Topics in Neurology: Management of Neuropathy and Evaluation of Concussion

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No Disclosures

Goals

- What is neuropathy
- Evaluation and treatment strategy for neuropathy

(focus on painful peripheral neuropathy)

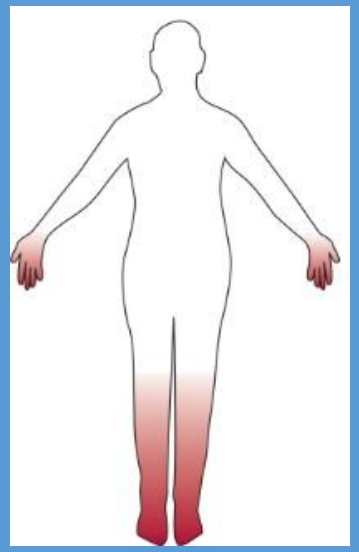
- What is concussion
- Concussion guidelines/recommendations

(focus on 2013 updated AAN guidelines)

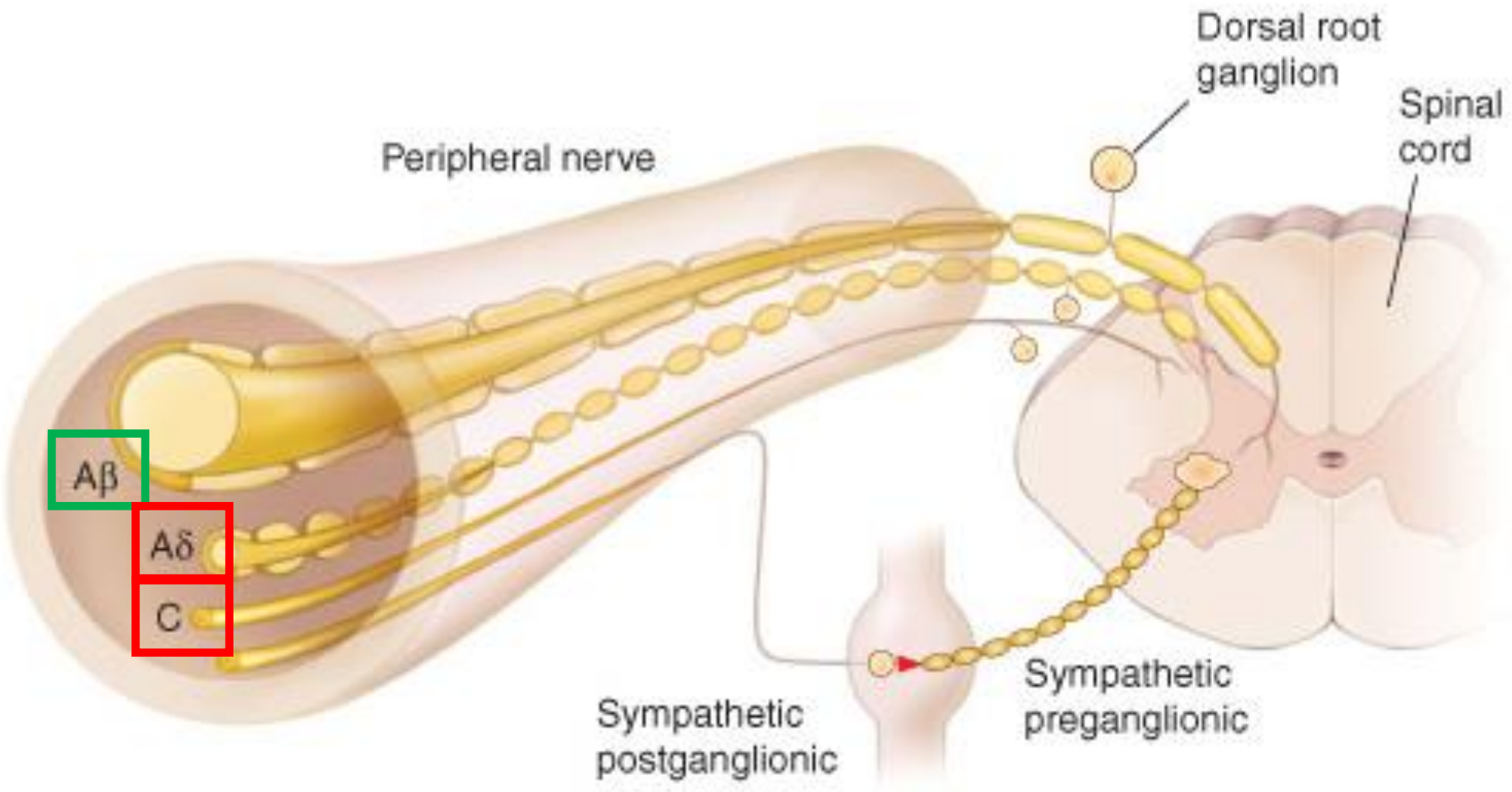
- Questions/Discussion

Peripheral Neuropathy

- Affects approximately 2-8% adults, incidence increases with age
- Various methods of classification
  - Axonal, demyelinating, neuronal
  - Small fiber, large fiber
  - Sensory, motor, autonomic
  - Acute, subacute, chronic, recurrent
  - Acquired, hereditary, autoimmune antibody mediated
  - Focus today on distal symmetric painful polyneuropathy



- There is no FDA approved treatment for small fiber neuropathy


Dorsal root ganglion
Spinal cord
Peripheral nerve
Aβ
Aδ
C
Sympathetic postganglionic
Sympathetic preganglionic

Strategic Approach

- Prevention in patients at risk (i.e. diabetes, prediabetes, gastric bypass, HIV)
- Determine underlying cause (may have multifactorial etiology)
- Medications alone or in combination (oral, topical, different mechanisms of action)

Some Main Causes of Neuropathy

- Diabetes, prediabetes (Likely related to metabolic syndrome and inflammatory nerve damage)
- Alcohol
- Thyroid disease
- Vitamin B12 deficiency, Vitamin B6 toxicity (100 mg daily may cause toxicity)
