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.

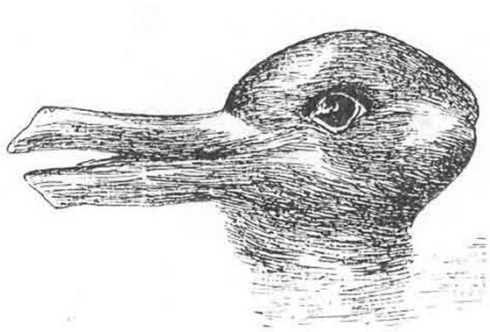
tail is a whip

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

PAIN & REWARD: A CONTINUUM

FUNCTIONAL RELATIONSHIP

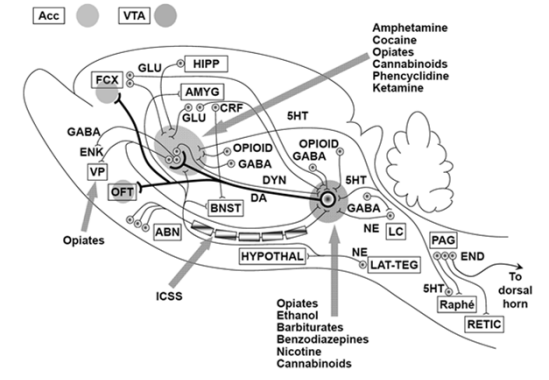
- Pain → ↓ reward
- Reward → ↑ analgesia (i.e., ↓ pain)
- Common currency: pain ↔ pleasure
- Motivation-decision model (Fields)
  - highest priority (e.g., childbirth)

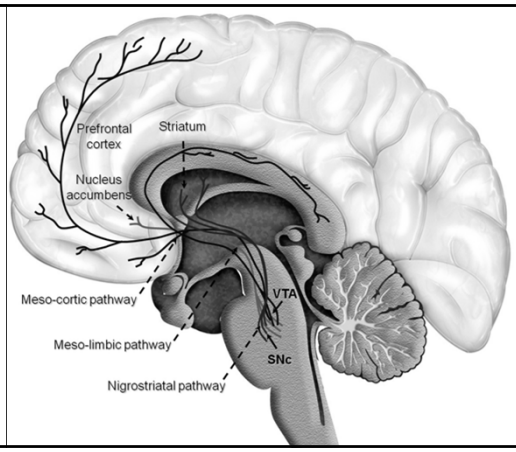
PHILOSOPHY

- **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…"**

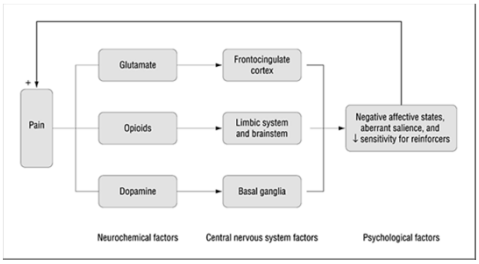
NEUROANATOMY

- **Nociception processing networks**
  - **lateral: sensory**
    - **thalamocortical projections to 1^0 & 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

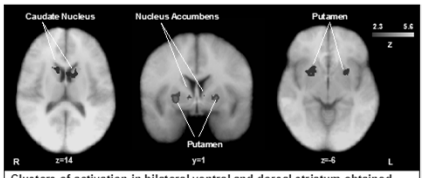
PAIN & PTSD

- 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

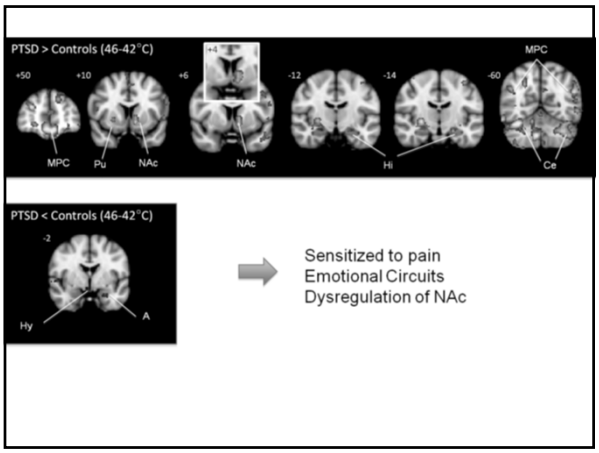
- Pain – conditioned stimulus
  - "mutual maintenance“
- ↑ Opiodergic tone in PTSD
  - sensitized pain (glutamatergic)
  - prophylactic use of opioids

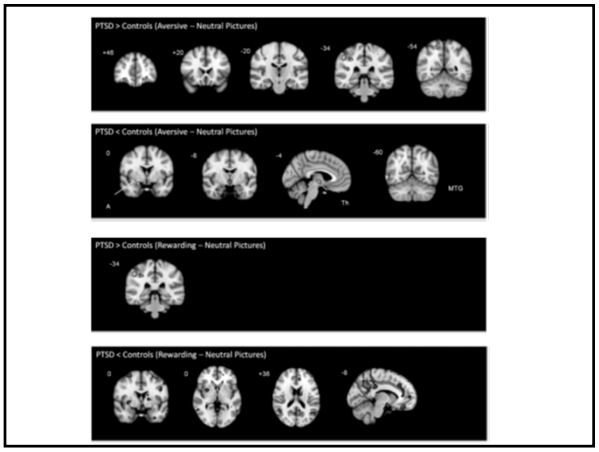
PTSD & REWARD



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)

Elman et al, Biological Psychiatry, 2009

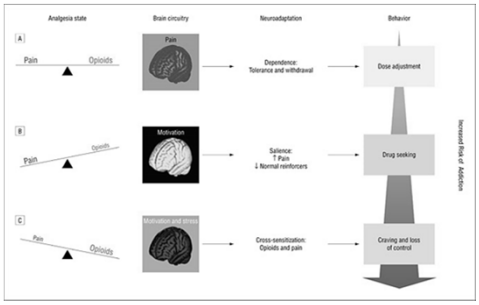




PAIN & SCHIZOPHRENIA

- **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**

Schematic diagram of potential mechanisms involved in drug-related motivational changes during adequate treatment, undertreatment, or overtreatment of pain with opioid analgesics



Elman, I. et al. Arch Gen Psychiatry 2011;68:12-20.

ARCHIVES OF GENERAL PSYCHIATRY

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

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