3D VOLUMETRY & DIFFUSION TENSOR IMAGING POSTPROCESSING, APPLIED RESEARCH RESULTS

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DEMENTIA/MILD CONGITIVE IMPAIRMENT - POSSIBILITIES, OPTIONS

- Visual rating – sulcii, ventricles, extracerebral liquorspaces – e.g. Scheltens-scale
- Planimetry – simple 2D measurements – the width of the III. ventricle or measuring the ventricle/brain ratio
- Volumetry – half automatized measurement to assess brain volumen data, cortical thickness, etc.
- Diffusion tensor imaging (DTI) – half automatized measurement to assess white matter data

- Resting state – half automatized measurement to assess functional connectivity impairment
- Automatized measurement to assess all above in the future…

DEMENTIA/MILD CONGITIVE IMPAIRMENT - POSSIBILITIES, OPTIONS

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VOLUMETRY

Pros:

- It is (can be) detailed and accurate
- Good predictor in early stages as well

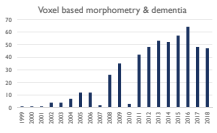
Cons:

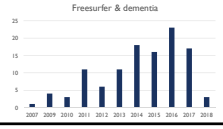
- Slow (can be)
- Needs dedicated software and routine
- Database is needed and hard to interpret results on single subject

MOST OFTEN USED SOFTWARE

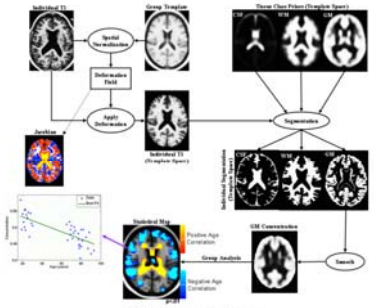
2 softwares are widely used in research

- SPM (voxel based morphometry toolbox)
  - Developed by UCL and Zürich universities
  - multimodal processing, analysis sw. (fMRI, PET, EEG)
  - Runs on windows, but the ui tidious and you better get familiar with Matlab
  - Faster than Freesurfer
- Freesurfer
  - Harvard developed
  - Needs Linux enviroment
  - You better get familiar with VMs if you don't dedicate a computer for it
  - Gives a wide type and amount of data
  - Slow (?)



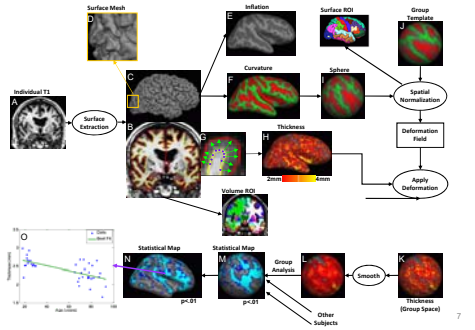


VBM Analysis Pipeline Overview



VBM Processing Stream

FreeSurfer Analysis Pipeline Overview



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VBM VS. FREESURFER

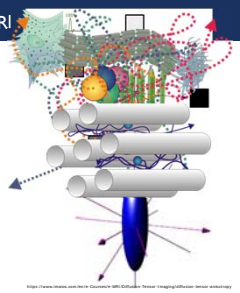
- VBM uses linear and non-linear deformation for intersubject analysis
- Freesurfer uses white matter geometry data (mesh) to inflate brain for intersubject analysis
- In essence VBM is Statistical Parametric Mapping of regional segmented tissue density or volume *
  - The exact interpretation of gray matter density or volume is complicated, and depends on the preprocessing steps used *
  - It is not interpretable as neuronal packing density or other cytoarchitectonic tissue properties *
  - The hope is that changes in these microscopic properties may lead to macro- or mesoscopic VBM-detectable differences

VBM VS. FREESURFER

- In Freesurfer one derives morphometric measures from geometric models of the cortical surface
- The yellow line is the surface boundary between cortical white matter and cortical gray matter known as the white surface; this represents the inner boundary of cortex.
- The red line is the boundary between the gray matter and dura and/or CSF; this is referred to as the pial surface.
- The cortex is modeled as a surface model which is a mesh of triangles as shown in the Figure. Each triangle is known as a face. The place where the corners of the triangles meet is called a vertex.

