Pain After Traumatic Brain Injury

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Disclosure
• Michael Andary is on the Speakers Bureau for Allergan, Manufacturer of Botox

Pain After Traumatic Brain Injury - Overview
• Statement of the problem
• Some of the painful conditions
• Management of the conditions
• Role of opioids
• Other management strategies for painful conditions
• Chronic Pain after TBI
Is Pain Common After TBI?
• In the US VA system of all the veterans with a TBI diagnosis:
  – the majority also had a mental health disorder
  – approximately half have both PTSD and pain

Cifu 2013

Is Chronic Pain Common After TBI? (II)
Namptiaparampil JAMA 2008
• Literature review of 23 studies and 4206 patients
• 57.8% had chronic headache
• Among 3289 civilians
  – 75.3% of mild TBI patients had chronic pain
  – 32.1% of moderate or severe TBI
• Among 917 veterans
  – 43.1% had chronic pain

Is Chronic Pain Common After TBI? (III)
Namptiaparampil JAMA 2008
• They tried to sort out if the pain was due to psychological problems and/or PTSD.
• Their conclusions:
  – Chronic pain is a common complication of TBI
  – It is independent of psychologic disorders such as PTSD and depression
  – Is common even among patients with apparently minor injuries to the brain.
Is Chronic Pain Common After TBI? (IV)
Comments Nampiaparampil JAMA 2008
• This paper reviews multiple studies with multiple methodologies
• These reviews almost exclusively deal with people who come to the doctor with complaints
• We really do not know what happens to the patients with TBI who don't follow up

Is Chronic Pain Common After TBI? (V)
Comments (II) Nampiaparampil JAMA 2008
• The true prevalence of all patients with TBI and chronic pain is almost surely significantly less than the numbers reported above
• On the other hand, this is probably close to the prevalence of problems that we see clinically, because they have entered the healthcare system

Is the High Prevalence of Pain After TBI a New Finding?
Not a Chance!
**TBI/CHRONIC PAIN**

- 104 Referred TBI Patients Systemically Evaluated for Chronic Pain
  - 95% of patients with mild TBI had chronic pain
  - 22% of patients with moderate/severe TBI had pain
- Pain location in mild TBI:
  - 89% Headaches
  - 51% Neck/Shoulder
  - 45% Back
  - 20% Chest/Extremities

-Uomoto JM, Esselman PC, 1992

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**Prevalence of Pain in TBI**

- Chronic Pain was reported in:
  - 58% of 53 mild TBI
  - 52% of 79 mod/severe TBI
- Headaches most common

-Lahz Archives PM&R 1996
  (Australia)

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**Other Older Studies That Look at the Prevalence of Low Back Pain in Patients with Soft-Tissue Neck Injuries**

- 42% (Retrospective)
  - Braaf et al, NY State J Med 1955
- 35% Hohl, JBJS 1974
- 42% Gargan, JBJS 1990
  - (43 subjects in 8-12 year follow-up. Legal settlement did not cure symptoms)
What About Pain and Depression?


- One year follow up of 158 patients admitted to IPR after moderate to severe TBI.
  - Depression assessed with Patient Health Questionnaire-9 (PHQ-9) ≥ 10
  - Pain assessed by numerical score or ≥ 4 out of 10
- They looked at baseline, and one year follow-up.

What About Pain and Depression? (II)


- Baseline - pain: 70%; depression: 31%
- 1 year - pain: 34%; depression: 22%
- Comorbid pain and depression declined from 27% at baseline to 18% at year 1.
- Pain was significantly associated with depression
  - baseline - (relative risk: 2.62, P=.003) and at
  - 1 year - (relative risk: 7.98, P<.001).

What About Pain and Depression? (III)


- Their conclusions:
  - Pain and depression are common
  - Although their frequency declined over the first year after injury, the strength of their association increased.
  - Assessment and treatment of both conditions simultaneously may lead to improved outcomes, both early after TBI and over time.
- Comment: How much treatment did they get?
  - They did get treated at UW in Seattle
  - How does this effect function?
Where is the Pain?
Brown - Brain Injury 2011

- Retrospective phone survey of 34 patients 15 or more years after moderate to severe TBI. (Toronto)
- 79% reported some MSK complaint within the last 30 days
- Comment – it is unclear the cause of these complaints, and how much is due to aging

Where is the Pain?
Brown - Brain Injury 2011

- These MSK complaints do not have any recognizable pattern
- These patients with pain report a lower level of function.
**Does Pain Correlate With Any Other Factors?**

Fogelberg - Arch PMR 2012

- 174 moderate or severe TBI patients
- Phone follow-up one year after discharge
- Were compared to a healthy comparison group.
- 44% of the TBI group had sleep disturbance
- Sleep problems were worse when they co-occur with depression, anxiety, and pain.

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**TBI, Pain and Sleep**

Fogelberg - Arch PMR 2012

- TBI group was worse than the comparison group in:
  - significantly longer to fall asleep (sleep latency)
  - used more sleep medications (medication use)
  - reported worse effects on daytime functioning
- There was a trend towards pain interfering with sleep

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**What Does That Leave Us With?**

- We are left with a potentially bad situation
- These are patients with cognitive problems, chronic pain, depression, anxiety, post traumatic stress disorder, sleep disturbance, and daytime fatigue with poor function.
- Treatment should be very easy!
Pain Behaviors

Poor Sleep

Disability

Depression / Anxiety/PTSD

Impaired Cognition

**Viscous Circle**

Which Comes First?

**BRAIN PAIN SYNDROME**

What is causing the symptoms and behaviors?

- No imaging studies are able to document the complex biochemical, physiological, and anatomic causes for the symptoms
- Psychological issues and operant conditioning make this complicated

**Unproven Hypothesis/Theory:**

- There is a pathophysiological process in the CNS that is causing persistent pain, sleep and memory problems, depression, anxiety, and other symptoms
- CNS injury leads to altered information processing and impaired coping mechanisms, which over time cascades into other problems
Chronic Pain After TBI

- It looks common
- How much literature is there that is a problem?

Pain and mild traumatic brain injury: the implications of pain severity on emotional and cognitive functioning
Weyer, Brain Inj. 2013

- 66 patients with mild TBI and symptoms
- Compared high pain vs low pain groups
- Cognitive tests were similar
- High pain had more emotional residuals: Anger, Aggression, Anxiety, Depression and Paranoia and Suspicion
- “CONCLUSIONS: High chronic pain exacerbates the emotional aspect of (concussion) and, therefore, should be given special observance in treatment settings.”
- Duh!

Chronic Pain After TBI

- It looks common
- How much literature is there that is a problem?
- Answer: Some
- How about treatment strategies?
Traumatic Brain Injury/Chronic Pain Syndrome: A Case Comparison Study

Andary MT, Crewe N, Ganzel S, Haines-Pepi C, Kulkarni MR, Stanton DF, Thompson A, Yosef M.

Archives of Physical Medicine and Rehabilitation 73(10):994A, October 1992

- Retrospective cohort study
- Comparison of 12 TBI/CP patient vs 12 with CP only treated in an interdisciplinary team.
- Outcomes – Both groups returned to work at same rate 75%. TBI/CP group took longer (459 days) to CP (295 days) from intake to discharge. Actual treatment time was less.
- In our hands this took a long time
Proposed Etiology for Chronic Pain CNS Hypotheses

"Wind Up"

FIGURE 57-2 Proposed pathways for chronic pain transmission.

Proposed Etiology for Chronic Pain CNS Hypotheses

Immediate Central Sensitization

FIGURE 57-3 Theorized mechanisms of immediate central sensitization.

Proposed Etiology for Chronic Pain CNS Hypotheses

Late Central Sensitization

FIGURE 57-4 Theorized mechanisms of late central sensitization.
Very Brief Summary of Their Treatment Recommendations Studies Done in Non-TBI Patients

- Understand and treat pain generators
- Use medications (non opioid primarily)
  - Antidepressants
  - Anticonvulsants
  - Anti-spasticity Medications
- understand the treatment appropriate role of certain drug classes vs the role of nonpharmacological treatment approaches.

