Neuropsychiatric Imaging in Addiction, TBI and Other Behavioral Disorders
Evidence-Based Approach

14th Annual Cardiovascular Conference
World Golf Village
Friday April 12, 2013
## Disclosure of Relevant Financial Relationships

<table>
<thead>
<tr>
<th>Name</th>
<th>Commercial Interests</th>
<th>Relevant Financial Relationships: What Was Received</th>
<th>Relevant Financial Relationships: For What Role</th>
<th>No Relevant Financial Relationships with Any Commercial Interests</th>
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<tbody>
<tr>
<td>John C. Tanner, D.O., FASAM</td>
<td>Reckitt Benckiser</td>
<td>Honorarium</td>
<td>Consultant &amp; Speaker</td>
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<td>Alkermes</td>
<td>Honorarium</td>
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</table>
John C. Tanner, D.O., FASAM, CCFC

- Medical Director for the Intervention Project for Nurses (Florida’s impaired practitioner program for Nurses)
- Vice-president of staff and former medical director at Wekiva Springs Center - psychiatric hospital in Jacksonville, Florida
- Director at Large for the American Society of Addiction Medicine’s Board of Directors
- American Board of Addiction Medicine Certified
- On Board of Directors for the Brain Health Foundation (not for profit brain research organization developed for the Jacksonville Psychiatric Society)
- Private Addiction and Behavioral Medicine since 1984

Disclosures

Speaker and Consultant for: Reckitt Benckiser and Alkermes
Learning Objectives

Gain an understanding about the role of new neuroimaging and scanning modalities as an aid in the understanding of psychiatric disorders, brain trauma and addictions:

- The brain is vulnerable to TBI, acquired addiction(s) to psychoactive substances and other pathologic processes in ways that may increase susceptibility to emotional and mood deregulation.
- Newer brain imaging and scanning techniques help identify more subtle changes that could not be seen with older imaging techniques.
- Proper identification of TBI injury and these other underlying brain pathologies may lead to better outcomes and recognition of improved ways to treat and protect the brain.
New brain imaging techniques

Brookhaven National Laboratory  1961
Pre-PET Headgear
New brain imaging techniques
New brain imaging techniques

Sometimes, we don’t like what we find
Neuropsychiatric Imaging

**Topics**

- Imaging modalities and applications
- Clinical indications for neuropsychiatric imaging
- Collaborating on what to order and when
- Correlating clinical and imaging diagnoses to enhance diagnosis
- Use of imaging in evaluating response and titrating medications
- Case studies
Imaging Modalities and Applications Utilized

- 3.0 Tesla MRI
  - Structures - Gray Matter
  - Connectivity - Diffusion Tensor Imaging
  - Chemical – MR Spectroscopy (MRS)
  - Volumetric Analysis of Structures (NeuroQuant)
  - Functional MRI (fMRI)

- PET/CT
- SPECT
Clinical Indications & Disease Processes

- Trauma (TBI)
- Addictions
  - Alcohol
  - Drug
  - Process addictions (e.g. Gambling, Sex, Shopping, etc.)
- Potential Neuropsychiatric Co-morbidities
  - Schizophrenia
  - Bipolar Disorder
  - Major Depressive Disorder
  - Anxiety Disorders – PTSD, OCD, OCPD, Fear / Anxiety
  - ADHD
  - Autism Spectrum and other Developmental Disorders
  - Cognitive Disorders – Alzheimer's, Other dementias
  - Eating Disorders
Dopamine pathways
Addiction and Co-Morbid Imaging Signatures

- Models
- Clinical observation correlation
- Imaging helps identify
  - Structure
  - Connectivity
  - Function
- Correlates: Models, Observation and Imaging
The cues can activate multiple areas of the brain 1,2,3. fMRI imagery of the brain’s reward system demonstrates that:

1. Alcohol cues activate the brain in alcohol-dependent individuals compared with social drinkers1.
2. Findings may lead to better interventions for the treatment of alcohol dependence4.

