· Course Objectives

Course participants will first learn various methods for traditional identification of different kinds of lesions and abnormalities with in a scan, based on standard clinical review of the images.

Participants will be informed and come away with a basic knowledge of neuroimaging quantification techniques and how to conduct them.

Participants will learn fundamentals of how to extract clinically relevant information from commercially available programs as well as those that are open source.
Neuropsychologia, Volume 8, 1970

Two other journals

Cortex
Journal of Comparative and Physiological Psychology

Neuropsychological investigation with Luria’s methods 1984

“One of the main trends in Luria’s concept of psychological function is that complex behavioral processes are not "localized" but are distributed throughout the brain in "functional systems."

Neurophysiological evidence of these considerations has been found, e.g., in cerebral blood flow studies, and the newest histological findings concerning the diversity of human brains give further support.

Why we need to study networks

Oral Reading of a nonsense word

The Challenge of Scale and Complexity

One Cubic Millimeter =

80,000 Neurons
200,000 Glial Cells
4.5 million synapses
Virtual Dissection of Erin Bigler's Brain

A Bit More History

Operating theatre at the Montreal Neurological Institute ca. 1958. Assisting Wilder Penfield with the procedure is Herber Jasper (monitoring EEG up upper left portion of picture) and Brenda Milner (back to camera and interacting with patient).


The first EMI scanner designed by Hounsfield in 1971 was disassembled in the late 1970s and transferred from Atkinson Morley’s Hospital to the Science Museum in London.

Sir Godfrey Hounsfield

Introduced in the United States in 1973 at the Mayo Clinic.

Back to Arnold Starr’s HSE Case


Dense amnesia in a professional musician following herpes simplex virus encephalitis.

Interesting 3-D presentation of neuroimaging findings, with quantitative neuroimaging, but what does this tell us about neural systems, networks and neuropsychological outcomes?

Amnesia
neu2201.unsw.wikispaces.net/Amnesia

INS Symposium
Barbara Wilson
Morris Moscovitch
Erin Bigler

Neuropsychological assessment
In comparison to healthy controls, patients were cognitively impaired in several neuropsychological domains (Table 2). Patients had a significantly impaired working memory when compared with healthy controls (digit span test) and a substantial impairment in both verbal and visual learning and episodic memory (RAVLT/ROCF). Executive dysfunction became evident as increased error rate on the Go/No-Go test and a decreased semantic fluency. In contrast, the patients’ response times were

Fast Forward – 2018: What is Old, What’s New?

RESEARCH PAPER
J Neural Neurosurg Psychiatry 2018;0:1–9.

Beyond the limbic system: disruption and functional compensation of large-scale brain networks in patients with anti-LGI1 encephalitis
Josephine Heine,1 Harald Pols,1 Utta A. Kopp,1 Florian Wegner,2 Florian Them Bergh,3 Thomas Mönte,3 Claus-Peter Wandinger,3; Friedrich Paul,3 Thorsten Bartsch,4 Carsten Frühe4,5,6

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Correlations with memory performance. Alterations in functional connectivity significantly correlated with memory performance in patients with anti-LGI1 encephalitis (p<0.05, corrected for multiple comparisons). A better working memory performance was associated with higher functional connectivity between the dorsal DMN and the left middle/superior temporal and parahippocampal gyrus, the left temporal pole as well as the cingulate cortex (digit span test, p=0.012). Likewise, episodic memory function was better with increased connectivity between the ventral fraction of the DMN and the left inferior temporal gyrus and fusiform cortex (RAVLT interference, p=0.005). This points to a potential functional compensatory mechanism.
During the acute phase, hippocampal T2/FLAIR hyperintensities on routine MRI were seen in the majority of patients (21/27 patients; 77.7%); unilateral in 8/27 patients (29.6%); bilateral in 13/27 patients (48.1%)), while in 6 patients (22.3%) no hippocampal abnormalities were present (Table 1). At the time of resting-state data acquisition (follow-up), initial hyperintensities evolved into unilateral (in 55.6%) or bilateral (55.6%) visually detectable hippocampal atrophy, while 11.1% of the patients showed no hippocampal atrophy (Table 2). Furthermore, patients and controls did not differ on global measures of whole brain volume (1.223 ± 0.33 × 10^6 mm³ vs 1.191 ± 0.29 × 10^6 mm³, p=0.697) and total grey matter volume (0.567 ± 0.01 × 10^6 mm³ vs 0.591 ± 0.01 × 10^6 mm³, p=0.172) at follow-up. VBM analysis revealed no further cortical volume change and there was no evidence of structural white matter damage as assessed using DTI.

