

2017 認知巡迴工作坊

臨床應用：科學化與醫療的舞曲

神經影像在神經與精神疾病的應用

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中國醫藥大學附設醫院 放射線部

2017. Jul. 10



2017



07 認知巡迴 10 工作坊 腦動一夏

來場認知神經科學初體驗 地點：高雄醫學大學、濟世大樓915

09:10 心腦同源：認知神經科學縱橫談
10:00 中央 張智宏教授

10:10 安全第一：磁振造影安全大小事
11:00 中山 莊子肇教授

11:10 不只這樣：連神經走向也看得出
12:00 高醫 周銘鐘教授

國立政治大學 台灣心智科學腦造影中心
國立政治大學 心理系

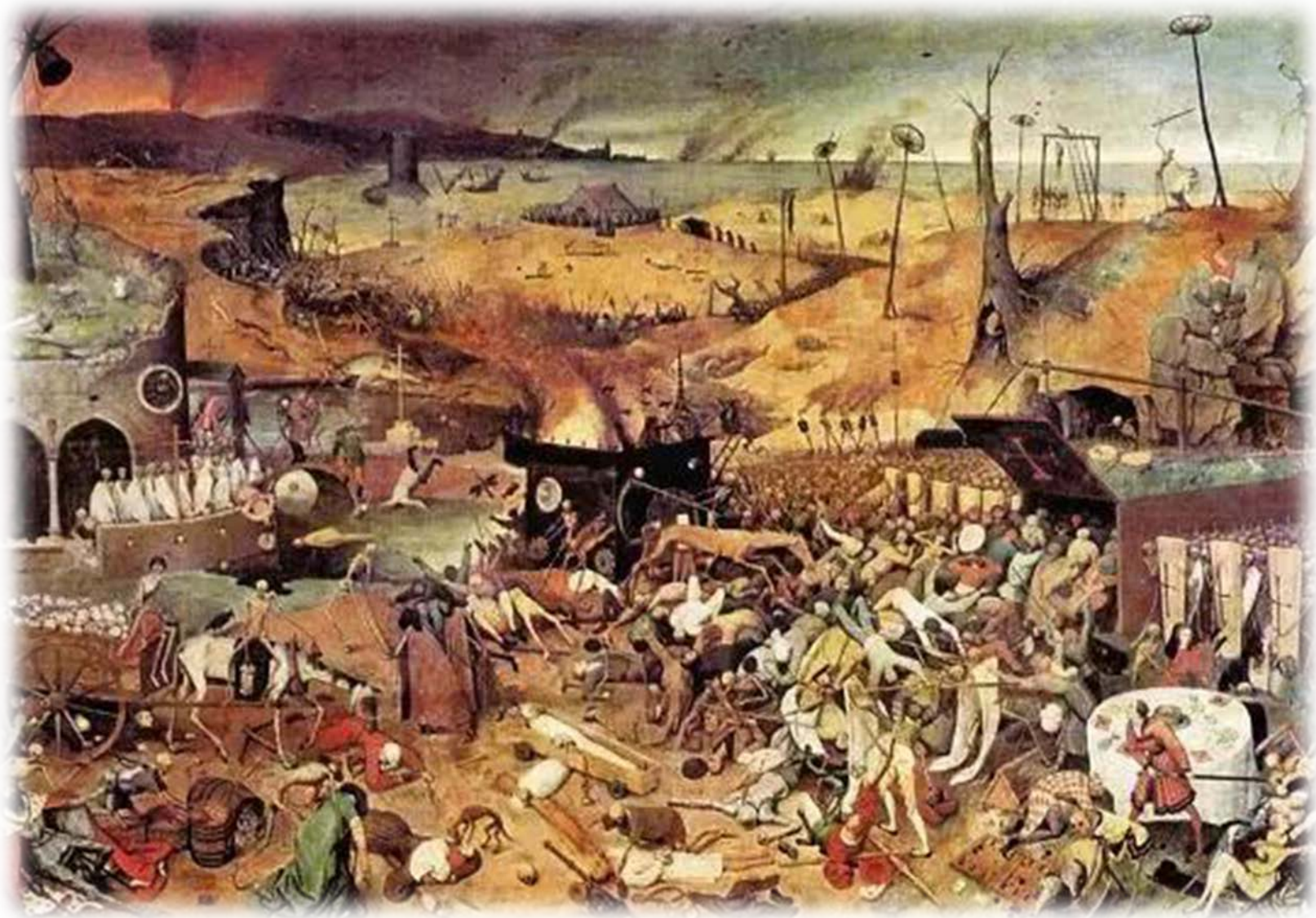
13:10 見微知著：數學居然算得出大腦
14:00 政大 張葶葶教授

14:10 臨床應用：科學化與醫療的舞曲
15:00 中國醫 陳君明 博士後研究員

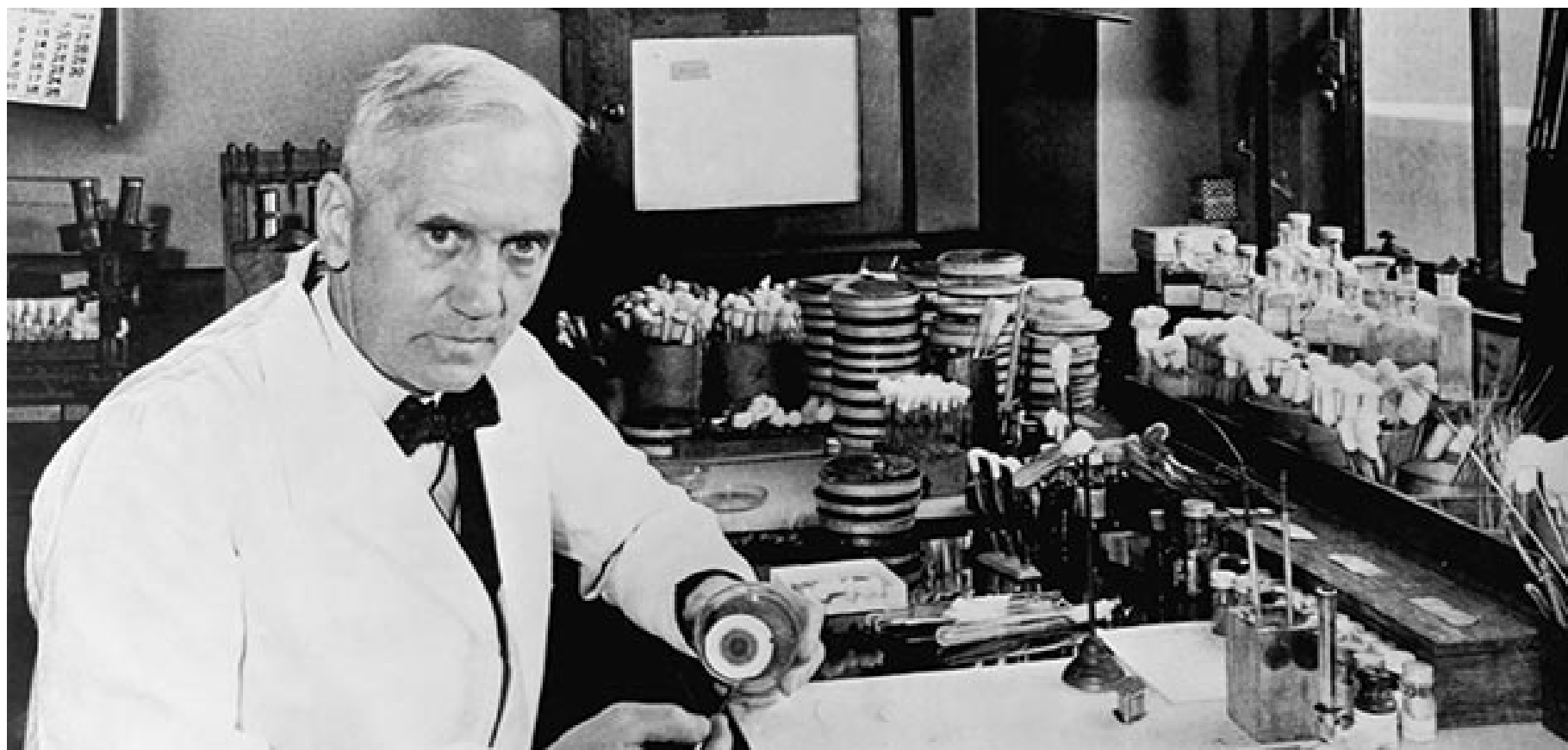
15:10 最終賽局：讓決策思考變得科學
16:00 政大 陳尹華 博士後研究員