Final Conclusion Zasler et al

- “Pain management of persons with TBI can be challenging… there is much that can be offered to patients and their families if the evaluating professionals have been appropriately trained and educated in pain assessment and management within a holistic and functionally oriented biopsychosocial framework.” (emphasis added)

Chronic Pain After TBI

It looks common

- How much literature is there that is a problem?
  - Answer (Some)
- How about treatment strategies?
  - Answer - (Virtually None!)
- There is very little specific treatment information
  - Why??
- Its difficult and takes a long time – who gets funding for this?
- Welcome to Rehabilitation
What Do We Do With Patients With Multiple Problems?

“We Do Not Treat The Disease In The Patient; Rather We Treat The Patient Who Has a Disease”
- Hippocrates 500 B.C.

Old medical model
- Diagnose
- Treat underlying cause
- Symptoms resolve

Rehabilitation/Functional Model (bio-psycho-social)
- Identify symptoms/behaviors
- Underlying pathology is not treatable or is unknown
- Must treat/improve behaviors
- Function improves

We should already be treating the TBI problems of Cognitive, Perceptual Motor and Psychological and Biopsychosocial Dysfunction
- Interdisciplinary Rehabilitation including the multiple therapies to try to help this patient be a whole person
- The therapy for pain has a lot of overlap with the interdisciplinary team
Treatment Approach: Try to Break Down Each Problem

- Specific pain problems
- Depression
- Anxiety
- Post Traumatic Stress Disorder
- Headache
- Sleep disorders
- Fatigue

Treating Specific Pain Problems

- Many of the acute physical injuries (fractures, nerve injuries, contractures, deconditioning, strains, will respond to:
  - Physical and Occupational Therapy
  - Functional activity
  - Medications
  - Surgeries
  - Injections
  - Other

Treatment of Post Traumatic Headaches

- Most of the headaches can be classified into other headaches such as:
  - Migraine up to 38%
  - Probable migraine up to 25%
  - Tension-type headache in up to 21%
  - Cervicogenic headache in up to 10%  \textit{Lucas 2012}
- Meds (triptans, antidepressants, anti seizure, botulinum toxin)
- Activity, counseling
Treatment of Psychological Problems – Depression, Anxiety, PTSD

• Activity: PT, OT, Vocational Therapy, Recreational Therapy, Family and Community Reintegration, Exercise
• Psychology - Cognitive Behavioral Therapy (CBT)
• Medications – many of these can help with more than one problem: i.e. sleep, anxiety, PTSD, depression and neuropathic pain
• Psychiatry – help with medications and behavioral strategies

Assessment and Treatment of Sleep Disorders

• Sleep study – Sleep apnea is common
• Medications – side effects can be a problem
• Daytime activity – exercise, functional activities (interdisciplinary treatment)
• Psychology – sleep hygiene

What Do We Do With the Patient With Chronic Pain?

• We routinely treat other problems where we do not know the etiology of the problem (HTN, Cancer)
• Therefore:
  – Treat individual symptoms (if you can); e.g. depression, pain, deconditioning
  – Eventually the whole person needs to be considered and a functional rehabilitation approach can help
Treatment of Chronic LBP: Does Anything Work??
What does the evidence show?
Have we made much progress since we were bloodletting?
Are we wasting money?

What Does This Medical Device Do?

- Circa 1750-1810
- Tobacco Smoke Enema
- Blows smoke up your … Arse!

• Acknowledgement to Richard Sallis MD former president of American College of Sports Medicine

• Used for resuscitation of drowning victims

**FIGURE 1-16** An attempt at resuscitating an apparently drowned person using the modified Dutch method. One resuscitator is assisting respiration by massaging the chest. The second is instilling tobacco smoke through the rectum. (From *Month, 1885*, with permission.)
• Was also used to treat other painful bowel conditions

This became accepted medical practice

• In the 1780s the Royal Humane Society installed resuscitation kits, including smoke enemas, at various points along the River Thames, and by the turn of the 19th century, tobacco smoke enemas had become an established practice in Western medicine.

• Such a treatment was considered by Humane Societies to be as important as artificial respiration.

Doctors and society have been convinced of some pretty ineffective treatments over the years
In 1964 the Surgeon General announces that smoking is harmful to health. It is controversial!! What treatments are we doing now that we will look back on and say “what were we thinking…”?

Why Don’t We Just Give Everybody Opioids?

Answer: Because they do not work.

Opioid Interventions—Cochrane library intervention reviews (I)

**Opioids for chronic low-back pain.**
“Based on our results, the benefits of opioids in clinical practice for the long-term management of chronic LBP remains questionable.” Deshpande The Cochrane Library 2010

**Long-term opioid management for chronic noncancer pain.**
“Patients who are able to continue opioids long-term experience clinically significant pain relief. Whether quality of life or functioning improves is inconclusive.” Noble Cochrane 2010
Do Opioids Improve Outcome in Non-malignant Pain in Denmark? (I)  
Eriksen et al Pain 2006

- National random sample of 10,066 of 16,684 completed a self-administered questionnaire.
- Participants reporting pain were divided into opioid and non-opioid users.
- Chronic/long-lasting pain (>6 months)
- The analyses were adjusted for age, gender, concomitant use of anxiolytics and antidepressants and pain intensity.
- Opioid usage was associated with very severe pain, poor self-rated health, not being engaged in employment, higher use of the health care system, and a negative influence on quality of life as registered in all items in SF-36.

Do Opioids Improve Outcome in Non-malignant Pain in Denmark? (II)  
Eriksen et al Pain 2006

- Because of the cross-sectional nature causative relationships cannot be ascertained.
- “However, it is remarkable that opioid treatment of long-term/chronic non-cancer pain does not seem to fulfill any of the key outcome opioid treatment goals: pain relief, improved quality of life and improved functional capacity.”

What Does the Literature Say About Rate of Addiction?

Does the National Enquirer actually have more information than the New England Journal of Medicine??

- No trial evaluating the efficacy of opioids was longer than 16 weeks.
- Opioids are commonly prescribed for chronic back pain and may be efficacious for short-term pain relief.
- Long-term efficacy (> 16 weeks) is unclear.
- Substance use disorders are common and "aberrant medication-taking behaviors" occur in up to 24% of cases.


- Thirty-four trials with 5,546 patients were included with 4,212 patients contributing some information on opioid adverse events
- Only two studies lasted longer than four weeks, and only one was as long as eight weeks!!
- It is possible that this might limit how general the results might be, as some tolerance to adverse events with opioids with longer use is expected.

Long Term Opioids for Chronic Non-Malignant Pain – What is the literature missing?

- Reasonable studies showing long-term efficacy.
- Studies showing function, QOL, safety, addiction, tolerance, and continued pain relief.
- Pain relief alone may not improve function
- The reports of addiction, dose escalation, over-dose are relatively rare in the literature, yet clinicians see these things.
- These are very common medicines.
- Where is the data??
When is absence of proof, Proof of absence?

I am of the view that opioids for non malignant pain meets that criteria.

Opioids for Chronic Non-Malignant Pain
Where is the evidence??

• Why is this so poorly studied?
• Where is the functional data?
  – If people feel better in the short term but lay around all day, is this good?
• Why are governmental agencies (NIH) not funding long term scientific studies?
• What do clinicians do with short term data, and short term patient expectations when long term outcome and chronic disease is what we are dealing with??

Prescription drug abuse deadlier than use of illegal drugs

• Many emergency rooms see more patients overdosing on prescription drugs than heroin and cocaine.
Not treating pain can lead to malpractice

- Some doctors are getting sued for inadequate treatment of pain.

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Medical Marijuana for Chronic Pain and Brain Injury

- "medical value in the treatment of brain diseases such as Alzheimer’s and Parkinson’s"

http://www.herbalmission.org/
Smoked cannabis for chronic neuropathic pain: a RCT Ware CMAJ 2010

- RCT of 4 concentrations of THC including zero.
- Smoke for 5 days then wash out for 9 days.
- “A single inhalation of 25 mg of 9.4% THC herbal cannabis three times daily for five days reduced the intensity of pain, improved sleep and was well tolerated.”
- Quality of Life and Mood did not improve
- What about function?
- How about long term use? 5 days is not chronic

MM and Chronic Pain

- Some of the best studies that support the use of MM have limitations in my view.
  - Length of treatment
  - Functional outcome
  - No measure of cognitive problems
- Are doctors supposed to medicate our patients so they can sit on the couch and not think?
- Is this better than Opioids?? Maybe

Which Treatments Work for Chronic LBP?
Cochrane Back Review Group has reviewed more than 600 RCT

<table>
<thead>
<tr>
<th>Beneficial</th>
<th>Likely to be beneficial</th>
<th>Unlikely to be beneficial</th>
<th>Ineffective or harmful</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise therapy</td>
<td>Analgesics</td>
<td>Bed rest</td>
<td>Facet joint injections</td>
</tr>
<tr>
<td>Behavioral therapy</td>
<td>Back schools in occupational settings</td>
<td>EMG biofeedback</td>
<td>Traction</td>
</tr>
<tr>
<td>Multidisciplinary treatment programs</td>
<td>Massage</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>NSAIDs</td>
<td></td>
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</tr>
</tbody>
</table>

van Tulder et al. Best Pract Res Clin Rheumatol. 2002;16:761-778 (A)
Cognitive Behavioral Therapy May Reduce Back Pain  
*Lamb Lancet 2010*

- 701 patients were randomized to receive either advice alone or advice plus CBT
- CBT targeted behaviors and beliefs about physical activity and avoidance of activity
- Roland Morris functional scale and pain scales improved more in CBT.
- Cost was about $4,500/patient probably about $3000 for quality-adjusted life year.

