Midterm Exam Feedback

- Initial Scoring: $M = 32.26 \ (SD = 9.37)$
- No “Bad” Items
- Two Items “Iffy”: #s 9, 10
  - $M$ Score > 1 $SD$ Below Mean
  - Rescored Full Credit for All Students
  - Rescore: $M = 37.12, \ SD = 7.80$
- Adjust Average Score: Add 5 Points
  - Final Score: $M = 41.84, \ SD = 7.45$

Clinical Disruptions of Consciousness

- Concussion
  - Temporary Disturbance of Consciousness
  - Results from Closed-Head Injury
- Coma
  - Chronic Loss of Consciousness
  - Failure to Arouse to Vigorous/Painful Stimuli
- Stupor
  - Chronic Loss of Consciousness
  - Responds to Vigorous/Painful Stimulation

“The Ding”
Yarnell & Lynch (1973)

- College Football Players (18 Games)
  - Mild Concussion vs. Broken Limbs
  - Memory Tests
    - Recall Examination on Field
    - Recall Impact, Play in Progress
- No Loss of Consciousness
  - Immediate Disorientation
  - Loss of Memory Within Minutes
    - Sometimes Lucid Interval Before Amnesia
Coma
Jennett & Plum (1972)
- Loss of Consciousness
  - No Communication
  - No Response to Stimulation
    - Auditory
    - Visual
    - Somatosensory Reflexes
  - No Signs of Emotion
- Vegetative Function OK
- Eyes Closed
  - But No Sleep Cycles

Vegetative State
Jennett & Plum (1972)
- Follows Coma (usually within 1 month)
- Wakefulness without Consciousness
  - No Communication
  - Partial Response to Stimulation
    - Auditory, Visual Startle
      - Sometimes Brief Orientation
    - Withdrawal to Noxious Somatosensory Stimulus
  - Few Signs of Emotion
    - Sometimes Reflexive Crying, Smiling
- Eyes Open
  - Sleep Cycles

Incidence of PVS in Severe Head Injury
Braakman et al. (1988)

Anatomy of Coma and Vegetative State
- Coma: Posterior Brain Stem
  - Reticular Formation
    - Periaqueductal Gray
    - Parabrachial Nucleus
- PVS: Diencephalon
  - Thalamus
  - RF Intact
    - Continues to Generate the Sleep-Wake Cycle

Glasgow Coma Scale
Teasdale & Jennett (1974)

Best Eye Response
1 - No eye opening
2 - Eye opening to pain
3 - Eye opening to verbal command
4 - Eyes open spontaneously

Best Verbal Response
1 - No verbal response
2 - Incomprehensible sounds
3 - Inappropriate words
4 - Confused
5 - Oriented

Best Motor Response
1 - No motor response
2 - Extension to pain
3 - Flexion to pain
4 - Withdrawal from pain
5 - Localises Pain
6 - Obeys commands

Range of Scores: 3 - 15
< 8, Severe
9-12, Moderate
>12, Mild

Reticular Activating System Rediscovered?
- Moruzzi & Magoun (1949)
  - Lesions, Stimulation in Cats
    - Anterior Lesions - Hypersomnia
    - Posterior Lesions - Insomnia
  - "Desynchronized" EEG
    - Sign of Cortical Activation
- RAS Extends into Thalamus
A “Proto-Self”?

- Two Types of Self-Consciousness
  - Core Self
    - On-line Conscious Awareness
    - Distinguishes Self from Nonself
  - Autobiographical Self
    - Narrative Personal History
- Unconscious Proto-Self
  - Associated with RF
  - Monitors Physical Condition of the Organism
  - Anything More than Homeostatic Regulation?

