Update on MRI and Mild Traumatic Brain Injury

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Director
Virginia Institute of Neuropsychiatry
Clinical Assistant Professor
Virginia Commonwealth University
Introduction

• Importance of magnetic resonance imaging (MRI) in patients with traumatic brain injury (TBI)
Overview

• History of structural brain imaging
• Modern techniques for measuring MRI brain volume
History of Structural Brain Imaging

• 1970s: Computerized tomography (CT) scans
CT scan in a patient who fell from a second-story window shows:
- large subdural hematoma (*)
- subarachnoid blood (yellow arrows) .
History of Structural Brain Imaging

• 1970s: CT scans
• 1980s: Magnetic resonance imaging (MRI) scans
MRI scan

A patient undergoing an MRI examination of the head.
Magnetic resonance imaging (MRI scan) of the brain
MRI in TBI

• Radiologists interpretations are based on simple visual inspection. They typically find:
  • Patients with moderate to severe traumatic brain injury usually have multiple abnormalities on MRI.
  • Patients with mild traumatic brain injury usually have little to no abnormalities on MRI.
History of Structural Brain Imaging

- 1970s: CT scans
- 1980s: MRI scans
- 1990s: Brain volume measurement
MRI in TBI

- Summary of MRI brain volumetry through 2000
  - Traumatic brain injury causes brain atrophy.
  - Brain volumetry was performed by human operator with computer assistance.
  - Brain volumetry took about 15 hr per subject/MRI.
  - Brain volumetry was confined to research settings.

References
History of Structural Brain Imaging

- 1970s: CT scans
- 1980s: MRI scans
- 1990s: Brain volume measurement
- 2000s: Automated brain volume measurement
  - FreeSurfer
FreeSurfer Methods
Segmentation and Volumetry
FreeSurfer Methods

A. T1-weighted structural
B. Surface reconstruction
C. Inflation
D. Coregistration
Inflation
FreeSurfer Methods

a) Inflation and spherification

b) Mapping to common space and comparison to brain atlas

c) Return with brain regions mapped
Typical MRI Slice
Segments Differentiated
Automated Brain Volume Measurement

• 2000s: FreeSurfer
  • Limitations
    • Not available for commercial use
    • Restricted to research settings
History of Structural Brain Imaging

• 2000s: Alzheimer’s Disease Neuroimaging Initiative
  • Standardized collection of MRI data
  • Online database with normal control MRI data

References
History of Structural Brain Imaging

• 1970s: CT scans
• 1980s: MRI scans
• 1990s: Brain volume measurement
• 2000s: Automated brain volume measurement
  • FreeSurfer
  • ADNI
• 2007: NeuroQuant®
History of Structural Brain Imaging

• 2007: NeuroQuant®
  • Developed by CorTechs Labs
  • Based on FreeSurfer
    • Computer-automated analysis of brain MRI volume
  • Commercially available
  • FDA-approved method

References
NeuroQuant® Segmented Brain Image

Image size: 256 x 256
View size: 591 x 518
WL: 133 WW: 255
History of Structural Brain Imaging

• 2007: NeuroQuant®
  • FDA-approved method
    • Cleared for marketing by the US FDA [510(k) K061855] as a medical device to measure brain MRI volume in human subjects
    • Highly reliable with the earlier approach based on computer-assisted, manual identification of brain regions
    • “Brain ruler”

Reference
http://www.cortechs.net/products/neuroquant.php
History of Structural Brain Imaging

Reference
http://www.cortechs.net/products/neuroquant.php
# NeuroQuant® Standard Report

