Greetings from Minneapolis
Learning Objectives

- Discuss pathophysiology explaining development of chronic persistent pain
- Review interdisciplinary rehabilitative and psychological treatment choices
- Appreciated low importance of pharmacotherapy
- Explore how patient expectation predicts pain treatment outcomes

So, how do we treat the individual pain patient in front of us?

So, how do we treat the individual pain patient in front of us?

Hmhh... Spoiler Alert: Crystal-clear answer on 3rd last slide!

What are we measuring...

(1) Nociceptive Pain: arises from the activation of peripheral nerve endings (nociceptors) that respond to noxious stimulation (e.g. localized, sharp, squeezing, stabbing, or throbbing)
  - Somatic (for example, muscles, joints)
  - Chronic somatic pain typically well localized & often results from degenerative processes (such as arthritis)
(2) Visceral (internal organs) (poorly localized, dull, crampy, or achy)
(3) Neuropathic Pain: resulting from injury to, or dysfunction of, the somatosensory system. (burning, shooting, electric, or tingling)
  - Central pain: caused by a lesion or disease of the central somatosensory nervous system
(4) Psycho-social-spiritual-emotional Pain / Total Pain
(5) Persistent (Chronic) Pain
  - Pain beyond expected time of healing
How Do We Manage Acute (vs chronic?) Pain in

No Needless Pain: The Children’s Comfort Promise
https://vimeo.com/20329079

Nociceptive Pathways & Primary Sites of Action of Analgesics
Opioids
- Tramadol ("weak")
- Morphine ("strong")

4 WHO-Principles
- "By the clock"

Multimodal (Opioid-sparing) Analgesia

Basic Analgesics
- Acetaminophen / Paracetamol
- NSAIDs

Opioids
- Pre-synaptic nerve terminal
  - Neurotransmitter release
- Post-synaptic nerve terminal:
  - Membrane hyperpolarization
  => suppress neuronal excitability

Nociceptive Pathways & Primary Sites of Action of Analgesics

Injury

Opioids

Acetaminophen (Paracetamol)

NSAIDs

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Integrative Therapies
- Such as:
  - Massage
  - Distraction
  - Deep Breathing
  - Biofeedback
  - Aromatherapy
  - Hypnosis
Nociceptive Pathways & Primary Sites of Action of Analgesics

Periaqueductal grey (endorphins)

Integrative (non-pharmacological) therapies

-Opioids

NSAIDs

Acetaminophen (Paracetamol)

Injury

Thalamus

Nociceptive Pathways & Primary Sites of Action of Analgesics

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Regional Anesthesia
- Neuraxial infusion
- Peripheral/Plexus Nerve block
- Neurolytic block
- Intrathecal port/pump
- Intraventricular opioids?

Adjuvants
- Alpha-Agonist
- Gabapentinoids
- TCA/Antidepressants
- NMDA-Antagonists
- Na-channel blockers
- Antispasmodics
- Muscle relaxants
- Corticosteroids
- Bisphosphonates

Integrative Therapies
Such as:
- Massage
- Distraction
- Deep Breathing
- Biofeedback
- Aromatherapy
- Hypnosis

Psychology
- CBT

Rehabilitation
- Exercise, Physical Therapy
- Sleep Hygiene
- OT

Spirituality

Friedrichsdorf S: 10th Annual Pediatric Pain Master Class, Minneapolis, MN, June 17-23, 2017
Don't have enough staff for pediatric pain control...?

Funny, how there is always enough staff to restrain a child.

Why, then, isn’t my pain treatment always successful?

Opioid Analgesia = Self-fulfilling Prophecy?

- Expectation of the success of a pain treatment can markedly influence its effectiveness
- Authors informed subjects the drug would (1) have no effect, (2) diminish the sensation of pain, or (3) make the pain worse
- 22 healthy adults were exposed to pain-provoking heat and also given the opioid remifentanil
Opioid Analgesia = Self-fulfilling Prophecy?

- Saline (Placebo)

Opioid Analgesia = Self-fulfilling Prophecy?

- Remifentanil infusion started (unknown to subject)

Opioid Analgesia = Self-fulfilling Prophecy?

