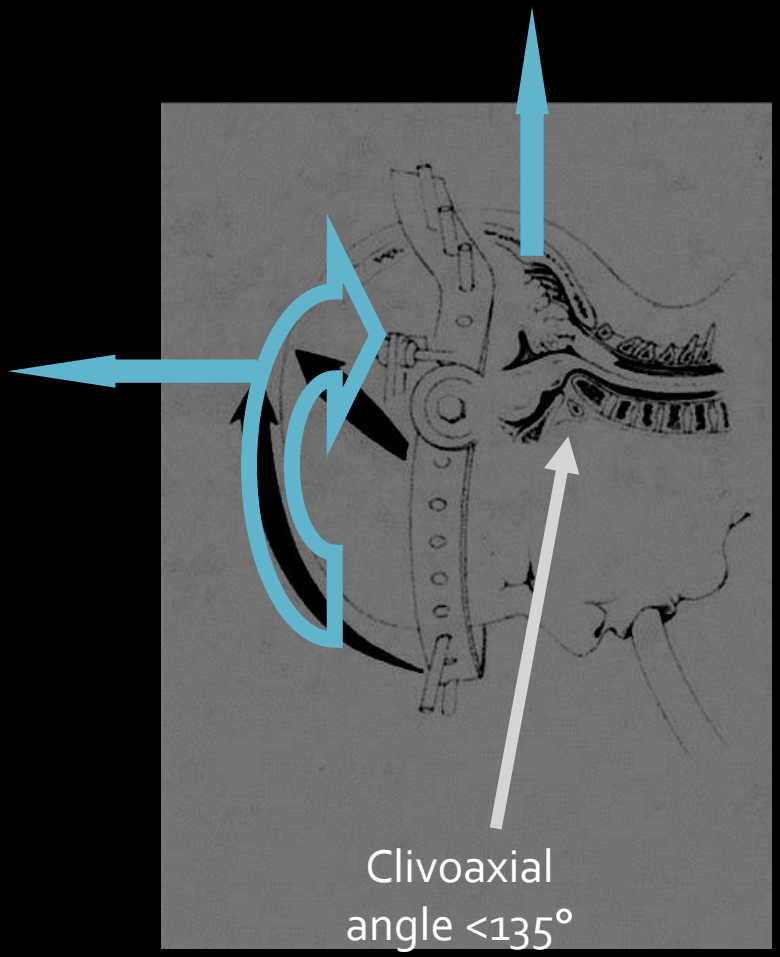
Traction reduction
To reduce the basilar invagination

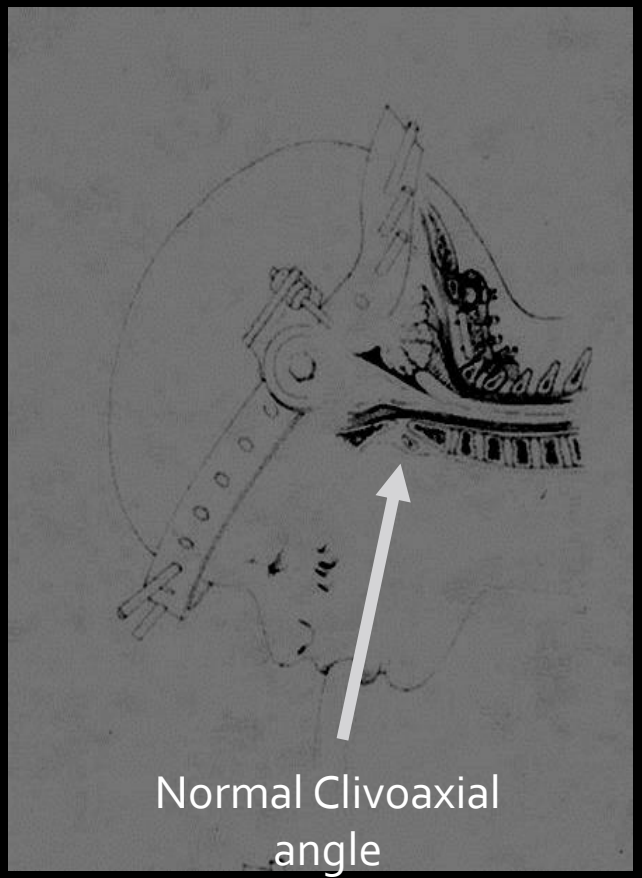
flexion



extension

Open reduction to normalize the clivo-axial angle and relationship of the skull to spine



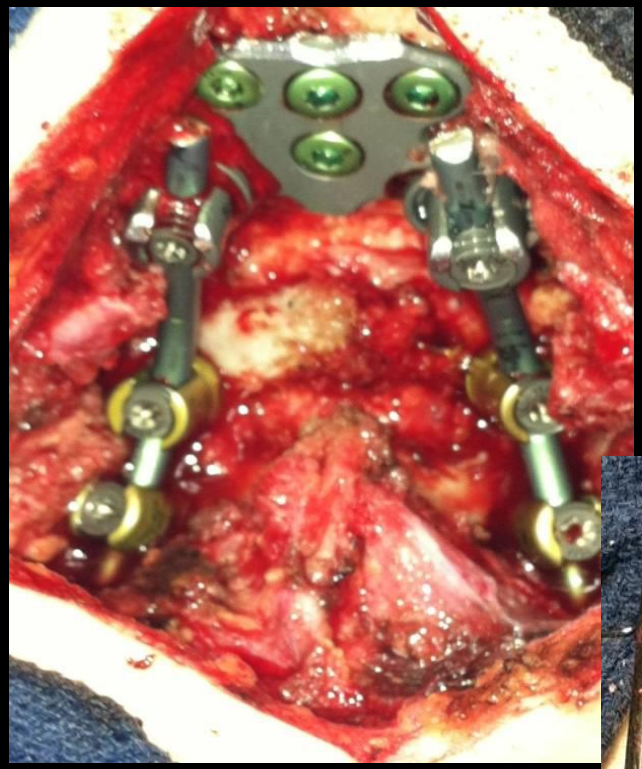


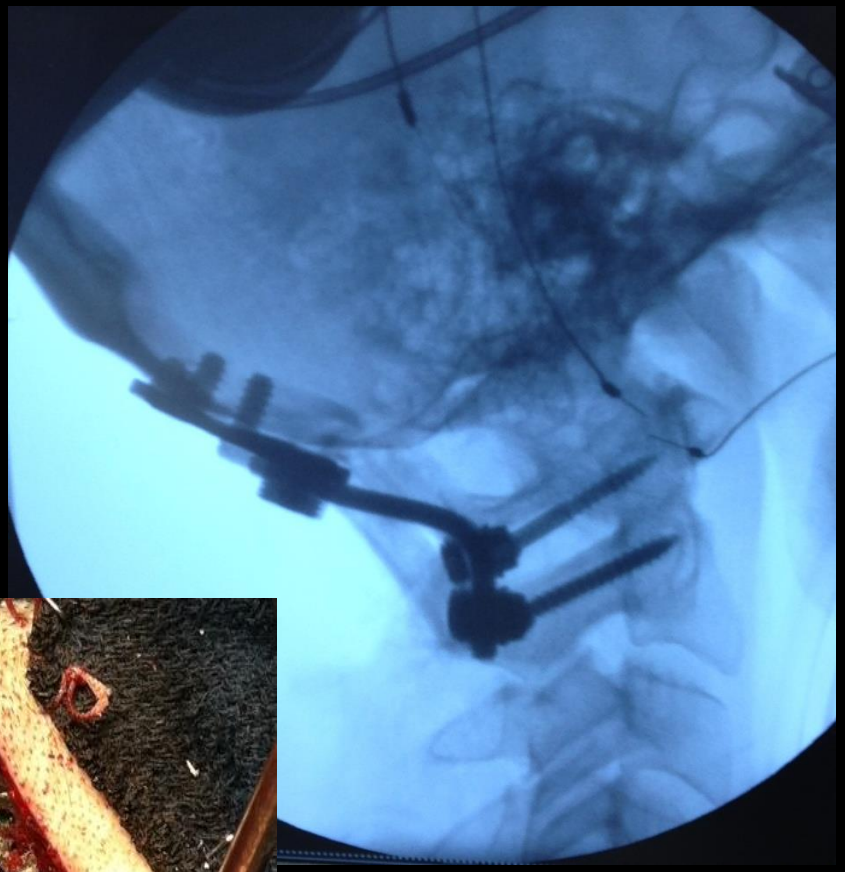
Modified from Kim, Rekate, Klopfenstein, Sonntag 2004

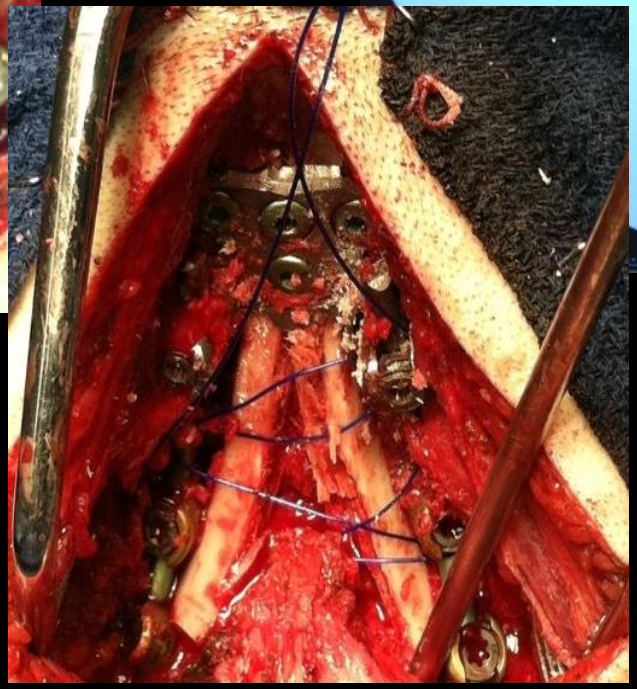
Radiological Measurements

- Clivo-axial angle
- Basion to odontoid interval
- Occipito-cervical angle
- Mandible to C2 interval
- Orbital Axial angle
- Iterative process

Fusion and Stabilization







Postoperative wound at 7 days and 1 month

Decreased Neck rotation after surgery does not appear to be an issue

- 5 weeks after fusion/ stabilization occiput to C1C2
- Few patients complain of lost range of motion

- Does cranios-pinal fusion relieve the pain and improve neurological deficits?

Preliminary results

Craniocervical Instability in Hereditary Hypermobility Syndromes : Retrospective Cohort Analysis of 20 Consecutive Patients undergoing Cranio-spinal Fusion

Fraser C. Henderson Sr MD
Clair Francomano MD
Jessica Adcock MS
Kelly Tuchman BS
George Malloch Brown

Symptoms Prior to Surgery (% of participants)

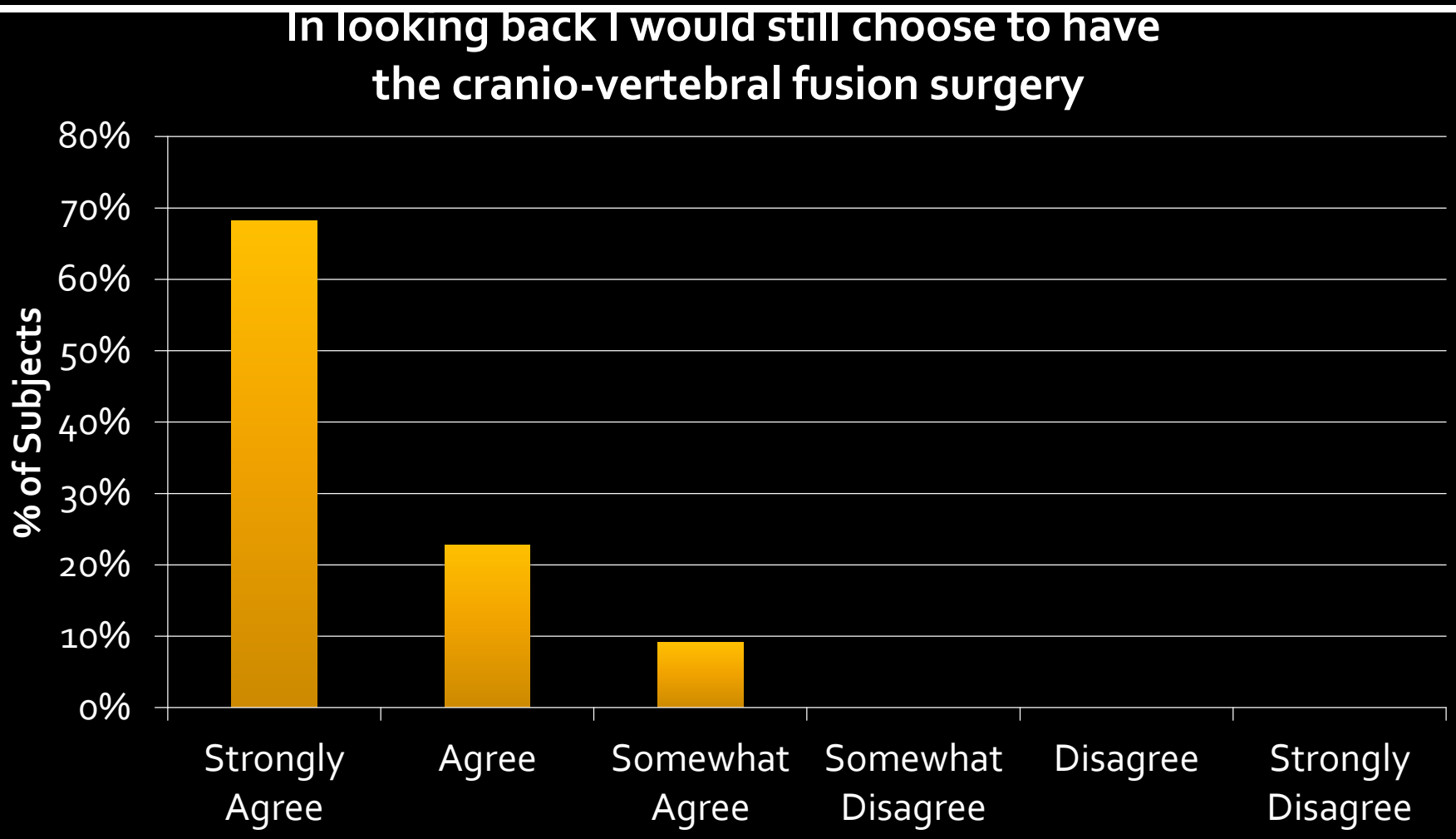
- Headaches (100%)
- Fatigue (100%)
- Dizziness (95.4%)
- Muscle pain (95.4%)
- Upper extremity weakness (90.9%)
- Joint pain (86.3%)
- Neck pain (83.3%)
- Balance problems (82.8%)
- Memory problems (81.8%)
- Night awakenings (81.8%)
- Upper extremity numbness (77.3%)
- Walking problems (77.3%)
- Hands and feet turning cold (72.7%)
- Lower extremity numbness (72.7%)
- Visual problems (72.7%)
- Lower extremity weakness (63.6%)
- Vertigo (59.1%)
- Hearing problems (59.1%)
- Speech problems (59.1%)
- Frequent daytime urination (59.1%)
- GERD (59.1%)
- Swallowing/choking problems (54.5%)
- Nocturia (54.5%)
- IBS (50.0%)
- Tremors/ dystonia (45.5%)
- Fainting (36.4%)
- Numbness in back (31.8%)
- Sleep apnea (22.7%)