**Accession Number:** 277625  
**Referring Physician:** ROSS, DAVID MD  
**Exam Date:** 2010/11/02 12:00:00 AM

## Morphometry Results

<table>
<thead>
<tr>
<th>Brain Structure</th>
<th>Volume (cm³)</th>
<th>% of ICV (5%-95% Normative Percentile*)</th>
<th>Normative Percentile*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hippocampi</td>
<td>7.71</td>
<td>0.51 (0.43-0.59)</td>
<td>47</td>
</tr>
<tr>
<td>Lateral Ventricles</td>
<td>18.66</td>
<td>1.23 (0.28-3.36)</td>
<td>41</td>
</tr>
<tr>
<td>Inferior Lateral Ventricles</td>
<td>1.13</td>
<td>0.07 (0.07-0.25)</td>
<td>7</td>
</tr>
</tbody>
</table>

## Age-Matched Reference Charts*

![L & R Hippocampus](chart1.png)  
![L & R Inferior Lateral Ventricle](chart2.png)
### 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>530.42</td>
<td>33.41</td>
<td>544.54</td>
<td>34.30</td>
<td>-2.63</td>
</tr>
<tr>
<td>Cortical Gray Matter</td>
<td>238.78</td>
<td>15.04</td>
<td>239.66</td>
<td>15.10</td>
<td>-0.37</td>
</tr>
<tr>
<td>Lateral Ventricle</td>
<td>11.99</td>
<td>0.75</td>
<td>10.80</td>
<td>0.68</td>
<td>9.91</td>
</tr>
<tr>
<td>Inferior Lateral Ventricle</td>
<td>0.75</td>
<td>0.05</td>
<td>0.55</td>
<td>0.03</td>
<td>30.02</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>3.98</td>
<td>0.25</td>
<td>4.02</td>
<td>0.25</td>
<td>-0.97</td>
</tr>
<tr>
<td>Amygdala</td>
<td>1.98</td>
<td>0.12</td>
<td>1.95</td>
<td>0.12</td>
<td>1.32</td>
</tr>
<tr>
<td>Caudate</td>
<td>4.07</td>
<td>0.26</td>
<td>3.67</td>
<td>0.23</td>
<td>10.33</td>
</tr>
<tr>
<td>Putamen</td>
<td>5.23</td>
<td>0.33</td>
<td>4.30</td>
<td>0.27</td>
<td>19.55</td>
</tr>
<tr>
<td>Pallidum</td>
<td>1.31</td>
<td>0.08</td>
<td>1.32</td>
<td>0.08</td>
<td>-0.83</td>
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<tr>
<td>Thalamus</td>
<td>7.66</td>
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<td>6.95</td>
<td>0.44</td>
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<tr>
<td>Cerebellum</td>
<td>65.25</td>
<td>4.11</td>
<td>66.08</td>
<td>4.16</td>
<td>-1.25</td>
</tr>
</tbody>
</table>

*The Asymmetry Index is defined as the difference between left and right volumes divided by their mean (in percent)*.
Reliability of NeuroQuant®

• NeuroQuant is reliable with FreeSurfer (Kovacevic, Rafii et al. 2009).

• NeuroQuant® is reliable with a computer-supported manual technique using NeuroMorphometric software (Brewer, Magda et al. 2009).

• The segmentation error rate of NeuroQuant® was found to be very low (9 out of 822) (Heister, Brewer et al. 2011).

Reference


Validity of FreeSurfer

- FreeSurfer is valid in assessing traumatic brain injury
  - Merkley, Bigler et al. 2008
  - Bigler, Abildskov et al. 2010
  - McCauley, Wilde et al. 2010
  - Strangman, O'Neil Pirozzi et al. 2010
  - Warner, Youn et al. 2010
  - Hudak, Warner et al. 2011

References


Validity of NeuroQuant®

- NeuroQuant is valid in assessing traumatic brain injury
  - Ross, Ochs et al. 3 articles in press

References
Case example: Patient LK

• History
  – 57 years old
  – MVA on 06/11/09

Case example: Patient LK

- History
  - 57 years old
  - MVA on 06/11/09
  - Traumatic brain injury (TBI), mild
  - Headaches, neuropathic
  - Muskuloskeletal injuries