Locked-In Syndrome

- Full Consciousness
  - Anarthria, Aphonia
    - Loss of Articulate Speech, Vocalization
  - Quadriplegia
    - Paralysis of Limbs
- Preserved Auditory, Visual Function
  - Startle, Orienting
  - Localization, Fixation, Pursuit
- Preserved Communication
  - Blinking, Vertical Eye Movements
  - Preserved Emotion

“Locked-In” Syndrome

- Follows Coma
- Largely Immobile
- Limited Responsiveness
  - Vertical Eye Movements
  - Blinking
- Anterior Brain Stem
  - Pons
  - Excludes Reticular Formation

How Do You Get “Locked In”?

- Most Motor Pathways Pass Through Anterior Brainstem
- Damage At or Below Trigeminal Nerve (V)
- Spares
  - Afferent Nerves
    - Olfactory Nerve (I)
    - Optic Nerve (II)
  - Efferent Nerves
    - Oculomotor Nerve (III)
    - Trochlear Nerve (IV)

Management and Rehabilitation of the Persistent Vegetative State

- “Persistent” Can Become “Permanent”
  - Should the Qualifiers be Dropped?
- Recovery vs. “Post-Vegetative State”
  - Differentiated Response to Environment
    - Internal (Bowel, Bladder discomfort)
    - External (Pain)
- Physical Therapy
- Electrical Stimulation of Brainstem
- Cognitive Stimulation

Recovery from Coma, PVS

West County Times, 04/07/03

- Tustin, Ca. Woman
- In “Coma” for 1 year
  - 1 Day After Giving Birth
  - 10 Minutes After Brain-Tumor Surgery
- Recovery after 1 Year
  - Turned Toward Mother, “Smiled”
  - Can Now Lift Arms, Hold Child
    - Cannot Walk, Talk, or Smile
  - Communicates by Rolling Eyes
Recovery from the Persistent Vegetative State
Levin et al. (1991)

% Recovering

< 6 Months <1 Year < 3 Years

Duration of PVS

Terri Schiavo (1963-2005)

- 1990
  - Respiratory/Cardiac Arrest
- 1998
  - Husband Petition to Remove Tube
  - Parents Appealed
  - State, Federal Involvement
- 2002 CT Scan
- 2005 Autopsy

Minimally Conscious State
Giacino et al. (2002)

- Partial, Inconsistent Consciousness
  - Communication Inconsistent but Intelligible
    - Contingent Vocalization
    - Spontaneous Verbalization, Gesture
  - Partial Response to Stimulation
    - Auditory Localization
      - Inconsistent Command Following
    - Sustained Visual Fixation
      - Inconsistent Sustained Pursuit
    - Localizes Noxious Stimuli
      - Automatic Movements
    - Reaches for Objects, Accommodates to Shape
    - Contingent Smiling, Crying

Brain Activity
in Minimally Conscious State
Schiff et al. (2005)

- 2 Patients in MCS
  - 1 with Damage to Left Temporal Lobe
- Passive Stimulation
  - Light Touch of Hands
  - Auditory Narratives of Familiar Events
    - Familiar Voice
    - Auditory Passages Without Semantic Content
    - Reversed Speech

Response to Somatosensory Stimulation
Schiff et al. (2005)

- Primary Somatosensory Area
  - “Anatomic Hand Area”

Response to Verbal Stimulation
Schiff et al. (2005)

- Activation of Language Centers
  - Recognition of Speech
  - Discrimination of Nonspeech
- Speech vs. Nonspeech
  - Pt. 1, Damaged Wernicke’s area
  - Pt. #2, “Reduced Engagement”
Brain Activity to Speech Stimulation
Schiff et al. (2005)

ERP Responses to Patients’ Own Names
Perrin et al. (2006)

- “Cognitive” Event-Related Potentials
  - N1, P2, N2
  - P3: Orienting Response to Unexpected Stimulus
- Own First Name vs. Other First Name
- Patients
  - Persistent Vegetative State
  - Minimally Conscious State
  - Locked-In Syndrome
  - Age-Matched Controls

ERP Amplitudes
Perrin et al. (2006)

Evidence of Semantic Processing
Perrin et al. (2006)

Conclusions and Implications
Perrin et al. (2006)

- Ambiguity of P3
  - Does Not Necessarily Entail Conscious Perception
  - Also Occurs in Subliminal Stimulation
  - “Automatic” component of Speech Comprehension?