References:
Extended-release naltrexone modulates brain response to drug cues in abstinent heroin-dependent patients

- Studied 17 abstinent i.v. heroin users w/fMRI during exposure to visual heroin-related cues and matched neutral images before and 10-14 days after injection of extended-release naltrexone (XRNTX)
- Whole brain analysis of variance of fMRI data showed main effect of XRNTX in the medial frontal gyrus, precentral gyrus, cuneus, precuneus, caudate and the amygdala.
- fMRI response was decreased in the amygdala, cuneus, caudate and the precentral gyrus and increased in the medial frontal gyrus and the precuneus.
- Higher plasma levels of naltrexone's major metabolite, 6-beta-naltrexol, were associated with larger reduction in fMRI response to drug cues after XRNTX in the precentral, caudate and amygdala clusters.
- Data suggests XRNTX pharmacotherapy of opioid-dependent patients may, respectively, decrease and potentiate prefrontal and limbic cortical responses to cues and effect may related to XRNTX metabolism.
- Further evaluation of the brain fMRI response to drug-related cues and of the 6-beta-naltrexol levels as potential biomarkers of XRNTX therapeutic effects in patients with opioid dependence is needed.

The rewards of music listening: Response and physiological connectivity of the mesolimbic system.
Activation during sex anticipation period

Cortical activation during anticipation period.

Regions with significant signal increases during anticipation period [erotic anticipation × emotional anticipation] (conj. $p < 0.05$ uncorrected, $x: -1, y: 1, z: -10$).

Gender differences in cerebral activation when viewing erotic stimuli in fMRI

For analysis of specific activation, the contrast images of all groups were entered into a two-sample t-test. Interaction-related increase in MR signal is superimposed on three orthogonal sections of 3-D T1 weighted standard brain.

When viewing erotic film excerpts, statistical parametric maps of areas activated more prominently in men compared with women. Results show activation of left thalamus, left amygdala, anterior cingulate, bilateral orbitofrontal.
Gender differences in cerebral activation when viewing erotic stimuli in fMRI

- When viewing erotic film excerpts, statistical parametric maps of areas were more prominently activated in women in mid-luteal phase, compared with women scanned during their menses (paired t-test).
- Results show a superior activation of women in mid-luteal phase in the orbitofrontal, cingulate cortex and left insula.

Reference:
University Clinic Essen 03/01/2006; Elke Gizewski, MD, Elke Gizewski
fMRI images of a woman's brain throughout an orgasm

- More than 30 areas of the brain are active during the event, including those involved in touch, memory, reward and even pain.
- PFC becomes more active during orgasm, whether it’s achieved through physical touch or thought alone.
- PFC evidently “shuts off” during orgasm – especially a region of the orbitofrontal cortex (OFC), which is involved in the process of self-control.
Face perception is modulated by sexual preference

Forty heterosexual and homosexual men and women viewed photographs of male and female faces and assessed facial attractiveness. Sexually relevant faces elicit stronger neural responses in the reward circuitry, where the value of stimuli is represented.
Sample Protocol - Systems Model

Schizophrenia - neural integration problem

- Structural MRI without contrast including Quantitative Volumetric Analysis - longitudinal over time
- Volume of structures decreases over time
- May begin locally in specific areas, but diffuses throughout the brain
- Results from Neuropil elimination (dendrite pruning) and/or Neuron death (apoptosis)
- MRI - Diffusion Tensor Imaging - Connectivity Models - Demyelinating/Myelin Development - spatially diffuse
- MR Spectroscopy - reduced NAA in the DLPFC among other areas
- Functional - fMRI - Working memory, cognitive - task based designs - network connectivity
During performance of an identical pairs continuous performance attention task, bipolar patients showed increased activation of the VLPFC, as well as limbic and paralimbic structures, suggesting that reciprocal connections between these regions play a role in bipolar neuropathology. Working memory tasks are similarly associated with increased activation in the VLPFC, left thalamus and left caudate, and decreased activity in the ACC. Furthermore, increases in the VLPFC (Brodmann area 10) in patients with bipolar disorder have been associated with increasing working memory load. Together, these findings suggest that performance of continuous performance and working memory tasks is associated with over-activation of striato- and thalamo-frontal portions of the ALN, with
Bipolar patients demonstrate significant deficits in performance on a variety of attention tasks, particularly tasks involving elements of executive function.

Bipolar disorder represents the consequences of dysregulation of the anterior limbic network that includes traditional limbic structures and portions of the frontal cortex and cerebellum that have been found to be active in both emotional regulation and specific cognitive processes.