高雄醫學大學 非線性分析及優化研究中心
高雄醫學大學 心理學系 / 醫教系

共同主辦



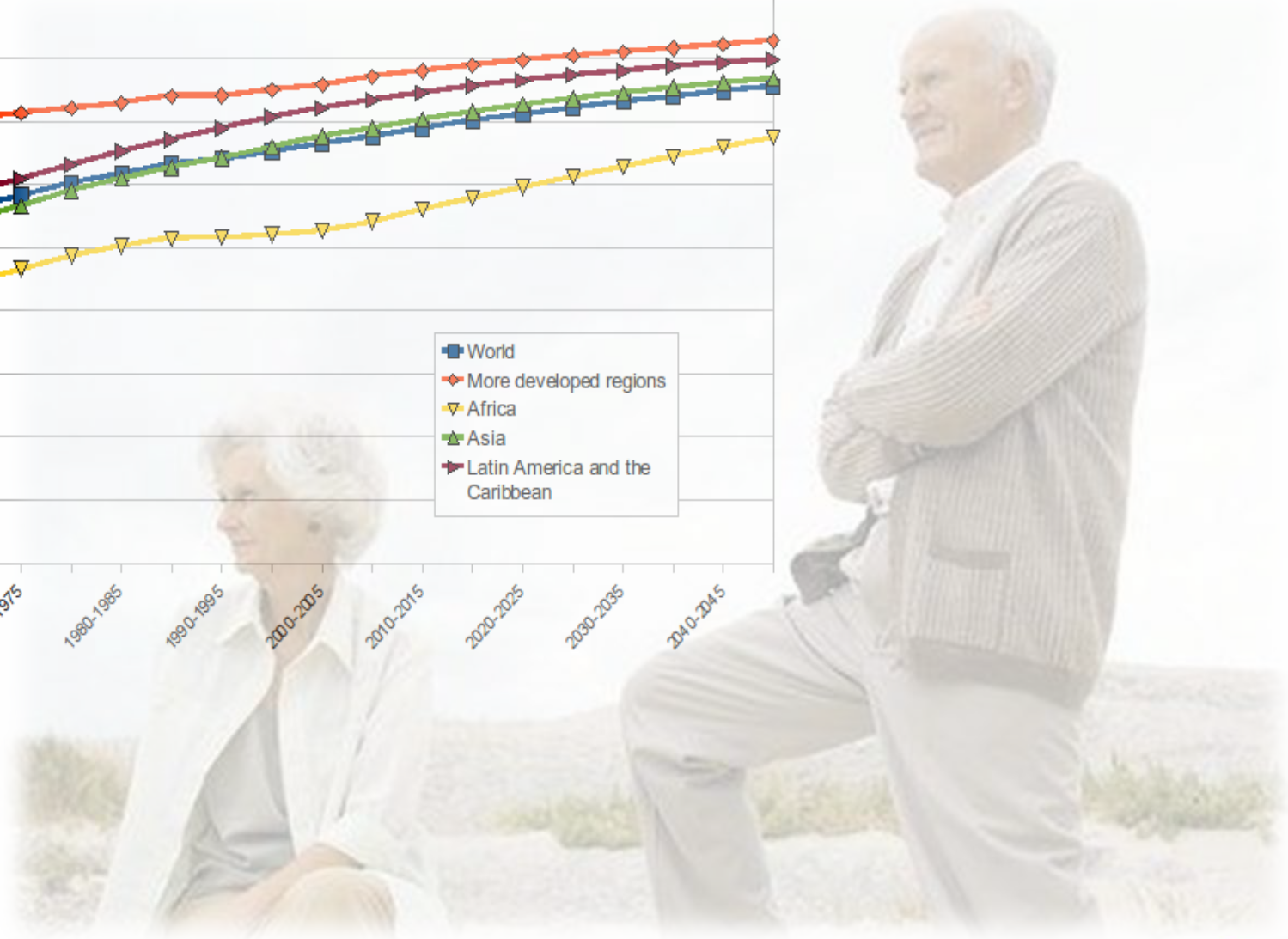
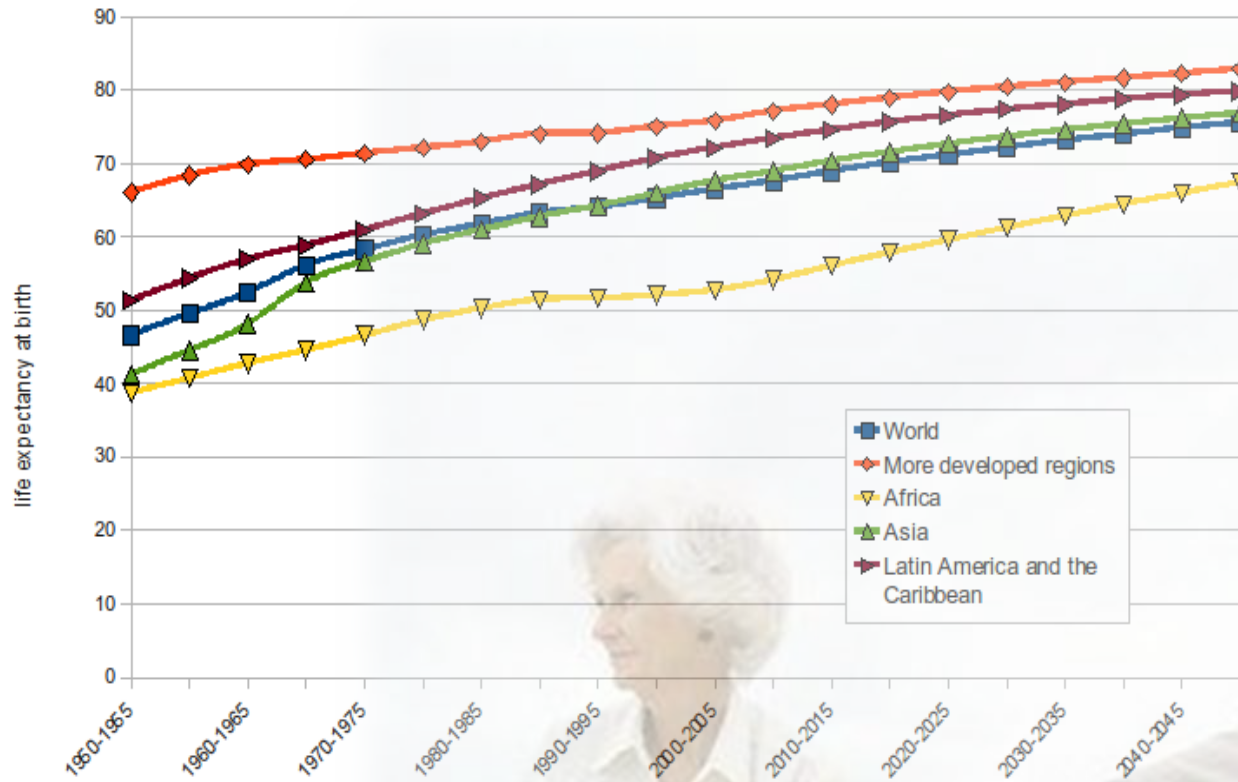