What Counts as Evidence of Consciousness?
Coma
General Anesthesia

Conscious Activity in the Vegetative State
Owen et al. (2006)

- 23 y/o Woman
  - TBI after Auto Accident
- Dx of Vegetative State
  - 5 Months Unresponsive
  - Preserved Sleep Cycle
- fMRI
  - Speech vs. Noise
    - Ambiguous Words
    - Creak, Beam, Ceiling
  - Imagery Instructions
Voluntary Brain Activity in the Persistent Vegetative State
Monti et al. (2010)

- 54 Patients: PVS = 23; MCS = 31
  - 16 Healthy Controls
- Motor and Spatial Imagery Tasks
  - Hitting a Ball on a Tennis Court
  - Walking Familiar Street or House
- fMRI of Regions of Interest
  - Motor: Supplemental Motor Area
  - Spatial: Parahippocampal Gyrus

fMRI Response to Imagery Tasks
Monti et al. (2010)

Imagine Playing Tennis
Owen (2013)

Useful for Communication?

- Asked Factual Yes-No Questions
  - “Do You Have Any Brothers?”
- Motor/Spatial for Yes/No
  - (Counterbalanced)
- Interrogator Blind to Correct Answers

Differential Response to Command
Cruse et al. (2011, 2012); Owen (2013)

- Patients in PVS, MCS
- Respond to Signal
  - Squeeze Right Hand
  - Wiggle Left Toe
- Classify EEG Activity in Premotor Cortex
  - 9/12 Normal Controls (75%)
  - 3/16 PVS (19%)
  - 5/23 MCS (22%)
Differential Response to Command
Cruse et al. (2011, 2012); Owen (2013)

- Patient in PVS for 5 Years
- Imagination Tasks
  - Playing Tennis
  - Moving Around House
- 5 Yes/No Questions Answered Correctly

Imagining for Communication
Monti et al. (2010); Owen (2013)

Conclusions About PVS and MCS

- Some Evidence of Intentional Activity
  - Specific Response to Instructions
- But Only in Small Minority of Patients
- Doubt Clinical Criteria for MCS
  - PVS > MCS
- Use Technique for Diagnosis
- Use Technique for Communication
  - Medical Decisions
    - Confirm Advance Directives
    - Life Support, Limited Treatment

General Anesthesia as “Controlled Coma”

- Sedation
- Loss of Consciousness
  - Analgesia
  - Amnesia
- Immobility
  - Lack of Voluntary Motor Behavior
    - Anesthetic Agents
    - Reflexive Response
  - Muscle Relaxants

Pain Relief in Pre-19th-Century Surgery

- Tolerate
- Alcohol
- Opiates (Laudanum)
- Bite Board
- Physical Restraint
Ether Day
First Demonstration of Ether as an Anesthetic Agent
William Morton, October 16, 1846

Surgeon: J.C. Warren
Anesthetist: W.T.G. Morton
Patient: Gilbert Abbot
Massachusetts General Hospital

Sedation Anxiety
Muscle Relaxation
Lack of Response

Balanced Anesthesia

Anesthesia Awareness
Analgesia Pain

Pre-Anesthetic Procedure
• Pre-Operative Visit
  – Exchange Information
  – Informed Consent
• Sedative Premedication
  • Benzodiazepine
    – Diazepam, Midazolam
  • Barbiturate
    – Thiopental
  • Propofol
    – Relieve Preoperative Anxiety
    – Facilitate Induction of Anesthesia

Inducing Anesthesia
• Rapid Sequence Induction
  – Short-Acting Barbiturate, Propofol
    • Intravenous
  • Inhalation (Mask) Induction
    – Nitrous Oxide in Oxygen
  • Muscle Relaxant