DIFFUSION WEIGHTED MRI

- Diffusion: Random (Brownian) motion of EC water molecules
- Hindering elements ↔ Tissue microstructure
  - CSF: ≈ free, isotropic
  - Grey matter: hindered, isotropic
  - White matter: restricted, anisotropic
  - Early pathological changes on cellular level ↔ disruptions
- Dedicated MRI-sequence → diffusion profile

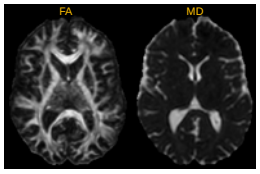


https://www.imaios.com/en/e-Courses/e-MRI/Diffusion-Tensor-Imaging/diffusion-tensor-anatomy

DTI – TENSOR MODEL

- Diffusion profile ≈ ellipsoid (tensor)
  - 6 independent components
  - Gaussian process
- Tensor eigenvalues – shape and orientation
  - Color coding,
  - Tractography
- Scalar parameters:
  - Fractional anisotropy (**FA**: Shape – how stretched is the ellipsoid?)
  - Mean diffusivity (**MD**: Size – „volume" of the ellipsoid)

http://www.diffusion-imaging.com/2013/10/what-is-diffusion-tensor.html



EXPLORE… – DTI

- Movement correction
- EPI correction (T1 registration)
- Susceptibility correction (induced distortion)
- Eddy current correction
- Tensor fitting
  - Outlier rejection

MILD COGNITIVE IMPAIRMENT=MCI

- Affects elderly most often
- Memory decline (noticed by patient or relatives)
- Mild decline in cognitive functions
- Self-care intact
- Dementia criteria are not met
- MCI most often precedes dementia
  - Conversion to dementia from MCI is about **10-15%**, compared to 1-4% in healthy elderly, which means they are **risk population** (Mitchell et al. Neurobiol Aging 2007)

MCI SUBTYPES

Amnestic MCI (aMCI): (memory impairment)		**Non-amnestic MCI (naMCI):** (executive, spatial-visual, language function impairment)	
Single-domain	Multi-domain	Single-domain	Multi-domain
Progression leads most often to **Alzheimer type dementia**		Progression leads most often to **non Alzheimer type dementia** (fronto-temporal dementia, Lewy-body dementia, Parkinson disease)	

AIMS

- To find a good clinical predictor
- To find potential central nervous structural differences that are helping clinicians to differentiate amnestic and non-amnestic subtype and to establish a proper diagnosis

METHODS

- Demographic and psychosocial status
- depression and anxiety tests (to exclude pseudodementia):
  - Geriatric Depression Scale (GDS)
  - Spielberger Trait- and Anxiety Scale (STAI)
- Cognitive function exploration:
  - Addenbrooke Cognitive Tests (AKV)
  - Mini Mental State Examination (MMSE) (exclude developed dementia)
  - Rey Auditory and Verbal Learning Test (RAVLT)
  - Trail Making Test A and B (TMT)
- MR scanning (3T Philips Achieva, 3D-T1, T2, Flair, DTI, T2-FFE, resting state)

SUBJECTS

62 subjects were involved

24 healthy control	**18 naMCI**	**20 aMCI**
Mean age: 65,5 years (SD: 7,6)	Mean age: 71 years (SD: 7,3)	Mean age: 71 years (SD: 11,3)

- No significant differences in age, sex and education between the 3 groups ($p>0,05$)
- **Excluding criteria:**
  - dementia: MMSE, age- and education specific cutoff values (min. limit: 21, max. limit: 27)
  - depression: GDS – no recent or actual depression episode (no sign. group diff. ($p > 0.1$))
  - trauma, epilepsy, mental retardation, psychotic episode or organic psychosindrome