Cognitive Behavioral Therapy

- This has been shown to be effective in almost all the other symptoms seen in these TBI patients.
  - PTSD
  - Anxiety
  - Depression
  - Sleep disturbance
- It seems the rehabilitation team should embrace this

Nonpharmacologic Approaches: 
Best Evidence for Efficacy in CLBP

- Exercise therapy
- Behavioral therapy
- Multidisciplinary treatment programs
  - Cognitive behavioral therapy
  - Patient education
  - Supervised exercise
  - Selective nerve blocks
  - Other strategies

Behavioral treatment for chronic low-back pain

- Only seven high quality studies
- Combined respondent-cognitive therapy and progressive relaxation therapy are more effective than wait list controls (WLC) on short-term pain relief.
- However, it is unknown whether these results sustain in the long term. No significant differences could be detected between behavioral treatment and exercise therapy.
- “Whether clinicians should refer patients with CLBP to behavioral treatment programs or to active conservative treatment cannot be concluded from this review.”
- We don’t know much

How do you treat chronic pain if you cannot cure it?

- If you can treat the pain, then cure it!!
- If not, treat the patient, not the pain
- Be honest with the patient
- The physician must decide the pain is not treatable
- Focus on treating pain behaviors and suffering
- The patient must eventually agree the pain is not curable

Approach to Chronic LBP: Summary (I)

- Address goals and expectations of patient and include education
- Assure patients of reasonable outcome
- Encourage continued activity/exercise
- Consider psychosocial factors
- Pharmacologic therapy to relieve
  - Best evidence for TCAs, NSAIDs
- Consider surgery only after 2- to 4-month trial of other therapies

Approach to Chronic LBP: Summary (II)

• I am not convinced we are doing a good job of improving this problem
• Does that mean we get to recommend any treatment we like?
• Rehab techniques and manipulation are as good as anything we have at this stage.

End of Talk
How Big of an Effect are We Really Having?
Summary of Evidence for Exercise Therapy in CLBP: Cochrane Review

- Meta-analysis of 43 RCTs (N=3907)
- Systematic review of 43 trials evaluating exercise for CLBP
- Mean improvements in pain and function* (100 Pt scale)
  - Pain vs no treatment= 10.2
  - Pain vs conservative treatments= 5.93
  - Function vs no treatment= 3.0
  - Function vs conservative treatments= 2.37
- Individually designed programs that include stretching/strengthening give best results
- These are NOT dramatic improvements

Ann Intern Med. 2005 May
Pain Behaviors vs. Pain

- If you can treat the pain, then do it!
  - The other problems (contractures, disability, pain behaviors, deconditioning, depression, suffering) will reverse themselves without a lot of problems.
- If you cannot... recognize the problem and treat the patient.
  - Treatment must focus on pain behaviors and rehabilitation, not cure.

A Randomized, Controlled Trial of Manual Therapy and Specific Adjuvant Exercise for Chronic Low Back Pain (I)

- A single blind, RCT
- Four groups
  1. Tailored exercise plus manipulation
  2. Tailored exercise plus Sham manipulation
  3. Nonspecific exercise plus manipulation
  4. Nonspecific exercise plus Sham manipulation
- The nonspecific program consisted of general stretching and aerobic conditioning
- 6 weekly sessions with twice daily exercise
- Seventy-two out of 100 patients completed the study.

A Randomized, Controlled Trial of Manual Therapy and Specific Adjuvant Exercise for Chronic Low Back Pain (II)

- Specific activity and manipulation group reported significant reductions in pain (Good)
- Specific exercise and sham manipulation reported worse perceived disability (Bad)
- Not much difference reported in the other groups
- Manual therapy with specific exercise appears to be beneficial in treating chronic low back pain.
- Despite improvements in pain, perceived function did not improve.
- Further studies are needed to examine the long-term effects

- No trial evaluating the efficacy of opioids was longer than 16 weeks.
- Opioids are commonly prescribed for chronic back pain and may be efficacious for short-term pain relief.
- Long-term efficacy (> 16 weeks) is unclear.
- Substance use disorders are common and "aberrant medication-taking behaviors" occur in up to 24% of cases.


- Thirty-four trials with 5,546 patients were included with 4,212 patients contributing some information on opioid adverse events.
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- It is possible that this might limit how general the results might be, as some tolerance to adverse events with opioids with longer use is expected.

Opioids for Neuropathic Pain (I) Eisenberg et al JAMA 2005

- Twenty-two articles met inclusion criteria
- Opioids were used to treat central or peripheral neuropathic pain of any etiology
- Eight articles met criteria as intermediate-term (median = 28 days; range = 8-56 days)
- None met criteria as long term.
Opioids for Neuropathic Pain (II)
Eisenberg et al JAMA 2005

• Meta-analysis of 6 intermediate-term studies showed a drop of 14 points on a 100 point scale when compared to placebo. (P<.001)
• Number needed to harm (NNH): nausea - 3.6; constipation 4.6; drowsiness - 5.3; vomiting - 6.2; and dizziness - 6.7
• “…all 8 intermediate-term trials demonstrated opioid efficacy for spontaneous neuropathic pain.”
• Is there functional data or Quality of Life information?
• I am not sure this is really efficacy.

Opioid Interventions-Cochrane library intervention reviews (II)

• NSAIDS or paracetamol, alone or combined with opioids, for cancer pain.
• “Thirteen out of 14 studies found no difference, or low clinical difference, when combining an NSAID plus an opioid versus either drug alone.”
McNicol ED,). The Cochrane Library. 2010;11;1-68

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• Reasonable studies showing long-term efficacy.
• Studies showing function, QOL, safety, addiction, tolerance, and continued pain relief.
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• These are very common medicines.
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Opioids for Chronic Non-Malignant Pain
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- Why is this so poorly studied?
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  - If people feel better in the short term but lay around all day, is this good?
- Why are governmental agencies (NIH) not funding long term scientific studies?
- What do clinicians do with short term data, and short term patient expectations when long term outcome and chronic disease is what we are dealing with??

Disability Compensation Influences the Number of Disabled Workers – *(If you pay more to sit, more will sit!)*

<table>
<thead>
<tr>
<th>Disability Income as % of Normal</th>
<th>All Claims</th>
<th>Back Claims</th>
</tr>
</thead>
<tbody>
<tr>
<td>49%</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>57%</td>
<td>1.4</td>
<td>2.1</td>
</tr>
<tr>
<td>80%</td>
<td>3.1</td>
<td>5.6</td>
</tr>
</tbody>
</table>


Disability compensation influences number of disabled workers
Physicians Should Not Treat Low Back Pain, Politicians Should”

Alf Nachemson Orthopedic Surgeon

Malingering

• Definition: intentional production of false or grossly exaggerated physical or psychological symptoms motivated by external incentives
• Is very rare!!!

Malingering

• This is very rare
• Chronic pain patients often act like malingers; but they are not
• Accusing patients of malingers ruins any chance to deal with the real issues
• Malingering is not recognized by IASP as a medical diagnosis
Malingering

- There is no scientific proof that they are malingering.
- It does not help in treatment.
- Challenging a person's integrity is not proven, effective treatment.
Fifteen randomised placebo-controlled trials were included.
- Four investigations with 120 patients studied intravenous opioid testing.
- Eleven studies (1025 patients) compared oral opioids with placebo for four days to eight weeks.
- Six of the 15 included trials had an open label follow-up of 6-24 months.