- Remifentanil (subject being told “started infusion”)
Subjects were told remifentanil was stopped (but it wasn’t...)

Are these our chronic pain patients?


In contrast, negative treatment expectancy abolished remifentanil analgesia.


Thermal pain itself causes activation of a so-called pain circuit, which encompasses numerous brain regions including somatosensory cortex, cingulate cortex, insula, thalamus, and brainstem.

Expectation of increased pain was accompanied by more neural activity in the hippocampus, midcingulate cortex, and medial prefrontal cortex—brain areas that mediate mood and anxiety—than was observed in these regions during expectation of analgesia.

Conversely, individuals who expected drug to mitigate their pain showed increases in anterior cingulate cortex and striatum, signs that descending mechanisms of pain inhibition were engaged.

A drug with a true biological effect may appear to be ineffective to a patient conditioned to expect failure.
Introduction

Persistent (Chronic) Pain in Children

- Pain lasting > 3-6 months: Time definition arbitrary
- Pain that extends beyond the expected period of healing and hence lacks the acute warning function of physiological nociception
- Chronic Pain in children is the result of a dynamic integration of biological processes, psychological factors, and sociocultural factors considered within a developmental trajectory. Pediatric Chronic Pain Task Force 2012 American Pain Society

Metaanalysis 2011 (King et al.)

- Chronic and recurrent pain prevalent in children and adolescents
- girls > boys
- increasing with age
- psychosocial variables impacting prevalence: anxiety, depression, low-self-esteem, other chronic health problems, lower socioeconomic status
- Range
  - Headaches: 8-83%
  - abdominal pain 4-53%
  - musculoskeletal (incl. back) pain 4-49%
  - pain combinations 4-49%
- Mean prevalence
  - Headaches: 23%
  - abdominal pain, musculoskeletal pain, and pain combinations: 11-38%
Why did you come to pain clinic?

**Fear of Pain**
- Plays a significant role in relation to functional disability and depressive symptoms in the context of pediatric chronic pain
  - Appears to play both a facilitative and inhibitory role in relation to treatment response:
    - may hinder improvements in disability & depressive symptoms
    - declines are strongly associated with positive functional outcomes
  - Meta-analysis: Robust, positive association between pain-related fear and disability
  - Consistent with fear-avoidance model of chronic pain, findings suggest that pain-related fear may be important target for treatments intended to reduce pain-related disability

**Catastrophizing [“Awfulizing”]**
- A set of negative emotional / cognitive processes such as magnification, rumination and pessimism about pain sensations and feelings of helplessness when in pain.
  - **Rumination**: Parent anxious preoccupation with pain
  - **Magnification**: Parent amplification of the significance of pain
  - Significant link between child and parent catastrophizing
- Kids have higher pain ratings, if either child or mother displays high pain catastrophizing
• Pejorative implication, i.e. pain is not “organic” and therefore not real or serious

Chronic Pain Pathophysiology

• Many different chronic and recurrent pain syndromes, in both adult and pediatric populations, are now considered manifestations of an underlying vulnerability rather than separate disorders.


• Considerable evidence, especially from twin studies, points to a role of shared biological sensitivity: “pain vulnerability”, “pain sensitivity”, or “central sensitivity syndrome”.


### Chronic Pain Pathophysiology

**Biology**
- Genetics (40-50%)
- Microtrauma
- Infection
- Injury

**Social**
- Early life stressors = acquired vulnerability (50-60%)
- School
- Adverse Events
- Parents
- Catastrophizing

**Psychology**
- Anxiety
- Depression
- Stress Sensitivity

**Disordered Pain Processing:** Imprecise encoding of threat?
- Fear of Pain
- Catastrophizing

**Functional Primary Pain Disorder**

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### Sleep & Persistent Pain

- **Majority of children with chronic pain have sleep difficulties; problems with:**
  - Sleep initiation
  - Maintaining sleep
  - Early morning awakening

- **Insomnia: 12-18 years with chronic pain: 54% (vs 20% control)**

- **Sleep problems are persistent (50% vs 20%) and associated with negative impact for youths with chronic pain**

