PSYCHOLOGICAL MANAGEMENT AND PHARMACOTHERAPY OF PATIENTS WITH CHRONIC PAIN AND DEPRESSION, SCHIZOPHRENIA AND PTSD

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WHY PAIN AND PSYCHIATRY?

- Psychiatry
  - subjective phenomena reflected in behavior
  - associated with distress &/or functional impairment
BODY – MIND

- Permeated human cognition for over 3,000 years
- Homer: will of Gods → behaviors motivations
- Millennium later: Plato & “psyche”
- Plato & Freud: behavior – conflict of rational, instinctual & emotional forces
- Aristotle: body – mind amalgamation, holistic & indivisible nature
- Descartes: body – mind dualism
  - mind: spiritual domain, no physical qualities
BODY – MIND

- Identity (Pavlov, Kandel)
- Independence (Freud, Wundt)
- Interaction (Hippocrates: bodily humors (yellow and black bile, phlegm, and blood; Descartes))
Four blind people encounter an elephant

leg is a tree trunk.

tail is a whip

trunk is a hose

side is a wall
BODY – MIND

• Dualism – a state of two parts

• Duality – a dual state or quality
  • e.g., both wave & particle properties
EPIDEMIOLOGY

• >70 million Americans

• the most common concern

• annual cost ~ $100 billion
  • medical expenses
  • loss of earnings & productivity
DEMOGRAPHICS

• ↑ geriatric patients
• > 65 years
  • 4% early 1900s
  • 12% now
  • projected > 20% in 25 yrs

• ↑ risk for pain-related conditions
  • 50% of community-dwelling
  • 80% of nursing home residents
"Hey! My lower back pain! It's gone!"
FUNCTIONAL RELATIONSHIP

- Pain $\rightarrow \downarrow$ reward
- Reward $\rightarrow \uparrow$ analgesia (i.e., $\downarrow$ pain)
- Common currency: pain $\leftrightarrow$ pleasure
- Motivation-decision model (Fields)
  - highest priority (e.g., childbirth)
PHILOSOPHY

• **Aristotle** (*Rhetoric*): “We may lay it down that Pleasure is a movement, a movement by which the soul as a whole is consciously brought into its normal state of being; and that Pain is the opposite.”

• **Spinoza** (Ethics Part 3, *Definitions of the emotions*)
  • Two extremes on the same scale: "a passive state wherein the mind passes to …”
    • pleasure – “a greater perfection”
    • pain – "a lesser perfection”

• **Nietzsche** (*The gay science*): pleasure and pain are “so knotted together that whoever wants as much as possible of the one, must also have as much as possible of the other…”
NEUROANATOMY

• Nociception processing networks
  • lateral: sensory
    • thalamocortical projections to $1^0$ & $2^0$ somatosensory cortex
  • medial: emotional/motivational coloring of pain ($1^0$ & $2^0$ pain affect & pain unrelated affect)
  • limbic & reward structures
SCHEMATIC OVERVIEW OF THE INTERFACE BETWEEN NEUROBIOLOGICAL & PSYCHOLOGICAL FACTORS INVOLVED IN THE EXPERIENCE OF CHRONIC PAIN
INTERFACE BETWEEN NEUROBIOLOGICAL & PSYCHOLOGICAL FACTORS INVOLVED IN THE EXPERIENCE OF CHRONIC PAIN

• Frontocingulate
  • chronic pain → brain reorganization (via glu) → emotional & cognitive impairments → negative affective states & compromised decision-making → ↑ dysphoria → ↑ pain

• Subcortical systems
  • acute pain → ↑ DA
  • chronic pain → ↓ DA → ↓ motivation
PHYSICAL AND EMOTIONAL PAIN: TWO SIDES OF THE SAME COIN

- fMRI work (O'Connor et al, 2008):
  - grief-related emotional pain: periaqueductal gray, insula and the anterior cingulate cortex
  - physical pain: reward/motivational circuits
- International Association for the Study of Pain: An unpleasant sensory and emotional experience associated with actual or potential tissue damage
- DSM-IV: Axis1 Pain Disorder (3/5 criteria)
  - A. Pain . . . is of sufficient severity to warrant clinical attention
  - B. Pain causes clinically significant distress or impairment in social, occupational, or other important areas of functioning
  - C. Psychological factors
PHYSICAL PAIN

- DSM-IV, Axis III, medical conditions

- Distinction of Axis I & III is not obvious
  - share clinical characteristics, symptom severity & functional impairment
  - blurring of diagnostic boundaries in lay language; the term *pain* is used interchangeably
PAIN & THE BRAIN: IMPLICATIONS FOR EMOTIONAL & MOTIVATIONAL PROCESSING

- Chronic pain
  - not a unitary sensation
  - modulated by genetic, environmental, cognitive & emotional factors

- Majority neuropathic
  - caused by CNS alterations
    - spinal cord pathways: hyperalgesia & allodynia
    - emotional/motivational circuits: negative affective states & drive to eliminate pain
COMORBIDITY OF PAIN & PSYCHIATRIC DISORDERS

- Pain → emotional abnormalities in healthy
- Neuropsychopathology → ↑ pain
  - diathesis-stress theory