*Would the FDA approve any drug after an 8 week trial for Diabetes, Hypertension, or any other chronic disease??

BRAIN – PAIN SYNDROME

Chronic Pain After Traumatic Brain Injury
TBI Brain Pain Overview

- General TBI
- Mild TBI
- Pathology
- Legal complications/Malingering
- Symptoms
- Treatment, Seizures

EPIDEMIOLOGY OF TBI

- Incidence: 180 to 230/100,000
- Prevalence: As high as 1/200
- Ages: 15 to 24 and over 70 (two peaks)
- Associated with – ETOH, drugs and low socioeconomic status
- Etiology: MVA, Falls, GSW
- TBI causes 50% of traffic fatalities
- Male-Female: 2:1
- Survival: Half in PVS die in one year. 
  Rest is unknown
  (DeLisa 1988 and Kusen’s 1990)
DEGREES OF SEVERITY OF TBI
NO UNIVERSAL AGREEMENT

- **Mild** - LOC < 20 min, GCS – 13 to 15
  - No focal findings, no abnormal x-rays, home in 48 hours

- **Moderate** - 20 min < LOC < 6 hrs
  - Initial GCS of 8-12, PTA 1-24 hrs

- **Severe** - LOC for > 6 hrs
  - Only about 10% of all cases

- **Persistent Vegetative State** – No volitional movements.
  - May have sleep – wake cycle, yawning, lip smacking, tracking
  - (Cope in Krusens 1990)

COMA

Has numerous definitions

1. A) Not opening eyes
   - B) Not obeying commands
   - C) Not speaking understandable words

2. Glasgow coma scale of 8 or less

GLASCOW COMA SCALE

IS AN EASY BEDSIDE TEST THAT IS A MORE PRECISE AND OBJECTIVE MEASURE OF DEPTH OF UNCONSCIOUSNESS

GIVES A SCORE OF 3-15

- EYE OPENING
- MOTOR RESPONSE
- SPEECH
GLASGOW COMA SCALE

EYE OPENING

4. SPONTANEOUS
3. OPENS TO VOICE
2. OPENS WHEN PINCHED
1. EYES CLOSED

GLASGOW COMA SCALE

• VERBAL RESPONSE

5. ORIENTED
4. CONVERSANT, BUT CONFUSED
3. INTELLIGIBLE, BUT NONSENSE
2. SOUNDS, BUT NOT WORDS
1. SILENT
   1T – TRACHEOSTOMY

GLASGOW COMA SCALE

BEST MOTOR RESPONSE

6. FOLLOWS COMMANDS
5. PURPOSEFUL (PULLS EXAMINER)
4. WITHDRAWS OWN HAND
3. FLEXES TO PAIN (DECORTICATE)
2. EXTENDS TO PAIN (DECEREBRATE)
1. NO RESPONSE TO PAIN
MILD TRAUMATIC BRAIN INJURY

MINOR TRAUMATIC BRAIN INJURY
POST CONCUSSION SYNDROME
MINOR CONTUSION SYNDROME
POST TRAUMATIC VASOMOTOR NEUROSIS
POST TRAUMATIC NERVOUS INSTABILITY
POST TRAUMATIC SYNDROME

- Headaches, inattention, poor memory, anxiety, irritability, lethargy, dizziness, depression, giddiness, photophobia
- Litigation and secondary gain are discussed as factors that make this syndrome worse but there is no data to support this.


ACRM REVISED DEFINITION OF MILD TBI*

A patient with MTBI (mild traumatic brain injury) is a person who has had a traumatic induced physiological disruption of brain function, as manifested by at least one of the following:

1. Any period of loss of consciousness
2. Any loss of memory for events immediately before or after the accident
3. Any alteration in mental state at the time of the accident (e.g., feeling dazed, disoriented or confused)
4. Focal neurological deficit(s) which may or may not be transient but where the severity of the injury does not exceed the following:
   a. Loss of consciousness of approximately 30 minutes or less
   b. After 30 minutes, an initial Glasgow Coma Scale of 13 to 15
   c. Post-traumatic amnesia not greater than 24 hours

*Formulated by the Mild Traumatic Brain Injury Committee of the Head Injury Interdisciplinary Special Interest Group to the American Congress of Rehabilitation Medicine (May 24, 1991).

(Katz, Am Fam Phy 1992)

Grading of Concussion - Subset of Mild TBI

- **Grade 1** – Confused but conscious (e.g., dazed, dizzy, problems following directions, “inability to maintain a coherent stream of thought”)
  – Symptoms usually clear in less than 15 minutes
- **Grade 2** – Similar symptoms to grade 1 but also develops amnesia. (No LOC)
  – Symptoms usually last longer than 15 minutes
- **Grade 3** – Any loss of conscious for a few seconds or longer
  (American Academy of Neurology and Brain Injury Association)
Sports concussion is defined as a complex pathophysiological process affecting the brain, induced by traumatic biomechanical forces. Several common features that incorporate clinical, pathologic and biomechanical injury constructs that may be utilised in defining the nature of a concussive head injury include:

1. Concussion may be caused either by a direct blow to the head, face, neck or elsewhere on the body with an "impulsive" force transmitted to the head.
2. Concussion typically results in the rapid onset of short lived impairment of neurologic function that resolves spontaneously.

3. Concussion may result in neuropathological changes but the acute clinical symptoms largely reflect a functional disturbance rather than structural injury.
4. Concussion results in a graded set of clinical syndromes that may or may not involve loss of consciousness. Resolution of the clinical and cognitive symptoms typically follows a sequential course.
5. Concussion is typically associated with grossly normal structural neuroimaging studies. No changes were made to the definition by the Prague Group beyond noting that in some cases post-concussive symptoms may be prolonged or persistent.

"Vienna recommendation that injury grading scales be abandoned in favor of combined measures of recovery to determine injury severity (and/or prognosis) and hence individually guide return to play decisions received continued support."
Prague Agreement Statement
McCrory Clin J Sport 2005

• Simple Concussion
  In simple concussion, an athlete suffers an injury that progressively resolves without complication over 7–10 days.

• Complex Concussion
  Complex concussion encompasses cases where athletes suffer persistent symptoms (including persistent symptom recurrence with exertion), specific sequelae (e.g., concussive convulsions, prolonged loss of consciousness (>1 minute) or prolonged cognitive impairment following the injury.

Sport Concussion Assessment Tool (SCAT)

For more information see the “Symptoms and Agreement on return to play” and the “Contributors” sections of the Concussion Assessment Tool II (CAT II) from the Journal of Neurotrauma (vol. 17, no. 10) and the Concussion Assessment Tool (CAT) (J Neurotrauma vol. 20, no. 10) from the British Journal of Sports Medicine and Catz (2007) in the British Journal of Sports Medicine, pp. 661–668. Copyright 2008. BISS: Concussion in Sport Group

What should I do?
If athlete suspected of having a concussion should be removed from play, and then seek medical evaluation.

Signs to watch for:
Problems could arise over the next 24 hours. You should not be allowed to play and should go to a hospital if any of the following apply:

- The athlete is drowsy or confused.
- The athlete is not aware of their surroundings.
- The athlete has memory loss.
- The athlete is agitated or irritable.
- The athlete has headaches.
- The athlete has a sensitivity to light or sound.
- The athlete has vomiting or nausea.
- The athlete has any changes in vision.
- The athlete has any changes in behavior.
- The athlete has any changes in mental status.
- The athlete has any changes in cognitive function.
- The athlete has any changes in physical function.

What is complex concussion?

The SCAT can be used to assist with the assessment of concussions as follows:

1. Assess the athlete for symptoms and signs of concussion.
2. If symptoms persist for more than 15 minutes after the injury, refer to a healthcare professional.
3. If symptoms persist for 24 hours after the injury, refer to a healthcare professional.
4. If symptoms persist for more than 7 days after the injury, refer to a healthcare professional.

For more information see the “Symptoms and Agreement on return to play” and the “Contributors” sections of the Concussion Assessment Tool II (CAT II) from the Journal of Neurotrauma (vol. 17, no. 10) and the Concussion Assessment Tool (CAT) (J Neurotrauma vol. 20, no. 10) from the British Journal of Sports Medicine and Catz (2007) in the British Journal of Sports Medicine, pp. 661–668. Copyright 2008. BISS: Concussion in Sport Group

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What is simple concussion?