Symptoms Improved After Surgery
% participants reporting improvement

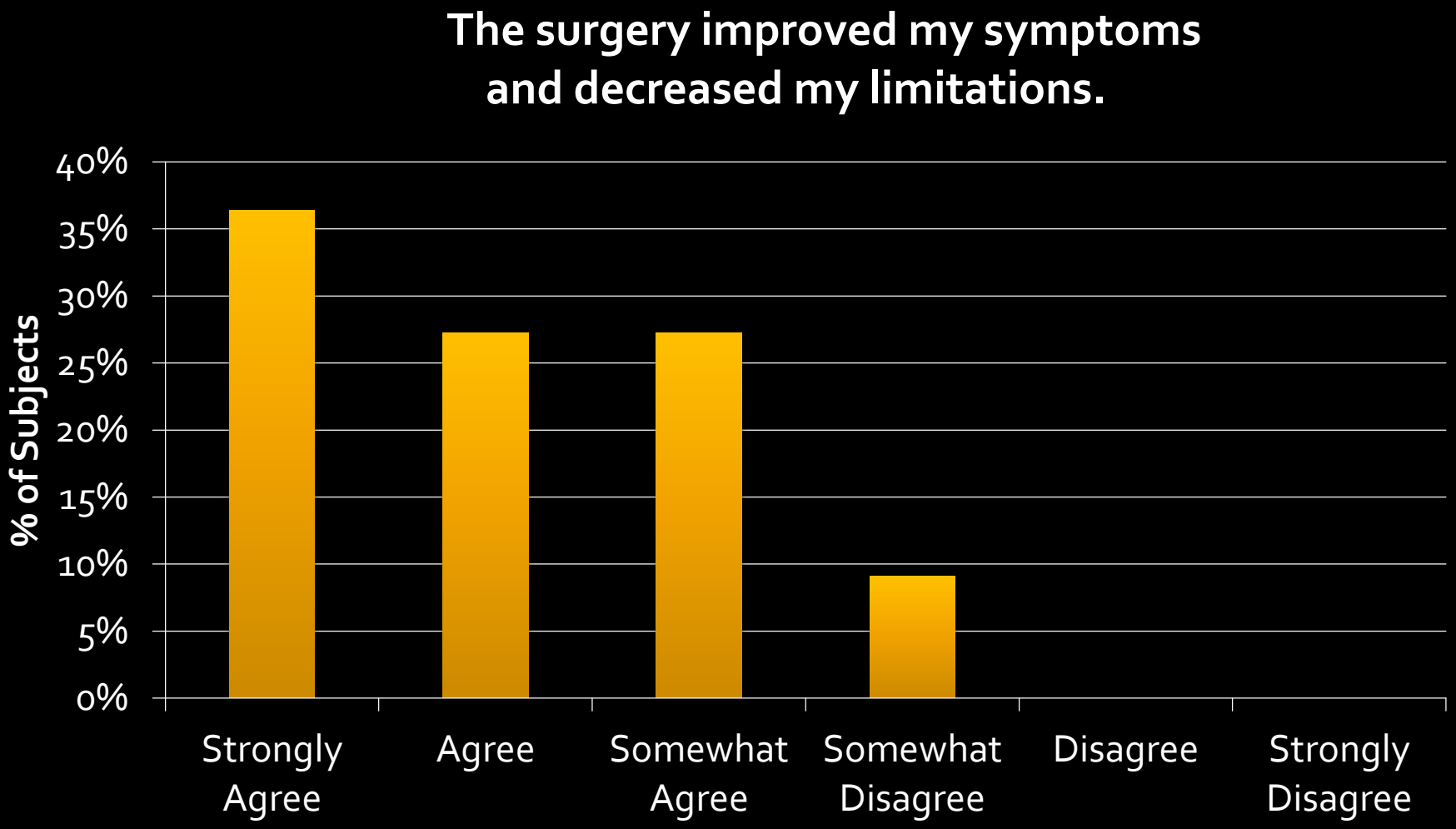
Vertigo (92.3%)
Headaches (81.8%)
Balance problems (77.8%)
Upper extremity numbness (76.5%)
Dizziness (71.4%)
Speech problems (69.2%)
Neck pain (68.4%)
Memory problems (66.7%)
Upper extremity weakness (65.0%)
Walking (64.7%)
Fainting (62.5%)
Hearing problems (61.5%)
Swallowing/choking problems (58.3%)
Lower extremity numbness (56.3%)
Visual problems (56.3%)
Numbness in back (57.1%)
Lower extremity weakness (57.1%)

Tremors (50.0%)
Muscle pain (38.1%)
Frequent daytime urination (38.5%)
Hands and feet turning cold (37.5%)
Fatigue (36.4%)
Night awakenings (33.3%)
GERD (30.8%)
Nocturia (25.0%)
Sleep apnea (20.0%)
IBS (18.2%)
Joint pain (26.3%)

Patient Opinions Regarding Surgery



Opinions Re Surgery



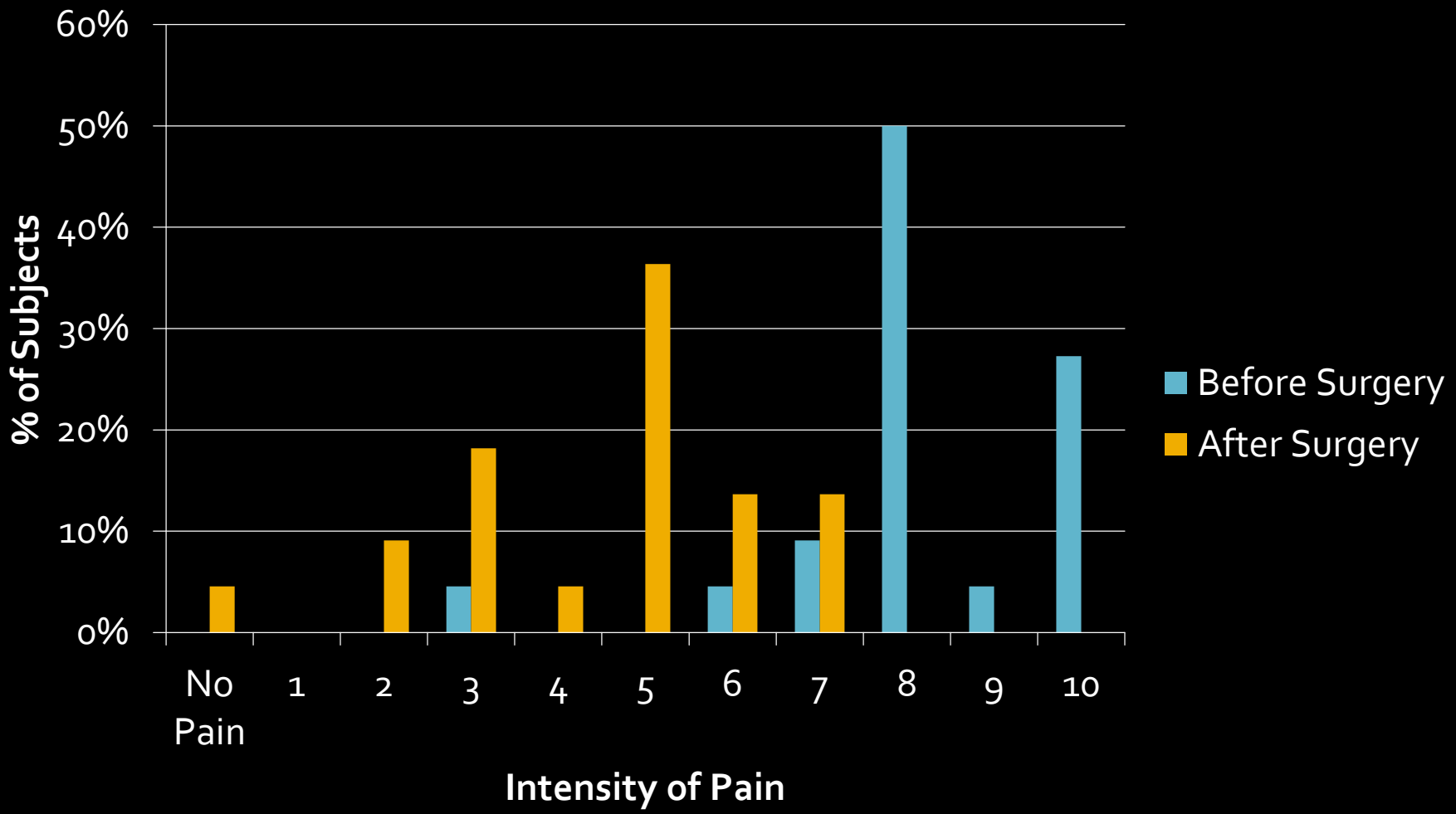
Average Headache (0-10)

- Participants reported headache
  before surgery (M = 8.18, SD = 1.62)
  after surgery significantly less headache pain (M = 4.50, SD = 1.82)

  - $t(21) = 6.532$, **$p<0.001$,**

  - (M_{diff} = 3.68, SD_{diff} = 2.64),
  - 95% CI [2.51-4.85]

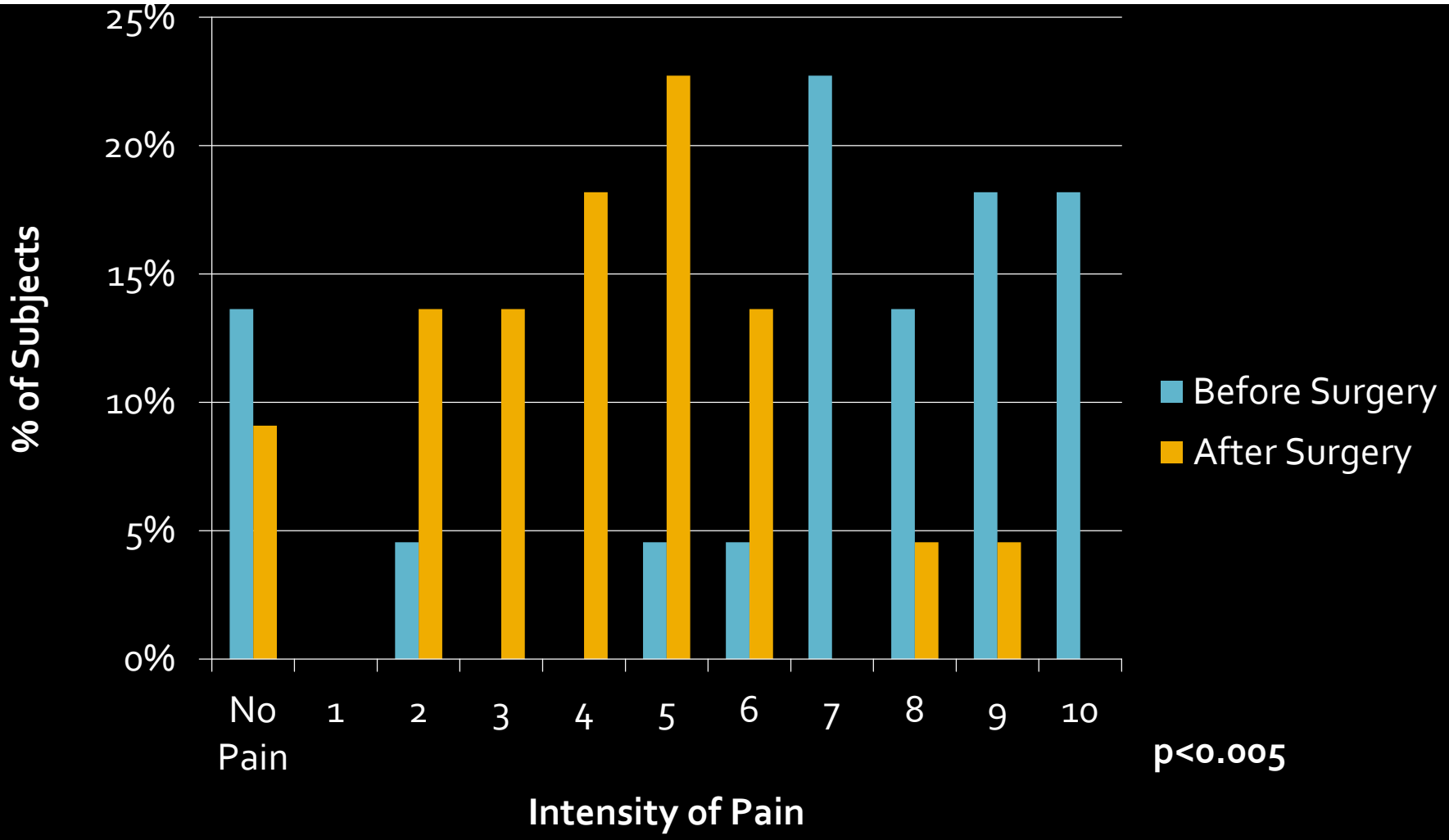
Average Headache



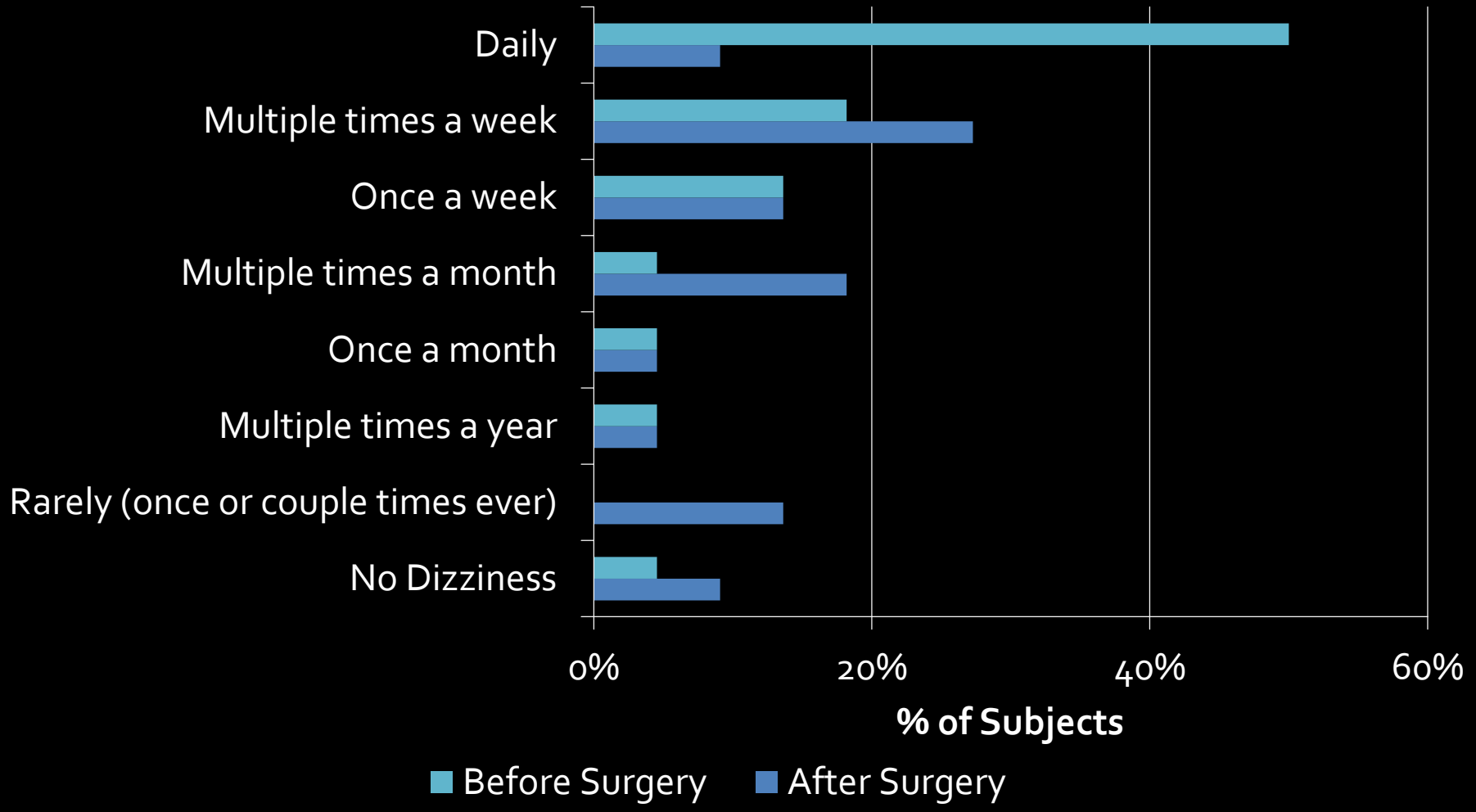
In craniocervical instability, headache can result from co-morbid conditions