Results showed that alcoholics' long-term (but not short-term) memory performance correlates significantly with thalamic CT density numbers in the region of the dorsomedial nucleus and with third ventricle/intracranial width ratio.
From early biological work and the first T1 nuclear magnetic resonance (n.m.r.) animal image in 1974, whole-body patient images, by using a two-dimensional Fourier transform method were achieved in Aberdeen in 1980 with a 0.04 T vertical resistive magnet. Different pulse sequences produce images dependent by different amounts on proton density, T1 and T2, and for clinical work it is advantageous to use more than one pulse sequence to image pathology. The slow improvement of spatial resolution with increasing standing magnetic field strength is discussed and information on the T1 and T2 contrast dependence is reviewed: it suggests that the gains from high fields may be less than believed hitherto. Electrocardiogram gating can be used to produce moving images of the beating heart; blood flow can be imaged and surface radiofrequency coils are used for improved detail. N.m.r. imaging has considerable potential for studying response to therapy; mental states and dementia; tissue generation; discriminating body fat and body fluids. Other nuclei such as 23Na can be imaged and the potential to image fluorine-labelled pharmaceuticals could be very exciting; n.m.r. contrast agents are now being developed. Images formed from T1 values measured for each pixel are very useful for diagnosis, but the numerical values themselves are less valuable for distinctive pathological identification. With 15 companies manufacturing n.m.r. imagers and over 200 in use in hospitals, the technique is rapidly becoming established in diagnostic clinical practice and some typical uses are presented.


"As these techniques become more and more automated, we should be able to quantify directly a variety of parameters of the brain, including the amount of white versus gray matter, ventricular volume, hemispheric volume, subcortical nuclei, normal asymmetries, etc. These anatomic measurements may be critical parameters with respect to manifestations of certain neurological disorder states. Accordingly, the statistical emphasis that has played such an important role in neuropsychology needs to be applied to brain imaging as well." - 1989


196 Subjects: 4 years of image analysis


200 Subjects: 4 years of image analysis


97 Subjects: 3 years of image analysis

Automated Image Analysis and Supercomputing Game Changers!!

FreeSurfer* as an automated platform introduced in 2003 and BYU’s Super Computer comes online in 2006

2008 Use to Date: 320 scans used

21,370 hours or 890 days or 2.45 years of processor “time” based on standard single computer time to calculate the FreeSurfer analysis.

The supercomputer did it in roughly a week’s time!

Why is image Quantification Important?
Why is image Quantification Important?

**Proposal for a hierarchical, multidimensional, and multivariate approach to investigate cognitive aging**

Alejandra Machado,†, Joel Barros, Yolanda Molina, Ana Pimentel, Leticia Díaz-Ríos, Icíar Westman, Daniel Ferrer,∗

†Research Unit of Mental Health and Neuropsychological Disorders, University of Vigo, Vigo, Spain

∗Department of Neurology, Hospital Universitario de Canarias, La Laguna, Tenerife, Spain

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**Table 1. The association of age with MRI measures (ORR) model.**

<table>
<thead>
<tr>
<th>Brain compartment</th>
<th>Model</th>
<th>Markers</th>
<th>Number of markers</th>
<th>β1</th>
<th>SE</th>
<th>P1</th>
<th>P2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gray matter</td>
<td>1</td>
<td>Control thickness</td>
<td>61</td>
<td>248.36</td>
<td>0.046</td>
<td></td>
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<tr>
<td></td>
<td>2</td>
<td>Control volume (V)</td>
<td>61</td>
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<td></td>
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<tr>
<td></td>
<td>3</td>
<td>Control volume (V)</td>
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<tr>
<td></td>
<td>4</td>
<td>Subcortical structures (V)</td>
<td>11</td>
<td>234.34</td>
<td>0.012</td>
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<td></td>
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<tr>
<td>Cortical system</td>
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<td>Control thickness + white matter (V)</td>
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**Figure:**

- Image with bar chart showing quantitative analysis.
- Image with graphs illustrating statistical data.
- Image with tables summarizing experimental results.

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**Conclusion:**

Image quantification is crucial for elucidating the structural and functional changes associated with cognitive aging. By employing a hierarchical, multidimensional, and multivariate approach, researchers can gain deeper insights into the complex mechanisms underlying cognitive decline. Further studies are needed to validate these findings and explore potential therapeutic interventions.
Why is image Quantification Important?

What You Can Do Now!!
A Semiquantitative Approach

It All Begins with the Digital Imaging and Communications in Medicine (DICOM) File

National Academy of Neuropsychology: Series on Evidence-Based Practices

Bigler 2017: Evidence-Based Integration of Clinical Neuroimaging Findings in Neuropsychology
The hippocampus is affected early and severely in the AD pathological process (Braak and Braak, 1991; West et al., 1994), and the volume of this brain structure is the most widely applied (Jack et al., 2011b) and only qualified (Hill et al., 2014) MRI imaging biomarker in AD (p.480).
What is the LESION?

White Matter
- T1, T2, and FLAIR
- MRS
- Dendrite
- Astrocyte
- Oligodendrocyte
- Axon
- Nucleus
- Neuron
- Blood Vessel
- Axon Terminals

Cell death – atrophy/encephalomalacia
T1-based Volumetrics
Hemorrhage
GRE/SWI

When to measure?