 Evidence suggests that some pathological changes are developmental in origin while others may represent the consequences of lesions elsewhere in the anterior limbic network. Healthy network formation requires both increased myelination of white matter tracts and synaptic pruning of gray matter. Subcortical structures, such as the amygdala, basal ganglia, and thalamus, are mature by puberty, and increased striatal volume in patients with bipolar disorder suggests a failure of pruning in at least a portion of the subcortical portion of the anterior limbic network.

Progressive losses of volume in the VLPFC may be related to the excitotoxic effects of increased glutamate release in the PFC that may in turn be a consequence of over-activity in subcortical structures.
What is the risk for addiction & MH after TBI?

The brain is fragile and susceptible to TBI and other pathologic processes that may result in disease states characterized by persistent changes in brain structure and function placing one at risk for addiction and emotional dysregulation.
Wasn't it Woody Allen who said, "The brain is my second favorite organ"?

The brain is worth protecting from even "minor trauma" - whatever the cost!
SPECT scans Single Photon Emission Computed Tomography (SPECT or SPET)

- Used to track cerebral blood flow, detect blood flow changes and brain metabolic activity.
- SPECT studies require a small amount of a gamma-emitting radioisotope (typically iodine-123, technetium-99m, xenon-133, thallium-201 or fluorine-18).
- Highlights cerebral functioning by emphasizing active brain cells showing heavy blood flow and less active cells with light blood flow.
- Pathology is detected by identifying over-active areas, under-active areas, and asymmetrical activity.
- Creation of 3D images is achieved when gamma camera record multiple 2D cross-sectional images of blood flow and cell activity. These images are then tomographically reconstructed into 3D images by the computer.
- SPECT Scanning may offer functional information that is frequently not attainable with other imaging procedures.
SPECT scans:

Normal

TBI

Source: braininspect.com
SPECT scans:

Bipolar Disorder

Source: braininspect.com
SPECT scans:

Normal

Depression

Source: braininspect.com
PET scan shows us minute by minute, in a time-lapsed sequence, just how quickly cocaine begins affecting the brain.

PET Scan

Normal brain activity

Same brain 4 weeks after being given amphetamine for 10 days

Decreased brain activity continues for up to 1 year after 10 days of amphetamine use

Chemical - MR Spectroscopy (MRS)

- Safe (No X-Rays)
- Noninvasive
- Provides a snapshot of the neurochemistry within a defined volume of interest
- Significantly increases the accuracy and specificity of conventional MR imaging in differentiating between disease states
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<table>
<thead>
<tr>
<th>ppm</th>
<th>Metabolite</th>
<th>Properties</th>
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</thead>
<tbody>
<tr>
<td>0.9-1.4</td>
<td>Lipids</td>
<td>Products of brain cell destruction</td>
</tr>
<tr>
<td>1.3</td>
<td>Lactate</td>
<td>Product of anaerobic glycolysis</td>
</tr>
<tr>
<td>2.0</td>
<td>N-acetylaspartate (NAA)</td>
<td>Neuron cell marker</td>
</tr>
<tr>
<td>2.2-2.4</td>
<td>Glutamine (Gtx)/GABA</td>
<td>Neurotransmitters</td>
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<tr>
<td>3.0</td>
<td>Creatine (Cr)</td>
<td>Energy metabolism</td>
</tr>
<tr>
<td>3.2</td>
<td>Choline (Cho)</td>
<td>Cell membrane marker</td>
</tr>
<tr>
<td>3.5</td>
<td>myo-inositol (ml)</td>
<td>Glial cell marker, osmolyte, hormone receptor mechanisms</td>
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<tr>
<td>1.48</td>
<td>Alanine</td>
<td>Present in meningiomas</td>
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Magnetic Resonance Spectroscopic Imaging and Relevance to Addiction

Summary of reported metabolite changes with drugs of abuse

<table>
<thead>
<tr>
<th></th>
<th>N-acetylaspartate</th>
<th>Choline</th>
<th>Creatine</th>
<th>myo-inositol</th>
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</thead>
<tbody>
<tr>
<td>Amphetamine</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Increase (TL) None (PFC)</td>
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<tr>
<td>Methamphetamine</td>
<td>Decrease (BG, FGM)</td>
<td>Increase (FMG)</td>
<td>Decrease (BG)</td>
<td>Increase (FGM, FWM)</td>
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<tr>
<td>MDMA</td>
<td>Decrease (FGM, HP) None (FGM, PWM, NC, HP, OCC)</td>
<td>—</td>
<td>—</td>
<td>Increase (PWM) None (FMG, PWM, OCC)</td>
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<tr>
<td>Cocaine</td>
<td>Decrease (FMG, TAH)</td>
<td>Increase (BG)</td>
<td>Increase (PWM)</td>
<td>Increase (FGM)</td>
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### Magnetic Resonance Spectroscopic Imaging and Relevance to Addiction