- Chiari malformation
- Atlanto-axial instability
- Vertebral instability
- Pseudotumor cerebri
- Occipital neuralgia
- TMJ Syndrome
- Intracranial thrombosis
- Hypercoagulability ,Hughes Syndrome, migrainous TIAs
- Neuro-immunological disorders- Hashimoto's thyroiditis /encephalopathy, Anti-NMDA Ab, PANDAS, neuro-Behcet's

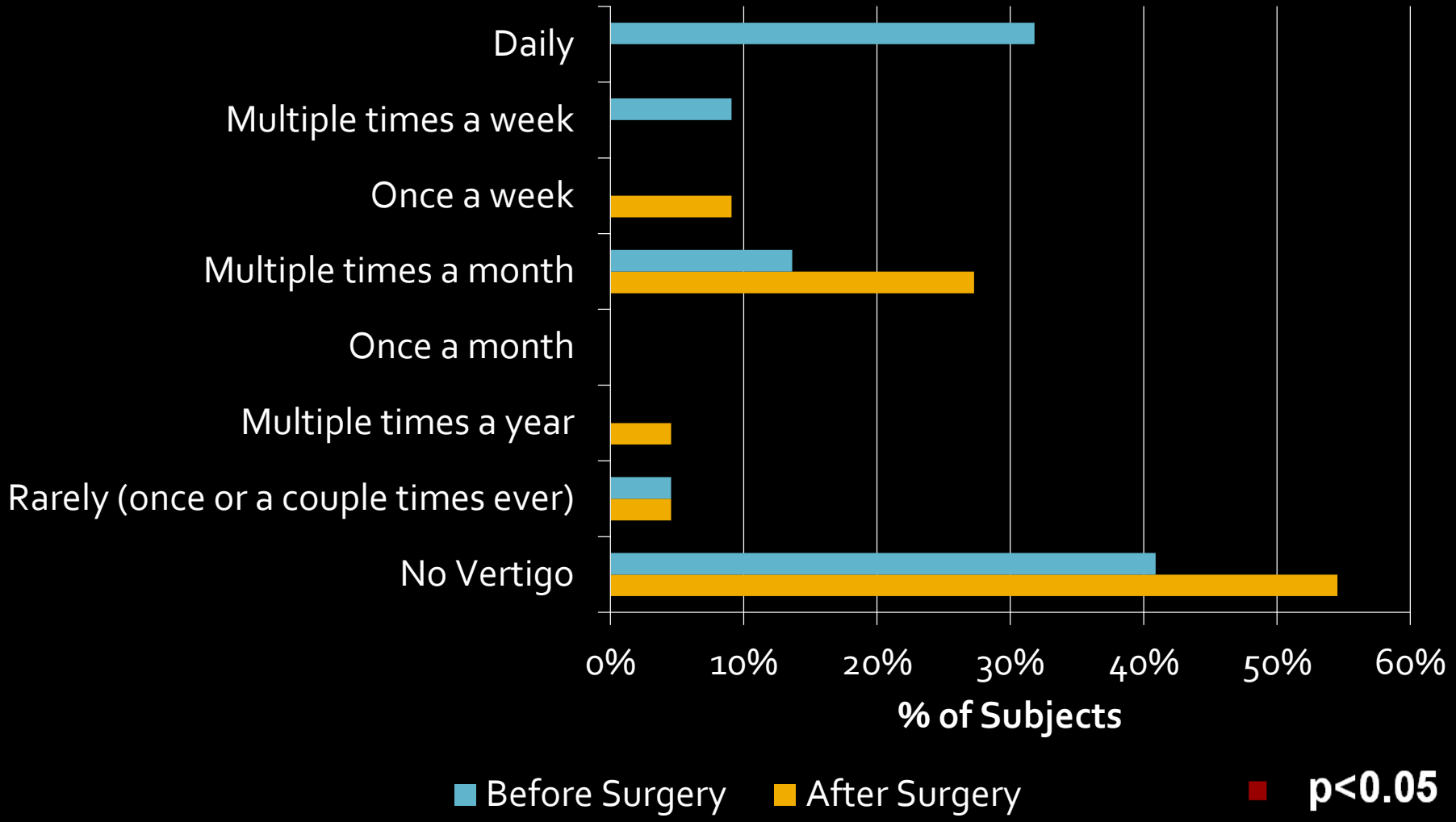
Average Neck Pain



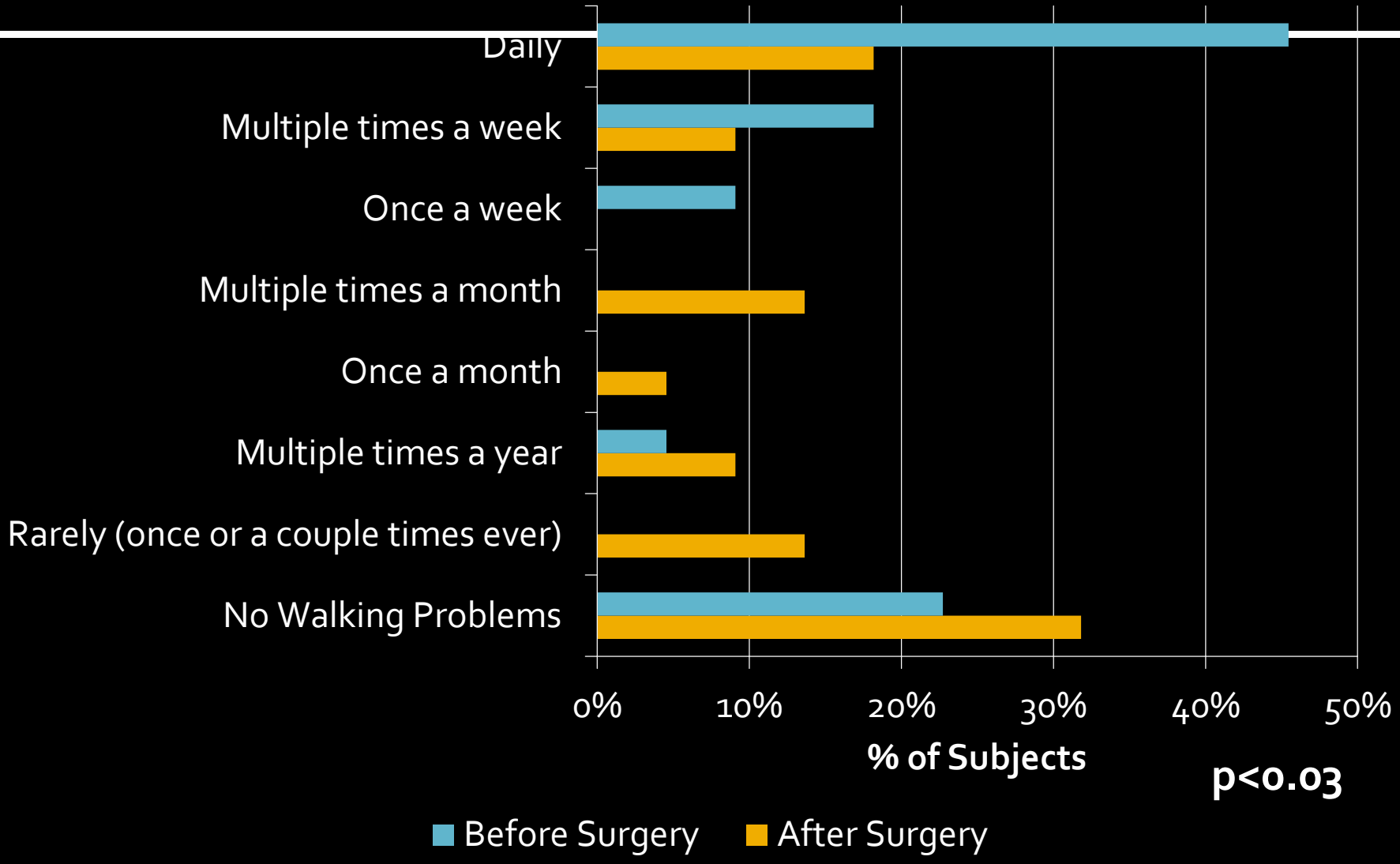
Frequency of Dizziness



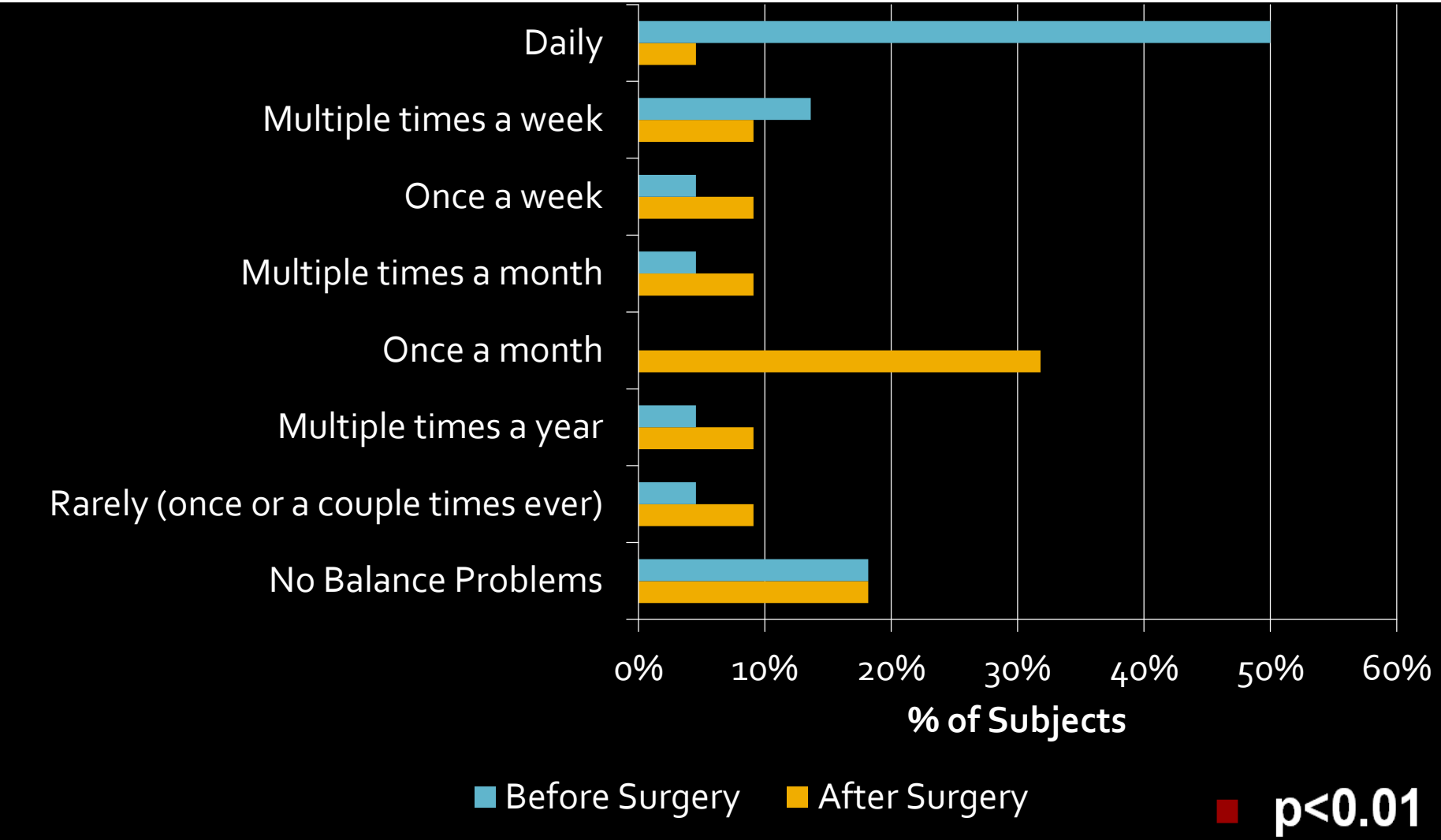
Frequency of Vertigo



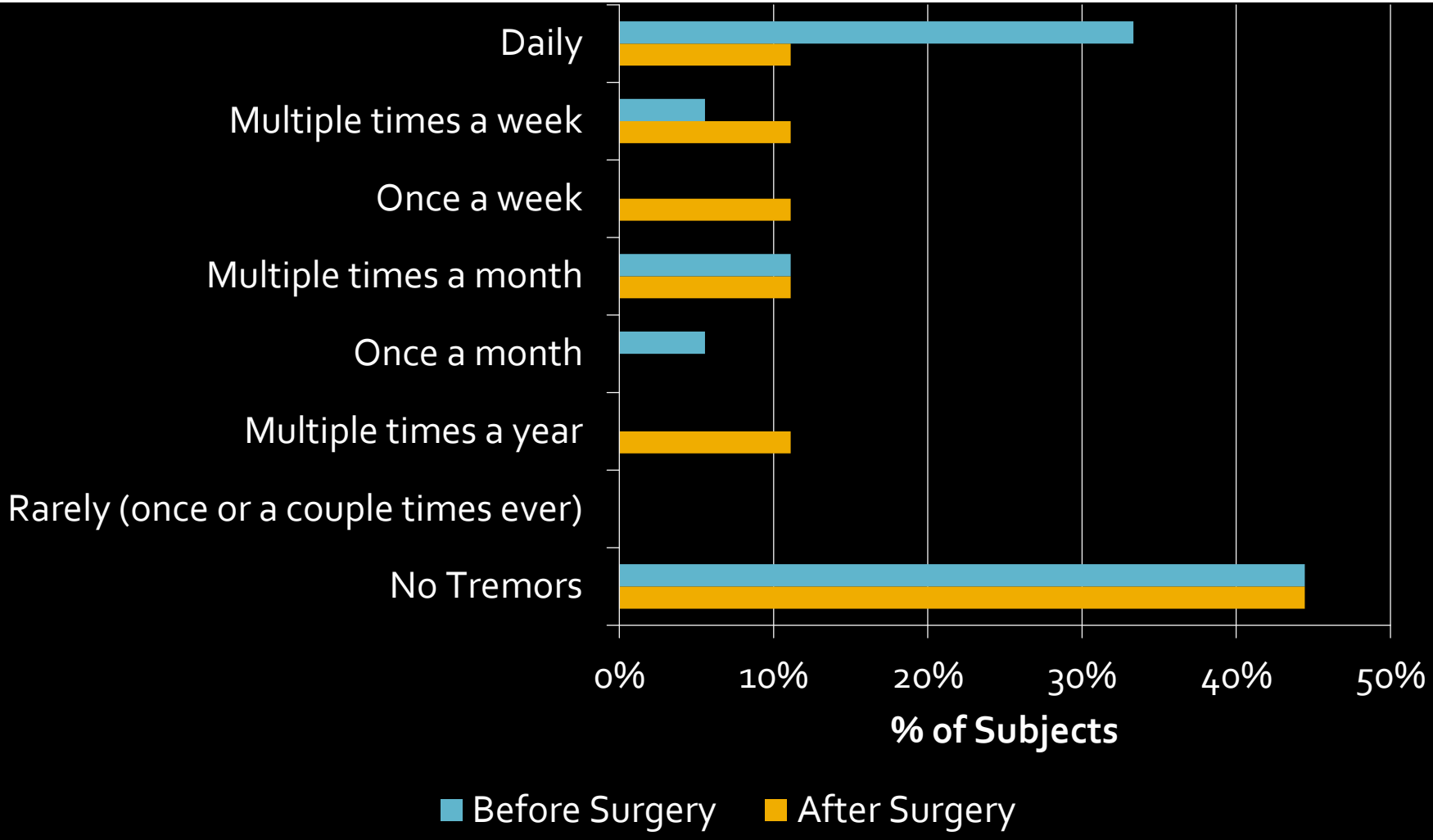
Frequency of Walking Problems



Frequency of Balance Problems



Frequency of Tremors



Karnofsky Performance Status Scale

100% - Normal; no complaints; no evidence of disease.
90% - Able to carry on normal activity; minor signs or symptoms of disease.
80% - Normal activity with effort; some signs or symptoms of disease.
70% - Cares for self; unable to carry on normal activity or to do active work.
60% - Requires occasional assistance, but able to manage personal needs.
50% - Requires considerable assistance and frequent medical care.
40% - Disabled; requires special care and assistance.
30% - Severely disabled; hospital admission is indicated
20% - Very sick; hospital admission necessary for supportive treatment
10% - Moribund; fatal processes progressing rapidly.
0% - Dead