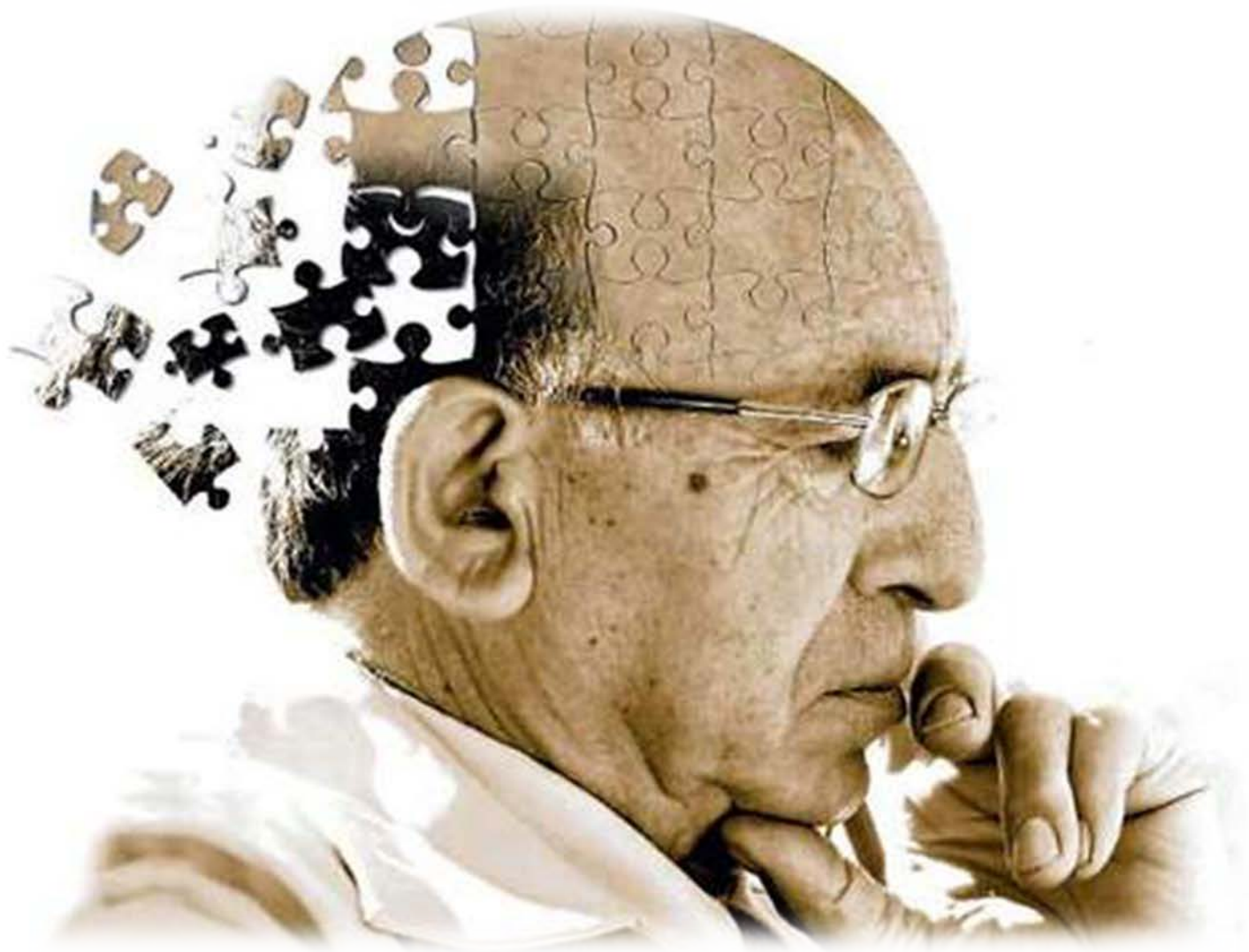


亞歷山大弗萊明

Life Expectancy at Birth by Region, 1950-2050.

Source: UN World Population Prospects, 2008.





Stress



Affected Diseases

- **Neurodegenerative disorders**
 - Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease, Amyotrophic lateral sclerosis (ALS)
- **Neurodevelopmental disorder**
 - ADHD
- **Mental disorder**
 - Major depression, schizophrenia, bipolar disorder, anxiety disorder...

Difficulty

- Unclear mechanisms
- Progressive (neurodegenerative illness)
- Heterogeneous (mental illness)
 - Symptom (subtype)
 - Treatment outcome
 - Recurrent
- Lose the ability to enjoy life!!

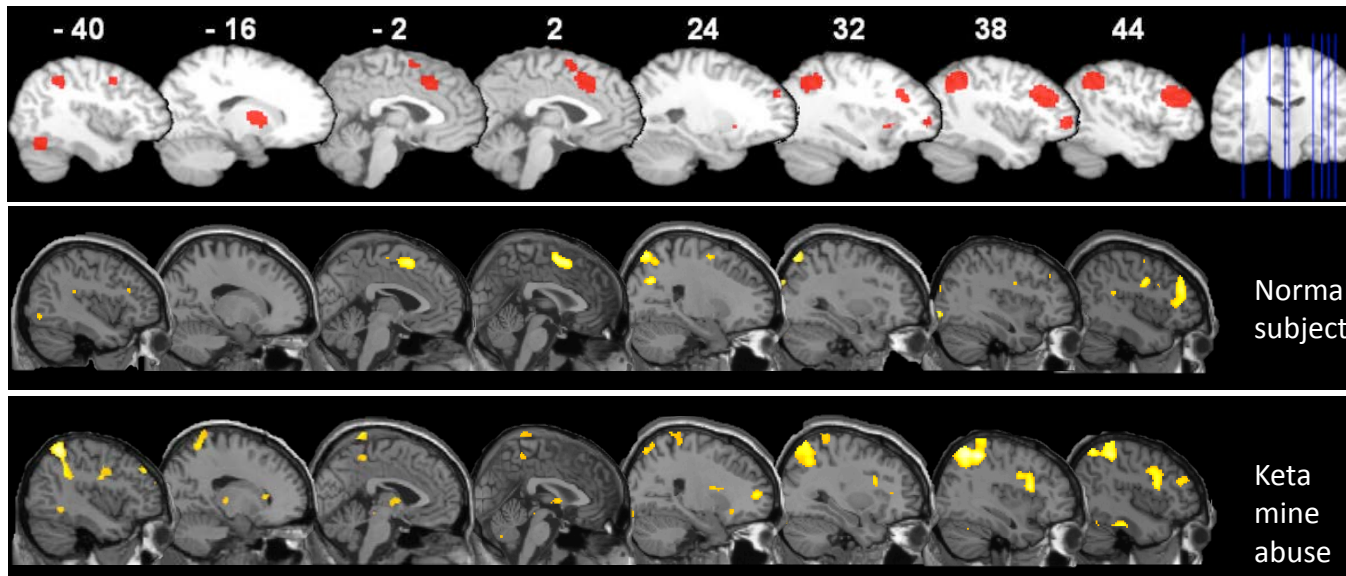
**Cognitive
neuroscience**

Neuroimaging

**Clinical
Medicine**

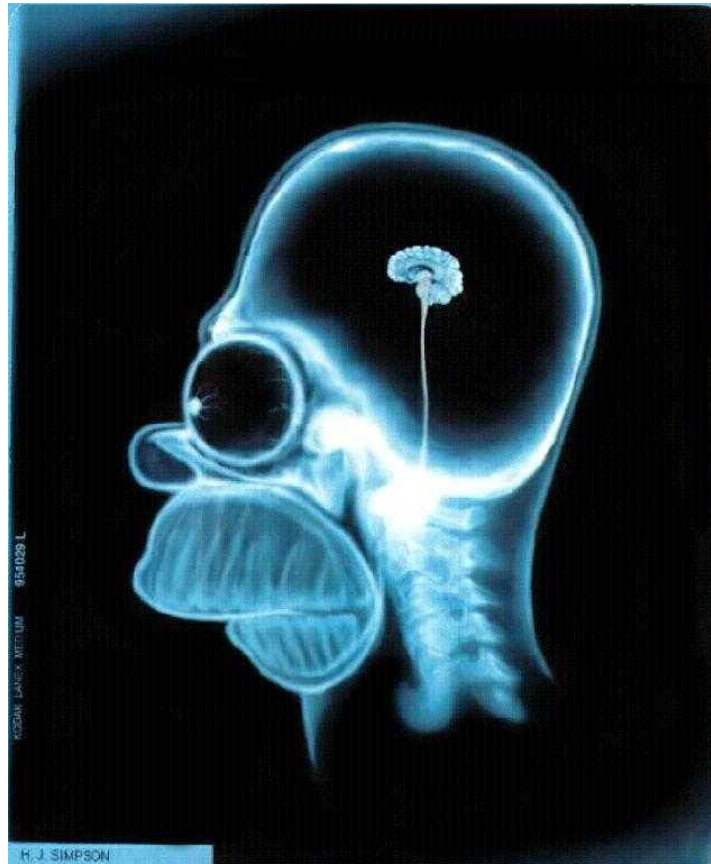


Why neuroimaging?



		Correction Rate		Error Rate		Avg. Reaction Time (ms)
		No-Go	Go	No-Go	Go	
Normal	R	98% (49/50)	100% (50/50)	2% (1/50)	0% (0/50)	436.66
	L	98% (49/50)	100% (50/50)	2% (1/50)	0% (0/50)	465.18
Ketamine	R	98% (49/50)	96% (48/50)	2% (1/50)	4% (2/50)	534.42
	L	98% (49/50)	52% (26/50)	2% (1/50)	48% (24/50)	569.81

What's neuroimaging??



Everything that can image your brain

Neuroimaging in hospital

- **Magnetic Resonance Imaging (MRI)**
- Computed Tomography (CT)
- Positron Emission Tomography (PET)
- Single Photon Emission Computed Tomography (SPECT)
- Electroencephalography (EEG)
- Ect...