Case example: Patient LK

• 08/01/09: 1.5 Tesla MRI of brain:
  • Radiologist’s interpretation:
    – Normal

Case example: Patient LK

- **08/01/09**: 1.5 Tesla MRI of brain:
  - Radiologist’s interpretation:
    - Normal

- **03/04/10**: 3.0 Tesla MRI of brain:
  - Radiologist’s interpretation:
    - Two linear white matter hyperintensities in left frontal lobe subcortically, nonspecific

---

Case example: Patient LK

- **08/01/09:** 1.5 Tesla MRI of brain:
  - Radiologist’s interpretation:
    - Normal

- **03/04/10:** 3.0 Tesla MRI of brain:
  - Radiologist’s interpretation:
    - Two linear white matter hyperintensities in left frontal lobe subcortically, nonspecific
  - NeuroQuant Standard Analysis:
    - Hippocampal volume = 0.29 % of intracranial volume (less than 1st normative percentile)

# NeuroQuant®

## Age-Related Atrophy Report

### Patient Information

<table>
<thead>
<tr>
<th>Field</th>
<th>Value</th>
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<tbody>
<tr>
<td>Patient ID</td>
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<tr>
<td>Patient Name</td>
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<td>Sex</td>
<td>M</td>
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<tr>
<td>Assignment ID</td>
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<tr>
<td>Referring Physician</td>
<td>ROSS DAVID MD</td>
</tr>
<tr>
<td>Exam Date</td>
<td>2010/03/04 12:00:00 AM</td>
</tr>
</tbody>
</table>

### Morphometry Results

<table>
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<tr>
<th>Brain Structure</th>
<th>Volume (cm³)</th>
<th>% of ICV (5%-95% Normative Percentile*)</th>
<th>Normative Percentile*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hippocampus</td>
<td>4.37</td>
<td>0.29 (0.43-0.60)</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Lateral Ventricles</td>
<td>11.99</td>
<td>0.30 (0.03-3.11)</td>
<td>34</td>
</tr>
<tr>
<td>Inferior Lateral Ventricles</td>
<td>2.30</td>
<td>0.15 (0.06-0.24)</td>
<td>74</td>
</tr>
</tbody>
</table>
NeuroQuant® Extended Analysis

• Developed at VIN
• Compares data to normal controls
  • Alzheimer’s Disease Neuroimaging Initiative (ADNI) database (Jack et al)
  • 20 normal control subjects (10 men, 10 women)
  • Age: 68.3 yr (mean), 60.0 - 71.5 yr (range)
• 15 brain regions compared to normal controls
• All patients compared to normal controls, even patients less than 50 years old

Experience with NeuroQuant® at the Virginia Institute of Neuropsychiatry

• Over 100 NeuroQuant® analyses since 2010.
• Quality control
  • Prior to data collection, communicate with radiology center
  • NQ website: “NeuroQuant-Compatible MRI Scanners Setup”
Experience with NeuroQuant® at the Virginia Institute of Neuropsychiatry

Example of scanner setup from NQ website:
“NeuroQuant-Compatible MRI Scanners Setup”
Experience with NeuroQuant® at the Virginia Institute of Neuropsychiatry

• Quality control
  • Prior to data collection, communicate with radiology center
  • NeuroQuant® software automatically checks several parameters
  • Visual inspection of each set of segmented brain images
  • Inspection of the numerical and statistical results of the analyses
### NeuroQuant® Extended Report: Example of p. 1

