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

Igor Elman, M.D.
Cambridge Health Alliance/Harvard Medical School
March 30, 2012

DISCLOSURE OF FINANCIAL INTERESTS OR OTHER AFFILIATIONS

I have read the APA policy on full disclosure and I declare that (covering the past twenty-four months):

Neither I nor any member of my immediate family have a significant financial interest in or affiliation with any commercial organization(s) that may have a direct or indirect interest in the material presented in the program.

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

PAIN & REWARD: A CONTINUUM

FUNCTIONAL RELATIONSHIP
• Pain → ↓ reward
• Reward → ↑ analgesia (i.e., ↓ pain)
• Common currency: pain → 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\textsuperscript{o} & 2\textsuperscript{o} somatosensory cortex
  - medial: emotional/motivational coloring of pain (1\textsuperscript{o} & 2\textsuperscript{o} pain affect & pain unrelated affect)
  - limbic & reward structures
SCHEMATIC OVERVIEW OF THE 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: Axis I 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"
- ↑ Opiodergic tone in PTSD
  - sensitized pain (glutamatergic)
  - prophylactic use of opioids

PTSD & REWARD

Clustering of activation in bilateral ventral and dorsal striatum obtained from voxel-wise contrasts of imagery pain minus blanks collapsed across splinter type in Control (N=24) vs PTSD (N=30) 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 view. (p<0.05 corrected)

Elman et al, Biological Psychiatry, 2009
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
ADDITION-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
<table>
<thead>
<tr>
<th>REFERENCES</th>
</tr>
</thead>
</table>