It's our routine

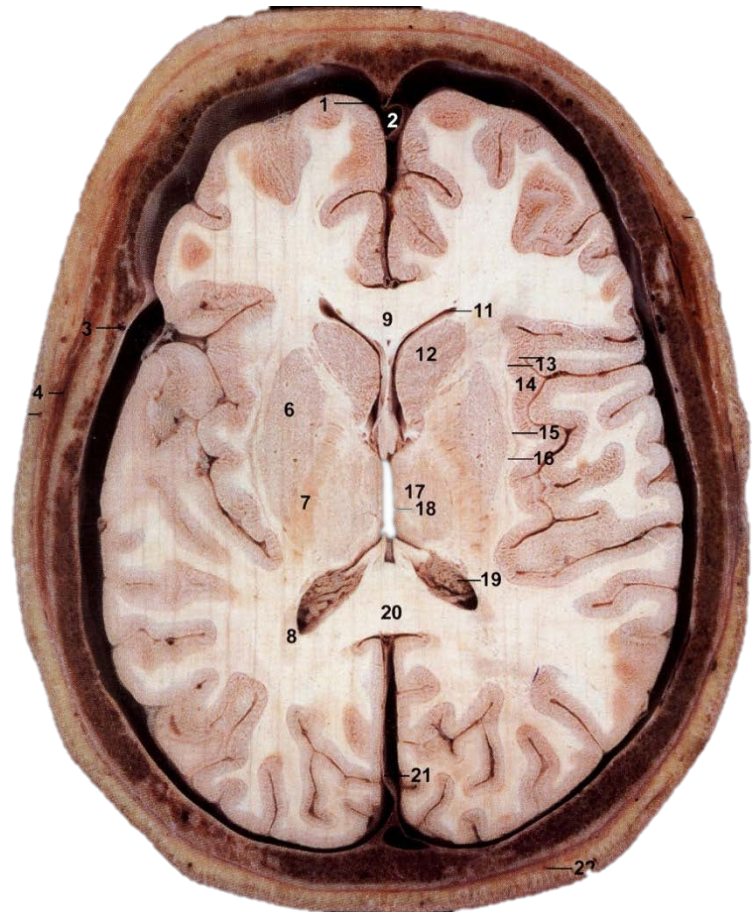
- Use for diagnosis for long.
- The limitation of human eyes
 - Intensity
 - Contrast
 - Texture
 - (Subjectively)
 - (Empirically)
 - (Individually)



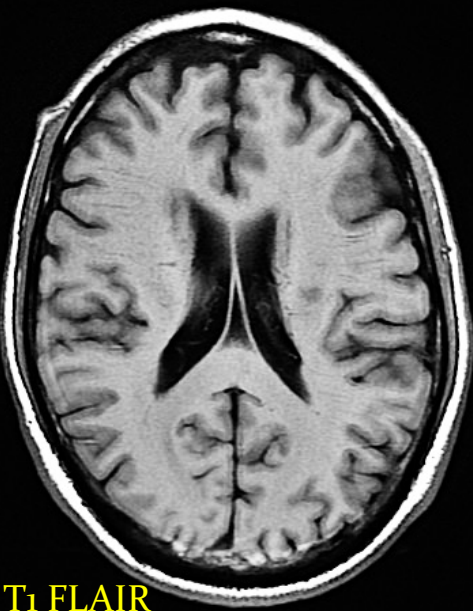
Why we love this big monster?



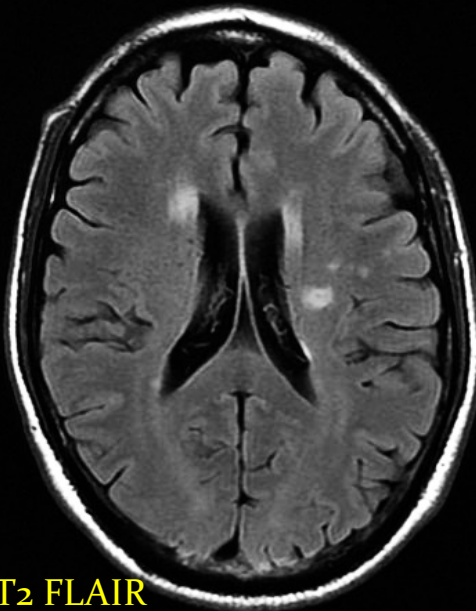
It looks fantastic!!



It creates lots of images



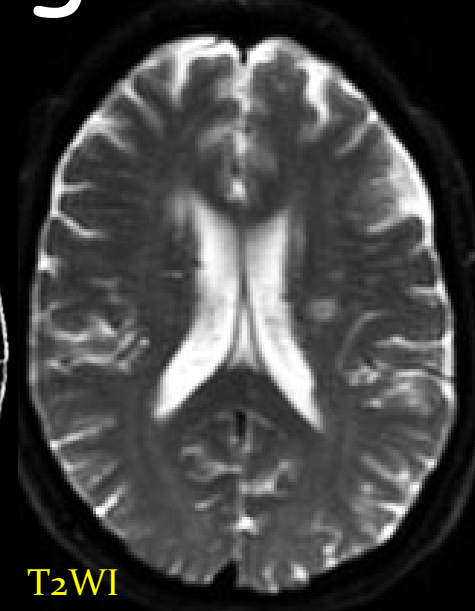
T1 FLAIR



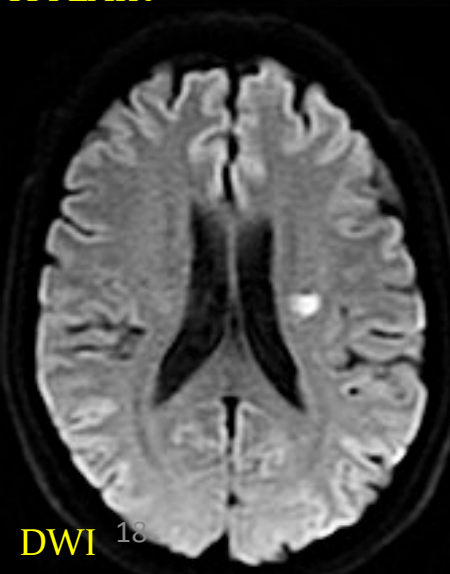
T2 FLAIR



T2 Gra



T2WI



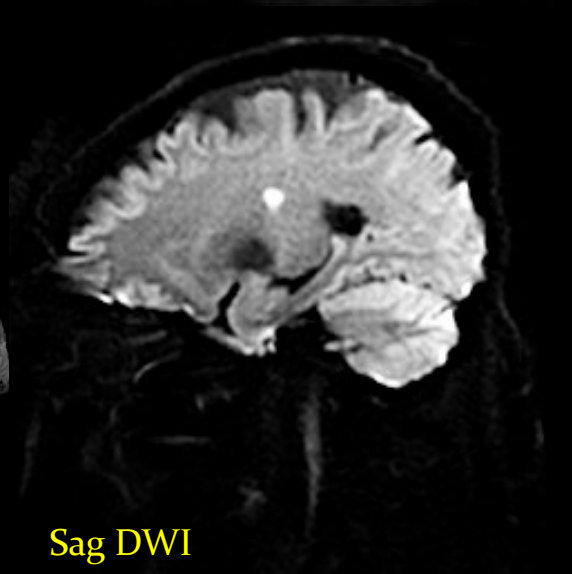
DWI 18



Cor T2WI

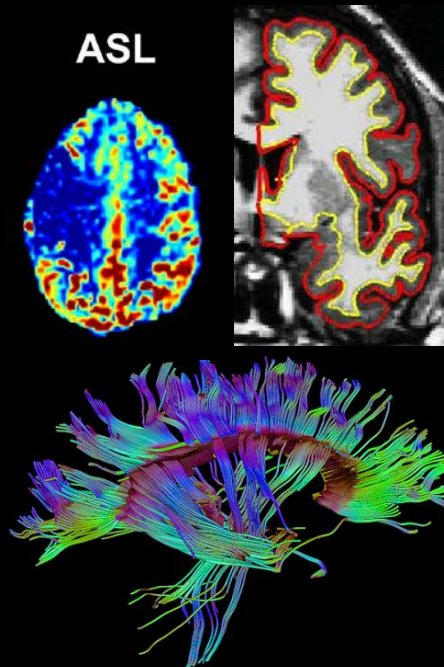
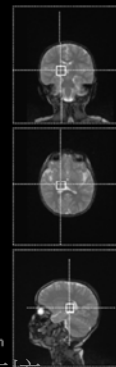
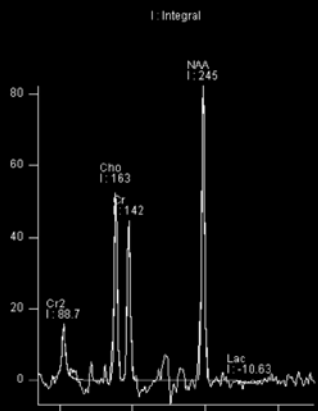
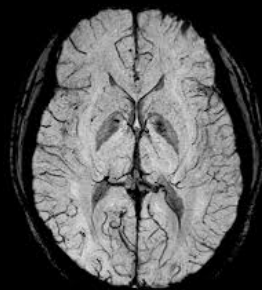
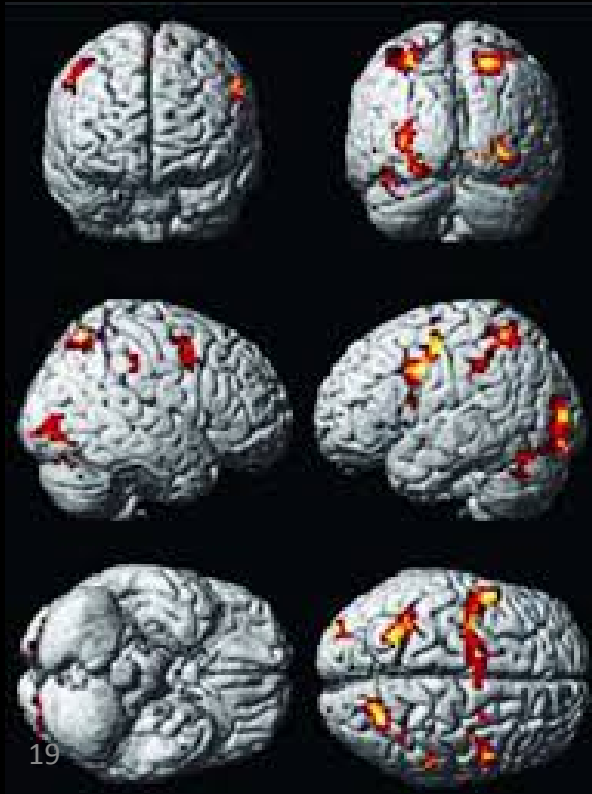
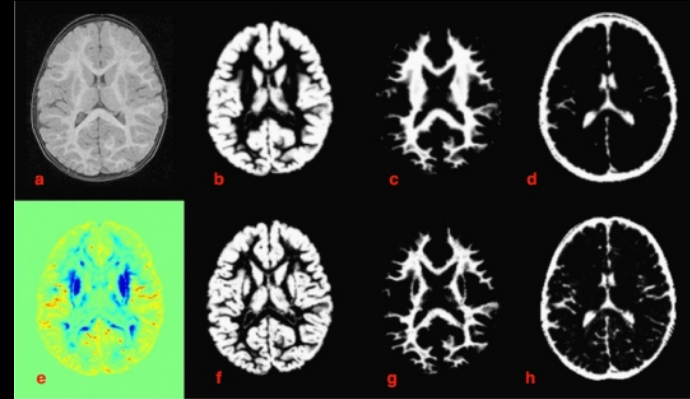
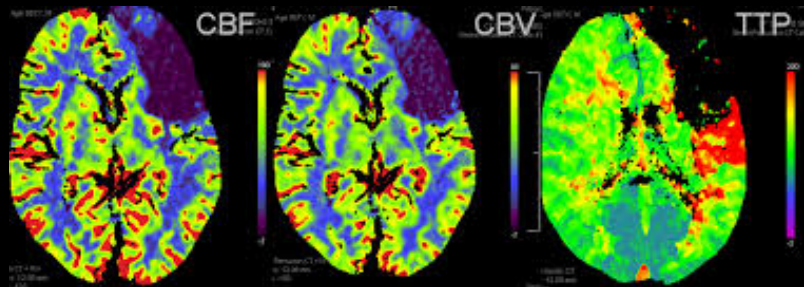