- **Sleep difficulties at 10 to 11 years uniquely predicted pain at ages 12 to 13 years, suggesting that early intervention using sleep interventions may be a promising direction for future research**

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*Stephen McMahon: Neurobiological basis for pain vulnerability. IASP Congress 2014*  
Chronic pain may be due to imprecise encoding of threat

Lorimer Moseley


- Pain can be considered a response, not just a stimulus
- Encoding non-nociceptive information predictably coincident with nociceptive input underpins the response to subsequent similar events
- Precision with which multi-sensory information (temporal, proprioceptive, spatial) about the painful event is encoded and represented in brain will determine the degree to which the painful response will subsequently generalize to similar events.

Bin your DIMs & seek your SIMs

Lorimer Moseley

Negative Interpretation Bias

- Tendency to appraise ambiguous situations in a negative or threatening way, specifically in ambiguous situations that could indicate pain and bodily threat, mediated the association between pain catastrophizing and recent pain experiences.

**School & Chronic Pain**

- Long-term school impairment -> poorer academic and occupational achievement, increase educational costs, development of psychiatric disorders
  

- Parental pain catastrophizing and parental protective response to child pain each individually predict school attendance rates and reports of overall school impairment.
  

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**How did you become pain free?**

(Andrew = Physical Therapist)

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**Mental Health & Pain**

- Affective, anxiety, & behavior disorders early risk factors of chronic pain (rather than vice versa)
  

- Metaanalysis of chronic pain trials: Girls ↑ anxious and ↑ depressed than boys
  

- New musculoskeletal pain 10-17 year-olds (<1 month): ↑ depressive symptoms = ↑ pain-related disability and ↓ QoL 4 months later
  
Mental Health & Pain

- **National Longitudinal Study of Adolescent to Adult Health** (n=14,790)
  Chronic pain in adolescence associated with higher rates of internalizing mental health disorders reported in adulthood

  - anxiety disorders (21.1% vs 12.4%)
  - depressive disorders (24.5% vs 14.1%)

Functional Primary Pain Disorder

- Chronic pain disorder that after appropriate medical assessment cannot be explained in terms of conventionally defined medical disease based on biochemical or structural abnormalities
- Associated with significant disruption of everyday life and often incapacitation
- Not typically responsive to conventional medical therapy but responsible for the consumption of enormous medical resources
- Often disparaging or pejorative implication, i.e. pain is not “organic” and hence not real or serious

Primary Pain Disorders

- Primary headaches
- Centrally mediated abdominal pain syndrome (2016)
- Widespread musculoskeletal pain (“fibromyalgia”)
  - CRPS ????
- Majority of children experience pain at multiple sites
The Porcupine

“I Guess That Explains The Abdominal Pains”
Gary Larson, The Far Side

Primary Pain Disorder

Pain Problem

Medical Workup

Positive

Negative

Assume manifestations of underlying vulnerability

Chronic-on-acute

Medical Treatment

Referral to:
- Integrative Medicine
- Mental Health Therapist
- Pain Clinic

Pain Perception Gender Dependent?

Friends
Chronic post surgical pain (CPSP)


Chronic-on-acute Pain


- In USA > 3.7 million children


- At least 5% of children with sickle cell disease, inflammatory bowel disease, rheumatoid arthritis, congenital heart disease, or cancer are expected to display chronic pain in addition to their underlying somatic pain episodes

- 5% of children with sickle cell disease, inflammatory bowel disease, rheumatoid arthritis, congenital heart disease, or cancer are expected to display chronic pain in addition to their underlying somatic pain episodes
Chronic Pain: Survivors of Childhood Cancer

- **Prevalence of pain during treatment:** Outpatient 9-26%, inpatient 39-54%
  
  
  

- **Prevalence of pain conditions after treatment:** 12% pain/abnormal sensation; 15.5% migraines; 20.5% other headaches; using prescription analgesics higher among survivors than siblings
  
  

How long can we wait?

- Unknown at what point clinical deterioration begins

- Wait-times for chronic pain treatment of 6 months or longer are medically unacceptable: significant decrease in health related quality of life and psychological well being (metaanalysis, 24 studies)


- 2/3 of US pediatricians felt it was not their primary responsibility to treat chronic pain


**Pediatric Pain Screening Tool (PPST)**


Interdisciplinary Pain Clinic

How do you feel now?