- Drug induced (chemotherapy)
- Monoclonal gammopathy
- Paraneoplastic neuropathy
- Vasculitis
- HIV
- Hereditary
- Berreliosis
- Amyloidosis

EVALUATION OF DISTAL SYMMETRIC POLYNEUROPATHY: THE ROLE OF LABORATORY AND GENETIC TESTING (AN EVIDENCE-BASED REVIEW)

Muscle Nerve 39: 116–125, 2009

J.D. ENGLAND, MD,[1] G.S. GRONSETH, MD,[2] G. FRANKLIN, MD,[3] G.T. CARTER, MD,[4] L.J. KINSELLA, MD,[5] J.A. COHEN, MD,[6] A.K. ASBURY, MD,[7] K. SZIGETI, MD, PHD,[8] J.R. LUPSKI, MD, PHD,[9] N. LATOV, MD,[10] R.A. LEWIS, MD,[11] P.A. LOW, MD,[12] M.A. FISHER, MD,[13] D. HERRMANN, MD,[14] J.F. HOWARD, MD,[15] G. LAURIA, MD,[16] R.G. MILLER, MD,[17] M. POLYDEFKIS, MD,[18] A.J. SUMNER, MD[19] Report of the American Academy of Neurology, the American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation

- Approximately 75% of neuropathies have an identifiable cause
- Initial screening can include:
  - CBC, CMP, ESR, TSH, Vitamin B12, Folate, SPEP, Immunofixation, HgbA1C, RPR
- Patient's with cryptogenic neuropathy should have further evaluation including EMG/NCS testing (skin biopsy, autonomic testing for small fiber neuropathy)

Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis

Nanna B Finnerup, Nadine Attal*, Simon Haroutounian, Ewan McNicol, Ralf Baron, Robert H Dworkin, Ian Gilron, Maija Haanpää, Per Hansson, Troels S Jensen, Peter R Kamerman, Karen Lund, Andrew Moore, Srinivasa N Raja, Andrew S C Rice, Michael Rowbotham, Emily Sena, Philip Siddall, Blair H Smith, Mark Wallace*

