Inception, Total Recall, & The Brain: An Introduction to Neuroscience
Part 2

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Summary from September 4

- Gross Anatomy of the Brain
- Neuron and Neuronal Communication
- Memory & Emotion
  - Henry Molaison
  - Phineas Gage
- Limbic System & Emotional Circuitry
- CNS Disorders: changes in memory and information processing
  - PTSD
PTSD: A Complex Disorder with Frequent Co-morbidities

- **Major Symptoms**
  - Hyperarousal to Traumatic Memory
  - Emotional Dysregulation

- **Common co-Morbidities**
  - Major Depression
  - Anxiety Disorders
  - Impulsivity/Violent Behavior
  - Substance Abuse
Underlying Neurobiology: Anatomy & Neurochemistry
A Common Thread in PTSD and co-Morbidities: Hypothalamic-Pituitary-Adrenal Axis Disturbance

Key Considerations

➤ Regulatory Peptides
  ▪ CRF
  ▪ AVP

➤ Feedback Regulation
  ▪ Glucocorticoids

➤ Rhythm Disturbance
  ▪ Sleep
  ▪ Cardiovascular
  ▪ Core Temperature
  ▪ Activity
Plasma Vasopressin is Elevated in Combat Veterans with PTSD

In veterans with PTSD (far left)

- PTSD w/o MDD
- PTSD with MDD

Plasma AVP in veterans with PTSD (far left) and controls that were 1) veterans that experienced trauma but not PTSD (TC; center column) or healthy civilians (right)

Plasma AVP in veterans with PTSD (far left) and controls that were 1) veterans that experienced trauma but not PTSD (TC; center column) or healthy civilians (right)

de Kloet et al (2008)
Vasopressin Receptors

There are three vasopressin (AVP) receptors: V1a, V1b, and V2

V1a receptor is the most widely distributed CNS subtype and mediates the social and emotional effects of AVP

V1b receptor is found on ACTH-producing cells in the pituitary

V2 receptor is found on kidney cells and mediates the antidiuretic effect of AVP, and is not found in the brain
Predatory Conditioned Fear – A Translational Model of PTSD

Imaging Protocol

ferret

5 min stimulus

5 min control

Physiology

ferret

heart rate

blood pressure

respiratory rate

40 sec
Emotional Memory Disturbance: The Memory of Fear is Worse Than Fear Itself

**Method:** Male rats were exposed to a ferret (a natural predator and an unconditioned stimulus, UCS) paired with sucrose (conditioned stimulus, CS). Fourteen days later, the males were exposed to sucrose alone. Result: BOLD activation showed hyperarousal in response to sucrose alone in regions linked to fear and memory retrieval.
V1a Receptor Blockade is Effective in a Conditioned Fear Animal Model of PTSD

- V1a antagonist significantly reduced hyperarousal in brain regions mediating fear & memory when given two weeks after traumatic fear conditioning
- Normal fear responses & arousal patterns were unaffected (not shown)
Functional Neuroimaging in PTSD: Negative Emotional States

AMI: Amygdala
IFG: Inferior Frontal Gyrus
ACC: Anterior Cingulate Cortex
VM PFC: ventromedial prefrontal cortex

Hyperactivation

Hypoactivation
Alzheimer’s Disease: Symptoms

- Memory loss that disrupts daily life
- Challenges in planning or problem solving
- Difficulty completing familiar tasks
- Confusion with time or place
- Trouble with visual images and spatial relationships
- New problems with words when speaking or writing
- Mood and personality changes
Alzheimer’s Disease

- An estimated 5.2 million Americans have Alzheimer's Disease
- 6th leading cause of death in the United States
- $203 billion: the direct costs of caring in the United States in 2013
- In 2050: 14 million people will have AD
- In 2050: $1.2 trillion: direct costs
The cortex shrivels up, damaging areas involved in thinking, planning and remembering.

Shrinkage is especially severe in the hippocampus, an area of the cortex that plays a key role in formation of new memories.

Ventricles (fluid-filled spaces within the brain) grow larger.
The Alzheimer’s Brain: Microscopic Changes

- Alzheimer’s tissue has many fewer nerve cells and synapses than a healthy brain.
- **PLAQUES**, abnormal clusters of protein fragments, build up between nerve cells.
- Dead and dying nerve cells contain **TANGLES**, which are made up of twisted strands of another protein.

alz.org / braintour
The Alzheimer’s Brain: Tangles

- tau helps the tracks stay straight
- Tau collapses and disintegrates
- Transport system collapses leading to cell death
Brain scans show evidence of Alzheimer’s disease 20 years before symptoms arise (far left), 10 years before (middle), and after the onset of symptoms (right). Beta amyloid, a protein associated with the disease, is more visible in people who develop the disease (top row) than in those who don’t. The more color in the scan, the more beta amyloid is present in the brain.

Bateman et al (2012)
Alzheimer’s Disease: Treatment

- Drugs slightly slow progression but not disease-modifying
  - Namenda (NMDA receptor)
  - Aricept (Cholinesterase inhibitor)

- Drawing on Genetics
  - Family with Early Onset Alzheimer’s (age 45)
  - Crenezumab: anti-amyloid beta antibody
  - Prophylactic intervention
What We Learned Today

1. Basic Neuroanatomy

2. Neuron & Synaptic Transmission

3. Functional Neuroanatomy of Memory

4. PTSD: An affective disorder of memory and emotion

5. Alzheimer’s Disease: A neurodegenerative disorder

6. Imaging Technologies as a Tool for Understanding Circuitry
Thank you for your time and attention