- Intensive Interdisciplinary Pediatric Chronic Pain Rehabilitation:
  - e.g. 3-week inpatient program costs ($31,720)
  - Health care expenses $61,988 in year before admission; $14,189 the year after admission
  - Cost of missed work was $12,229 in year prior and $1,189 in year after

Excerpt From "Little Stars" By Moonshine Movies (58Min; 2014) https://Www.YoutubE.com/Watch?T=13&V=Bb1Fhxfjdwi
The Exit Interview

- Pain is real!
- Positive Expectation = Self-fulfilling prophecy

Exit Interview:
What is the Hard Work...and non-negotiable...?

- Physical Therapy
  - Daily home exercise

Myths, Mirrors, Magic and no Morphine?
Physical Therapy

- Physical activity reduces risk for depression in female adolescents

- Adolescents with chronic pain: lower physical activity level

Graded Motor Imagery

- Process of thinking about moving without actually moving.
  Cortical reorganization and associated changes in somatosensory cortex activity and anatomy in certain types of chronic pain (e.g. CRPS; lower back pain)

- degree of cortical reorganization correlated with pain intensity

Myths, Mirrors, Magic and no Morphine?
**Integrative modalities**

- **Integrative modalities effective in management of pediatric pain**

- **Hypnosis**

- **Guided imagery**

- **Yoga**

- **Acupuncture**

- **Massage**

- **Biofeedback**

**Exit Interview: What is the Hard Work...and non-negotiable...?**

- **Physical Therapy**
  - Daily home exercise

- **Integrative Medicine**
  - Self-Hypnosis
  - Biofeedback
  - Progressive Muscle relaxation, etc.
  - Daily home exercise
    - Passive Massage, Acupuncture

**How does this stuff work...?**

- The periaqueductal gray and descending pain modulation:

- Distraction significantly increased activation of cingulo-frontal cortex including orbitofrontal & perigenual anterior cingulate cortex (ACC), as well as periaqueductal gray (PAG) & the posterior thalamus.

- Active distraction techniques, such as imagery, appear to modulate endorphine release in the midbrain, including the periaqueductal gray and thereby increase activity of descending inhibiting pathways thereby decreasing nociception from the dorsal horn resulting in gate pain modulation during distraction.

- Springer! Bishop is a distinguished neurosurgeon at the prestigious medical center and is an expert in the field of pain management. His research on the effects of distraction techniques on pain modulation has been groundbreaking. His work has significantly contributed to the understanding of how the brain processes pain, and his findings have led to the development of new, effective pain management strategies. In his lecture, Bishop emphasized the importance of understanding the neural mechanisms underlying pain modulation to improve pain treatment outcomes.
How did you become pain free?

Exit Interview:
What is the Hard Work...and non-negotiable...?

- **Physical Therapy**
  - Daily home exercise
- **Integrative Medicine**
  - Self-Hypnosis
  - Biofeedback
  - Progressive Muscle relaxation, etc.
  - Daily home exercise
  - Passive: Massage, Acupuncture
- **Psychology** (...if missing school, anxiety, depression...)

Exit Interview
Psychology


Exit Interview: What is the Hard Work...and non-negotiable...?

**Physical Therapy**
- Daily home exercise

**Integrative Medicine**
- Self-Hypnosis
- Biofeedback
- Progressive Muscle relaxation
- Daily home exercise

**Psychology** (...if missing school, anxiety, depression...)
- Sports/Exercise
- Sleep-hygiene
- Social: Having daily fun
- School: Attending full-time (or school-re-entry plan)

**Normalize Life**

Exit Interview
Back to normal life

Exit Interview:
What is the Hard Work...and non-negotiable...?

- **Physical Therapy**
  - Daily home exercise
- **Integrative Medicine**
  - Self-Hypnosis
  - Biofeedback
  - Progressive Muscle relaxation
  - Daily home exercise
  - Passive: Massage, Acupuncture
- **Psychology** (...if missing school)
- **Normalize Life**
  - Sports/Exercise
  - Sleep-hygiene
  - Social: Having daily fun
  - School: Attending full-time (or school-re-entry plan)
- **Family Coaching**
- **Medications**...???