Lancet Neurol 2015; 162–73

	Total daily dose and dose regimen	Recommendations
Strong recommendations for use		
Gapabentin	1200–3600 mg, in three divided doses	First line
Gabapentin extended release or enacarbil	1200–3600 mg, in two divided doses	First line
Pregabalin	300–600 mg, in two divided doses	First line
Serotonin-noradrenaline reuptake inhibitors duloxetine or venlafaxine*	60–120 mg, once a day (duloxetine); 150–225 mg, once a day (venlafaxine extended release)	First line
Tricyclic antidepressants	25–150 mg, once a day or in two divided doses	First line†

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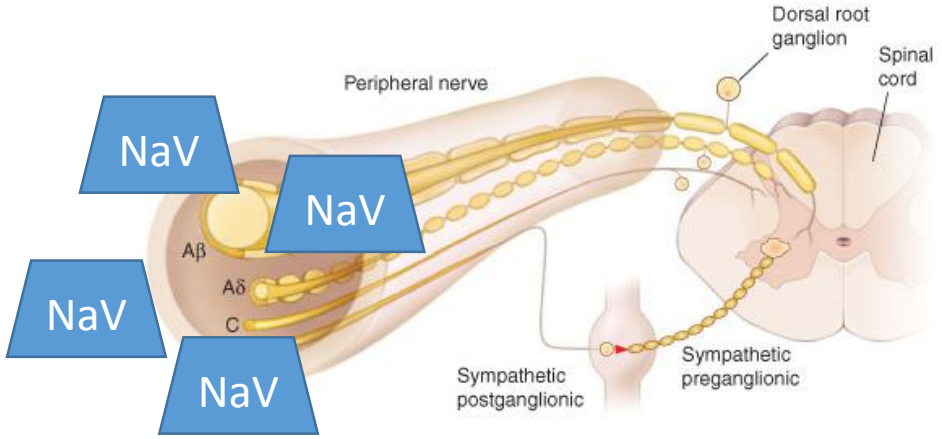
	Total daily dose and dose regimen	Recommendations
Weak recommendations for use		
Capsaicin 8% patches	One to four patches to the painful area for 30–60 min every 3 months	Second line (peripheral neuropathic pain)‡
Lidocaine patches	One to three patches to the region of pain once a day for up to 12 h	Second line (peripheral neuropathic pain)
Tramadol	200–400 mg, in two (tramadol extended release) or three divided doses	Second line
Botulinum toxin A (subcutaneously)	50–200 units to the painful area every 3 months	Third line; specialist use (peripheral neuropathic pain)
Strong opioids	Individual titration	Third line§

Mechanisms

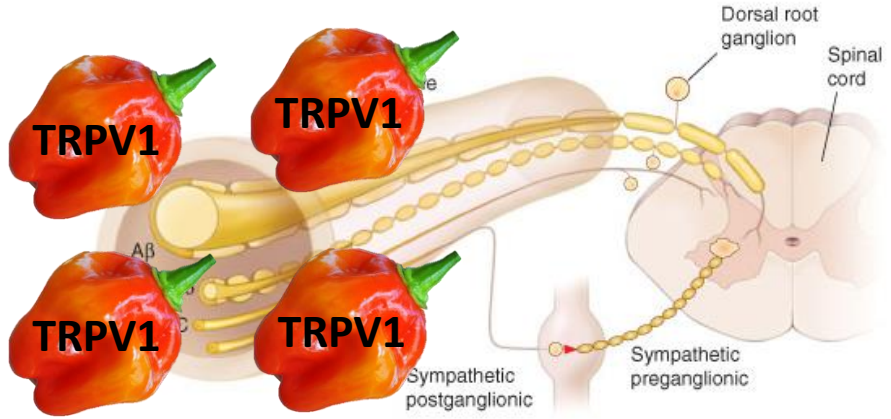


- Sodium Channel (i.e. NaV 1.7) upregulation and sensitization from peripheral nerve damage
- Results in hyperactivity (ectopic) activity in nociceptive neurons