#### Summary of reported amino acid changes with drugs of abuse

<table>
<thead>
<tr>
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<th>Glutamate</th>
<th>GABA</th>
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<tbody>
<tr>
<td>Methamphetamine</td>
<td>Decrease in frontal gray matter</td>
<td>________</td>
</tr>
<tr>
<td></td>
<td>(Ernst &amp; Chang, 2008)</td>
<td>________</td>
</tr>
<tr>
<td>Cocaine</td>
<td>________</td>
<td>Decrease in prefrontal cortex</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Ke et al., 2004)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Decrease in OCC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Hetherington et al., 2000)</td>
</tr>
<tr>
<td>Opiates</td>
<td>Decrease in ACC</td>
<td>________</td>
</tr>
<tr>
<td></td>
<td>(Yucel et al, 2007)</td>
<td>________</td>
</tr>
<tr>
<td>Cannabis</td>
<td>Decrease in basal ganglia</td>
<td>________</td>
</tr>
<tr>
<td></td>
<td>(Chang et al., 2006)</td>
<td>________</td>
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<tr>
<td>Alcohol</td>
<td>Increase in ACC</td>
<td>Decrease in ACC</td>
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<td></td>
<td>(Lee et al, 2007)</td>
<td>(Lee et al, 2007)</td>
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<tr>
<td></td>
<td>Decrease in BG</td>
<td>Decrease in OCC</td>
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<tr>
<td></td>
<td>(Miese et al., 2006)</td>
<td>(Behar et al., 1999)</td>
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<tr>
<td>Nicotine</td>
<td>No change in HP</td>
<td>Decrease in OCC</td>
</tr>
<tr>
<td></td>
<td>(Galliant et al., 2008)</td>
<td>(Epperson et al., 2005)</td>
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Magnetic Resonance Spectroscopic Imaging and Relevance to Addiction

<table>
<thead>
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<th>Metabolite</th>
<th>Decrease</th>
<th>Increase</th>
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<tbody>
<tr>
<td>N-acetylaspartate (NAA)</td>
<td>Methamphetamine, MDMA, Cocaine, Opiates, Cannabis, Alcohol, Nicotine, Toluene</td>
<td>Cocaine (acute administration)</td>
</tr>
<tr>
<td>Choline (Cho)</td>
<td>Cannabis, Alcohol</td>
<td>Methamphetamine, Cocaine, Alcohol</td>
</tr>
<tr>
<td>Creatine (Cr)</td>
<td>Methamphetamine</td>
<td>Cocaine, Cannabis, Alcohol</td>
</tr>
<tr>
<td>Myo-Inositol (mI)</td>
<td>____</td>
<td>Amphetamine, Methamphetamine, MDMA, Cocaine, Alcohol, Toluene</td>
</tr>
<tr>
<td>Glutamate (Glx)</td>
<td>Methamphetamine, Opiates, Cannabis</td>
<td>Alcohol</td>
</tr>
<tr>
<td>GABA</td>
<td>Cocaine, Alcohol, Nicotine</td>
<td>____</td>
</tr>
</tbody>
</table>

Reductions in NAA and elevations in ml were observed almost universally, thus indicating that drugs of abuse in general have a profound impact on neuronal health, energy metabolism and inflammatory processes.

The next most common metabolite changes involved alterations in Cho and Cr, suggesting that methamphetamine, cocaine, cannabis, and alcohol influence cell membrane turnover as well as energy maintenance.

Methamphetamine, opiates, cannabis, and alcohol were found to alter Glx to some extent, while GABA was reduced by cocaine, alcohol, and nicotine, together suggesting that drugs of abuse impact neurotransmission.
Diffusion tensor imaging

Source: www.radnet.ucla.edu

Location of sensory motor area
Location of deep part of Broca area
Location of Sylvian fissure
Inferior longitudinal tract, temporal fibers
Superior temporal gyrus fibers
Superior temporal gyrus
Optic radiations
Location of angular gyrus
Projection fibers to supra marginal gyrus
Location of Heschl's gyrus

43mm from midline

On this image, the yellow horizontal line represents the AC-PC direction while the two vertical ones are perpendicular to the AC and PC respectively.