3D TOF MRA



Sag DWI

Even more!



Today's focus: MRI

- Structural
 - Diffusion Tensor Imaging
 - Quantitative Volumetric Analysis
- Functional
 - fMRI

Diffusion Tensor Imaging (DTI)

- A structure image to display/recon. the orientations of WM.

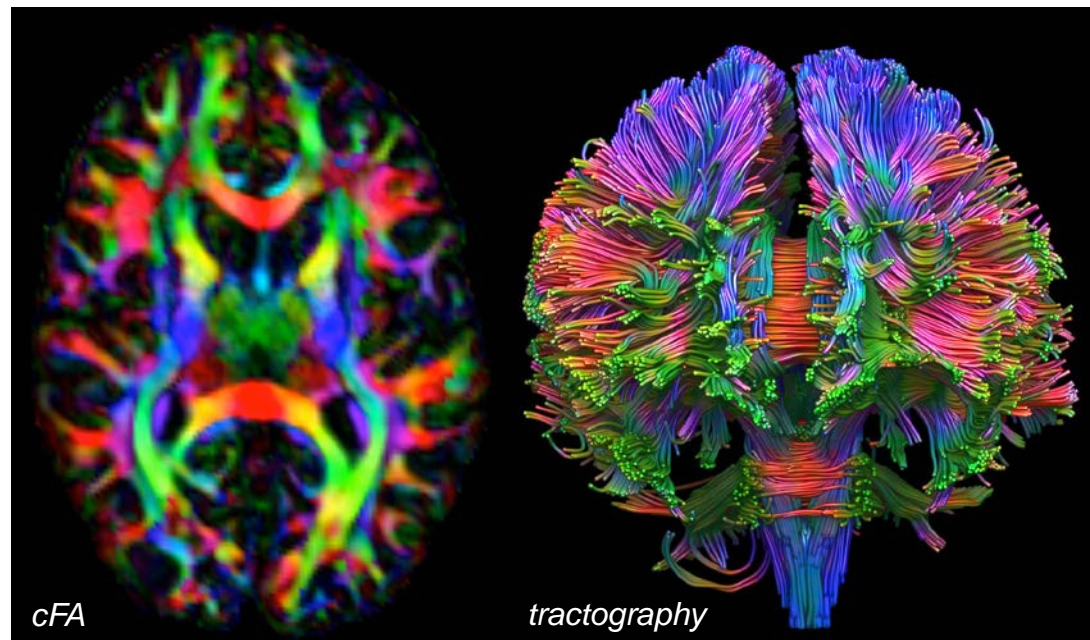
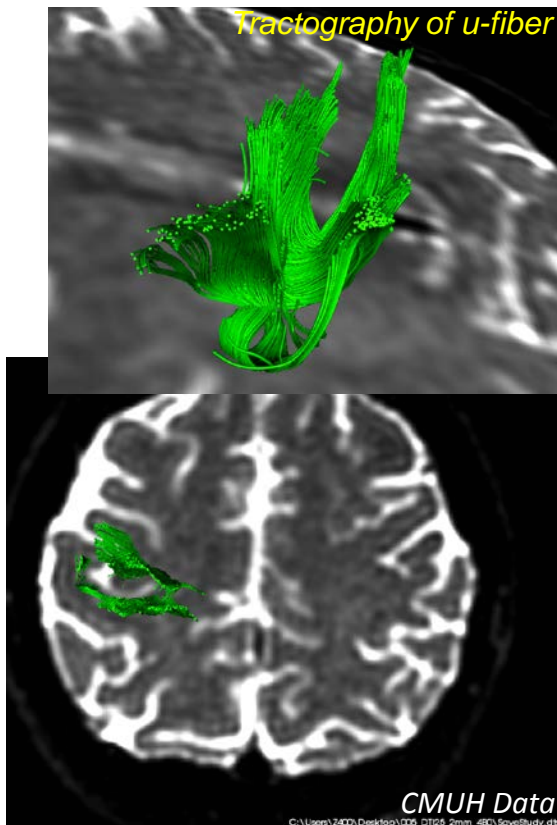
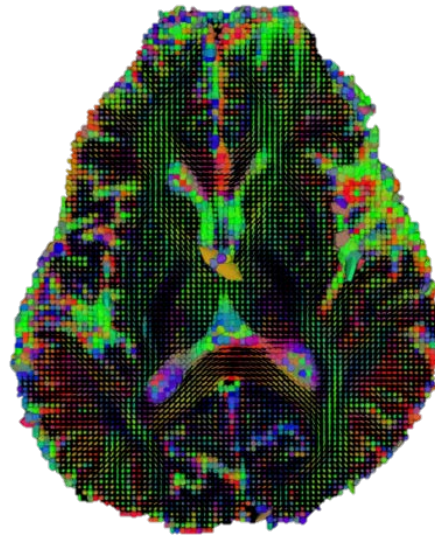


Image courtesy of Alexander Leemans

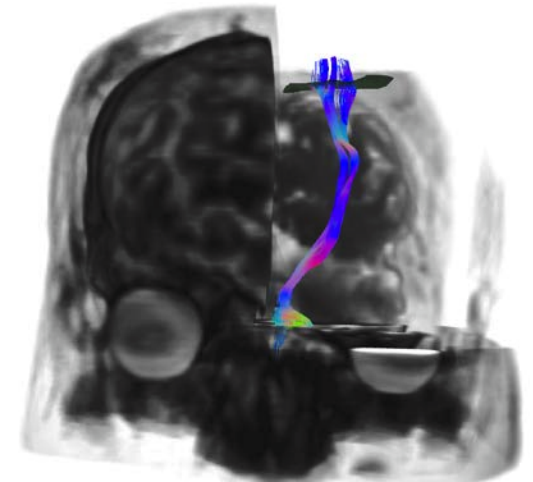
Tractography



Structure MRI



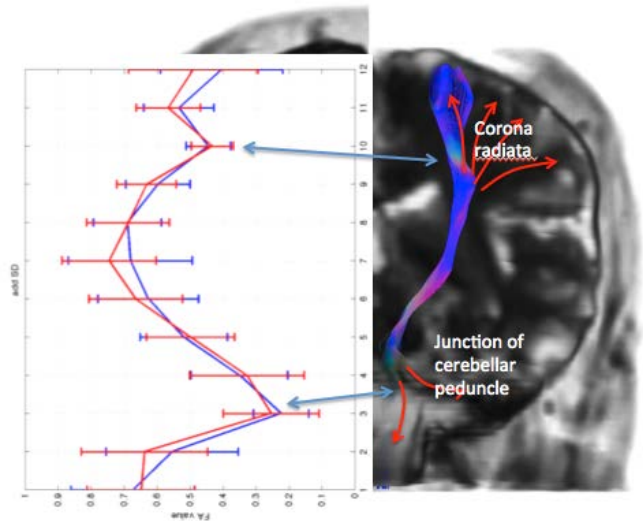
Diffusion MRI
(Tensor Map)