Karnofsky Performance Scale

- Retrospectively asked to provide a Karnofsky score pre- and post-surgery
- Participants reported significantly improved Karnofsky scores

  pre- $M = 57.73$, $SD = 15.72$

  post $M = 71.36$, $SD = 16.1$

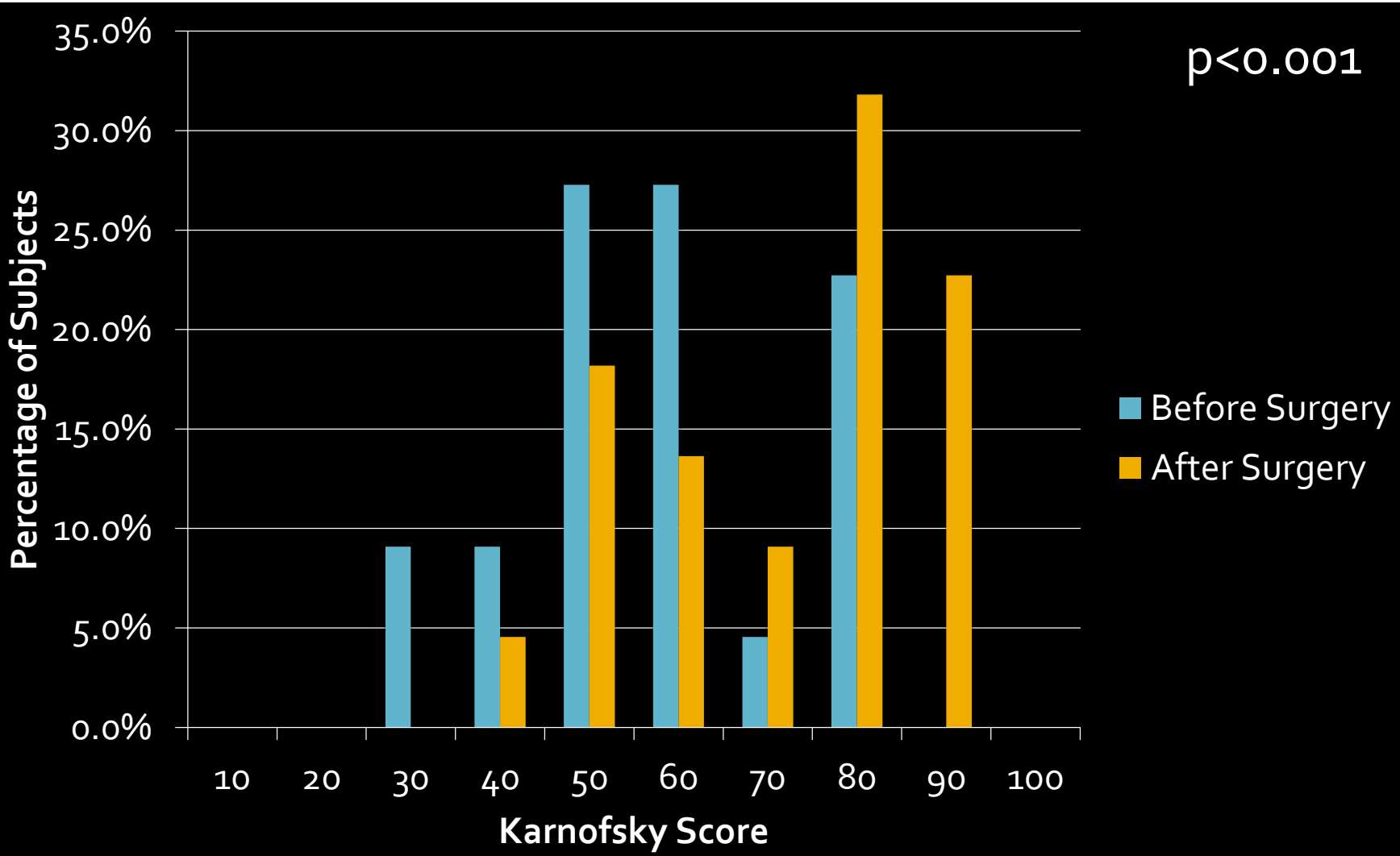
  $t(21) = 3.53$, ($M_{diff} = 13.63$, $SD_{diff} = 18.14$), 95% CI [5.59-21.68]

  p<0.001

At average 22 months s/p occipito cervical fusion

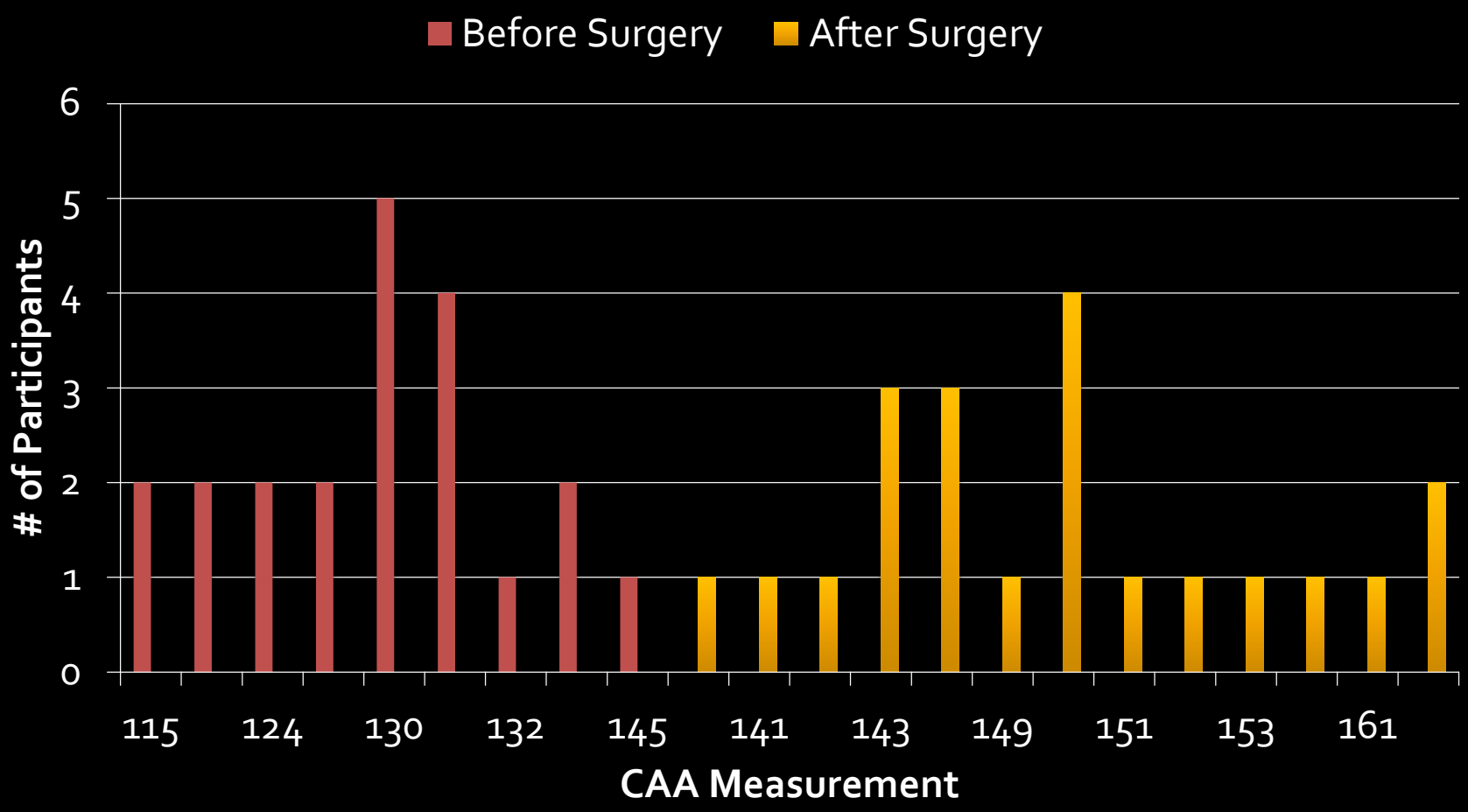
- 14/22 improved
- 5 no change
- 3 worse
- Overall the group (n=22) improved from 57 to 71 (KPSS /100)

Karnofsky Performance Scale



p<0.001

CXA measurements



Pitfalls : Complications of surgery

- rib harvest (occiput - C1-C2 graft)
- 13/18 (72.2%) reported persistent rib
- average pain 2.7 /10 (range 1-5)

- In some , delayed thoracic instability

- hardware profile causing pain- a high profile system resulted in our removal of hardware in 20% patients

- failed fusion if hardware removed too soon <1 year
- “Hardware failure” 8% (Vaccaro, 2008);
  modern systems <2%

Pitfall: incorrect expectations

- Surgery is not a panacea
- Most of the symptoms related to the underlying HCTD will not be improved
- Some symptoms will worsen
- Treatment requires ongoing pain management and medical management of the non-surgical problems

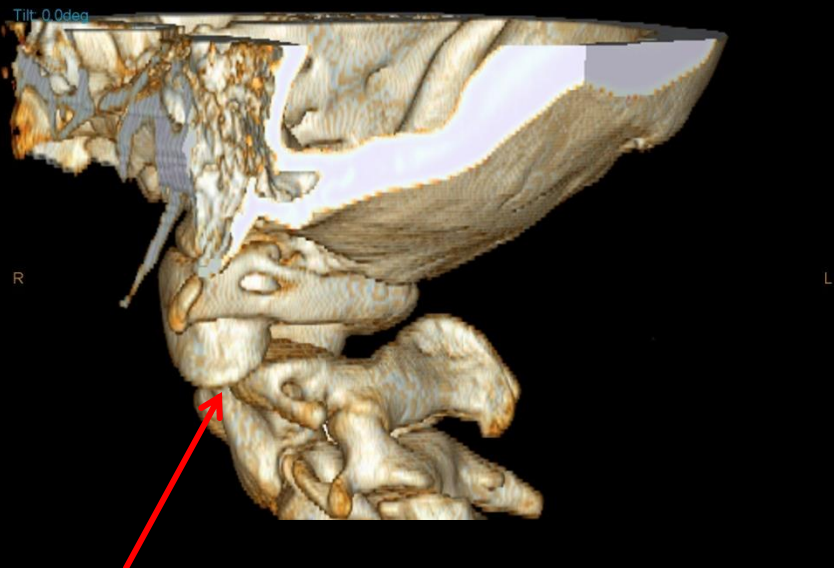
Cranio-vertebral instability, Chiari I malformation s/p decompression, stabilization/fusion

Completely disabled , pain 10/10, syncope, unable to stand or sit

Valedictorian
Worked through College in 3 yrs 3.98 average
Job
Married
Promotion
Several more neck surgeries