Brodman areas are listed in yellow numbers
Diffusion tensor imaging (DTI)

Source: www.radnet.ucla.edu

33mm from midline

On this image, the yellow horizontal line represents the AC-PC direction while the two vertical ones are perpendicular to the AC and PC respectively.

Brodman areas are listed in yellow numbers.
High Definition Fiber Tracking (HDFT)

A novel combination of processing, reconstruction, and tractography methods that can track white matter fibers from cortex, through complex fiber crossings, to cortical and subcortical targets with subvoxel resolution.

High Definition Fiber Tracking (HDFT)

- New high definition fiber tracking reveals damage caused by traumatic brain injury
- Current state-of-the-art diffusion tensor imaging (DTI) collects data points from 51 directions, while HDFT is based on data from 256 directions
- HDFT is able to identify disruptions in neural pathways with a clarity that other methods can not see
- Can virtually dissect 40 major fiber tracts in the brain to find damaged areas

Walter Schneider, Ph.D., professor of psychology at University of Pittsburgh Learning Research and Development Center (LRDC) led the team that developed the technology.
High Definition Fiber Tracking (HDFT)
High Definition Fiber Tracking (HDFT)
High Definition Fiber Tracking (HDFT)
Neurocircuitry and brain chemicals may be disrupted with a TBI or other brain pathology resulting in risks for addiction or psychopathology.
What is the TBI vulnerability of the brain that is not fully developed in the pediatric years?

MRI scans of healthy children and teens over time.

What role may TBI play in altering the known underlying mechanisms of relapse?

Reference:
1. Shaham et al., 2003
Stria terminalis and disruption

The stria terminalis has been indicated in a variety of functions, including:

• The activity of the bed nucleus of the stria terminalis correlates with anxiety in response to threat monitoring.

• It is thought to act as a relay site within the hypothalamic-pituitary-adrenal axis and regulate its activity in response to acute stress.

• It is also thought to promote behavioral inhibition in response to unfamiliar individuals, by input from the orbitofrontal cortex.

• Bilateral disruption of this pathway has been shown to attenuate reinstatement of drug seeking behavior in rodents.
Stria terminalis
Insula are important for anticipating negative events - does TBI impact this?
Insula - part of the negative arousal circuits. Would injury increase risk for addiction?
TBI and the hormonal system

Emotions have links to hormones

- Patients may experience problems in any of the hormonal system controlled by the pituitary (Agha A et al. J Clin Endocrinol Metab. 2007; 89 (10): 4929-4936)

- A patient who has pre-existing endocrine problems or is at-risk for hormonal imbalance should consult an endocrinologist within six months of any incident of head trauma (Ghigo E, Masel B. Brain Inj. 2005;19(9):711-24)
Emotional Effects of TBI

Many post-TBI patients show increased emotional labiality, and may laugh or cry inappropriately. Some will develop aggression and inappropriate social behaviors. Some of the common emotional changes following TBI include:

• Loss of motivation
• Impaired social judgment
• Increased risk-taking
• Disregard for the future
• Anxiety and/or depression
• Failure to recognize impact of one's behavior on others
• Sudden increase in libido with a loss of sexual impulse control
• Poor grooming and hygiene
• Loudness not associated with hearing loss.
• Indifference to the needs of others

Depression is a complex mental disorder with psychological symptoms. Patients with major depression exhibit abnormal metabolic activity and anatomy in specific brain regions, including:

- The basal ganglia
- The frontal cortex
- The thalamus

This suggests dysfunction of cortical-striatal and cortical-limbic reward pathways. TBI likely impacts on these critical structures in ways not previously understood.
“Psychiatric problems that may surface after TBI include depression, apathy, anxiety, irritability, anger, paranoia, confusion, frustration, agitation, insomnia or other sleep problems, and mood swings. Problem behaviors may include aggression and violence, impulsivity, disinhibition, acting out, noncompliance, social inappropriateness, emotional outbursts, childish behavior, impaired self-control, impaired self awareness, inability to take responsibility or accept criticism, egocentrism, inappropriate sexual activity, and alcohol or drug abuse/addiction.”