#### Extended Volumetric Analysis based on NeuroQuant® data

**Patient:**
**Location of MRI:**
**Date of MRI:**
**Date of report:**

<table>
<thead>
<tr>
<th>Region</th>
<th>LH Volume (% of ICV)</th>
<th>% tile rank</th>
<th>RH Volume (% of ICV)</th>
<th>% tile rank</th>
<th>Asymmetry Index %</th>
<th>% tile rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole Brain Parenchyma</td>
<td>35.732%</td>
<td>47.1%</td>
<td>35.450%</td>
<td>26.0%</td>
<td>0.791%</td>
<td>96.4% *</td>
</tr>
<tr>
<td>Forebrain Parenchyma</td>
<td>30.580%</td>
<td>37.4%</td>
<td>30.270%</td>
<td>17.1%</td>
<td>1.019%</td>
<td>97.4% *</td>
</tr>
<tr>
<td>Cortical Gray Matter</td>
<td>15.402%</td>
<td>72.9%</td>
<td>15.581%</td>
<td>71.6%</td>
<td>-1.158%</td>
<td>54.2%</td>
</tr>
<tr>
<td>Cerebral White Matter</td>
<td>13.473%</td>
<td>17.4%</td>
<td>12.955%</td>
<td>4.7% *</td>
<td>3.918%</td>
<td>100.0% *</td>
</tr>
<tr>
<td>Lateral Ventricle</td>
<td>1.514%</td>
<td>88.4%</td>
<td>1.680%</td>
<td>95.2% *</td>
<td>-10.370%</td>
<td>22.8%</td>
</tr>
<tr>
<td>Inferior Lateral Ventricle</td>
<td>0.225%</td>
<td>100.0% *</td>
<td>0.146%</td>
<td>99.9% *</td>
<td>42.688%</td>
<td>96.8% *</td>
</tr>
<tr>
<td>Total CSF</td>
<td>1.880%</td>
<td>93.3%</td>
<td>2.065%</td>
<td>96.8% *</td>
<td>-9.344%</td>
<td>35.1%</td>
</tr>
<tr>
<td>Caudate</td>
<td>0.270%</td>
<td>84.3%</td>
<td>0.282%</td>
<td>46.2%</td>
<td>3.052%</td>
<td>87.8%</td>
</tr>
<tr>
<td>Putamen</td>
<td>0.318%</td>
<td>47.1%</td>
<td>0.274%</td>
<td>15.6%</td>
<td>14.866%</td>
<td>91.4%</td>
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<tr>
<td>Pallidum</td>
<td>0.041%</td>
<td>10.5%</td>
<td>0.050%</td>
<td>37.2%</td>
<td>-37.405%</td>
<td>1.4% *</td>
</tr>
<tr>
<td>Thalamus</td>
<td>0.518%</td>
<td>38.0%</td>
<td>0.475%</td>
<td>5.0% *</td>
<td>8.622%</td>
<td>94.9%</td>
</tr>
<tr>
<td>Amygdala</td>
<td>0.105%</td>
<td>23.7%</td>
<td>0.113%</td>
<td>43.8%</td>
<td>-7.521%</td>
<td>25.0%</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>0.191%</td>
<td>0.3% *</td>
<td>0.255%</td>
<td>36.6%</td>
<td>-28.811%</td>
<td>0.1% *</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>4.488%</td>
<td>87.0%</td>
<td>4.397%</td>
<td>84.7%</td>
<td>2.081%</td>
<td>88.3%</td>
</tr>
<tr>
<td>Brain Stem</td>
<td>0.663%</td>
<td>6.0%</td>
<td>0.783%</td>
<td>12.8%</td>
<td>-16.573%</td>
<td>27.8%</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Whole Brain Parenchyma (L+R)</th>
<th>L+R Volume (% of ICV)</th>
<th>% tile rank</th>
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<tbody>
<tr>
<td></td>
<td>71.181%</td>
<td>35.5%</td>
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**Virginia Institute of Neuropsychiatry**

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(866) 586-8977 (fax)
www.VaNeuropsychiatry.org

**Patient information**

DOB:
### NeuroQuant® Extended Report:

**Example of p. 1: Zoom in**

**Virginia Institute of Neuropsychiatry**

---

**Extended Volumetric Analysis based on NeuroQuant® data**

**Patient:**  
**Location of MRIs:**

**Date of MRI:**  
**Date of report:**

<table>
<thead>
<tr>
<th>Region</th>
<th>LH Volume (% of ICV)</th>
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<tr>
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<td>2.065%</td>
<td>96.8% *</td>
<td>-9.344%</td>
<td>35.1%</td>
</tr>
</tbody>
</table>
NeuroQuant® Extended Report:
Example of p. 1: Zoom in