Medications?

RITALIN
So much easier than parenting.
Myths, Mirrors, Magic and no Morphine?

Hey, Fluffy… should we prescribe opioids for children with primary pain disorders…?

Opioids & Primary Pain Disorders

- Lack of evidence supporting long-term effectiveness
- Updated Cochrane Review: Effectiveness/safety of long-term opioid therapy for lower back pain remains unproven
- Even after adjusting for substantial number of potential confounders, opioids were associated with worse functioning in back pain patients at 6-month follow-up
- Chronic lower back pain: Increase in opioid use associated with increase in depression, and increase in depression associated with increase in opioid dose
- 109 patients with chronic pain over 7 years: NO relation between opioid dose change and clinical pain score


Pain Modulation Circuits

Cortex

[cingulo-frontal, incl. orbitofrontal & perigenual anterior cingulate]

Periaqueductal gray (PAG)

Dorsal Horn

Thalamus

On

Off

Active Integrative Strategies

Distraction

Stress

Anxiety

Depression

Catastrophizing

School absenteeism

Poor sleep hygiene

Perceived Injustice

Friedrichsdorf S: 10th Annual Pediatric Pain Master Class, Minneapolis, MN, June 17-23, 2017

Active Integrative Strategies

Distraction

Stress

Anxiety

Depression

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School absenteeism

Poor sleep hygiene

Perceived Injustice

1. Low-dose Amitriptyline (stimulates DIP)

2. Gabapentin (inhibits)

3. Acetaminophen

4. Ibuprofen (Celecoxib?)

5. Lidocain 5% patch

6. Melatonin

7. Vitamin D ?

8. SSRI ?


So, how do we treat the individual pain patient in front of us?

Crystal clear answer:

“IT DEPENDS”

-Socrates
Conclusion

- Chronic persistent pain usually not derived from peripheral nociceptive input (i.e. damage or inflammation)
- Many different chronic and recurrent pain syndromes now considered manifestations of underlying vulnerability rather than separate disorders
- Importance of rehabilitative, interdisciplinary team approach
- Opioids in absence of tissue injury or inflammation not indicated
- Patient expectation predict pain treatment outcomes

Your advice to become pain free?

Elana
Greetings from Minnesota

Nerstrand Big Wood State Park

ADDENDUM
“Deleted Scenes”

No pain without analgesia, no analgesia without pain... ???

Further Reading

Conquering Your Child’s Chronic Pain
A Pediatrician’s Guide for Reclaiming a Normal Childhood

HarperResource
$ 14.95
Persistent (Chronic Pain)

http://www.youtube.com/watch?v=4b8oB757DKc&feature=player_embedded

The mystery of chronic pain

https://www.youtube.com/watch?v=J6--CMhcCfQ
Further Links

- Video: Kiran Stordalen and Horst Rechelbacher Pediatric Pain, Palliative and Integrative Medicine Clinic Tour https://vimeo.com/122654881
- Short Movie Meet the Interdisciplinary Chronic Pain Clinic Team at Children’s Minnesota: LittleStars TV https://www.youtube.com/watch?v=138uB6uf6GW
- Video: Tour of the Kiran Stordalen and Horst Rechelbacher Pediatric Pain, Palliative and Integrative Medicine Clinic at Children’s Hospitals and Clinics of Minnesota in an overview of the three programs that are offered at Children’s under this title. https://www.childrens.org/1213157
- Short Movie LittleStarsFilm ‘Kali’s Story - Beyond the NICU’/This amazing pediatric palliative care short movie (7 min) features 8-year-old Kali’s journey at Children’s Hospitals and Clinics of Minnesota from NICU to today receiving care by the Pain & Palliative & Integrative Medicine program while inpatient, in the clinic, and at home (Jun 22, 2015) http://www.littlestars.tv/short-films/beyond-the-nicu

Table 1. ACTION-APS Pain Taxonomy (AAPT) for Chronic Pain