Other Conditions resulting in headache associated with EDS

C1-C2 instability

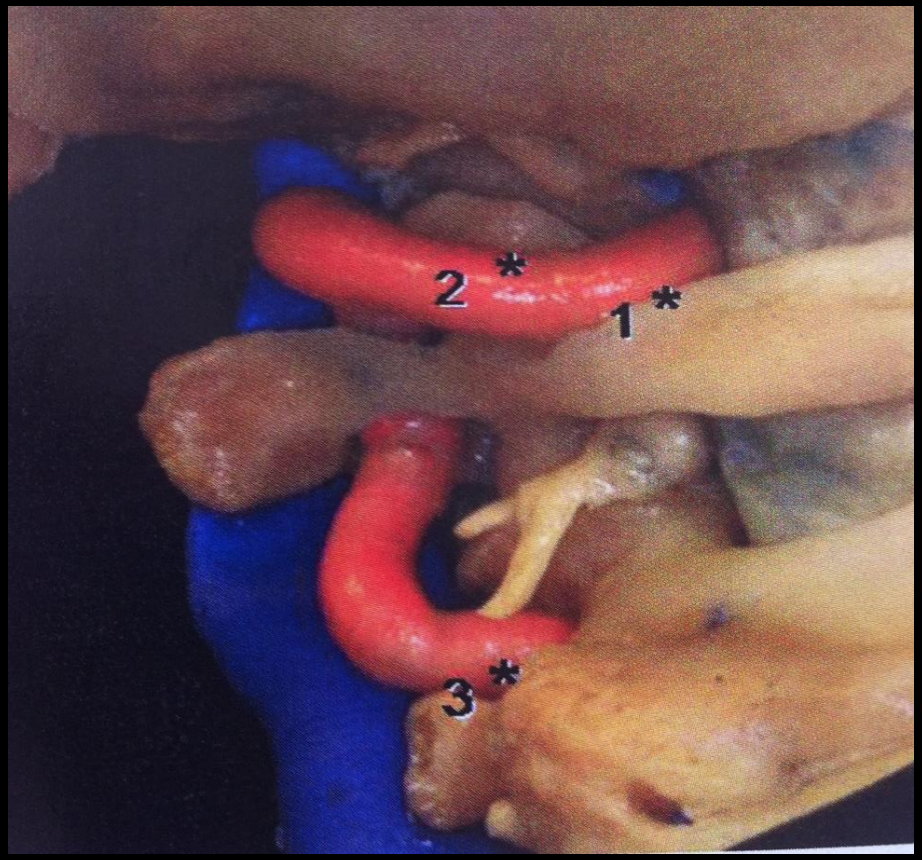


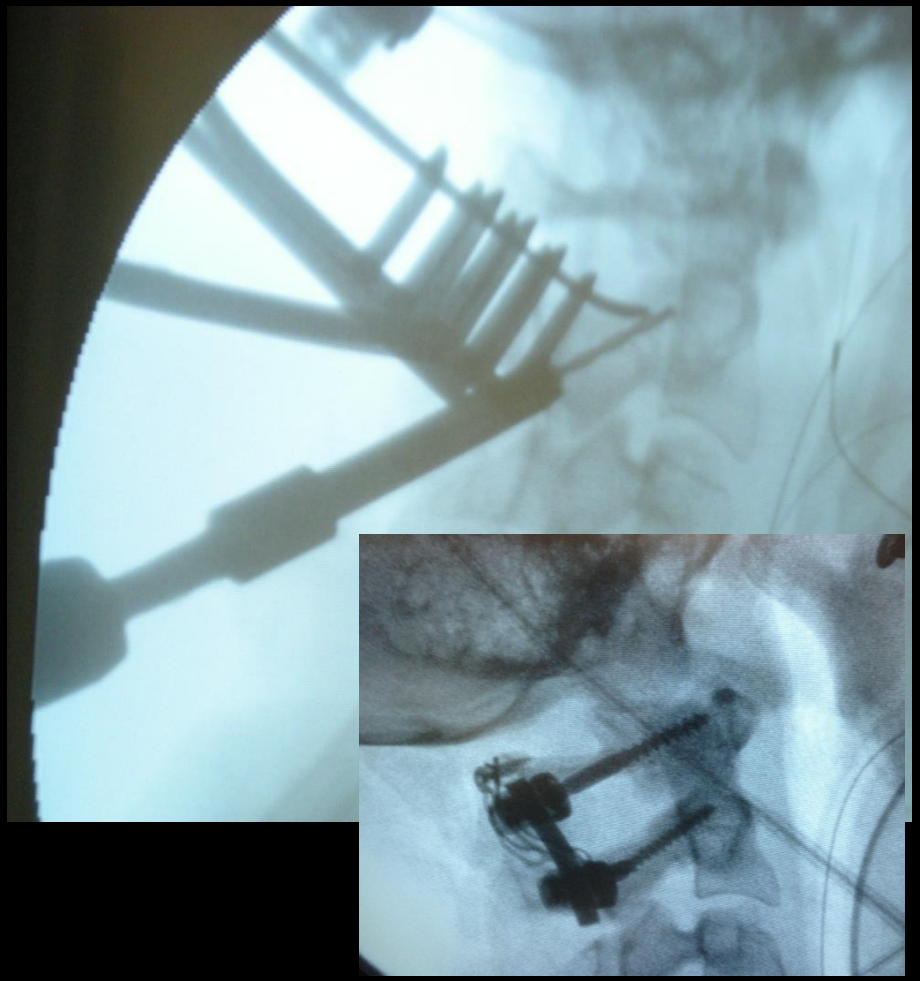
>44 degree angle between c1 and c2 on full neck rotation

Atlanto- axial instability

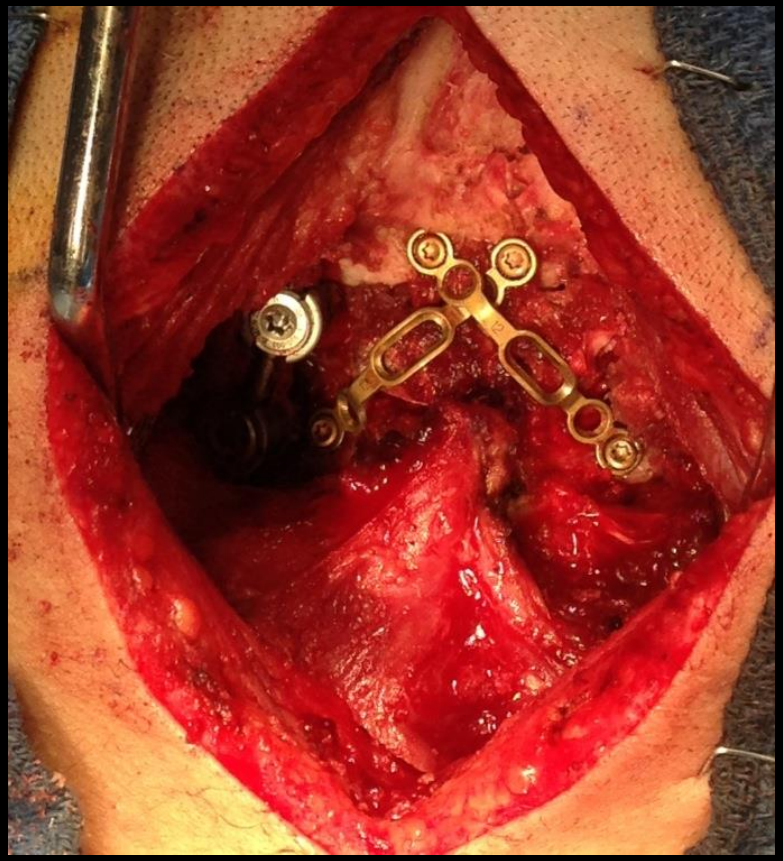
- Neck pain and headache, much worse when driving on bumpy roads
- Nausea
- POTS, dysautonomia
- Pain with neck turning
- Pain over the C1/2 spinous process
- decreased pinprick sensation
- Hyper-reflexia
- Dysdiadochokinesia
- Improved with neck brace
- CT confirmation : pathological rotation of C1 upon C2

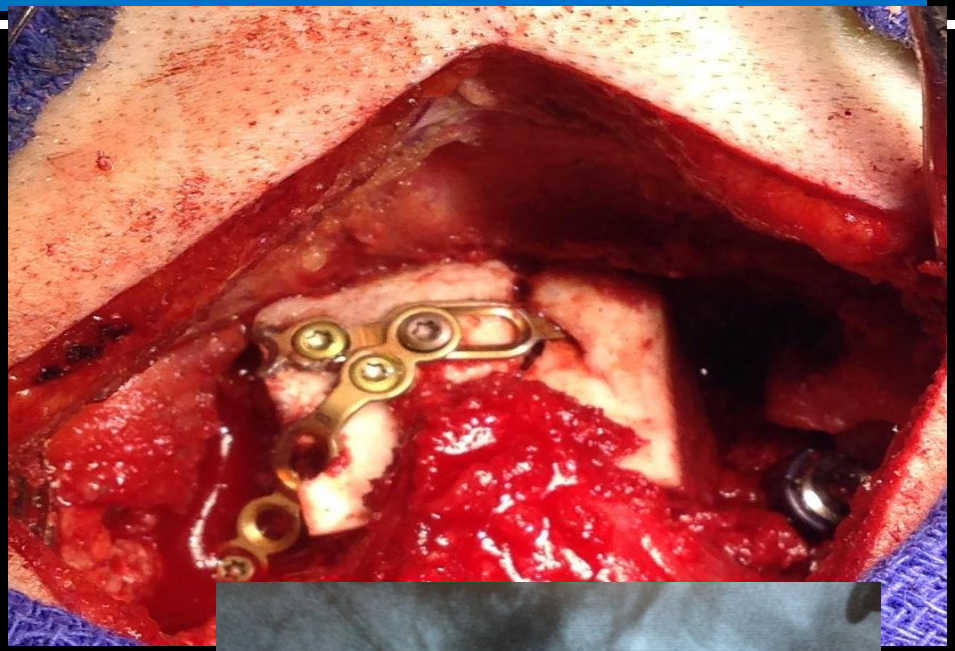
C1 C2 reduction stabilization

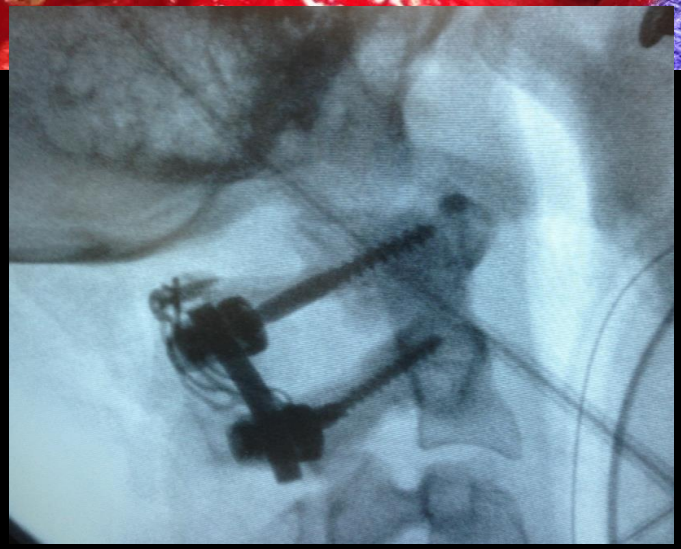




C1-C2 fusion with autograft or allograft







C1-C2 fusion stabilization

- Complications : graft site pain
  - we are now using allograft
- Mobilize on day of surgery with neck brace for 3-4 weeks
- one failure of fusion, no hardware failure to date

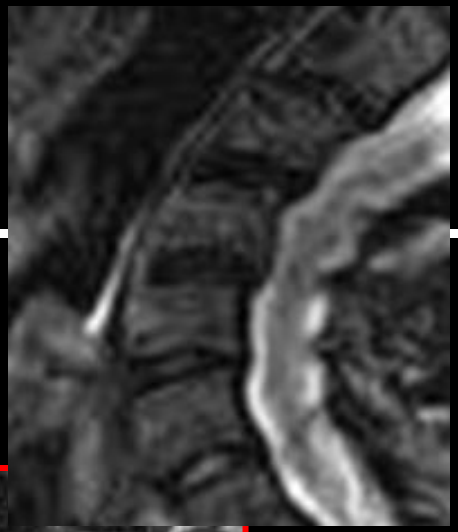
EDS Related
Cervical Segmental Instability syndromes

- discopathy is characteristic of EDS
- hyperangulation of the spine
- may manifest as a stretch myelopathy
- paresthesias of the hands and legs
- arm and leg weakness
- gait problems
- urinary urgency
- nausea, headache
- Pain between the shoulder blades

Findings associated with C45 instability

- Headache
- Head pressure
- vertigo
- Nausea
- Decreased visual acuity
- dysphagia
- Difficulty breathing when bending forward
- Sleep with head of bed at 30 degrees
- Pain across shoulders
- Interscapular painpain behind the TMJ

Cervical Segmental instability C45



Diagnosis of Clinical Instability in the Middle and Lower Cervical Spine Total of 5 or more = unstable

2 points each

- Anterior or posterior elements destroyed or unable to function
- Positive stretch test
- Dynamic Flexion-extension X-rays

* Total Sagittal plane translation > 3.5 mm or 20%

* Total Sagittal plane rotation > 20 degrees

- Resting X-rays
- Sagittal plane displacement > 3.5 mm or 20%
- Relative sagittal plane angulation > 11 degrees
- Spinal cord damage

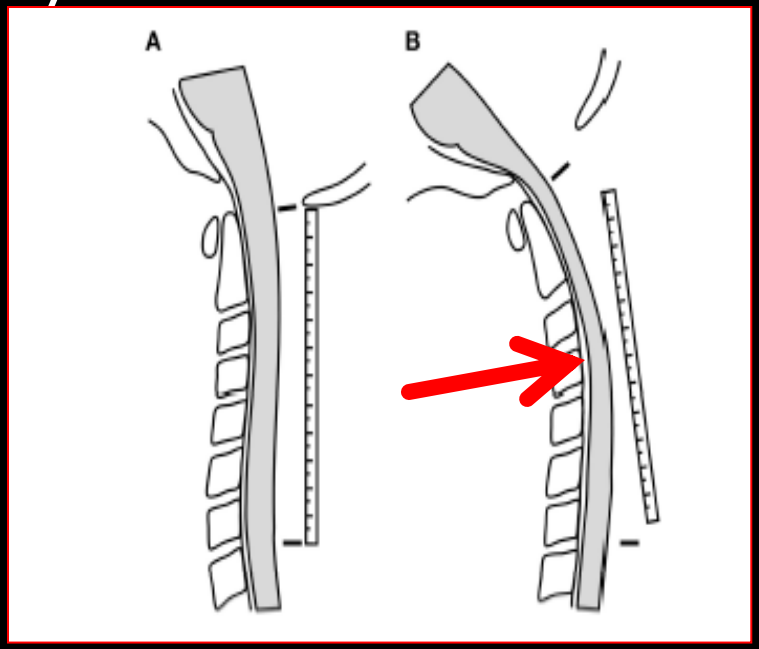
1 pt each

- Stenosis Sagittal diameter < 13 mm or Pavlov's ratio < 0.8
- Abnormal disc narrowing
- Nerve root damage
- Dangerous loading anticipated

- From White AA, Panjabi MM. Clinical Biomechanics of the Spine, 2nd ed. Philadelphia: Lippincott; 1990.

The myelopathy of cervical spondylosisis is the result of repetitive trauma , spinal cord distortion and tethering

The repetitive stretching of the spinal cord over the apex of the deformity



BENZEL E Neurosurgery Jan 2007 Suppl S1 P1

Stretch-Associated Injury in Cervical Spondylotic Myelopathy: New Concept and Review

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THE SIMPLE PATHOANATOMIC concept that a narrowed spinal canal causes compression of the enclosed cord, leading to local tissue ischemia, injury, and neurological impairment, fails to explain the entire spectrum of clinical findings observed in cervical spondylotic myelopathy. A growing body of evidence indicates that spondylotic narrowing of the spinal canal and abnormal or excessive motion of the cervical spine results in increased strain and shear forces that cause localized axonal injury within the spinal cord.

During normal motion, significant axial strains occur in the cervical spinal cord. At the cervicothoracic junction, where flexion is greatest, the spinal cord stretches 24% of its length. This causes local spinal cord strain. In the presence of pathological displacement, strain can exceed the material properties of the spinal cord and cause transient or permanent neurological injury.

Stretch-associated injury is now widely accepted as the principal etiological factor of myelopathy in experimental models of neural injury, tethered cord syndrome, and diffuse axonal injury. Axonal injury reproducibly occurs at sites of maximal tensile loading in a well-defined sequence of intracellular events: myelin stretch injury, altered axolemmal permeability, calcium entry, cytoskeletal collapse, compaction of neurofilaments and microtubules, disruption of anterograde axonal transport, accumulation of organelles, axon retraction bulb formation, and secondary axotomy. Stretch and shear forces generated within the spinal cord seem to be important factors in the pathogenesis of cervical spondylotic myelopathy.