<table>
<thead>
<tr>
<th>Tissue</th>
<th>L Volume</th>
<th>R Volume</th>
<th>% of ICV</th>
<th>% tile rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Putamen</td>
<td>0.318%</td>
<td>47.1%</td>
<td>0.274%</td>
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</tr>
<tr>
<td>Pallidum</td>
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</tr>
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Patient information

DOB:

Note: LH = left hemisphere. RH = right hemisphere. %tile = normative percentile. A/I = Asymmetry Index.
**−** indicates that the data were unreliable due to segmentation error.
**−** indicates a normative percentile which was statistically and clinically significant, defined as any of the following:
- A parenchymal region ≤ 5th normative percentile, consistent with atrophy
- A ventricular region ≥ 95th normative percentile, consistent with atrophy of the surrounding parenchyma
- Asymmetry index ≤ 2.5th or ≥ 97.5th normative percentile, consistent with atrophy of the smaller structure
- Asymmetry index ≤ 5th or ≥ 95th normative percentile for cases in which there were other unilateral, homodirectional signs of head or brain injury, including:
  - scalp contusions or lacerations
  - cranial fractures
  - unilateral brain abnormalities identified by the attending radiologist which are consistent with or associated with parenchymal atrophy
  - a second asymmetry index ≤ 5th or ≥ 95th normative percentile and homodirectional with the first asymmetry index

Inspection for image segmentation quality: NeuroQuant® segmented (color-coded) DICOM images were inspected visually by A.L.O. and D.E.R. The following segmentation errors were identified:
- None

Otherwise, the regions of interest were found to be accurately identified by the NeuroQuant® software.

Summary of positive findings: Abnormal volumes consistent with parenchymal atrophy were found in the following regions:
- The right whole brain parenchyma was significantly smaller than the left.
- The right forebrain parenchyma was significantly smaller than the left.
- The right cerebral white matter was significantly smaller than normal and was significantly smaller than the left.
- The right lateral ventricle was abnormally large.
- Both inferior lateral ventricles were abnormally large.
- The left inferior lateral ventricle was significantly larger than the right.
- The right total cerebral spinal fluid volume was abnormally large.
- The left pallidum was significantly smaller than the right.
- The right thalamus was abnormally small.
- The left hippocampus was abnormally small and significantly smaller than the right.

Virginia Institute of Neuropsychiatry

Patient information

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DOB:
NeuroQuant® Extended Report:
Example of p. 2: Zoom in

Virginia Institute of Neuropsychiatry

Note: LH = left hemisphere. RH = right hemisphere. %tile = normative percentile.
AI = Asymmetry Index.
“—” indicates that the data were unreliable due to segmentation error.
“*” indicates a normative percentile which was statistically and clinically significant,
defined as any of the following:
- A parenchymal region ≤ 5\textsuperscript{th} normative percentile, consistent with atrophy
- A ventricular region ≥ 95\textsuperscript{th} normative percentile, consistent with atrophy of the surrounding parenchyma
- Asymmetry index ≤ 2.5\textsuperscript{th} or ≥ 97.5\textsuperscript{th} normative percentile, consistent with atrophy of the smaller structure
- Asymmetry index ≤ 5\textsuperscript{th} or ≥ 95\textsuperscript{th} normative percentile for cases in which there were other unilateral, homodirectional signs of head or brain injury, including:
  - scalp contusions or lacerations
  - cranial fractures
  - unilateral brain abnormalities identified by the attending radiologist which are consistent with or associated with parenchymal atrophy
  - a second asymmetry index ≤ 5\textsuperscript{th} or ≥ 95\textsuperscript{th} normative percentile and homodirectional with the first asymmetry index