Maintaining Anesthesia
• Connection to Ventilator
  – Artificial Respiration
• Maintenance of General Anesthesia
  – Nitrous Oxide and Oxygen
  – Volatile Agent
    • Isoflurane
  – Intravenous Narcotics
    • Sufentanil, Propofol

Reversing Anesthesia
• Reverse Muscle Relaxation
  – Anticholinesterase Agent
    • Neostigmine
• Restore Normal Breathing
• Intravenous Narcotic Analgesic
  • Morphine
    – Post-Operative Pain
General Anesthesia as “Controlled Coma”

- Sedation
- Loss of Consciousness
  - Analgesia
  - Amnesia
- Immobility
  - Lack of Voluntary Motor Behavior
  - Reflexive Response
  - Muscle Relaxants

Mechanisms of General Anesthesia

- Originally, Purely “Empirical” Treatment
- Informal Theories
  - Alter Membrane Dynamics
    - Inhibit Action Potentials
    - Interfere Axonal Transmission
  - Interfere with Synaptic Transmission
    - Neurotransmitter Release
    - Neurotransmitter Uptake

Dual-Process Theory of General Anesthesia

- Inhibit Excitatory Neurotransmitters
  - N-methyl-D-aspartate (NMDA) receptors
- Potentiate Inhibitory Neurotransmitters
  - Gamma-Aminobutyric Acid (GABA) receptors

Single-Process Theories of General Anesthesia

- Dissolve in Lipid Bilayers of Neurons
  - Fat cells
- Form Plasma Membrane of Neuronal Cell
- Expansion of Cell Membranes
- Close Ion Channels
- Bind Directly to Proteins in Neuron
  - Stabilize Shape
    - Alters Suitability for “Lock and Key” Mechanism
  - Interferes with Synaptic Transmission
    - Mostly on Post-Synaptic Side

Pharmacological Mechanisms

- Halogenated Ethers
  - Alters Lipid Membrane
  - Alters Action of Sodium Pump
    - “Depolarization”
- Narcotics
  - Interfere with Postsynaptic Uptake
    - “Lock and Key”
Clinical Assessment of Consciousness

- Lack of Response
  - Verbal Command
  - “Surgical Stimulation”
- No awareness of pain during procedure
- No memory of surgical events

Loss of Consciousness

- <<1% Report Surgical Awareness
  - 0.2% of General Surgical Cases
  - 0.4-1.8% of Malpractice Claims
  - Post-Traumatic Stress Disorder
- “Light Planes” of Anesthesia
  - Caesarian Section
  - Trauma Surgery
  - Cardiopulmonary Bypass Surgery
  - Neurosurgery

Minimum Alveolar Concentration
Potency of Inhaled Anesthetic

- MAC
  - Prevents Movement to Stimulation
    - In 50% of Subjects
- MAC-Aware
  - Eliminates Awareness of Stimulation
    - In 50% of Subjects
- Analogy to Sensory Thresholds
- Standard of Care = 1.3 MAC

PRST Score
Autonomic Nervous System Index of Consciousness

- Blood Pressure
- Heart Rate
- Sweating
- Secretion of Tears

Central Nervous System
Indices of Consciousness

- Event-Related (Evoked) Potential
- EEG Power Spectrum
- Bispectral Index

Event-Related (Evoked) Potential

- Stimulus
  - Auditory
  - Visual
  - Somatosensory
- Components
  - Early (Brainstem)
  - Middle (Subcortical)
  - Late (Cortical)
- Auditory “AEP Index”
  - Abolish late components
  - Delay Midlatency Components
**EEG Power Spectrum**

- EEG Bands
  - Delta (0.5-4 Hz)
  - Theta (5-7 Hz)
  - Alpha (8-12 Hz)
  - Beta (18-30 Hz)
  - Gamma (30-50 Hz)
- Median $f < 2-3$ Hz
- Spectral Edge $f < 8-12$ Hz