Therapy: Na-Channel Blockers

- Carbamazepine and Oxcarbazepine – Effective for trigeminal neuralgia, not approved for peripheral neuropathic pain (PNP)
- Topical Lidocaine 5% – Effective for post herpetic neuralgia (PHN), mixed efficacy for PNP. (Less side effects)

Mechanisms

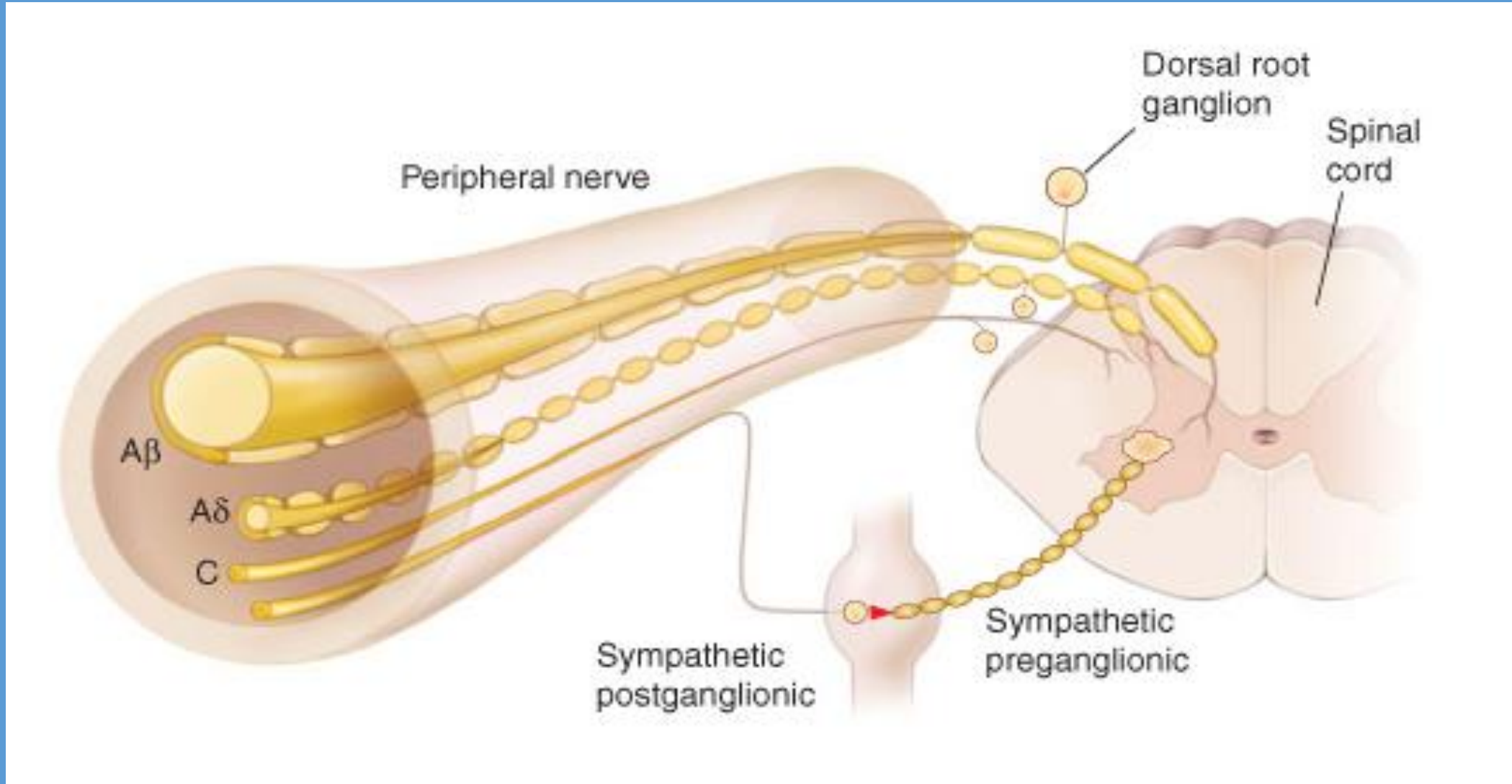


- TRPV1 (capsaicin) receptor upregulation results after peripheral nerve injury
- Even tiny sensory input can activate intense burning type pain