In simple concussion, an athlete suffers an injury that progressively resolves without complication over 7–10 days.
WHAT SYMPTOMS (INCLUDING PAIN) DO PATIENTS WITH MILD TBI REPORT OF AFTER MILD TBI?

DISABILITY IN MINOR TBI

- Prospective F/U of 424/538 admissions for mild TBI
- 3 months after TBI the symptoms were reported:
  - 79% - Headaches
  - 59% - Memory
  - 14% - Problems with ADL's
  - 34% - Now unemployed – previously employed
  - Lower socioeconomic status most affected
  - 69/424 - Had neuropsych testing and were abnormal
  - 31% - Had a previous TBI (hospitalized)
  - 6/424 - Had litigation (Rimel et al, Neurosurg 1981)

DO SURVEY QUESTIONAIRES “SUGGEST” SYMPTOMS THAT WOULD NOT OTHERWISE BE REPORTED? MILD TBI – SURVEY OF TREATING PHYSICIANS

- 122 MTBI – GCS < 12, normal CT, physicians were surveyed (retrospective from ER reports)
- 55% (67/122) responded
- 21% (14/67) had been to their primary care doctor for symptoms of MTBI (may be underestimated, i.e., orthopedics was listed as primary care)
- This suggests that questionnaires to subjects do not “suggest” symptoms
  - Jones, Viola, LaBian et al, APMR 1992
Slow Recovery After Concussion
(Bleiberg, NRH Research Update Fall 2000)

- Automated Neuropsychological Assessment Metrics (ANAM) were prospectively given to a large portion the West Point freshman (prior to and after TBI)
- This group sustained 23 boxing concussions
- ANAM was administered at 1 hour, then repeated at 1, 3 and 5 days
- There was slowed reaction time at 1 hour
- Most subjects showed little or no improvement between 1 and 24 hours and half still did not improve by 72 hours.
- This suggests that metabolic changes contribute to the damage and that an injury ‘evolves’ over time and parallels animal studies and anecdotal reports from patients.
- This may allow a window of treatment.

Does Every Study Report A High Incidence Of Problems After Mild Traumatic Brain Injury?

NEUROBEHAVIORAL OUTCOME AFTER MINOR TBI (I)

- Followed 57/155 only got F/U on 32/155 at 3 months
- Excluded: Previous TBI, H/O ETOH or drugs, Psychiatric Hospitalization
- Did neuropsych testing at 1 wk, 1 mo and 3 mo. Found deficits that largely improved
  - 1 mo – 56% had HA, 47% malaise, 35% dizzy
  - 3 mos – 48% had HA, 22% dizzy, 22% malaise
- Conclusion: Minor TBI “rarely” causes “chronic disability” or permanent cognitive impairment
- No data on disability/employment
  » From Levin et al, J Neurosurg 1987
NEUROBEHAVIORAL OUTCOME AFTER MINOR TBI (II)  Levin et al. Neurosurg 1987

• 3 month follow-up of 32/155 “has little power to detect small gains” (their words)
• No measure of “disability”
  – (e.g. employment, function, ADL)
• If all patients lost to follow-up had no symptoms at least 14/155 (9%) would have symptoms
  How can this be “rare”?  

Neuropsychological and Psychosocial Consequences of MTBI

• 20 MTBI and 20 CONTROL FRIENDS
• At 1 month 50% of patient and <40% of controls had HA (not statistically significant).
• At 1 year there were minimal differences in 2 groups except SIP, alertness behavior and communication
• Pain complaints other than HA not reported
• Low number of subjects limits power to detect differences
  » Dickman et al. J Neurol, Neurosurg, Psychiatry 1986

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• This suggests that questionnaires to subjects do not “suggest” symptoms
  » Jones, Viola, LaBan et al, APMR 1992
Is There Pathological Brain Damage After Mild Traumatic Brain Injury?

DIFFUSE AXONAL INJURY AND TRAUMATIC COMA IN PRIMATE (I)

Methods:
• Primates had one episode of controlled angular head acceleration without impact. (Animals were anesthetized initially, but not during trauma).
• Length of coma, behavioral recovery and neuropathology were documented.
• Animals were studied 2 hours to 50 days post-trauma.

(Gennarelli, TA et al, Ann Neurol 1982)
DAI AND PRIMATES (II)

Results:
- Sagittal acceleration caused less problems than oblique or lateral.
- DAI correlated highly with LOC and recovery.
- DAI was present in white matter of cerebral hemispheres and cerebellum and upper brainstem.
- DAI was characterized by axonal retraction balls and axonal morphology in white matter.
- Most common findings was white matter lesions with focal lesions in corpus callosum and superior cerebellar peduncle.

(Gennarelli, TA et al Ann Neurol 1982)

DAI IN PRIMATES (III)

- Concussion Group – LOC < 15 minutes
  - All had good recovery (no apparent deficit)
  - Did not have evidence for DAI
  - However in 2/8 (25%) had focal abnormalities in the hippocampus with loss of neurons and reactive changes

(Gennarelli, TA et al, Ann Neurol 1982)
DAI IN PRIMATES (IV)

• Conclusions:
  – Do not need impact to get severe DAI
    • i.e., Acceleration alone can cause problems.
  – DAI is unlikely to be due to secondary injury (hypoxia, ischemia, ICP elevation, etc.).
  – DAI is from the movement of the head (shear and tensile strains most likely).
    (Gennarelli, TA et al, Ann Neurol 1982)

Axonal Degeneration Induced by Experimental Noninvasive Minor Head Injury (I)

• Continuation of previous work in monkeys
• Used control monkeys put in apparatus but not accelerated
• After injury, there was no obvious problem and monkeys acted normal
  (Jane, Stewart and Gennarelli, J Neurosurg 1985)
Axonal Degeneration Induced by Experimental Noninvasive Minor Head Injury (II)

- Pathology showed abnormalities in the brainstem (inferior colliculus, pons, dorsolateral medulla)
- Occasional abnormality in cerebrum and then in the subcortical white matter and parasagittal region but not in the cortex
- Control monkeys had rare problems
- “Shearing may not be the etiology”

(Jane, Steward and Gennarelli J Neurosurg 1985)

AXONAL SWELLINGS IN MINOR TBI

METHODS

1. Anesthetized cats with small 11 mm craniectomy and saline fluid filled shaft was inserted outside the dura. A fluid percussion injury was induced.
2. All animals had uneventful recovery no overt neurologic abnormalities, no signs of discomfort, normal food intake.
3. Two days prior to inspection, horseradish peroxidase was inserted over motor cortex and deep cerebellar nuclei through craniotomy.
4. Anterograde labeled corticorubral, corticothalamic, corticoreticular, corticospinal, and cerebellar efferent tracts, most coursing through the brain stem.

(Povlishock, Becker Laboratory Investigation 1985)
Axonal Swellings in MILD TBI (II)

- Axonal swellings followed out to 21 days show the axons can:
  a) Persist unchanged
  b) Degenerate or
  c) Start a regenerative response
- There was no parenchymal or vascular changes
- The area of the brain injured was the brainstem and subcortical sites. Motor cortex and cerebellum were uninjured.
- Shear and tensile forces are not the major cause but is the “traumatic event itself”
- This follows the clinical course of improvement
  (Polvishock, JT and Becker, DP - Laboratory Investigation, 1985)

BRAIN – PAIN SYNDROME

Chronic Pain After Traumatic Brain Injury
Do Legal problems And/Or Malingering Cause These Symptoms?

“The first thing we do, let’s kill all the lawyers.”

King Henry VI 2nd part, Act IV, Scene 2

ACCIDENT NEUROSIS TBI (I)

- Personal experience of 200 cases of TBI
- 47 had “unequivocally psychoneurotic complaints”
- Lesser injuries caused greater neurosis (skull Fx, PTA, LOC)
- Predisposing factors: Low social class, personality factors (only 20/47), low IQ (“dullards”), “shiftless work record”, emotional instability, hypochondriasis
- 11/47 had HA, dizziness, irritability, poor concentration, noise intolerance (i.e. organic with neurosis)
- 9 had depression (organic)

> Miller, BMJ 1961
ACCIDENT NEUROSION TBI (II)
Miller, BMJ 1961

- Symptoms of accident neurosis
  - Latent period of weeks to months
  - HA – increasing over the years
  - Sleeplessness, Inconsistent memory, Self-pity
  - Inconsistent weakness/sensory changes
  - Arrives late with family member
  - Claims inability to work

- After settlement (50 cases)
  - 45 had complete recovery (“trivial residual symptoms”)
  - 3 had psychiatric symptoms without disability
  - 2 had psychiatric symptoms with disability
  - No clear method of F/U (systematic questionnaire)
  - No statistical analysis

- Does this meet current standards of scientific rigor??