Source: www.ninds.nih.gov/disorders/tbi/detail_tbi.htm
Statistically, a single TBI episode doubles the risk of a second one. Subsequently, the rates increase exponentially.

Purdue University research

- Studied football players for two seasons at Jefferson High School in Lafayette, Ind.
- 21 players completed the study the first season and 24 the second season
- Included 16 repeating players
- Helmet-sensor impact data from each player were compared with brain-image scans
- Cognitive tests were performed before, during and after each season
- Players received from 200 to nearly 1,900 hits to the head in a single season
- Two players exceeding 1,800 hits
- Helmet-sensor data indicated impact forces to the head ranged from 20 Gs to more than 100 Gs
- A soccer player “heading” a ball experiences an impact of about 20 Gs.
fMRI brain scans show differences among high school football players in a two-year study that suggests concussions are likely caused by many hits over time and not from a single blow to the head, as commonly believed. (Purdue University image/Thomas Talavage)
Case 1 - 61 Year Old Male
Depression, Memory Loss & Speech Deficit

• Imaging:
  a) MRI with and without contrast
    - MRI Diffusion Tensor Imaging
    - MR Spectroscopy
  b) PET/CT

• Findings:
  - Right dural AVM
  - Significant structural, diffusion and spectroscopic abnormalities in the right frontal lobe
61 Year Old Male with Depression, Memory Loss & Speech Deficit

PET/CT in black and white
61 Year Old Male with Depression, Memory Loss & Speech Deficit

MRI
61 Year Old Male with Depression, Memory Loss & Speech Deficit

MRI
61 Year Old Male with Depression, Memory Loss & Speech Deficit

Impression:
- Low grade glioma

Differential:
- Localized small vessel disease
- AVM with venous congestion
61 Year Old Male with Depression, Memory Loss & Speech Deficit

Choline (Cho) spike is seen due to gliosis/glioma
61 Year Old Male with Depression, Memory Loss & Speech Deficit

MR Spectroscopy & MRI localization
61 Year Old Male with Depression, Memory Loss & Speech Deficit
61 Year Old Male with Depression, Memory Loss & Speech Deficit

- Glioma
- Dural AVM

MR
Case 2 - 28 Year Old

Male

- Hx: Intractable Seizures – 5+ years, Depression
- Imaging:
  - MRI with and without contrast
    - MRI Diffusion Tensor Imaging
    - MR Spectroscopy
    - NeuroQuant
  - PET/CT
- Findings:
  - Significant structural, diffusion, spectroscopic and volumetric abnormalities
- Impression:
  - Mesial Temporal Sclerosis
  - Pre-clinical schizophrenia
Case 2 - 28 year old Male with Intractable Seizures - 5+ years, MRI Image w/o contrast
Case 2 - 28 year old Male with Intractable Seizures - 5+ years, PET Scan
Case 2 - 28 year old Male with Intractable Seizures – 5+ years, Depression

MR Spectroscopy

Myo-inositol peak c/w Mesial Temporal Sclerosis & MRI
Case 2 – 28 year old Male with Intractable Seizures – 5+ years, Depression

MR Spectroscopy & MRI localization

Myo-inositol peak c/w Mesial Temporal Sclerosis
Case 2 - 28 year old Male with Intractable Seizures – 5+ years, Depression

MR Spectroscopy & MRI localization

Abnormal Hunter’s Angle indicative of decreased neuronal activity as seen in schizophrenia

Temporal sclerosis is characterized by pyramidal cell loss and astrogliosis in the mesial temporal lobe, hippocampal formation, amygdala, and parahippocampal gyrus. MTS is usually a bilateral process with one side affected more than other in about 80% of patients.
Case 3 - 68 Year Old Male

Hx: Long term Depression

- Imaging:
  - MRI with and without contrast
  - MRI Diffusion Tensor Imaging
  - MR Spectroscopy
  - PET/CT

- Findings: Giant Cell Astrocytoma
- Impression: Tuberous Sclerosis
68 Year Old Male with Depression
68 Year Old Male with Depression

Giant Cell Astrocytoma in the ventricle
68 Year Old Male with Depression

PET/CT
Case 4 - 49 Year Old Female

- **Hx:**
  - ALL with chemotherapy (18 years ago),
  - AML with radiation therapy, chemotherapy, stem cell therapy (12 years ago)
  - Severe depression & cognitive decline - 1 year with rapid change - past 3 months