KEY WORDS: Apoptosis, Axon spheroids, Cervical spondylotic myelopathy, Focal axonal injury, Shear, Spinal cord stretch, Strain

Neurosurgery 56:1001–1112, 2005 DOI: 10.1227/01.NEU.0000156518.38370.2C www.neurosurgery-online.com

Cervical spondylotic myelopathy (CSM) is a well-described clinical syndrome that may evolve from a combination of etiological mechanisms. The strong association between a narrowed, spondylotic cervical spinal canal and the development of CSM has previously led to the formulation of a relatively simple pathoanatomic concept that a narrowed spinal canal causes compression of the enclosed cord, leading to local tissue ischemia, injury, and neurological impairment. However, this simple mechanism fails to explain the entire spectrum of clinical findings

ical studies of cervical mobility in patients with CSM, 2) histopathological studies of spinal cord tissue from CSM patients, and 3) biomechanical studies that have led to an improved understanding of the material properties and biomechanical behavior of spinal cord tissue under various physiological and pathological conditions. A growing body of evidence indicates that spondylotic narrowing of the spinal canal results in increased strain and shear forces, and that these pathological forces cause both widespread and localized axonal injury within the spinal cord. The term strain

Neurosurgery: May 2005 - Volume 56 - Issue 5 - pp 1101-1113

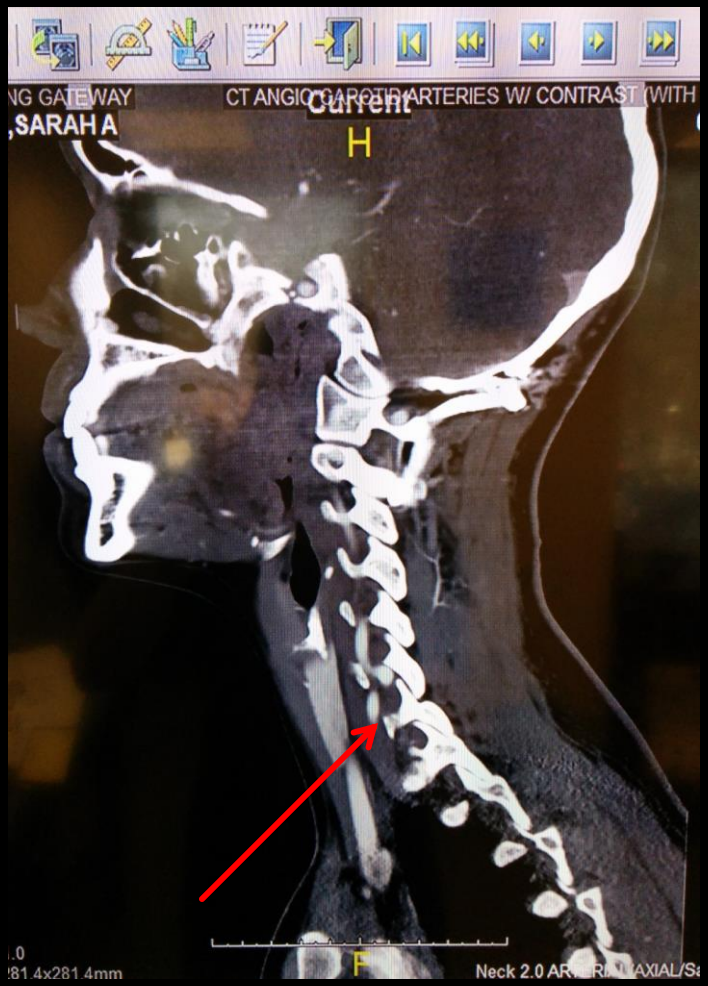
Sx associated with C2-3 instability

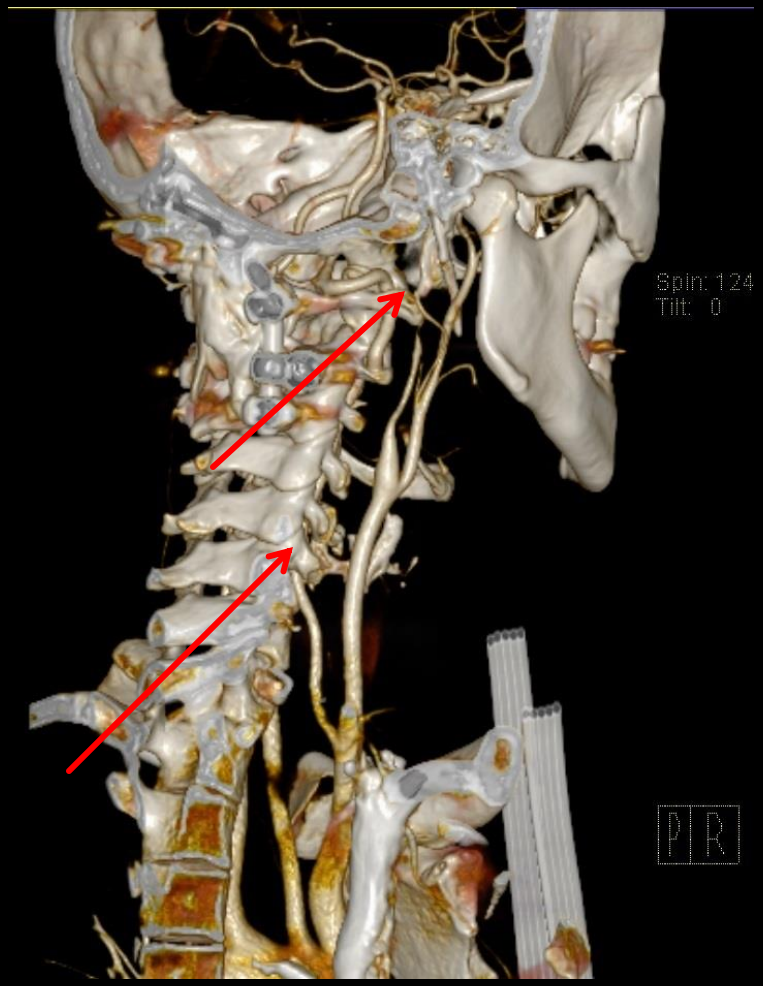
- Suboccipital and upper neck pain
- Headache
- Sometimes syncopal episodes
- Air hunger
- tics
- Eye pain
- Thoracic pain
- Gait changes

Sx associated with C6-7 instability

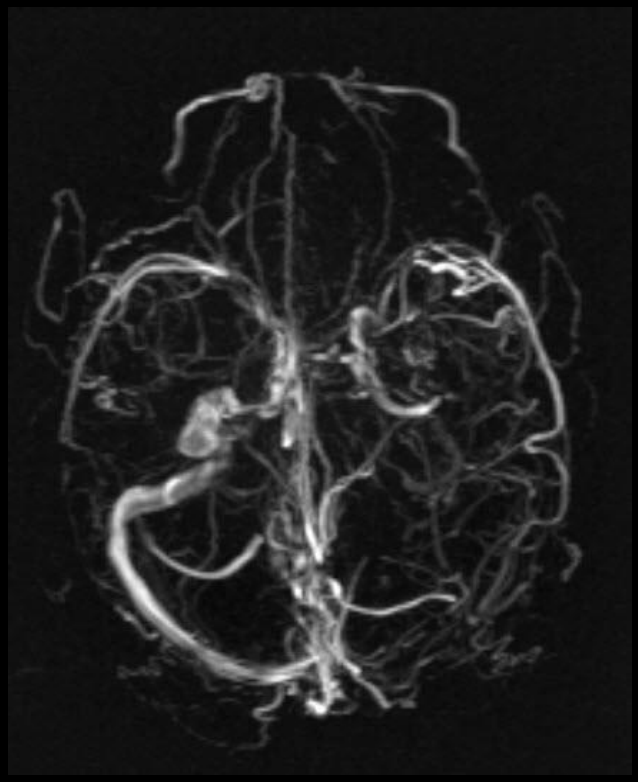
- Arm numbness and weakness
- Eye pain
- Nausea, vomiting
- Occipital neuralgia
- Poor balance
- Twitching arms
- Disturbed vision, conjunctival burning
- Ears feel clogged

Vertebral artery kinks and carotid dissection





Intracranial thrombosis



Tethered cord syndrome

- Stretching of the spinal cord by any structure that anchors the spinal cord to the spine
- In the EDS population this results from increased thickness and tightness of the filum terminale

Tethered cord syndrome

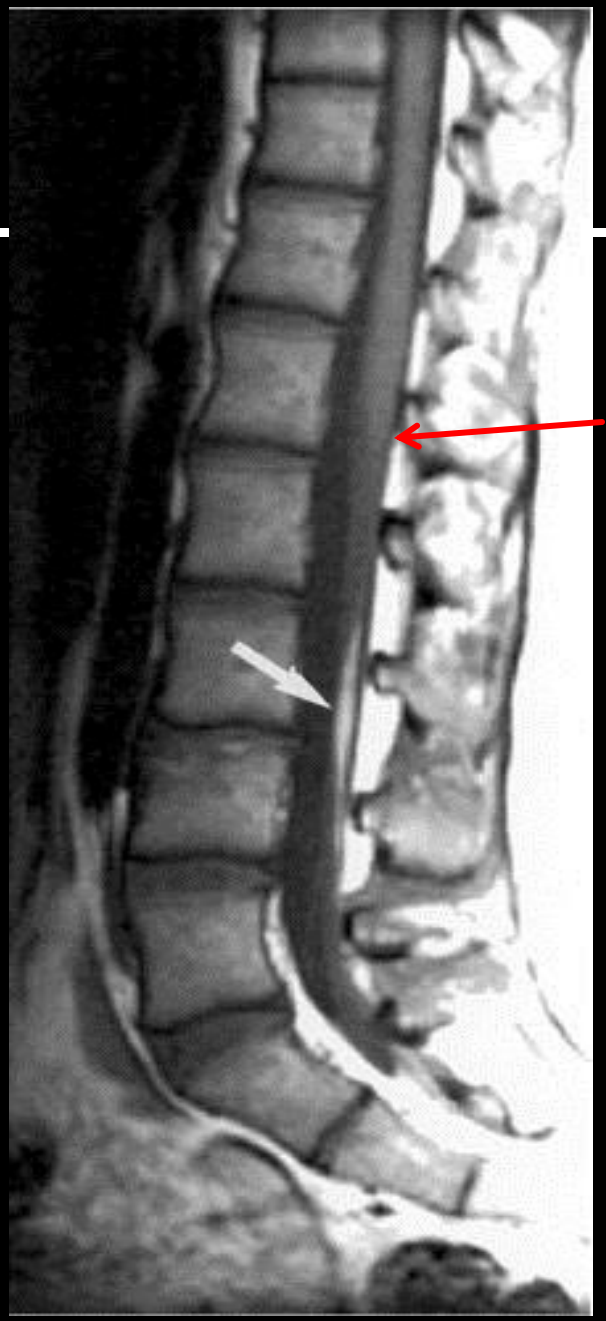
- Clinical diagnosis
- Weakness of the legs
- low back pain
- sensory loss, especially in the sacral dermatomes
- neurogenic bladder , urodynamics show large PVR, sphinchter detrussor dysynergia
- h/o growing pains, multiple UTIs, enuresis, toe walking, pidgeon toed, leg cramps, sleeping with knees bent, cannot walk uphill
- flat feet
- scoliosis

Unusual sx of tethered cord syndrome

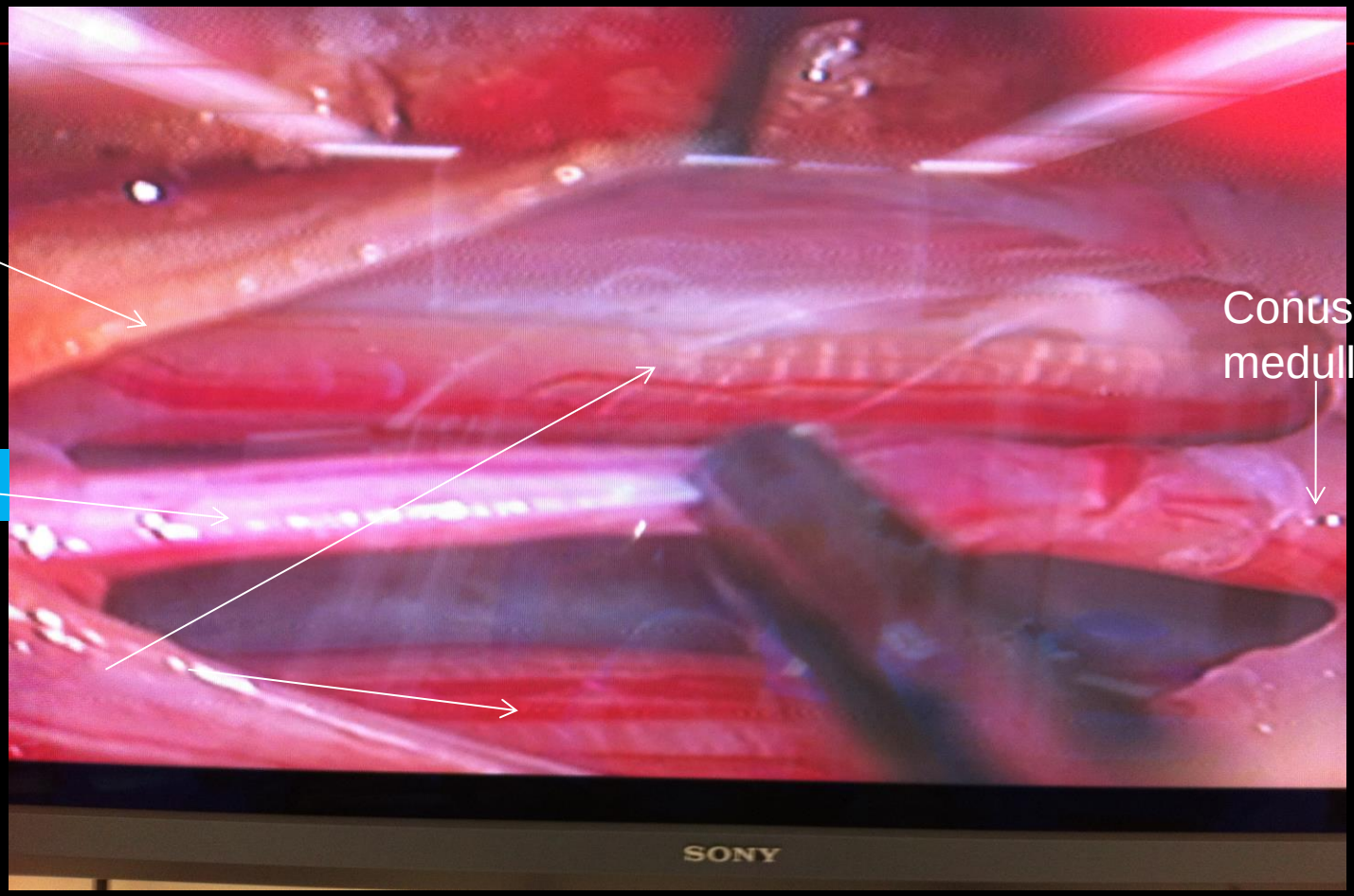
- Bowel incontinence
- Headache
- Stretch signs :severe back pain, tingling and nausea
- Light shock waves going down the legs
- Burning under the feet
- Fullness of pharynx / dysphagia