- Psychiatric conditions: entire diagnostic range from "Disorders Usually First Diagnosed in Infancy, Childhood, or Adolescence" to "Other Conditions That May Be a Focus of Clinical Attention"
PAIN & MAJOR DEPRESSIVE DISORDER

• MDD: the 2nd common disability (projected)
• Depressed vs. happy affective states → ↑ & ↓ pain in healthy & chronic pain
• MDD
  • ↑ prevalence
  • ↑ in severity → ↑ pain
  • pain → depressive symptomatology → MDD
• MDD + pain
  • ↑ symptoms severity of depressive symptoms
  • ↓ treatment outcomes
PAIN & MDD

• fMRI pain stimulus (Strigo et al., 2008): ↑ amygdala activity proportionally (to depressive symptoms)
• Recursive, partly shared neural systems
  • serotonergic and noradrenergic pathways
  • SNRI, TCA analgesic action
  • other treatment modalities (eg, TMS or VNS)
  • opioidergic abnormalities in MDD
• MDD and pain can trigger and perpetuate each other owing to overlapping neural and emotional alterations
• Assessment of pain function may provide important diagnostic & therapeutic leads in MDD
PAIN & PTSD

• Anxiety commonly comorbid with pain
  • poorer prognosis

• PTSD conditioned fear & anxiety syndrome
  • reward/motivational circuitry involvement

• Pain-PTSD link
  • neuroanatomy: dopamine terminal fields play key roles in stress, aversive responses & PTSD
  • pathophysiology: peritraumatic pain is among PTSD independent risk factors
  • timely morphine reduces the severity & prevents PTSD
PAIN & PTSD: MECHANISMS

• Pain – conditioned stimulus
  • "mutual maintenance"

• Up Opiodergic tone in PTSD
  • sensitized pain (glutamatergic)
  • prophylactic use of opioids
Clusters of activation in bilateral ventral and dorsal striatum obtained from voxelwise contrasts of monetary gains minus losses collapsed across spinner type in Control (N=26) > PTSD (N=20) subjects against a background representing the mean high-resolution anatomic image of the subjects included in the analysis. (Apparent activation in a ventricle represents artifact.) The x, y and z values are in accordance with the Harvard-Oxford subcortical structural atlas. A. Coronal view, B. Sagittal view and C. Axial views. (p<0.05 corrected)
PTSD > Controls (46-42°C)

-50 +10 +6 -12 -14 -60
MPC Pu NAc NAc Hi

PTSD < Controls (46-42°C)

-2
Hy A

Sensitized to pain
Emotional Circuits
Dysregulation of NAc
PAIN & SCHIZOPHRENIA

• DA pain & reward
• ↑↑ Endorphines in CSF & plasma
  • parallel severity of psychosis
  • pain insensitivity (Haslam, 1798; Kraepelin, 1919; Bleuler, 1924)
• reversal by opioid antagonism
• Molecular abnormalities in opioid genes: prodynorphin & proenkephalin
• Clinically: tissue damage, finger burns from cigarettes; grave medical outcomes; silent MI; delays in management of abdominal emergencies perforated bowel & ruptured appendix
Schematic diagram of potential mechanisms involved in drug-related motivational changes during adequate treatment, undertreatment, or overtreatment of pain with opioid analgesics.

ADDICTION-LIKE PHENOMENA

- Pseudo-addiction: compulsive seeking of opioid drugs driven by the desire to ameliorate inadequately treated pain or to avoid a feared opioid withdrawal

- Pseudo-opioid resistance: self-reported pain with adequate analgesia owing to unwarranted anxiety about an impending opioid dose reduction

- Therapeutic dependence: attempts to avoid a feared opioid withdrawal
ROLE OF PSYCHIATRISTS

• Recognize and treat subtle psychological processes
  • expression of feelings via pain concerns
  • defense mechanisms (denial & repression vs. lying & malingering)
• conscious and unconscious motivations
• Motivational enhancement
• Fostering compliance
TREATMENT STRATEGIES

• Numerous cognitive & behavioral strategies (e.g., cognitive restructuring, stress management & systemic desensitization)
• NIH Technology Panel
  • muscle relaxation techniques
• Psychopharmacology: opioids, antidepressants, dopamine agonists, cholinergic agents, adrenergic agents, anticonvulsants & neuroleptics
• Suicidality, comorbidities
PAIN & 2ND GENERATION ANTIPSYCHOTICS

• Dopamine the most extensively investigated neurotransmitter
• Some SGAs (clozapine, olanzapine & risperidone) enhance opioidergic system
  • clinically olanzapine overdose = opioid intoxication
  • both human & rodent models: analgesic/antinociceptive properties
• Therapeutic implications: if excess of central opioid activity is consequential to the schizophrenia neuropathology it is reasonable to expect amelioration of the symptoms through the blockade of opioid receptors
CONCLUSIONS

• Broad public health interest

• Additional clinical expertise

• Pain rooted in numerous specialties (neurology, medicine, surgery & anesthesiology)

• Integration of psychiatry into mainstream medical care

• Significance of attending in concert to both mental & physical problems