- **Imaging:**
  - MRI with and without contrast
  - MRI Diffusion Tensor Imaging
  - MR Spectroscopy
49 Year Old Female s/p chemo/XRT

• Findings:
  – Extensive structural, spectroscopic and diffusion abnormalities

• Impression:
  – Necrotic neoplastic lesion in left frontal lobe
  – Enhancing, probably neoplastic lesion anterio-medial to lesion above
  – 3 – 4 mm left to right midline shift

• Post – surgery: Brain cancer (GBM) – poor prognosis
49 Year Old Female s/p chemo/XRT
Imaging MRI with and without
49 Year Old Female s/p chemo/XRT

Imaging MRI with and without
49 Year Old Female s/p chemo/XRT

MR Spec

Choline (Cho) peak associated with cell wall synthesis in GBM tumor. Very low N-acetylaspartate (NAA) indicative of minimal neuronal activity and cognitive loss.
49 Year Old Female s/p chemo

MR Spec
49 Year Old Female s/p chemo/XRT

MR Spec

Cr: 29.2
Cho: 29.3
Cr2: 11.2
NAA: 44.9
49 Year Old Female s/p chemo

MR Spec

ppm

NAA

I: 77.0

Cr

I: 49.2

Cho

I: 38.6

Cr2

I: 26.3

86
49 Year Old Female s/p chemo/XRT

MRI
Diffusion Tensor Imaging

Lack of symmetry, fiber tracks displaced etc.
49 Year Old Female s/p chemo/XRT

MRI
Diffusion Tensor Imaging

Lack of symmetry, fiber tracks displaced etc.
49 Year Old Female s/p chemo

MRI
Diffusion Tensor Imaging
49 Year Old Female s/p chemo/XRT

MRI
Diffusion Tensor Imaging
49 Year Old Female s/p chemo/XRT

MRI
Diffusion Tensor Imaging
Case 5 - 29 Year Old Male

Hx:
Paranoid Schizophrenia
Inappropriate social interaction since kindergarten
Multiple sports related head injuries

Findings:
Multiple sub-ependymal nodules
Numerous quantitative volumetric abnormalities

Impression: Tuberous Sclerosis

Referred to the MuCusick Institute (Genetics) - Hopkins
Case 5 - 29 Year Old Male

Multiple sub-ependymal nodules
Case 5 - 29 Year Old Male

Hippocampal volume is only 13 percent of the norm consistent with schizophrenia.
Case 5 - 29 Year Old Male

### General Morphometry Report

**PATIENT INFORMATION**

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<th>Patient ID:</th>
<th>409658</th>
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<td>Accession Number:</td>
<td>1746N01</td>
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<tr>
<td>Sex:</td>
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| Exam Date: | 2012/02/29 04:11:48 PM |

### MORPHOMETRY RESULTS

<table>
<thead>
<tr>
<th>Brain Structure</th>
<th>LH Volume (cm³)</th>
<th>LH Volume (% of ICV)</th>
<th>RH Volume (cm³)</th>
<th>RH Volume (% of ICV)</th>
<th>Asymmetry Index (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forebrain Parenchyma</td>
<td>508.63</td>
<td>30.72</td>
<td>515.53</td>
<td>31.13</td>
<td>-1.35</td>
</tr>
<tr>
<td>Cortical Gray Matter</td>
<td>225.86</td>
<td>13.64</td>
<td>230.97</td>
<td>13.95</td>
<td>-2.24</td>
</tr>
<tr>
<td>Lateral Ventricle</td>
<td>6.34</td>
<td>0.38</td>
<td>6.36</td>
<td>0.38</td>
<td>-0.28</td>
</tr>
<tr>
<td>Inferior Lateral Ventricle</td>
<td>1.12</td>
<td>0.07</td>
<td>1.40</td>
<td>0.08</td>
<td>-21.57</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>3.81</td>
<td>0.23</td>
<td>3.67</td>
<td>0.22</td>
<td>3.69</td>
</tr>
<tr>
<td>Amygdala</td>
<td>1.66</td>
<td>0.10</td>
<td>1.74</td>
<td>0.11</td>
<td>-4.47</td>
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<tr>
<td>Caudate</td>
<td>4.12</td>
<td>0.25</td>
<td>4.78</td>
<td>0.29</td>
<td>-14.78</td>
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<tr>
<td>Putamen</td>
<td>6.14</td>
<td>0.37</td>
<td>6.16</td>
<td>0.37</td>
<td>-0.21</td>
</tr>
<tr>
<td>Pallidum</td>
<td>1.20</td>
<td>0.07</td>
<td>1.35</td>
<td>0.08</td>
<td>-11.98</td>
</tr>
<tr>
<td>Thalamus</td>
<td>9.13</td>
<td>0.55</td>
<td>10.07</td>
<td>0.61</td>
<td>-9.80</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>71.00</td>
<td>4.29</td>
<td>75.98</td>
<td>4.59</td>
<td>-6.78</td>
</tr>
</tbody>
</table>