Fiber Connection
(tractography)

Tractography-based Analysis

Group analysis



Left CST

Right CST

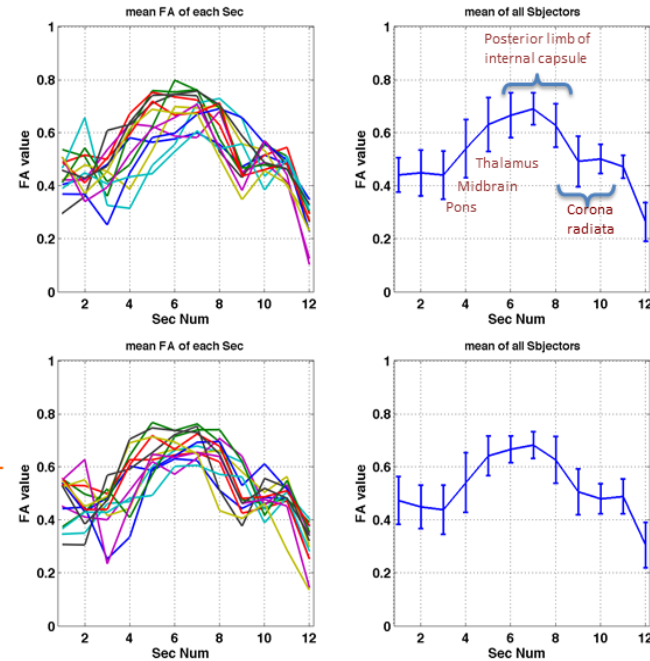


Fig.3a: FA distribution of right/left CST

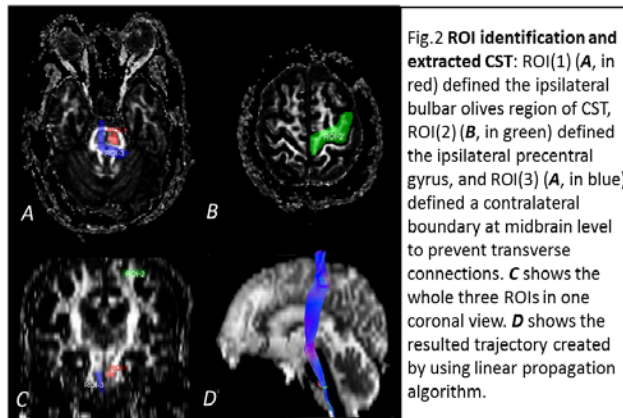
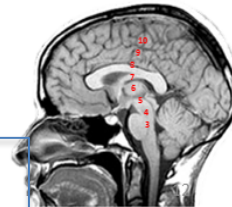
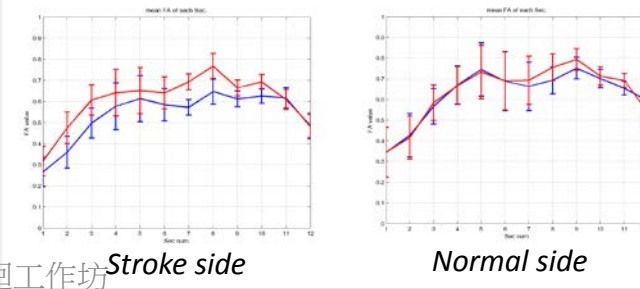


Fig.2 ROI identification and extracted CST: ROI(1) (A, in red) defined the ipsilateral bulbar olives region of CST, ROI(2) (B, in green) defined the ipsilateral precentral gyrus, and ROI(3) (A, in blue) defined a contralateral boundary at midbrain level to prevent transverse connections. C shows the whole three ROIs in one coronal view. D shows the resulted trajectory created by using linear propagation algorithm.

CST changes in single stroke patient



FA differences between MDD Non-remission / remission group

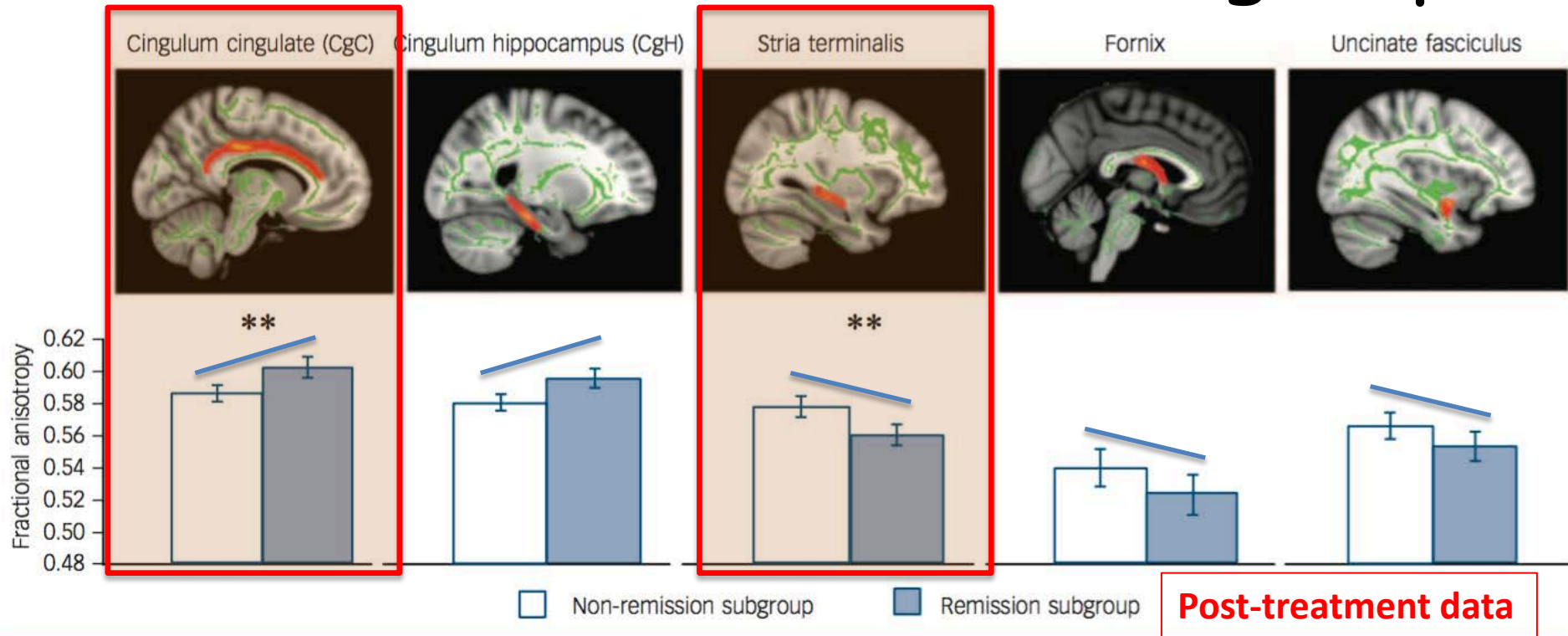


Fig. 2 Fractional anisotropy differences in preselected white matter tracts between the participants in the major depressive disorder group who reached remission (remission subgroup) and those that did not (non-remission subgroup).

The upper panel shows the five preselected white matter tracts (in red) and the white matter skeleton representing the centre of all white matter tracts (in green) overlaid on a standard brain. The lower panel shows fractional anisotropy differences between participants in the remission and non-remission subgroups. Fractional anisotropy for the stria terminalis and cingulum portion of the cingulum bundle was identified as the most significant predictors of remission (**).