A Study of the Effect of Legal Settlement on Post-Concussion Symptoms (I)

- All TBI with amnesia (at that time) were admitted to Royal Victoria Hospital in Belfast, Ireland.
- 46 patients needed medical legal reports (this prompted the admission to this study).
- Compared to 145 patients admitted previously to same hospital and previously reported.
  

Legal Settlement & MTBI Symptoms(II)

- They obtained data on 44/46 patients “difficult and tedious process”.
- Data gathering: 1) at hospitalization;
  2) 6 week F/U
  3) At time of Legal Report (mean 13 months).
  4) Legal Settlement (22 months).
  5) One year after Settlement
- Meticulously counted every case and the rare missing data.
  
  Fee and Rutherford 1988
Legal Settlement & MTBI Symptoms (III)

- Used standardized questionnaires
- PTA was grouped as: a) 15 minutes (49%), b) 15-59 minutes (26%), c) 60 minutes (26%)
- No difference in litigation group for: a) PTA, b) Sex, c) HA at 24 hours, d) CNS signs at 24 hr.
- Percent falls were less in litigation group
- 82% had made contact with “solicitor” (lawyer) within 2 months of accident.

Fee and Rutherford 1988

Legal Settlement & MTBI Symptoms (IV)

<table>
<thead>
<tr>
<th>Percent with Symptoms</th>
<th>Legal</th>
<th>General</th>
</tr>
</thead>
<tbody>
<tr>
<td>At legal report (13 months avg)</td>
<td>57%</td>
<td>51% - 6 week F/U</td>
</tr>
<tr>
<td>At Settlement (22 months avg)</td>
<td>39%</td>
<td>N/A</td>
</tr>
<tr>
<td>One year after injury settlement</td>
<td>34%</td>
<td>15% 1 year after settlement</td>
</tr>
</tbody>
</table>

Settlement did not cure the symptoms

Fee and Rutherford 1988

Legal Settlement & MTBI Symptoms (V)

- Early settlement did not significantly predict a lower symptom rate (31% early vs 36% late)
- This suggests that the prolonged emotional stress, or other factors associated with, prolonged litigation did not increase reported percentage of symptoms.

Fee and Rutherford 1988
Legal Settlement & MTBI Symptoms (VI)

Summary
- Only 12.5% of symptomatic litigants reported no symptoms (so called "cure") in the year after settlement. (2 of 16)
- Litigation patients are more likely to have symptoms at 1 year and about 3 years. Why?
  - Bad prognosis patients take legal action (and/or)
  - Litigation increases symptoms

Fee and Rutherford 1988

Legal Settlement & MTBI Symptoms (VII)

“There is nothing in this study to refute (earlier) conclusions that the condition results from an interplay of both organic and psychological factors”

Fee and Rutherford 1988
MILD TBI – LITIGATION/MALINGERING
PROSPECTIVE STUDY IN NEW ZEALAND

- 66 selected young working males (thus limiting compensation and more disabled people).
- 13/66 had symptoms 90 days post injury.
- 4/8 that could be found for 2 year follow-up still had problems.
- No litigation in these cases and full RTW despite symptoms suggests people have symptoms after MTBI not related to litigation or malingering

A Follow-Up Study of Accident Neurosis (I)

- Got follow-up of 35 out of possible 50 in U.K.
  - “No organic cause”
  - “Extreme Group”
- Various Injuries - 50% LBP other were arms, neck, gait and TBI
- Did home visits with structured interviews
- Average time between accident and settlement was 5 years.

Tarsh, Royston - Br J of Psych 1985

A Follow-Up Study of Accident Neurosis (II)

- RTW - only 8 of 30 unemployed did RTW
  - 4 of these at lower level job
- RTW was between 1 and 5 years after settlement.
- 10 of 35 had conversion reactions.
- One was in a nursing home.

Tarsh, Royston Br J of Psych 1985
A Follow-Up Study of Accident Neurosis (III)

- Their Suggestions were:
- Family roles of “Total Belief” and “Over-Protectiveness” seem important factors.
- Legal system could improve things by making payments over a period of time and contingent on whether the person: “cooperates to the fullest with all the help offered”.
- These psychological problems have a similarly poor prognosis, as if the illness is physically based.
- Should increase the monetary compensation.  
  Tarsh Royston Br J of Psych 1985

Malingering

- Reports remain anecdotal and hard to prove
- Forced choice testing for memory and somatosensory perception may be helpful
- Prospective studies that attempt to identify malingering or litigation factors have been unable to do so

Are there any related studies to look at whiplash pain and the prevalence of injuries and complaints?
CHRONIC WHIPLASH AND HEADACHES IN LITHUANIA (I)

- Retrospective questionnaire of accident “victims” identified from crash records of all rear-end collisions 1-3 years earlier
- Controls were (202), age and sex matched from population register. If they had a history of MVA, then they were excluded (17%)
- Most drivers at that time did not have personal injury insurance and disability compensation was “remote”


CHRONIC WHIPLASH AND HEADACHES IN LITHUANIA (II)

- 240 victims were contacted and 82% responded
- Neck pain reported in 35% of accident, and 33% of controls
- Headache reported in 53% of accident and 50% of controls
- None of the 202 people said they had permanent disabling symptoms caused by the car accident


CHRONIC WHIPLASH AND HEADACHES IN LITHUANIA (III)

- Questionnaires were mailed 1-3 years later
- Only 31/202 (15%) had any acute symptoms after the accident. (How does this compare to 33% of controls who have neck pain?)
- Only 2/202 had symptoms for > 1 month
- All “significant rear-end impact” defined as damage …that the police were called to the scene
- No comment on any accidents that went to hospital (Did anybody get hurt?)
- Family history of neck pain was most strongly associated with current neck pain

Do Patients With Chronic Pain Syndrome Have A High Prevalence Of Traumatic Brain Injury?

CHRONIC PAIN/TBI
• 11% (7/67) patients who presented with chronic pain in a rehab clinic were found to have TBI
• Diagnosis by history, and expanded MSE (digit repetition, new learning ability, constructional testing, proverb interpretation)
• Neuropsychological testing was abnormal in 5/5 tested  Anderson et al, APMR 1990

Do Patients With Traumatic Brain Injury Have Complaints Of Chronic Pain?
Whiplash/Psychological Reaction (I)

- Are psychological problems a consequence of or a cause of somatic complaints?
- Obtained data on 117/130 possible patients.
- Recruited by advertisement and physician referral.
- They estimated they obtained data from >1/2 of all whiplash injuries in their catchment area (Berne, Switzerland).

Radanov Pain 1996

Whiplash/Psychological Reaction (II)

- Whiplash - Hyperflexion/extension of neck
  - No - LOC, head impacts or post-traumatic amnesia
  - No fractures or dislocations
- All MVA covered by Swiss Insurance
  - Includes wage loss for time off work
  - Medical care covered
  - No compensation for pain and/or suffering

Radanov Pain 1996
Whiplash/Psychological Reaction (III)
- 21 of 117 had symptoms at 2 years
- 96 were asymptomatic
- Data collected average of 7 days and 3, 6 and 24 months post injury
- Frieberg Personality Inventory, Pain and Well-Being Scale
- Age, sex and education matched controls were obtained from the 96 symptomatic patients.

Radanov Pain 1996

Whiplash/Psychological Reaction (IV)
- Average Neck pain level (initial to 2 years) 5.3 to 4.8 (NS)
- Headache level 4.8 to 5.6 (NS)
  - 0 - 10 rating scale
- Control group at 2 year follow-up had zero pain levels. Initial pain numbers were not reported.
- Depression Scale - surprisingly no significant differences between groups.
- 10 other categories evaluated, with little relevant differences between groups.