Tethered Cord Syndrome Radiological findings

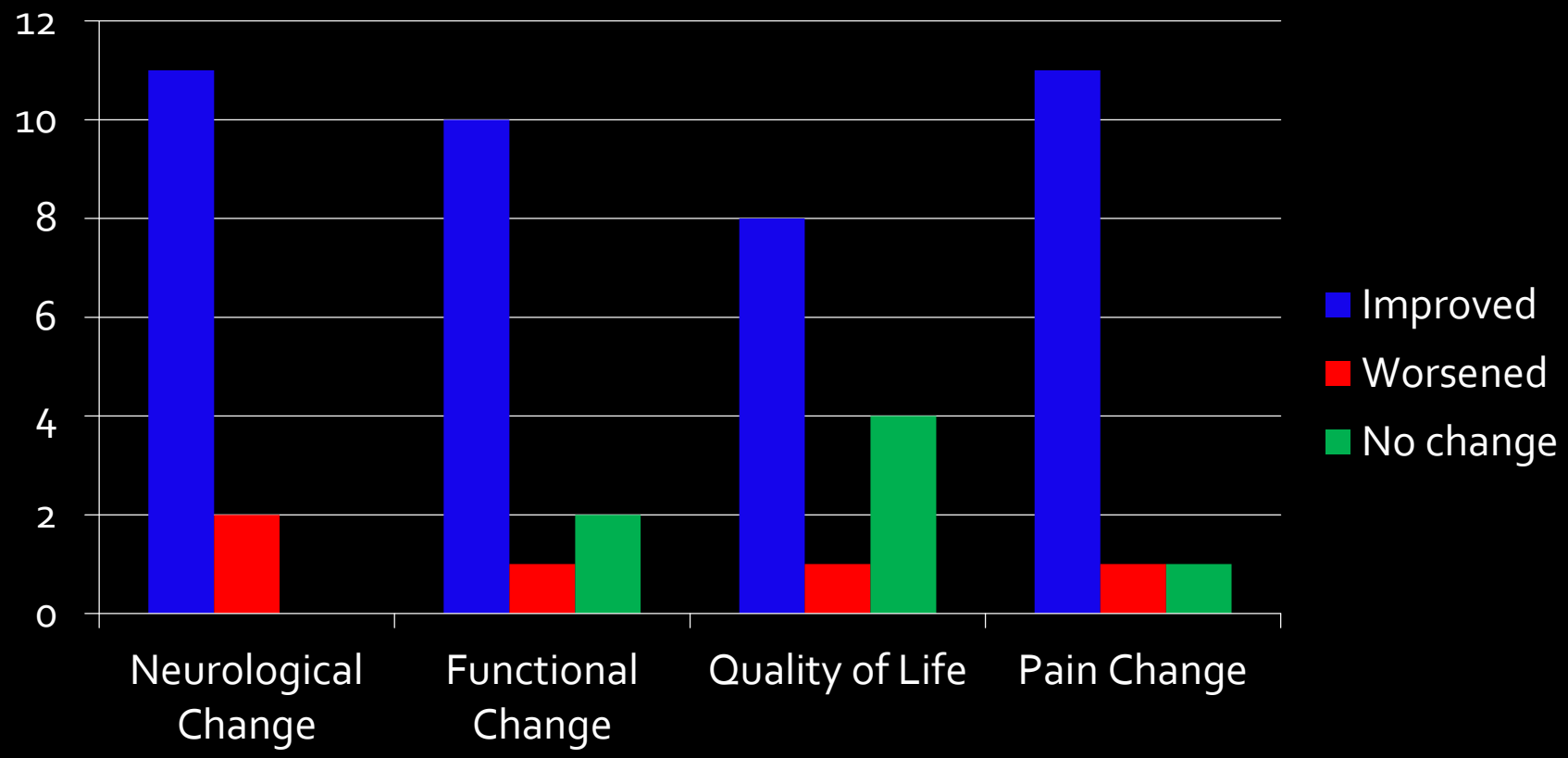
- Conus medullaris L 3
- In EDS, usually “radiologically occult”
- Fatty filum
- Scoliosis
- Syringomyelia
- Spinal bifida oculta
- Cauda equina appears stretched
- On prone MRI conus posterior



Tethered cord syndrome is the result of tension of the filum terminale and stretching of the spinal cord.
To relieve the tension, the filum terminale is clipped



Preliminary results : Tethered cord release n=13



Outcomes of un-tethering

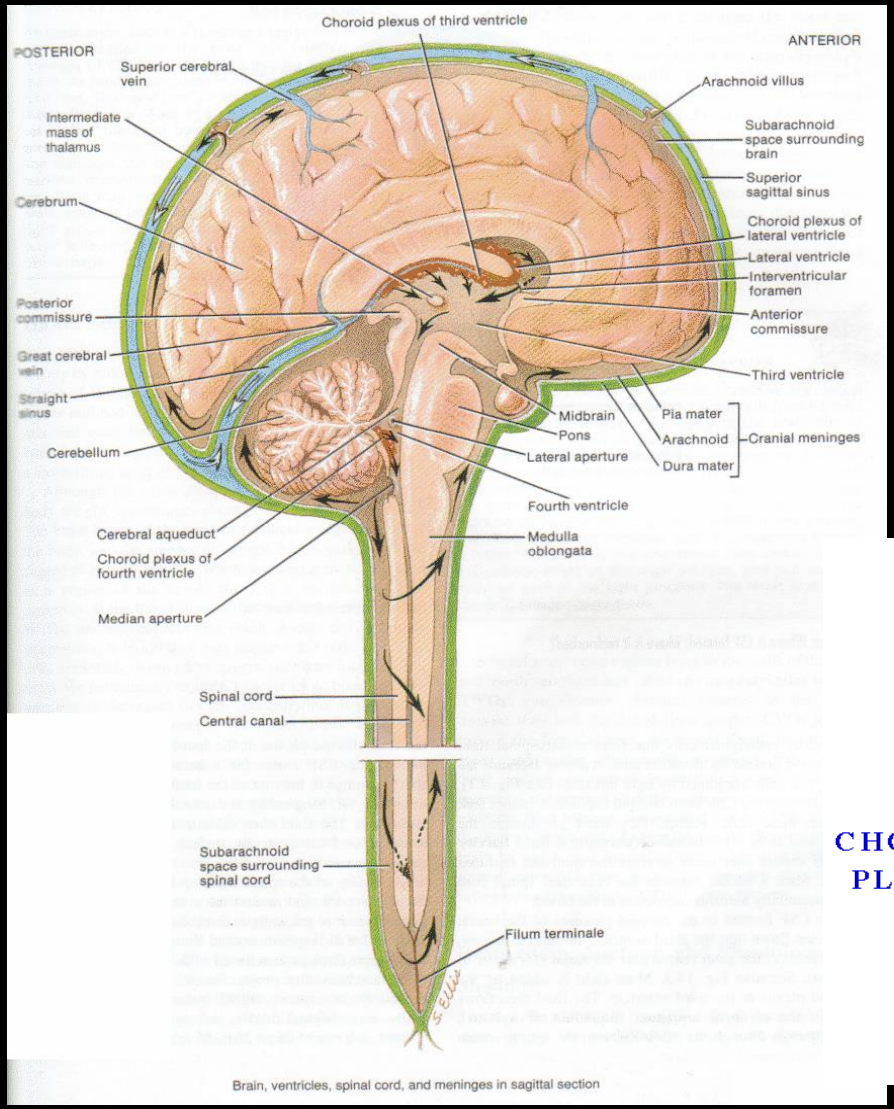
- Every patient surveyed, with the exception of one, said they would do the surgery again if they had the choice and said they would recommend it to a friend or family member
- Complications: subcutaneous hematoma, IV thrombosis, urethritis from catheter, pulmonary embolism
- Other complications: pseudomeningocoele

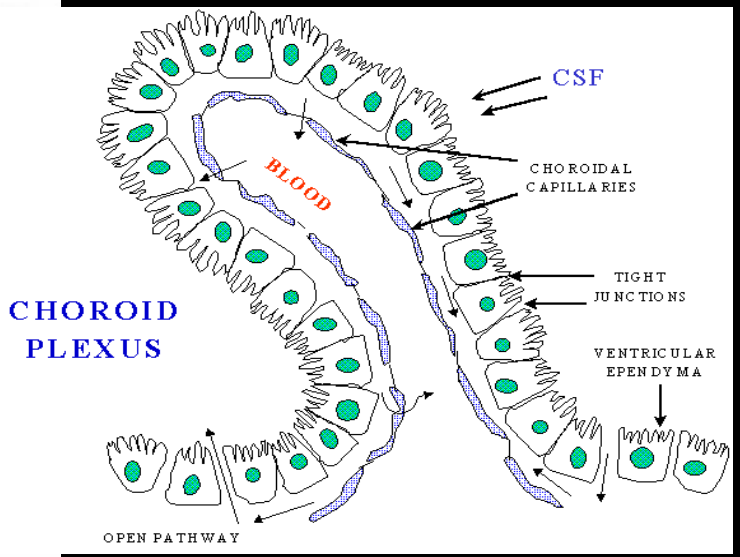
Tethered cord Syndrome Conclusions

- is a clinical diagnosis, more often radiologically occult in EDS patients
- In well selected patients, sectioning the filum terminale improves pain, function and neurological deficit in more than 85% of patients

Problems of Brain Water

Hydrocephalus





Benign Intracranial hypertension (pseudo tumor cerebri)

- Raised intracranial pressure with no evidence of “mass lesion”, hydrocephalus, infection or hypertensive encephalopathy
- Etiology:
  obesity, hyper-vitaminosis, pregnancy, menarche, menstrual irregularities, Addison’s disease, Fe^{++} def. anemia, polycythemia vera
  Oral contraceptives, steroid withdrawal, tetracycline, nalidixic acid

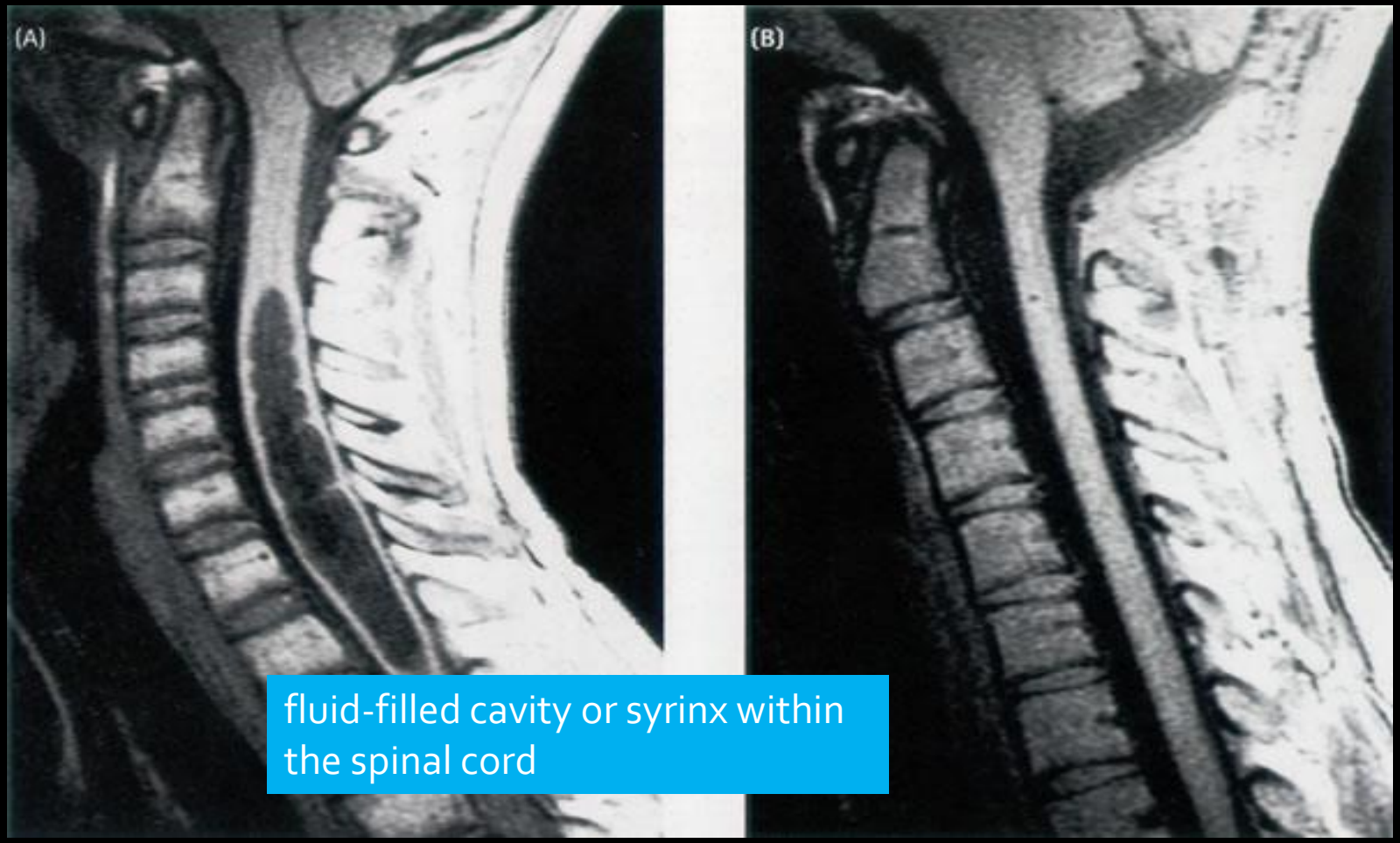
Clinical features of pseudotumor cerebri

- Usually 3rd and 4th decades
- Women > men
- Headache (94%)
- visual obscurations/blurring (68%)
- Pulse synchronous tinnitus or whooshing noise (58%)
- Retro-orbital pain (44%)
- Diplopia (38%)
- Visual loss (30%)
- Normal radiological (CT/MRI) studies
- LP: CSF pressure greater than 25 cm H2O

Treatment Benign Intracranial Hypertension

- Treat the underlying cause
- Weight loss
- Drugs- Acetazolamide
  - Thiazide diuretic
- Lumbo-peritoneal shunt
- Ventriculo-peritoneal shunt

Syringomyelia



fluid-filled cavity or syrinx within the spinal cord

Associations with syringomyelia

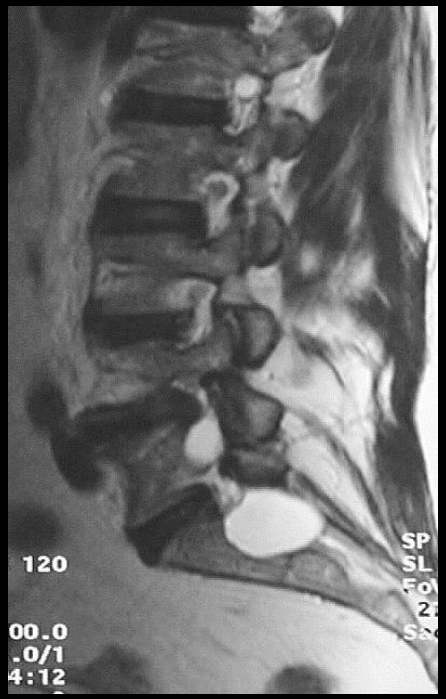
- Chiari malformation = most common cause
- Tethered cord causes small syrinx
- Other forms
  - Meningitis or arachnoiditis
  - Hemorrhage
  - Tumor
  - trauma

Treatment of syringomyelia

- Treat the underlying cause
  - Chiari
  - Tethered cord syndrome
- Rarely a syringo-subarachnoid shunt

Tarlov cyst syndrome

- Tarlov cyst or perineurial cysts
- abnormal cystic dilations arising from the posterior spinal nerve root, distal to the root ganglion



Clinical features of Tarlov Cyst Syndrome

Pain: sacral>lumbar, buttocks
Non-dermatomal
Perineal pain: dyspareunia, proctalgia

- exacerbated by standing, coughing, sneezing… Valsalva
- pain worsened by standing or sitting,
- Improved by lying flat

Urinary: frequency, urgency, incontinence
Bowel: constipation, rectal incontinence
Sensory: paresthesias, sacral sensory loss