Treatment:

- Capsaicin 8% topical patch – approved for peripheral neuropathic pain (PNP)
- Causes 30 minutes to 1 hour of massive activation pain fibers followed by degeneration of these fibers

Mechanisms: Ca-channel upregulation and central sensitization



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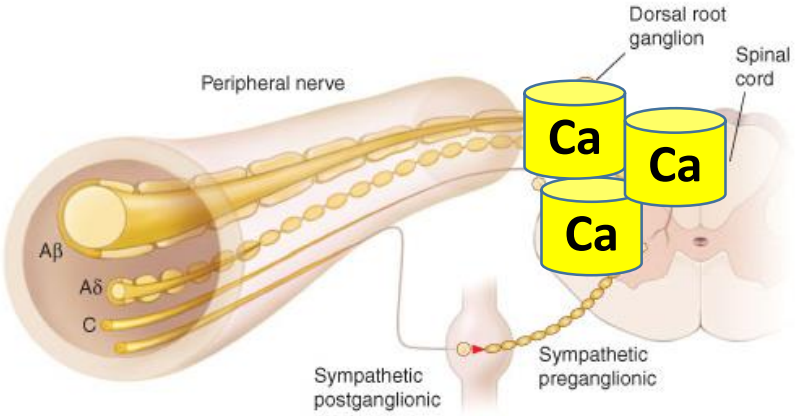
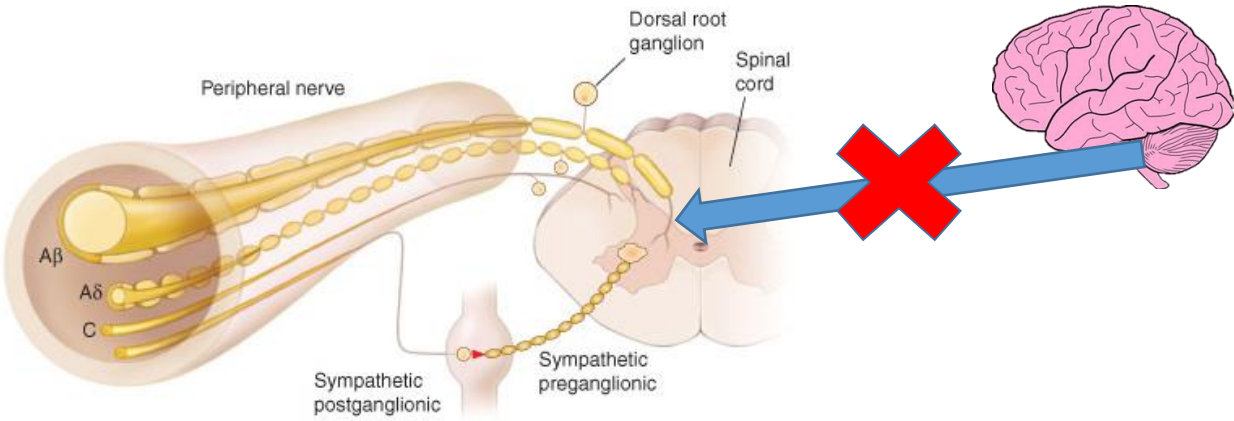


- Ca-channel upregulation occurs at the central presynaptic terminals of the primary afferent fibers in response to nerve injury
- Central sensitization can occur on second order neurons leading to activation of pathological pain sensation by ANY sensory input

Treatment: Ca-Channel Modulators

- Gabapentin, Pregabalin – Effective for PHN, PNP, central pain
- Few side effects with no significant drug interactions

Mechanisms



- Normally pain sense to the brain is followed by a descending inhibitory signal via noradrenaline and serotonin receptors
- In chronic pain there is decreased descending inhibition

Treatment:

- TCA- Amitriptyline: Effective for PHN, PNP, CP. Side effects common
- SNRI - Venlafaxine, Duloxetine: Effective for PNP. Less side effects

Other Treatments

- Opiods, Tramadol also have efficacy for neuropathic pain
- NSAIDS not effective