Radanov Pain 1996

Whiplash/Psychological Reaction (V)
- Well Being Scale - Symptomatic group did not improve over time like controls
- Nervousness Scale - which means “subjects prone to develop psychosomatic condition” or could have “serious somatic illness”
  - No differences at first evaluation
  - Got worse over time in the symptomatic group and much better in controls

Radanov Pain 1996
RANCHOS LOS AMIGOS SCALE

I. NO RESPONSE
II. GENERALIZED RESPONSE
   (MAY FOLLOW COMMANDS)
III. LOCALIZED RESPONSE
    (PRIMARILY INTERNAL STIMULI)
IV. CONFUSED AGITATED
    (FOLLOWS COMMANDS)
V. CONFUSED INAPPROPRIATE
   (INCONSISTENTLY ORIENTED)
VI. AUTOMATIC APPROPRIATE
    (REQUIRES MINIMAL SUPERVISION)
VII. PURPOSEFUL APPROPRIATE
     (INDEPENDENT LIVING)

GLASGOW OUTCOME SCALE

1. Death
2. Persistent Vegetative State
3. Severe Disability
4. Moderate Disability
5. Good Recovery

PRIMARILY USED IN RESEARCH
**DISABILITY RATING SCALE**

RATES PATIENTS OVER 10 LEVELS OF SEVERITY: NONE, MILD, PARTIAL, MODERATE, MODERATELY SEVERE, SEVERE, EXTREMELY SEVERE, VEGETATIVE STATE, EXTREME VEGETATIVE STATE.

---

**How does recovery occur after TBI??**

- Recovery of injured neurons
- Synaptic Alterations
- Neuronal Regeneration (sprouting)
- Growth/differentiation of new cells
- Functional Substitution

---

**FUNCTIONAL REORGANIZATION (I)**

- One area of the brain that is “hard wired” will change
  - If a peripheral nerve in the arm (primate) is cut that previously “assigned” brain will respond to different nerves
  - The converse can also occur. If the cortex is removed an adjacent portion of the brain will activate
- This often occurs very quickly (hours to days) that supports existing, unused brain connections and not sprouting

  » Whyte in DoLaa, 1998
FUNCTIONAL REORGANIZATION (II)

• Training and experience alter the neuronal representation in the brain
  – Primate studies support show that if the cortex is abated motor training recruits adjacent cortex
    – Nudo Science 1996
  – Human functional MRI studies show that with repeated practice of a motor task enlarges the motor cortex
    – Karn Nature 1995
  – Mental rehearsal can potentiate new motor cortex outputs almost as well as actual physical practice
    – Pascual-Leone, J. Neurophysiology, 1995

NEURONAL REGENERATION

Medication/Substance Effects
• Ganglioside GM-1 can improve motor function after SCI in humans and brain injury in animals
  – Geisler, NEJM, 1991
  – Dunbar, Behav Brain Res, 1993
• Nerve growth factor
• Adrenocorticotropic factor (ACTH)

NEURONAL REGENERATION/SPROUTING

• Occurs over weeks to months
• Experience and training probably contribute to fiber sprouting and development and maintenance of useful connections. Even forced use.
• Enriched environments (medications, toxins, etc) help
MECHANISMS OF FUNCTIONAL RECOVERY AFTER BRAIN INJURY

• Recovery is usually dramatic, but incomplete
• There are probably multiple levels of improvement

---

Functional Limitations often Improved with Rehabilitation

• Impaired Mobility
• Impaired Activities of Daily Living
• Impaired Instructional ADL’s
• Impaired Cognitive Function
• Impaired Communication
• Impaired Swallowing/Nutritional Intake
• Pain Behaviors
• Incontinence of Bowel or Bladder
**FUNCTIONAL RECOVERY**

- SEVERE DEFICITS CANNOT BE REVERSED
- SPECIFIC SKILLS CAN BE LEARNED, USUALLY THROUGH REPETITION
- THESE MUST BE TAILORED TO AN ANTICIPATED ENVIRONMENT

---

**Engram**

The neurologic pathway that allows automatic and fast motor activity. This often requires millions of repetitions.

---

**FUNCTIONALLY IMPAIRED TISSUE RESUMES FUNCTIONING IN THE FIRST FEW WEEKS**
SYNAPTIC ALTERATIONS

- Localized lesions can show changes in neurotransmitters and blood flow distant from the lesion.

- Neurotransmitter receptors on the cell membrane of neurons can change. There can be increased sensitivity similar to denervation supersensitivity. Whyte in DeLisa, 1998.
NEURONAL REGENERATION

• Sprouting of surviving neurons
• Occurs over months
• The importance is unknown

NEURONAL REGENERATION/SPROUTING

• Sprouting of existing axons
• Growth of new neurons (existing cells differentiate and contribute to different function)
• Occurs over weeks to months
• Experience and training probably contribute to fiber sprouting and development and maintenance of useful connections.
  – Even forced use
• Enriched environments (medications, training, etc) help
  Whyte, et al. in DeLisa, 1998
NEURONAL REGENERATION

• Medication/Substance Effects
  • Ganglioside GM-1 can improve motor function after SCI in humans and brain injury in animals
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    • Dunbar, Behav Brain Res, 1993
  • Nerve growth factor
  • Adrenocorticotropic factor (ACTH)

NEURONAL REGENERATION

• RESEARCH PRIMARILY IN NON-MAMMALS
• AGE DEPENDENT
• UNMYELINATED FIBERS SPROUT MORE
• PURPOSEFUL VERSUS RANDOM SPROUTING
• SHORT DISTANCE SPROUTING

FUNCTIONAL SUBSTITUTION

• USE ANOTHER STRATEGY TO ACCOMPLISH THE TASK USING INTACT NEURAL SYSTEMS
• VERY HARD TO STUDY AND DOCUMENT BECAUSE IF IT IS SUCCESSFUL THE STRATEGY IS INVISIBLE
PROGNOSTIC FACTORS IN TBI
EACH PERSON IS UNIQUE

• Duration of coma
• Post-traumatic amnesia
• Neurologic signs and deficits
• Physiologic indicators (CK-BB, LDH-1)
• EEG, SEP, BAEP, VEP
• Imaging – CT, MRI, PET
• Age
• Premorbid function
• Socioeconomic status – family
• Cognitive function
• Associated injuries – SCI, fractures, HO
  (Krusen’s 1990)

COMPARISON OF SUBJECTS VS. CONTROLS

<table>
<thead>
<tr>
<th></th>
<th>Subjects</th>
<th>Controls</th>
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<tbody>
<tr>
<td>Sex</td>
<td>% Males</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>Mean</td>
<td>Range</td>
</tr>
<tr>
<td>Marital Status:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>8%</td>
<td>8%</td>
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<tr>
<td>Married</td>
<td>58%</td>
<td>58%</td>
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<tr>
<td>Widowed</td>
<td>8%</td>
<td>2%</td>
</tr>
<tr>
<td>Separated/Divorced</td>
<td>25%</td>
<td>33%</td>
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<tr>
<td>Education (years completed)</td>
<td></td>
<td></td>
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<tr>
<td>Up to 9 Years</td>
<td></td>
<td></td>
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<tr>
<td>9 to 12 Years</td>
<td>50%</td>
<td>33%</td>
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<tr>
<td>Above 12 Years</td>
<td>12.17</td>
<td>12.58</td>
</tr>
<tr>
<td>Causative Factors:</td>
<td></td>
<td></td>
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<tr>
<td>Auto Injury</td>
<td>75%</td>
<td>8%</td>
</tr>
<tr>
<td>Work Related Injury</td>
<td>17%</td>
<td>20%</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DESCRIPTIVE FACTORS REVIEWED (II)

Medical
Onset & Location of Pain
Onset of Brain Injury
Medical Treatment at Onset
Loss of Consciousness
Post Traumatic Amnesia
Imaging and Electrodiagnostic Results
Surgical Procedures
Previous Pain Program Participation
Previous Pain Treatment Modalities
Balance Evaluation
Body Mass Index

Emotional & Behavioral Symptoms*
Depression
Delusions or Hallucinations
Paranoia
Decreased Initiative
Improved Social Relationships
Irritability or Aggression
Anxiety/Agitation
Indifference
Other

*Dimensions Based Upon Portland Adaptability Index
**TRENDS IN DATA FOR PRE-TREATMENT FACTORS**

<table>
<thead>
<tr>
<th>Factor</th>
<th>TBI/CP Subject</th>
<th>Chronic Pain Control</th>
<th>Student t p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Clinical Studies Performed (i.e., CT scans, MRI, EEG, EMG, Bone Scan) per person</td>
<td>1.8</td>
<td>1.3</td>
<td>0.04</td>
</tr>
<tr>
<td>Number of Normal Clinical Studies/Total Number of Clinical Studies</td>
<td>20/22</td>
<td>9/15</td>
<td>0.03</td>
</tr>
<tr>
<td>Average Number of Reported Specific Pain Treatments per Patient (Passive Modalities)</td>
<td>3.8</td>
<td>2.0</td>
<td>0.03</td>
</tr>
<tr>
<td>Number of People who Previously Participated in Pain Programs</td>
<td>4/12</td>
<td>5/12</td>
<td>0.03</td>
</tr>
</tbody>
</table>

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“The Art of Medicine consists of amusing the patient while nature cures the disease”

*Voltaire*

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**AMERICANS CAL ALWAYS BE RELIED ON TO DO THE RIGHT THING AFTER THEY HAVE EXHAUSTED ALL THE OTHER POSSIBILITIES.**

*(Winston Churchill)*
Who can benefit from inpatient rehabilitation?