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**Summary of positive findings:** Abnormal volumes consistent with parenchymal atrophy were found in the following regions:
- The right whole brain parenchyma was significantly smaller than the left.
- The right forebrain parenchyma was significantly smaller than the left.
- The right cerebral white matter was significantly smaller than normal and was significantly smaller than the left.
- The right lateral ventricle was abnormally large.
- Both inferior lateral ventricles were abnormally large.
- The left inferior lateral ventricle was significantly larger than the right.
- The right total cerebral spinal fluid volume was abnormally large.
- The left pallidum was significantly smaller than the right.
- The right thalamus was abnormally small.
- The left hippocampus was abnormally small and significantly smaller than the right.

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**Virginia Institute of Neuropsychiatry**

(804) 594-7046 (voice)
(866) 586-8977 (fax)
www.VaNeuropsychiatry.org

**Patient information**

DOB: __________
Case example: Patient KM

• History
  – 46 years old
  – Motor vehicle accident

• Diagnoses
  – Traumatic brain injury, mild
    • Cognitive impairment
    • Dysphoria
    • Impaired sleep and wakefulness
Case example: Patient KM

Radiologist’s interpretation: Normal
Case example: Patient KM

NQ Extended Report:
Lateral ventricles:
Asymmetry index = 74.4%
100.0 normative %tile
NeuroQuant® Illustrations

Cerebral cortex

Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions
NeuroQuant® Illustrations

Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions
NeuroQuant® Illustrations

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NeuroQuant® Illustrations

Lateral ventricles
caudate nucleus
Putamen
4th Ventricle
Thalamus

Hippocampus
Midbrain
Pons
Medulla oblongata

Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions
Case example: Patient KM

Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions
NeuroQuant® Illustrations

Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions
Radiologist vs. NeuroQuant®

<table>
<thead>
<tr>
<th></th>
<th>N positive/ Total N</th>
<th>% positive for atrophy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiologist atrophy</td>
<td>2/20</td>
<td>10%</td>
</tr>
<tr>
<td>NQ Extended atrophy</td>
<td>10/20</td>
<td>50%</td>
</tr>
</tbody>
</table>

Paired sign test, test statistic $M = -4.00$, $P=0.02$

Reference
Case Example: Patient DG

MRI scan 2 years after injury

- NeuroQuant® results:
- Lateral ventricle: L > R
- Hippocampus: L small; L < R
Case Example: Patient DG

MRI scan 2 years after injury

- NeuroQuant® results:
  - Lateral ventricle: L > R
  - Hippocampus: L small; L < R
Case Example: Patient DG

MRI scan 2 years after injury

- NeuroQuant® results:
  - Lateral ventricle: L > R
  - Hippocampus: L small; L < R
Progressive enlargement of left lateral ventricle: Patient DG

CT scan
Date of accident

MRI scan
2 years later

Higher level in brain

Right occipital horn of LV
Left occipital horn of LV

Right occipital horn of LV
Left occipital horn of LV
Progressive enlargement of left lateral ventricle: Patient DG

CT scan
Date of accident

MRI scan 2 years later

Lower level in brain

Right occipital horn of LV
Left occipital horn of LV
Right occipital horn of LV
Left occipital horn of LV

CT scan

MRI scan 2 years later
Longitudinal Analysis

- Literature review of longitudinal studies of brain volumetry in patients with TBI
  - Definitions
    - Longitudinal design: 2 points in time
    - Cross sectional design: 1 point in time

Reference:
Longitudinal Analysis
Longitudinal Analysis
Literature review of longitudinal studies of brain volumetry in patients with TBI

- Literature review of longitudinal studies of brain volumetry in patients with TBI*
  - 10 studies
    - Mild to severe TBI
    - Mean time between injury and first MRI: 2.5 mos
    - Mean time between 1st and 2d MRI: 13.2 mos

Reference:
Literature review of longitudinal studies of brain volumetry in patients with TBI