**Bispectral Analysis (BIS)**

- BIS Algorithm
  - High-Frequency Activation (14-30 Hz)
  - Low-Frequency Synchronization
  - Periods of "Nearly Suppressed" EEG
  - Presence of "Flat Line" EEG
- Bispectral Index
  - Awake = 100
    - 50% reduction in recall = 86
    - 95% reduction in recall = 64
    - Anesthetized < 60

**McSleepy, the Anesthesia Robot**

- Automated Delivery of Anesthesia
- Consciousness
  - Bispectral Index
- Muscle Relaxation
  - EMG Variant
- Pain (Proxies)
  - Heart Rate
  - Blood Pressure
- Met DaVinci, the Surgical Robot, in 2010
  - Performed Trans-Atlantic Prostatectomy in Italy

**Explicit vs. Implicit Memory Following General Anesthesia**

- Elective Surgery
- Isoflurane
  - No Nitrous Oxide
  - No Benzodiazepines
- Paired-Associates
  - Ocean-Water, Butter-Knife
  - $M$ Time = 50 min, $M$ Repetitions = 67
- Memory Tests
  - In Recovery Room; After 14 days

**Explicit and Implicit Memory Following General Anesthesia**

- Immediate Test

**Implicit Memory Following General Anesthesia**

- Mean Effect Size ($d$)

  - $< 12$ hrs
  - $12-36$ hrs
  - $> 36$ hrs
Nature of Explicit Memory Deficits in Surgical Anesthesia

- Loss of Consciousness
- Loss of Memory
  - Anterograde Amnesia?
  - Retrograde Amnesia
- Is the Patient Aware, and Then Forgets?

Is the Anesthetized Patient Aware During Surgery but Unable to Respond?

Isolated Forearm Technique
Tunstall (1977)

- Balanced Anesthesia
  - Induction
  - Muscle Relaxant
  - Maintenance
- Forearm Ischemia
  - Prevents Muscle Relaxant from Circulating to One Arm

Awareness During Caesarian Section
King et al. (1993)

<table>
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<th>% Aware</th>
<th>Incision</th>
<th>1 Min</th>
<th>2 Min</th>
<th>3 Min</th>
<th>End</th>
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<td>80</td>
<td>60</td>
<td>40</td>
<td>20</td>
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24 New Studies, 1993-2006
Deeprose & Andrade (2006)

- Assessment of Awareness
  - Isolated Forearm Technique
  - Auditory Evoked Potentials
  - Processed EEG
    - Bispectral Index
    - Spectral Edge Frequency
    - Narcotrend
- 44 Tests of Implicit Memory
  - “Mixed” Evidence Favoring Perceptual Priming
  - No Evidence Favoring Semantic Priming

Priming and Anesthesia
Iselin-Chaves et al. (2005, 2006)

- 48 Patients Receiving Isoflurane or Propofol
  - Unpremedicated
- 40 Words Presented 25 Consecutive Times
- Auditory Word-Stem Completion
  - Within 36 Hours of Surgery
  - Inclusion and Exclusion Instructions
- Anesthesia Monitored by BIS
  - Light = 61-80
  - Adequate = 41-60
  - Deep = 21-40
Performance in the Method of Opposition
Iselin-Chaves et al. (2005, 2006)

Applying the Process-Dissociation Procedure
Iselin-Chaves et al. (2005, 2006)

Reanalysis for “Maximum” BIS
Iselin-Chaves et al. (2005, 2006)

Anesthetic Effects on Memory
• No Explicit Memory for Surgical Events
  – By Clinical Definition of Adequate Anesthesia
• Spared Implicit Memory
  – Perceptual vs. Semantic Priming
  – Not An Artifact of Surgical Awareness
    • Clinically Adequate Anesthesia
      – Confirmed by EEG Monitoring
    • Process-Dissociation Procedure
      – Automatic vs. Controlled Influences
• Implicit Memory as Implicit Perception
  – No Conscious Perception of Primes