Questions to Answer

MECHANISMS OF FUNCTIONAL RECOVERY AFTER BRAIN INJURY

• Recovery is usually dramatic, but incomplete
• There are probably multiple levels of improvement

NEURONAL REGENERATION

• Medication/Substance Effects
  • Ganglioside GM-1 can improve motor function after SCI in humans and brain injury in animals
    • Geisler, NEJM, 1991
    • Dunbar, Behav Brain Res, 1993
  • Nerve growth factor
  • Adrenocorticotropic factor (ACTH)
ETIOLOGY OF PAIN IN MILD TBI (I)

Possible Peripheral Causes

- Muscle and ligament tears
- Greater occipital neuralgia
- Nerve root irritation
- Myogascial pain
- Somatic dysfunction
- Cranial bone abnormalities
- Migraine vascular spasm
- Skull fractures
- Dural tears

ETIOLOGY OF PAIN IN MILD TBI (II)

Central Nervous System

- Physiologic plastic CNS changes from nociception
- Brainstem seizures (Andy 1989)
- Pain behaviors may be related to operant and psychological factors

MINOR WHIPLASH AND MAJOR DEBILITATION

- A minority of patients will have post-concussion syndromes in addition to neck and spine pain.
- A retrospective study described 27 patients with major debilitation and neuropsychologic testing abnormalities (cognitive flexibility, non-verbal reasoning, new learning/memory, psychomotor ability and attention)
- No correlation between RTW and litigation.

-From Yarnell
Brain Injury 1988
CHRONIC PAIN AND TBI

• Treatment goals:
  • Identify deficits
  • Educate patient
  • Improve CPM function
  • Improve competencies
  • Improve physical limitations
  • Use appropriate medications
  • Educate about chronic pain
  • Decrease pain behaviors

Opioid Contracts or Agreements (I)

• This allows for all people involved to have expectations clearly written down.
• Things to cover in the agreement:
  – Opioids are addictive, dangerous and potentially fatal medications
  – Only one physician prescribes the medication
  – The goal of the medication is to improve function.
  – Complete relief of pain is not a goal
  – The medication does not cure the problem
  – If function decreases it may be due to the medication

Opioid Contracts or Agreements (II)

– The patient is still responsible for their health
– The medication will be tapered for breach of agreement
– There can be no other illegal drug use
– Drug tests will be ordered at the discretion of anybody on the treatment team.
– Medications need to be taken as prescribed diversion is unacceptable.
– Requests for escalation of dose suggests the medication is not working.
– Rules for refills (call in advance, do not request increase of dose without an appointment etc.)
– Other non-medication treatments are also required, psychology, PT, functional activity
How do you treat chronic pain if you cannot cure it?

- If you can treat (eliminate or decrease) the pain, then do it!!
- In any case, treat the patient, not just the pain
- Be honest with the patient
- The physician must decide the pain is not curable
- Focus on treating pain behaviors and suffering
- The patient must eventually agree the pain is not curable

Opiate Medications are not an easy cure and frequently cause side effects

Rush Limbaugh is not alone

Elizabeth Taylor, Robert Downey Jr., Kelsey Grammer, Tim Allen, Charlie Sheen, Billy Joel, Christian Slater, Ozzy Osbourne, Jack Osbourne, Ben Affleck, and Nick Nolte
Rush Limbaugh is not alone in using pain killers and becoming addicted

Elizabeth Taylor, Robert Downey Jr., Kelsey Grammer, Tim Allen, Charlie Sheen, Billy Joel, Christian Slater, Ozzy Osbourne, Jack Osbourne, Ben Affleck, and Nick Nolte

Rush Limbaugh’s story is not rare

- “I first started taking prescription painkillers some years ago when my doctor prescribed them to treat post surgical pain following spinal surgery.
- Unfortunately the surgery was unsuccessful, and I continued to have severe pain in my lower back and also in my neck due to herniated discs.
- I am still experiencing that pain. Rather than opt for additional surgery for these conditions, I chose to treat the pain with prescribed medication.
- This medication turned out to be highly addictive”
  www.rushlimbaugh.com

Opioids in chronic non-cancer pain: systematic review of efficacy and safety (I)
Kalso E, Pain. 2004

- Analyzed available randomised, placebo-controlled trials of WHO step 3 opioids for efficacy and safety in chronic non-cancer pain.
- The Oxford Pain Relief Database (1950-1994) and Medline, EMBASE and the Cochrane Library were searched until September 2003.
- Double-blind studies reporting on pain intensity outcomes using validated pain scales were included.
Fifteen randomised placebo-controlled trials were included.
- Four investigations with 120 patients studied intravenous opioid testing.
- Eleven studies (1025 patients) compared oral opioids with placebo for four days to eight weeks.
- Six of the 15 included trials had an open label follow-up of 6-24 months.

Would the FDA approve any drug after an 8 week trial for Diabetes, Hypertension, or any other chronic disease??

The mean decrease in pain intensity in most studies was at least 30% with opioids and was comparable in neuropathic and musculoskeletal pain.
- About 80% of patients experienced at least one adverse event, with constipation (41%), nausea (32%) and somnolence (29%) being most common.
- Length of treatment is four days to eight weeks.
- Six of the 15 trials had an open label follow-up of 6-24 months.
- Only 44% of 388 patients on open label treatments were still on opioids after therapy for between 7 and 24 months.

Is this efficacy?

The short-term efficacy of opioids was good in both neuropathic and musculoskeletal pain conditions.
- However, only a minority of patients in these studies went on to long-term management with opioids.
- The small number of selected patients and the short follow-ups do not allow conclusions concerning problems such as tolerance and addiction.
- The lack of addiction reports in the literature is amazing to me.
Do Opioids Improve Outcome in Non-malignant Pain in Denmark? (I)  Eriksen et al Pain 2006

- National random sample of 10,066 of 16,684 completed a self-administered questionnaire.
- Participants reporting pain were divided into opioid and non-opioid users.
- chronic/long-lasting pain (>6 months)
- The analyses were adjusted for age, gender, concomitant use of anxiolytics and antidepressants and pain intensity.
- Opioid usage was associated with very severe pain, poor self-rated health, not being engaged in employment, higher use of the health care system, and a negative influence on quality of life as registered in all items in SF-36.

Do Opioids Improve Outcome in Non-malignant Pain in Denmark? (II)  Eriksen et al Pain 2006

- Because of the cross-sectional nature causative relationships cannot be ascertained.
- “However, it is remarkable that opioid treatment of long-term/chronic non-cancer pain does not seem to fulfill any of the key outcome opioid treatment goals: pain relief, improved quality of life and improved functional capacity.”

Treatment of Chronic LBP  Back Letter 2004

- “The evidence on treatment of chronic back pain leaves general practitioners with few options”
- “Established treatments either do not work or have limited efficacy.”
- “Emerging treatments may still be regarded as controversial, or are not widely available.”  Bogduk 2004
Treatment of Chronic LBP
Back Letter 2004

• “Most individual therapies, are not particularly effective in resolving symptoms.”
  – This includes analgesics, nonsteroidal anti-inflammatory drugs, muscle relaxants, antidepressants, physical therapy, and manipulative therapy.
• “Exercise can be beneficial but is not a cure-all”
• “Multidisciplinary therapy based on intensive exercises improves physical function and has modest effects on pain.”
  
  
  Bogduk 2004