- Literature review of longitudinal studies of brain volumetry in patients with TBI*
  - Consistent pattern of brain atrophy
    - Total brain parenchyma
    - Gray matter and white matter
    - Hippocampi

Reference:
Literature review of longitudinal studies of brain volumetry in patients with TBI

- Literature review of longitudinal studies of brain volumetry in patients with TBI*
  - Atrophy correlated with important clinical variables
    - Duration of loss of consciousness
    - Duration of coma
    - Posttraumatic amnesia
    - Hypoperfusion seen on SPECT scanning
    - Functional status measured by FSE and GOS-E

Reference:
Literature review of longitudinal studies of brain volumetry in patients with TBI

- Literature review of longitudinal studies of brain volumetry in patients with TBI*
  - Effect sizes much larger for longitudinal design vs. cross-sectional design

Reference:
### Review of Longitudinal Studies

<table>
<thead>
<tr>
<th>Measure</th>
<th>Number of studies</th>
<th>Effect size for cross-sectional analysis (mean)</th>
<th>Effect size for longitudinal analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole brain parenchymal volume</td>
<td>6</td>
<td>0.6</td>
<td>1.8</td>
</tr>
<tr>
<td>Hippocampal volume</td>
<td>2</td>
<td>0.6</td>
<td>1.9</td>
</tr>
</tbody>
</table>

- Effect sizes between patients with TBI and normal controls.
  - For effect size $d$:
    - small = 0.3
    - medium = 0.5
    - large = 0.7 or greater

**Reference:**
Literature review of longitudinal studies of brain volumetry in patients with TBI

• Literature review of longitudinal studies of brain volumetry in patients with TBI
  • Conclusions
    • All studies found progressive brain atrophy in patients with TBI.
    • Greater rates of atrophy correlated with worse vocational outcome.
    • The longitudinal design was more powerful than the cross sectional design for detecting differences between patient and controls.

Reference:
VIN Longitudinal Study

• Design
  • 16 patients with mild TBI vs. normal controls
  • Longitudinal design
    • Each subject had 2 MRI scans, about 1 year apart

Reference:
### VIN Research: Test-retest Reliability

<table>
<thead>
<tr>
<th>Brain region</th>
<th>Intraclass correlation coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total intracranial volume, Brain parenchyma, Cerebrospinal fluid, Forebrain</td>
<td>0.95 – 1.00</td>
</tr>
<tr>
<td>parenchyma, Cortical gray matter, Cerebral white matter, Lateral ventricle,</td>
<td></td>
</tr>
<tr>
<td>Inferior lateral ventricle, Caudate, Hippocampus, Cerebellum, Brainstem,</td>
<td></td>
</tr>
<tr>
<td>Fourth ventricle</td>
<td></td>
</tr>
<tr>
<td>Thalamus, Amygdala, Exterior cerebrospinal fluid</td>
<td>&gt;.90</td>
</tr>
<tr>
<td>Putamen</td>
<td>&gt;.85</td>
</tr>
<tr>
<td>Third ventricle</td>
<td>&gt;.80</td>
</tr>
<tr>
<td>Pallidum</td>
<td>&gt;.75</td>
</tr>
<tr>
<td>Ventral diencephalon</td>
<td>&gt;.35</td>
</tr>
</tbody>
</table>

Test-retest reliability for NeuroQuant® volumetric measures were mostly excellent.

**Reference:**
## VIN Longitudinal Study

<table>
<thead>
<tr>
<th>Brain regions</th>
<th>Sig. (2-tailed)</th>
<th>Effect size d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole brain parenchyma</td>
<td>0.003*</td>
<td>1.5</td>
</tr>
<tr>
<td>Forebrain parenchyma</td>
<td>0.003*</td>
<td>1.4</td>
</tr>
<tr>
<td>Cortical gray matter</td>
<td>0.579</td>
<td>0.2</td>
</tr>
<tr>
<td>Cerebral white matter</td>
<td>&lt;0.001*</td>
<td>1.4</td>
</tr>
<tr>
<td>Cerebrospinal fluid</td>
<td>0.805</td>
<td>-0.1</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>0.004*</td>
<td>1.5</td>
</tr>
<tr>
<td>Brainstem</td>
<td>0.074</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Comparisons of progressive brain atrophy between patients with mild TBI and normal controls.