**** = most significant predictors of remission**

Meta-analysis - FA reduced areas in MDD

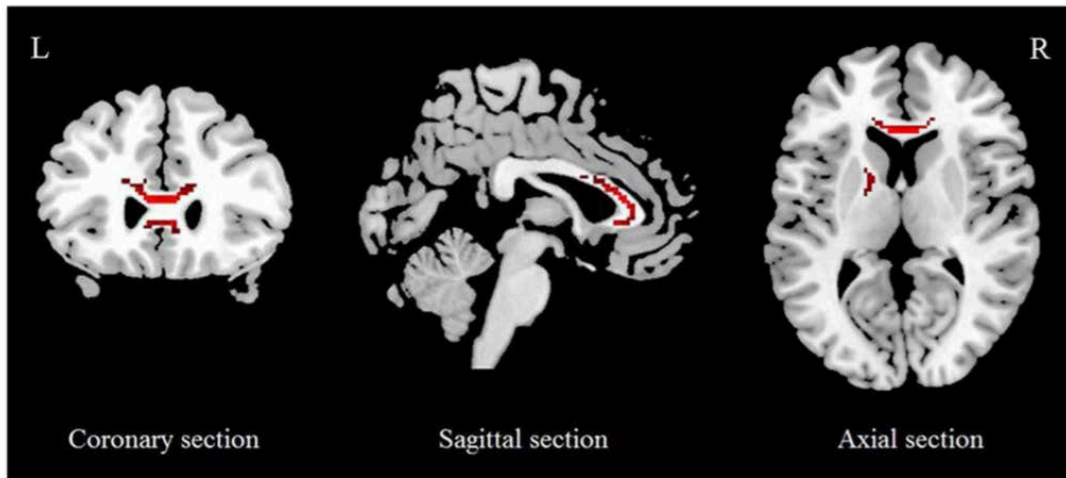


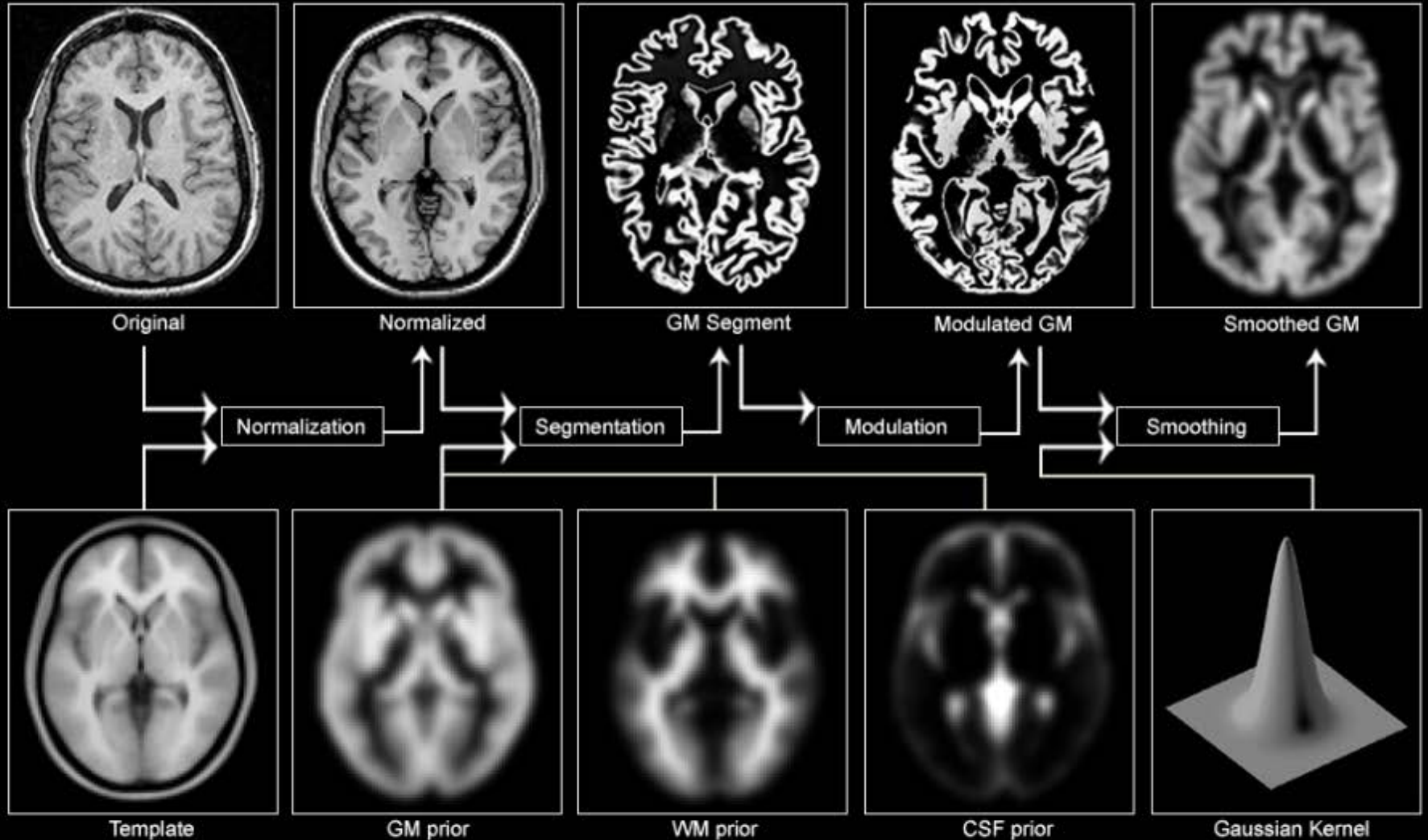
Figure 2. Regional FA reductions in the genu and body of the CC as well as the left ALIC in MDD patients compared with HCS. Significant clusters are overlaid on an MRICron template for Windows for display purposes only. Abbreviations: FA, fractional anisotropy; CC, corpus callosum; ALIC, anterior limb of internal capsule; MDD, major depressive disorder; HCS, healthy control subjects.

Region	Maximum			Cluster	
	MNI coordinates x, y, z	AES-SDM value	P value	Number of voxels	Breakdown (number of voxels)
Genu of CC	-6, 26, 10	-0.112	~0	499	Genu of CC (307) Body of CC (182)
Left ALIC	-14, 4, 8	-0.068	0.000098121	73	Left ALIC (49) Left PLIC (17)

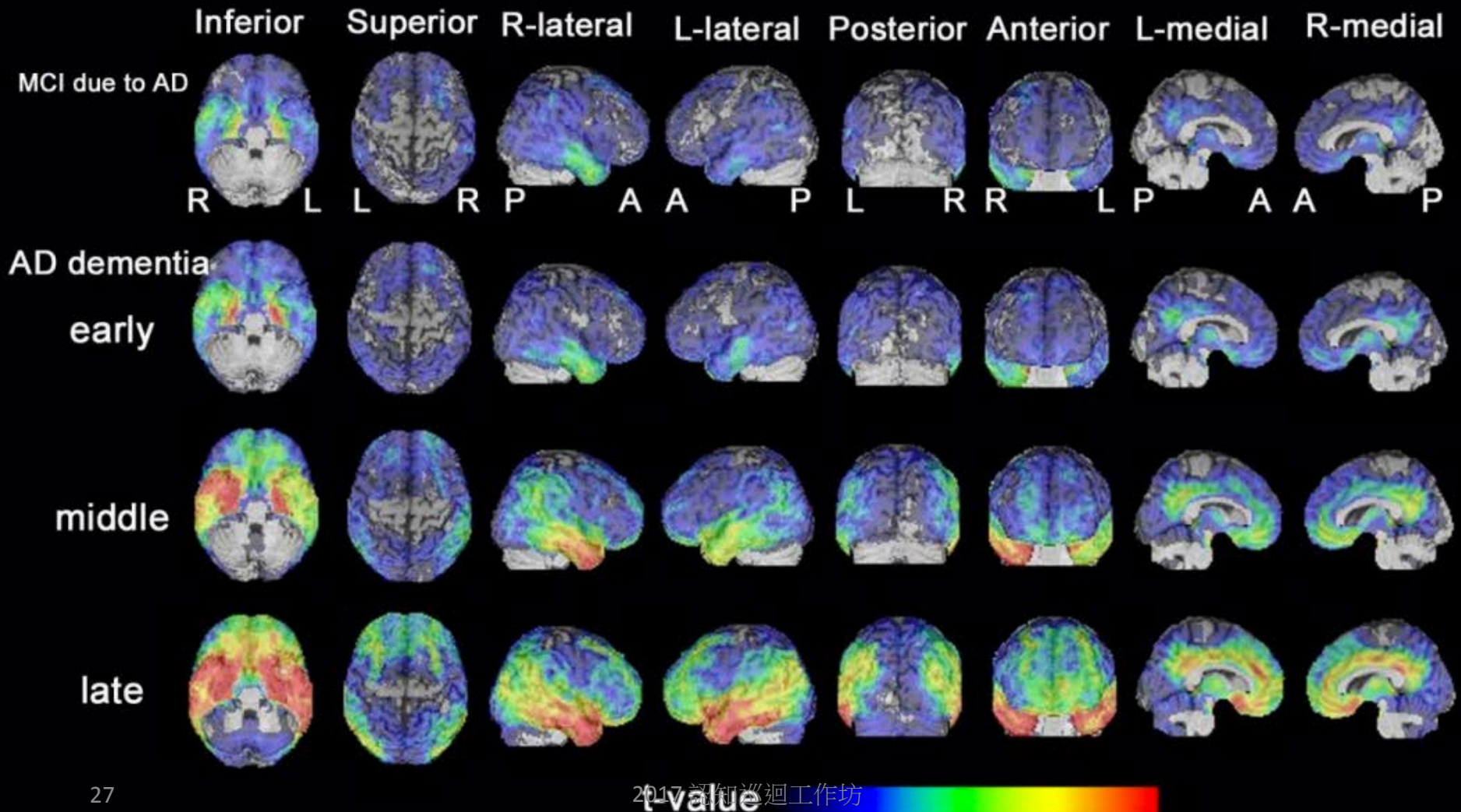
Table 2. Clusters of FA reductions in patients with major depressive disorder compared to healthy control subjects. Abbreviations: FA, fractional anisotropy; CC, corpus callosum; ALIC, anterior limb of internal capsule; PLIC, posterior limb of internal capsule; AES-SDM, anisotropic effect size-signed differential mapping; MNI, Montreal Neurological Institute.