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Summary

- Oral
  - Antidepressants (TCA, SNRI)
  - Anticonvulsants (Ca)
  - Anticonvulsants (Na)
  - Tramadol
  - Opioids

Consider combinations

+

- Topical
  - Lidocaine
  - Capsaicin

Concussion

- Complex process affecting the brain induced by trauma
  forces
- Approximately 3.8 million recreation and sport-related
  annually
- Approximately 9% of all high school injuries
  - Highest incidence in football, boy's hockey and boy's lacrosse
  - Females have a higher concussion rate
- History of concussion increases risk 3-6% of another co
- Recurrent concussion most likely to occur within 10 day

Lincoln, AM J Spots Med 2011

Giza, Neurology 2013

Table Concussion incidence in high school and collegiate competitions among commonly played sports

	Rate/1,000 games	
Sport	Males	Females
Football[6]		
High school	1.55	—
College	3.02	—
Ice hockey[14]		
High school	—	—
College	1.96	—
Soccer[6]		
High school	0.59	0.97
College	1.38	1.80
Basketball[6]		
High school	0.11	0.60
College	0.45	0.85
Baseball/softball[6,a]		
High school	0.08	0.04
College	0.23	0.37
Summary of 9 sports[6,b]		
High school	0.61	0.42
College	1.26	0.74

Diagnosis of Concussion

- Clinical diagnosis
- Careful history
- Physical and neurologic exam
- Ancillary testing such as: SCAT3, Sport Concussion Assessment Tool

McCrory, et. Al. Br J Sports Med, 2013

Management of Diagnosed Concussion

- Cognitive Restructuring
  - Educate
  - Reassurance
  - Reattribution of symptoms

- Diminish likelihood of developing chronic postconcussion syndrome

Retirement From Play After Multiple Concussions

- May obtain formal neurological and neurophysiological assessments
- Counseling regarding risks for developing chronic impairments
- Changes on imaging
- Permanent neurologic changes

Return to Play

- Athletes should not return to paly the same day of injury
- Graduated return

Graduated Return-to Play Protocol

Step	Rehabilitation Stage	Objective of Stage
1	No activity	Recovery
2	Light aerobic exercise	Increased heart rate
3	Sport-specific exercise	Add movement
4	Non-contact training drills	Exercise, coordination, cognitive load
5	Full-contact practice	Restore athletes confidence, coaching staff assess functional skills
6	Return to play	

Consensus Statement: 4th International Conference on Concussion in Sport
McCrory, et. Al. Br J Sports Med, 2013

- Concussion risk greatest in certain sports (football, boxing, hockey, lacrosse, soccer), in females (comparable sports), after prior concussion.
- Currently no evidence that soccer headgear, position played or specific helmet use alter risk.

RECOMMENDATION:

- Sports health providers should be educated to provide accurate information
- Athletes should be counseled regarding risks

- Concussion is a clinical diagnosis. Evaluation should include careful history, neurologic exam and may include ancillary validated concussion assessment tools (GCS, BESS, SAC, SCAT, CCT)

RECOMMENDATION:

- Athletic trainers should be educated to properly administer sideline tests
- Sports health providers may use these tests to assist in diagnosis/management

- CT scanning is of limited/minimal benefit after concussion

RECOMMENDATION:

- Routine CT scanning is NOT recommended for diagnosis of concussion
- Only used if intracranial/structural injury is suspected

- Risk factors for prolonged recovery include prior concussion, headache/migraine, “fogginess”, prior headache, learning disability.
- There is evidence of physiological and clinical vulnerability after concussion that supports removing injured player from contact risk.

RECOMMENDATION:

- Players with suspected concussion should be removed from play to minimize risk of repeat event or worse symptoms.
- Graded return to play should not be started until acute symptoms have resolved, off of medications

- Cognitive restructuring (reassurance, education, guidance) can reduce risk of chronic post-concussive symptoms.

RECOMMENDATION:

- Cognitive restructuring early after concussion

- Younger athletes take longer to recover from symptoms and cognitive impairment than adults.

RECOMMENDATION:

- Symptoms management and graded return to play should be managed more conservatively in high school and younger athletes.

Questions?

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- (916) 734-3588