Reference:
## VIN Longitudinal Study

<table>
<thead>
<tr>
<th>Brain region</th>
<th>Sig. (2-tailed)</th>
<th>Effect size d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole brain parenchyma</td>
<td>0.018*</td>
<td>-1.4</td>
</tr>
<tr>
<td>Forebrain parenchyma</td>
<td>0.016*</td>
<td>-1.4</td>
</tr>
<tr>
<td>Cortical gray matter</td>
<td>0.045*</td>
<td>-1.3</td>
</tr>
<tr>
<td>Cerebral white matter</td>
<td>0.817</td>
<td>-0.1</td>
</tr>
<tr>
<td>Cerebrospinal fluid</td>
<td>0.018*</td>
<td>1.6</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>0.04*</td>
<td>-1.3</td>
</tr>
<tr>
<td>Brainstem</td>
<td>0.201</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Comparisons of progressive brain atrophy between patient GOSE subgroups based on functional outcome.

### References:
Example of Progressive Ventricular Enlargement

Time 1

3D reconstruction of NQ segmented images

Time 2

Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions
Example of Progressive Ventricular Enlargement

3D reconstruction of NQ segmented images

Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions
Visualizing Progressive Atrophy

8/17/08 CT

Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions
Visualizing Progressive Atrophy

3/12/10 MRI

Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions
Visualizing Progressive Atrophy

8/17/08 CT

Courtesy of Michael Havranek, Medical Illustrator, Amicus Visual Solutions
Community Acceptance of NeuroQuant®

- NeuroQuant® is currently used in at least a dozen clinics and radiology centers across the USA:

  **West**
  
  Santa Rosa Imaging Center  
  3536 Mendocino Ave., Suite 280  
  Santa Rosa, CA 95403

  Dr. James Brewer  
  University of California, San Diego, CA

  San Joaquin Community Hospital  
  2615 Chester Avenue, Bakersfield, CA 93301

  Liberty Pacific Advanced Imaging  
  16130 Ventura Blvd., Suite 100, Encino, CA 91436

  Radnet, www.radnet.com  
  Sites in California

  **East**

  Lenox Hill Radiology & Medical Imaging Associates  
  61 East 77th Street, New York, NY 10075

  East River Medical Imaging, PC  
  519/523 East 72nd Street, New York, NY 10021

  Advanced Radiology  
  888 Bestgate Rd, Ste 101, Annapolis 21401

  Washington Radiology Associates  
  2141 K St. NW, Washington, DC 20037

  **South**

  Virginia Institute of Neuropsychiatry  
  364 Browns Hill Court, Midlothian, VA 23114

  Center for Neurorehabilitation Services  
  10710 Midlothian Turnpike, Suite 125, Richmond, VA 23235

  MRI CT Diagnostics  
  4668 Pembroke Blvd, Virginia Beach, VA 23455
MRI in Individual Patients

• Clinical implications
  • Objective signs of brain injury provide vindication for patients
  • Continuing brain atrophy can be a motivating factor for patients

• Forensic implications
  • Defense specialists often argue that a patient does not have any objective signs of brain injury
  • MRI may provide the best chance for objective findings of brain injury for many patients, especially patients with mild TBI
Recommendations

• Obtain NeuroQuantable MRI as soon as possible.
• Obtain follow up MRIs about 6 and 12 months later.
• In addition to NQ standard analysis, perform:
  • NQ Extended analysis
    • 15 brain regions (vs. 3 regions for NQ Standard)
  • Longitudinal analysis
    • % volume change per year

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