Dynamic Changes – Time post-injury
fMRI Contralateral Motor Activation

DTI Color Map

Blue – FA Positively Correlated with Motor Function

Traven et al., Developmental Science, 2016 and J Autism Dev Disord., 2015

The Future of Assessment – Gaming World, Meets Clinical Assessment and Standardization and Virtual Environments

The lesion localization Effects of TBI

Ever Changing, Improved Technology
Potential Components to Network Modeling

- Structural Imaging
- Volumetric/Shape Imaging
- Diffusion Tensor Imaging (DTI)
- DTI Tractography
- Resting State Functional MRI (rs-fMRI)
- Connectivity Matrix
- Network Plot
- Network Complexity

“Functional Systems” : These systems are organized so that each cortical zone contributes in a specific way in accordance with its position within the cortical hierarchy and in accordance with the rules of innervation and inhibition. Therefore, for a complex behavioral act to be performed in a precise and smooth manner, the coordinated and governed working of all cortical areas responsible for the elements of the act is a necessary condition.

It’s Time to Fully Integrate Neuroimaging with Neuropsychology. Clinical Neuropsychology WILL NOT advance without taking this step.

Neural Networks, Connectivity and Traumatic Brain Injury

- Principal strain at time of peak

Neuropsychology’s Failure in Understanding Mild TBI

"First, mTBI is a self-contained condition that resolves quickly without special treatment, a generally accepted conclusion by fair-minded neuropsychologists (xiii)"

Manfred F. Greiffenstein, Ph.D

"Could this possibly be an accurate statement? If not, why do neuropsychologists believe this to be the case?"

"Results indicate that, in contrast to the prevailing view that most symptoms of concussion are resolved within 3 months post-injury, approximately half of individuals with a single mTBI demonstrate long-term cognitive impairment."


"CONCLUSIONS AND RELEVANCE: In this cohort study of more than 350,000 veterans, even mild TBI without LOC was associated with more than a 2-fold increase in the risk of dementia diagnosis."
Madsen et al. Traumatic brain injuries (TBIs) can have serious long-term consequences, including psychiatric disorders. However, few studies have assessed the association between TBI and risk of suicide. *JAMA*. 2018 Aug 14;320(6):580-588. doi: 10.1001/jama.2018.10211.

**CONCLUSIONS AND RELEVANCE:**
In this nationwide registry-based retrospective cohort study individuals with medical contact for TBI, compared with the general population without TBI, had increased suicide risk.
Inferior Frontal Damage - TBI

Key: Lfx = Linear Fracture, Bfx = Basilar Skull Fracture, EDH = Epidural Hematoma, SDH = Subdural Hematoma, Lfx = Lateral Fracture, MS = Midline Shift
The Relation of Focal Lesions to Cortical Thickness in Pediatric Traumatic Brain Injury

Must Embrace the Heterogeneity of Brain Pathology

Heterogeneity in TBI
- Focal Encephalomalacia
- Focal Hemosiderin Deposition
- Focal White Matter Hyperintensities

Closed Head Injury: Right Side Weakness, Aphasia, Confusion
The Integration of Neuropathological with the Neuroimaging and Neuropsychological Outcome

How nice would it be?

White Matter Hyperintensity and Volumetrics in Mild TBI

CENC Study

Where Volumetric Differences Reside in CENC Case

Cerebral tract integrity relates to white matter hyperintensities, cortex volume, and cognition
What Should We Measure and When?
What Neuroimaging Modality Should Be Used

2 Weeks Post

5 Months Post
Diffusion Tensor Imaging

FA = low
ADC = high

IA = decreased
ADC = increased


Network Damage and the lesion localization Effects of TBI
Fig. 1. Representative example of DTI streamlines passing through the vicinity of a ∼4 mm³ CMB (red) in an old adult victim of mTBI. Arrows indicate a CMB in the left hemisphere, close to a streamline bundle belonging to the splenium of the corpus callosum. (A) Standard views (coronal, sagittal, and axial) of T1-weighted MRI are shown in addition to DTI glyphs associated with perilesional WM streamline bundles imaged acutely (orange) and approximately 6 months after injury (light blue). The splenium is notably asymmetric at both time points, with the asymmetry being most pronounced close to the CMB (inset). (B) Splenial streamlines ipsilateral to the CMB diverge briefly in its vicinity, and this is not found to occur contralateral to the CMB (inset). This asymmetry is also found at the time of the chronic scan. Abbreviations: DTI, diffusion tensor imaging; CMB, cerebral microbleed; mTBI, mild traumatic brain injury; MRI, magnetic resonance imaging; WM, white matter.
21st Century Neuroimaging Methods

- Structural Imaging
- Volumetric/Shape Imaging
- DTI Tractography
- Resting State Functional MRI (rs-fMRI)

Potential Components to Network Modeling

- Connectivity Matrix
- Network Plot
- Network Complexity

Why Neuroimaging is Critical in understanding SVT/PVT findings

"Every Behavior Has an Anatomy" – Norman Geschwind, M.D.
https://www.youtube.com/watch?v=uh8C2A2kkgps

IT'S MUCH MORE COMPLICATED IN THERE THAN WE THOUGHT.