DIAGNOSIS

aMCI: Petersen criteria (Petersen et al. 2009)	**naMCI**
• Subjective memory decline	• Memory functions are intact
• Daily activity intact	
• Objective memory decline (Rey test 1-5 or delayed remembrance, age specific cutoff values)	• Trail Making Test B or AKV sum (age, sex/education spec. cutoff values) • and VL/OM<3,2 (AKV)
• Intact global mental functions (MMSE)	
• Dementia criteria not met	

MR EXAMINATION PARAMETERS

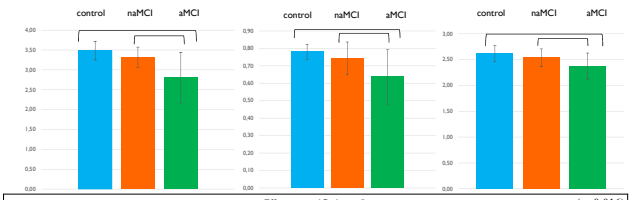
- 3D-T1 images were aquired on a 3T Philips MR
  - 3T Philips Achieva, sag. 3D-T1 (1 mm), axi. T2, FLAIR, DTI
- Processing: Freesurfer
  - Motion correction
  - BET
  - Talairach transformation
  - Segmentation
  - Normalization
  - Topology correction
  - Cortical model fitting
- Group wise statistics: SAS

REGIONS OF INTEREST

- **Hippocampus**
- **Entorhinalis cortex**
- **Gyrus parahippocampalis**
- Gyrus fusiformis
- Lobus parietalis superior
- Lobus parietalis inferior
- Gyrus cinguli posterior
- **Isthmus cinguli**
- **Precuneus**
- Gyrus temporalis superior
- Gyrus temporalis medius
- Gyrus temporalis inferior
- Gyrus supramarginalis
- **Amygdala**

BETWEEN GROUP DIFFERENCES: CONTROL VS. AMCI & NAMCI VS. AMCI

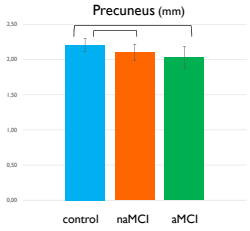
Entorhinal cortex (mm) | Hippocampus volumen (%) | Gyrus fusiformis (mm)



Effect size (Cohen d)			(p<0.016)
control – aMCI	1,6	1,4	1,2
naMCI - aMCI	1,2	0,8	0,8

VOLUMETRY – BETWEEN GROUP RESULTS: CONTROL VS. AMCI AND CONTROL VS. NAMCI

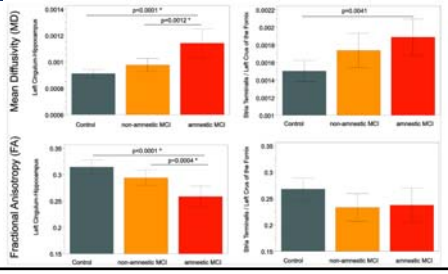
Precuneus (mm)



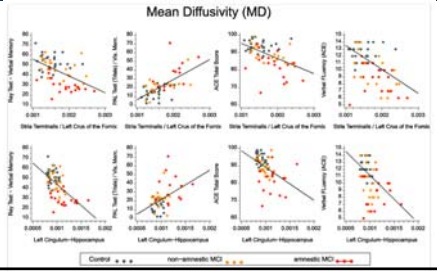
(p<0.016)