*The Asymmetry Index is defined as the difference between left and right volumes divided by their mean (in percent)*
29 Year Old Male fMRI Visual Paradigm
29 Year Old Male Visual-Motor Paradigm

More diffuse than expected for the norm
29 Year Old Male Visual-Motor Paradigm
Activation of the other side of the brain not expected
Case 6 - 53 Year Old WF w/DID

- Has dissociative identity disorder (DID) with multiple alter egos.
- The two most prominent are a 53-year-old white female and an 8-year-old white female - both are easily invoked.
- Severe sexual and physical trauma occurred at age 8.
- Received psychiatric treatment for 22 years.
- fMRI with word paradigm imaged in red for the eight-year-old and yellow for the 53-year-old.
- Eight-year-old is very predominantly left brain activity and very diffuse.
- 53-year-old is predominantly right brain activity and very localized.
- Verbal areas accessed are much greater for the 53-year-old than 48-year-old.
Identical verbal paradigm imaged in red & yellow then superimposed.
Case 7 - 16 YO WF w/TBI (MVA)

- Shearing occurs due to differential density of white matter and gray matter structures.
- Stretching and shearing result in the demyelination.
- Corpus callosum is an area where many fibers cross and a good area to identify injury.
- Step off can be seen on fiber tracts as well as significant asymmetry from injury.
- Cognitive changes can be restored for more frequently and fully than emotional and psychiatric changes which may be more permanent.

- Injury may result in decreased N-Acetyl Aspartine (NAA) seen or MRS with decreased neuronal activity and cognitive decline.
- Neuroplasticity may heal disrupted pathways.

See the “60 minutes special” on Gabby Gifford and how she was taught to speak through use of music accessing a different area of her brain.
Case 7 – 16 YO WF w/TBI (MVA)

- 16 year old went through windshield from the middle seat of the car she was riding in and back window of truck that was hit in front.
- No long term physical impairment
- Mild residual cognitive impairment
- Severe long-term depression with suicidal impulses and ideations
Case 7 - TBI in a 16 YO WEO Shearin
Case 7 - TBI in a 16 YO WF Shearing
Case 7 - TBI

- MRS is helpful to assess the degree of neuronal injury and predict patient outcomes.

- With diffuse axonal injury, imaging often underestimates the degree of brain damage.

- Clinical outcome correlates inversely with the NAA/Cr ratio.

- The presence of any lactate or lipid indicates a worse prognosis.
Case 8 - restless leg syndrome RLS

- White male in late 20s with severe restless leg syndrome
- MR spectroscopy showed a lactic acid spike in the region of the mid-cingulate gyrus where it crosses with the leg region of the motor cortex
- Not previously reported?
New neuroimaging and scanning modalities are available as an aid in the understanding of psychiatric, brain trauma and addictions for our patients:

- The brain is vulnerable to TBI in ways that may increase susceptibility to emotional and mood deregulation as well as acquired addiction(s).

- Newer brain imaging and scanning techniques help identify more subtle changes that could not be seen with older imaging techniques.

- Proper identification of TBI injury and underlying brain pathology with newer imaging and scanning may lead to better outcomes and recognition of improved ways to treat and protect the brain.
Summary (continued)

The use of a stronger (3.0 Tesla) MRI to evaluate brain structure (gray matter), analyzing connectivity with diffusion tensor imaging, chemical analysis with spectroscopy (MRS), volumetric analysis of structures (NeuroQuant) and functional (fMRI) along with PET/CT and MRI SPECT are valuable tools to help evaluate our patients with mental health and addiction problems.
Thank you for listening

Questions?