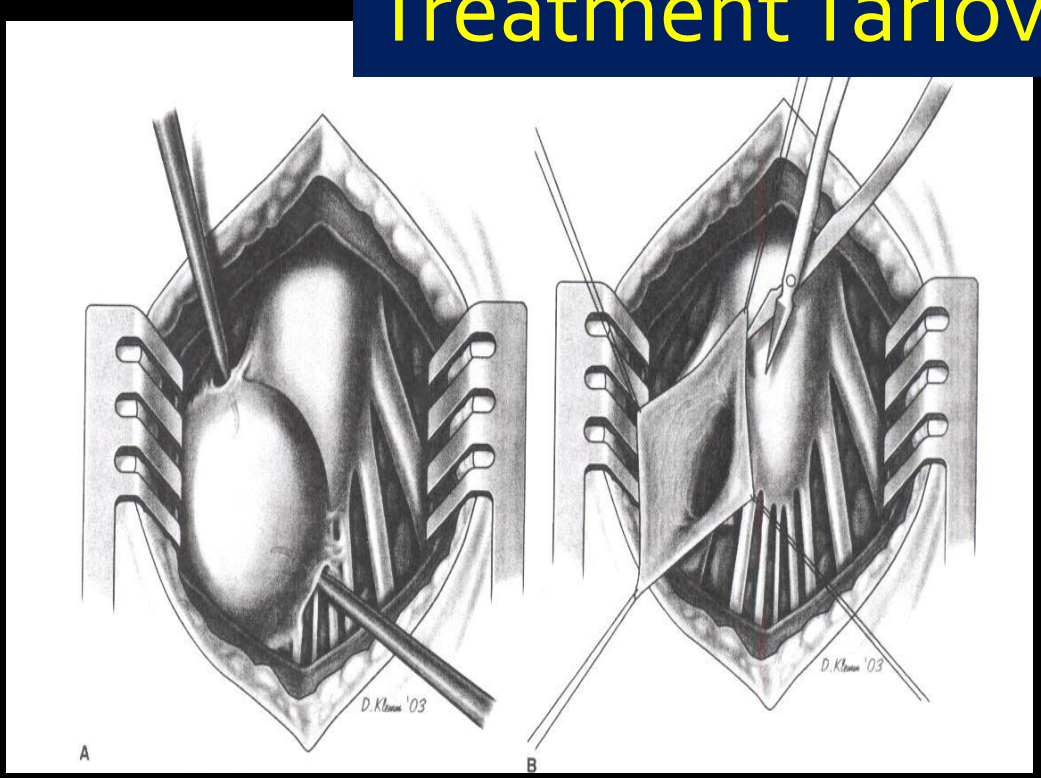
Non- surgical Management

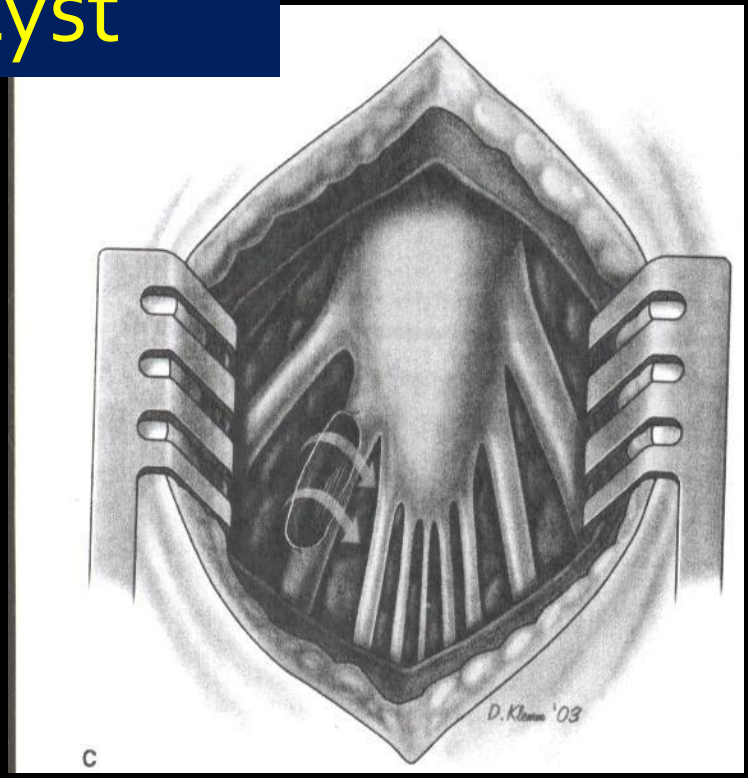
- Pain Meds: temporary relief
- Percutaneous aspiration

4/5 patients suffered recurrence of symptoms

AJNR 15: 293 -299, 1994

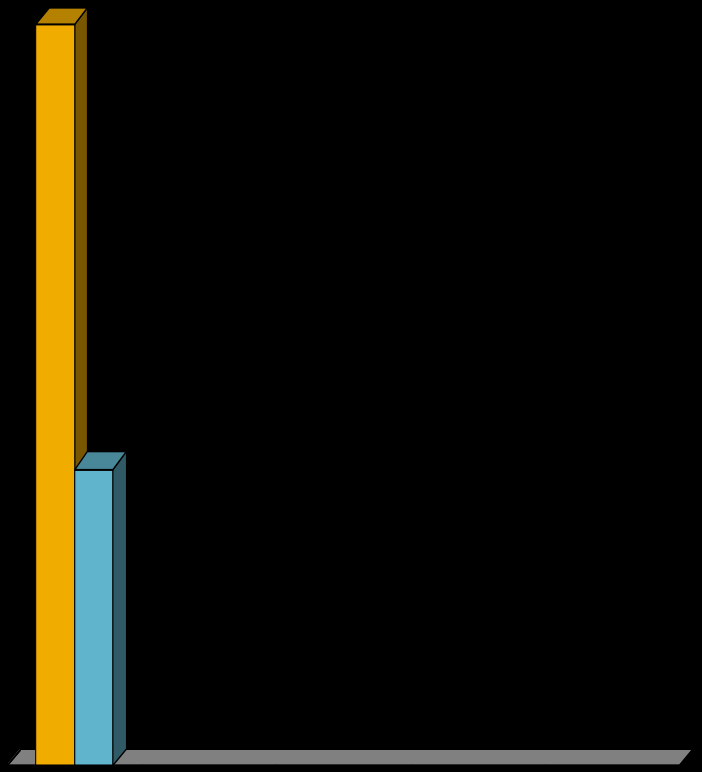
Treatment Tarlov Cyst





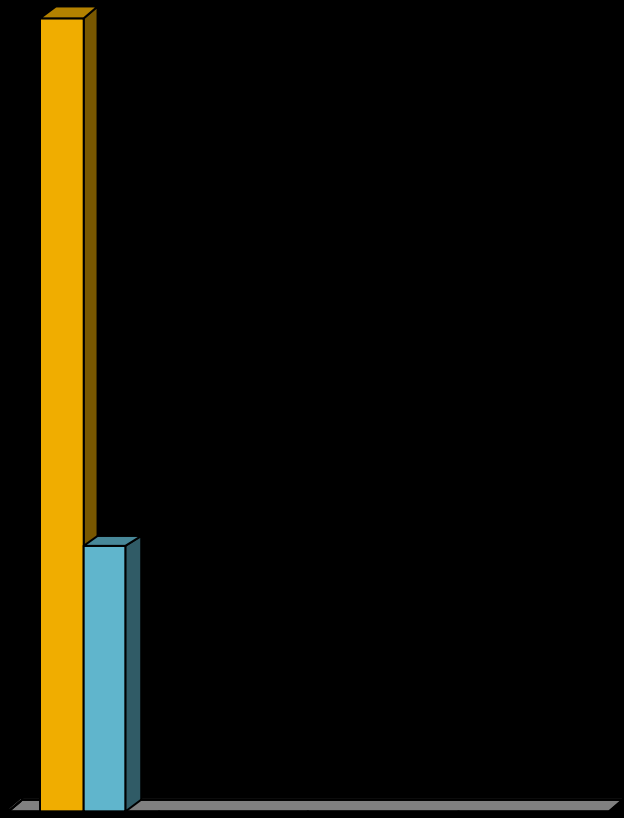
Sacral laminectomy, microsurgical stimulation to identify root fibers
Resection of redundant cyst wall, fusion/laminoplasty
+/- LP shunt

Results



Urinary symptoms

p .001



Pain p .001

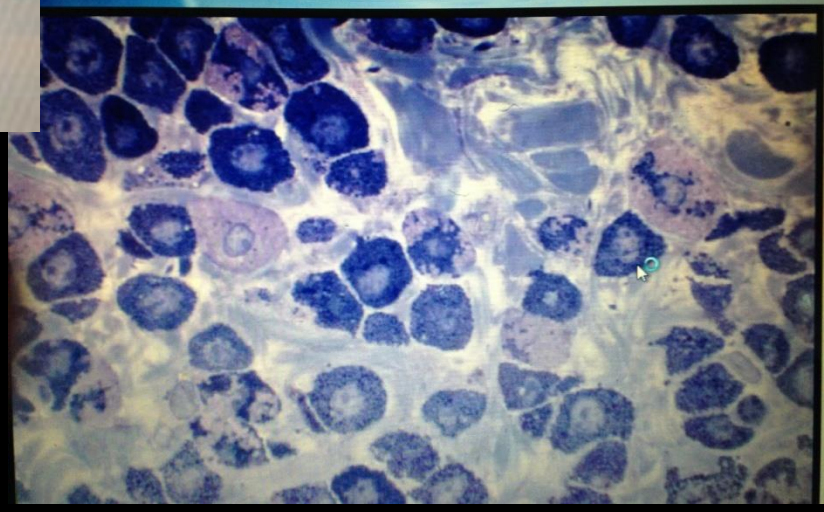
Mast cell activation syndrome MCAS impact upon brain fog , headache

Non Clonal Mast Cell Activation Syndrome
Hamilton et al JACI 2011

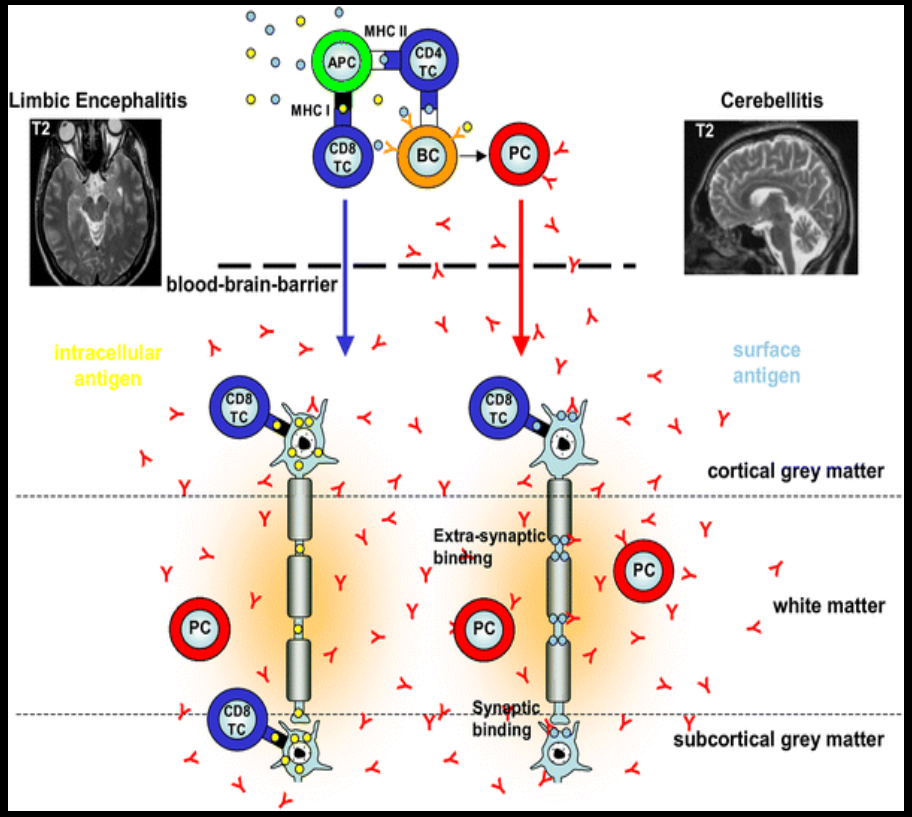
TABLE II. Signs and symptoms of patients with MCAS

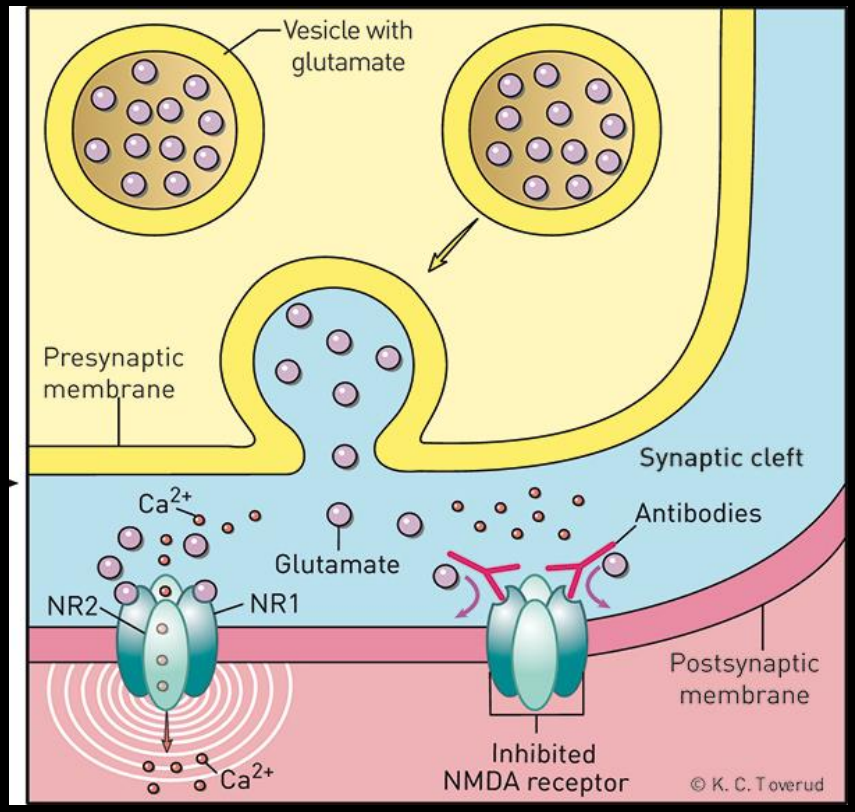
Sign or symptom	Total (%), n = 18
Abdominal pain	17 (94)
Dermatographism	16 (89)
Flushing	16 (89)
Headache	15 (83)
Poor concentration and memory	12 (67)
Diarrhea	12 (67)
Naso-ocular	7 (39)
Asthma	7 (39)
Anaphylaxis	3 (17)

kin Biopsy - Urticaria Pigmentosa



Dystonia, PANDAS and Paraneoplastic Limbic Encephalopathy





Conclusions

- headache and neurological deficits, in a patient with a hypermobility connective tissue disorder, should prompt consideration of cranio-cervical instability

  (Consensus Statement, Oct 2013)

- craniocervical instability, spinal instability and tethered cord syndrome result in deformative stress of the central nervous system

- deformative stress of the CNS appears to underlie the clinical manifestations of pain and neurological deficits

Conclusions

- Patients with craniocervical instability should be treated in a neck brace, physical therapy, activity limitation, medication, and have other disorders ruled out before consideration for surgery
- Patients with severe headache, neck pain, neurological deficits and appropriate radiological findings appear to benefit from correction of the deformity, stabilization and fusion
- Co-morbid conditions may require continued follow up

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