	Effect size (Cohen d)
control – aMCI	1,5
control - naMCI	1,1

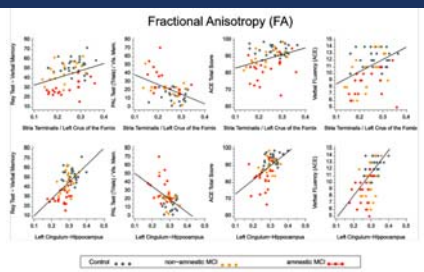
DTI (MD, FA) – BETWEEN GROUP RESULTS: CONTROL VS. AMCI AND CONTROL VS. NAMCI



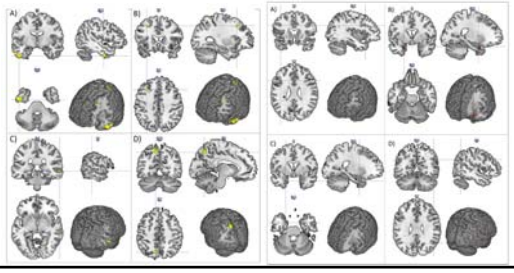
DTI (MD) – BETWEEN GROUP RESULTS: CONTROL VS. AMCI AND CONTROL VS. NAMCI



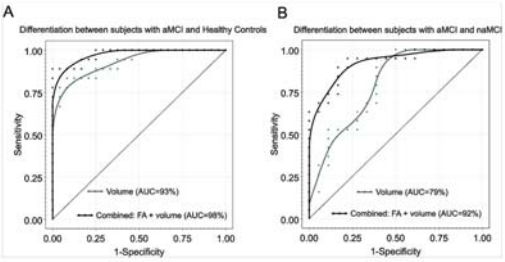
DTI (FA) – BETWEEN GROUP RESULTS: CONTROL VS. AMCI AND CONTROL VS. NAMCI



DTI (LOC) – BETWEEN GROUP RESULTS: CONTROL VS. AMCI AND CONTROL VS. NAMCI



DTI (ROC CURVES) – BETWEEN GROUP RESULTS: CONTROL VS. AMCI AND CONTROL VS. NAMCI



RESULTS - SUMMARY

- Volumetry: hippocampus, gyrus fusiformis, precuneus, enthorinal cortex
- DTI: hippocampus – left cingulum // stria terminalis – left crus of fornix

RESULTS - SUMMARY

- Volumetry: hippocampus, gyrus fusiformis, precuneus, enthorinal cortex
- DTI: hippocampus – left cingulum, stria terminalis – left crus of fornix
- Mild cognitive impairment subtype (amnestic – non-amnestic) differences are not only based on empiric data
- These structural differences are early predictors
- Amnestic MCI has a medial-temporal focus, while naMCI has a more diffuse involvement

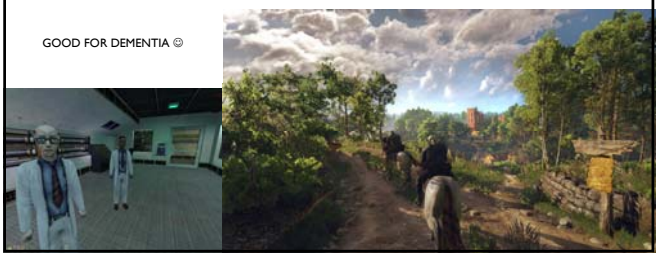
CONCLUSIONS

- Subtype grouping is useful in predicting developing dementia type and risks
- Structural MR analysis (3D-T1, DTI) is a very good clinical tool for clinicians
- Helps in disease follow-up and therapy adjustment

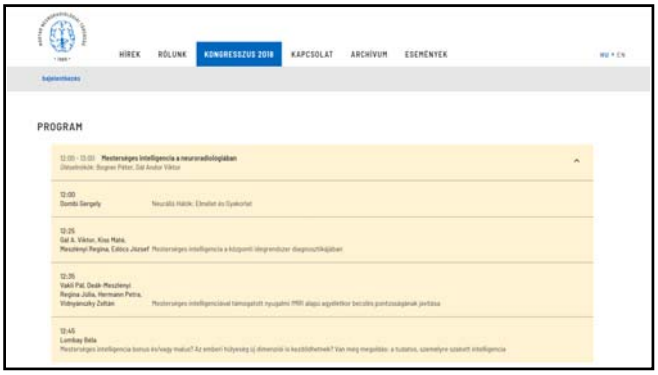
THE FUTURE…

WAIT…VIDEO GAMES?

GOOD FOR DEMENTIA ☺



AI?



THANK YOU FOR YOUR ATTENTION!