Voxel-Based Morphometry

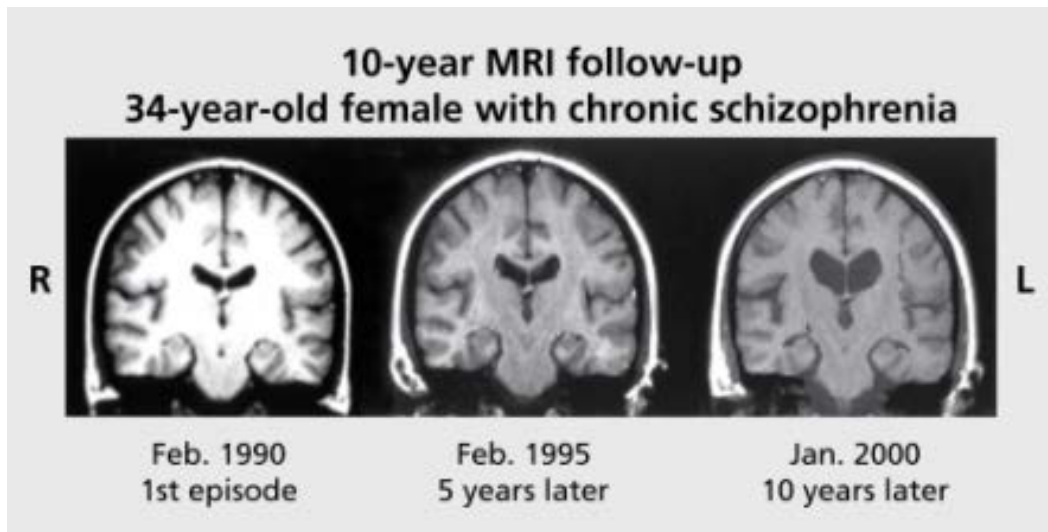
Pre-processing Overview



GM changes in AD



Brain atrophy in schizophrenia



DeLisi LE et al, 2006

- Smaller total brain volume.
- Enlarged ventricles.
- Reduced hippocampal and thalamic volume.
- Increased globus pallidus volume.

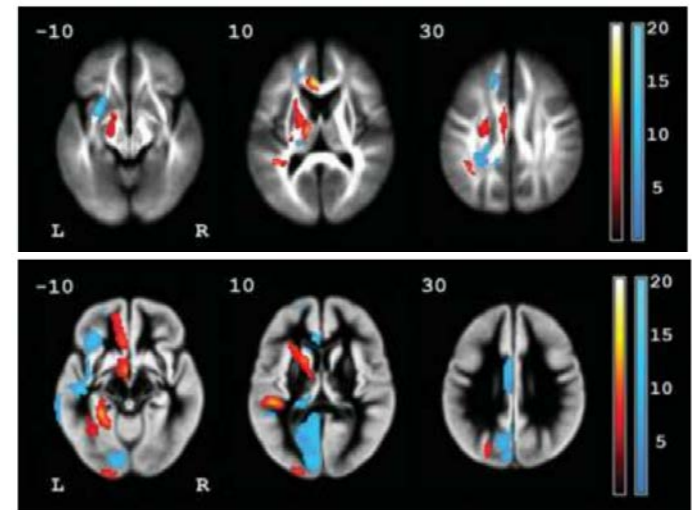


Figure 2. Gray-matter asymmetries. A number of gray-matter volume asymmetries, including the well-known right frontal and left occipital petalias and leftward asymmetry of the planum temporale, are seen. The color bars represent the *t* score at each voxel (red, leftward asymmetry; blue, rightward asymmetry). The voxel size is 2 mm × 2 mm × 2 mm. Only clusters of at least 200 voxels are shown.

Takao et al, 2010

Cortical thickness Analysis

- A image processing technique to evaluate cortical thickness *in vivo*. (Fischl 2000)
- Different approach form VBM.
- Several researches have demonstrate significant correlation between imaging and histological approach. (Rosas 2002, Cardinale 2014, Popescu 2016)

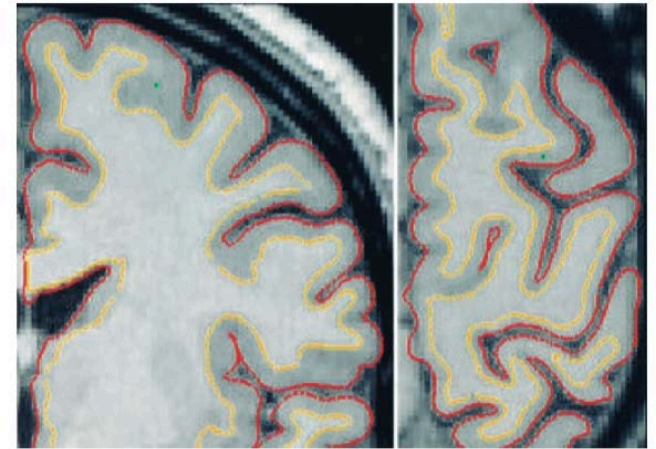
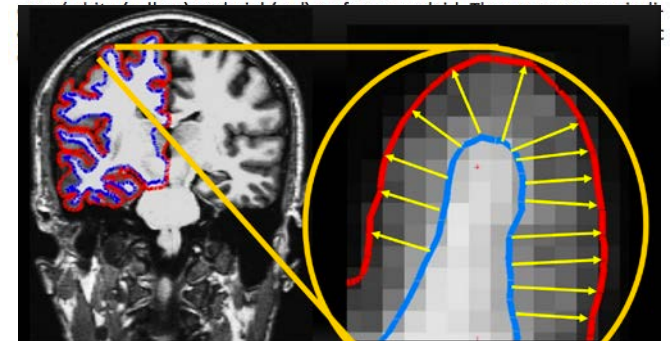
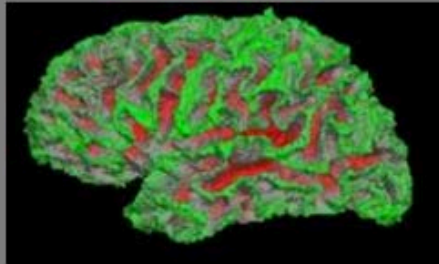


Fig. 1. Coronal (Left) and horizontal (Right) slices of the left hemisphere with

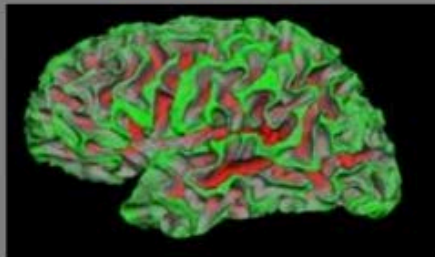


Processing steps

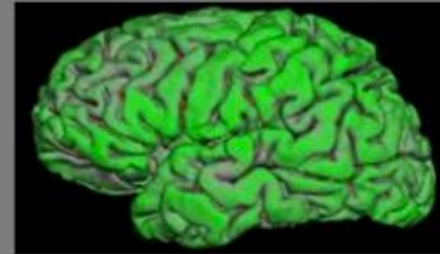
Surfaces



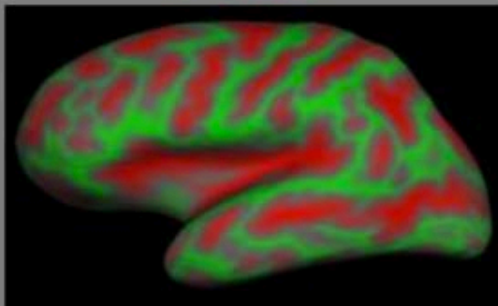
orig



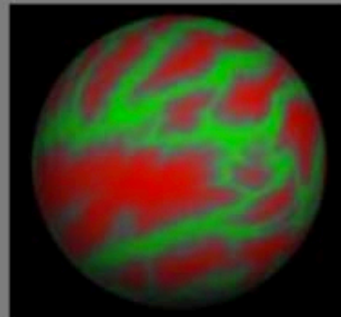
white



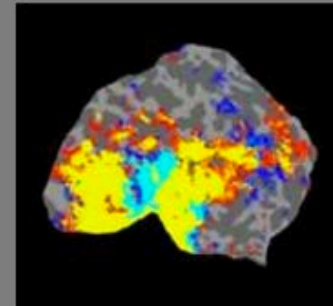
pial



inflated



sphere,sphere.reg



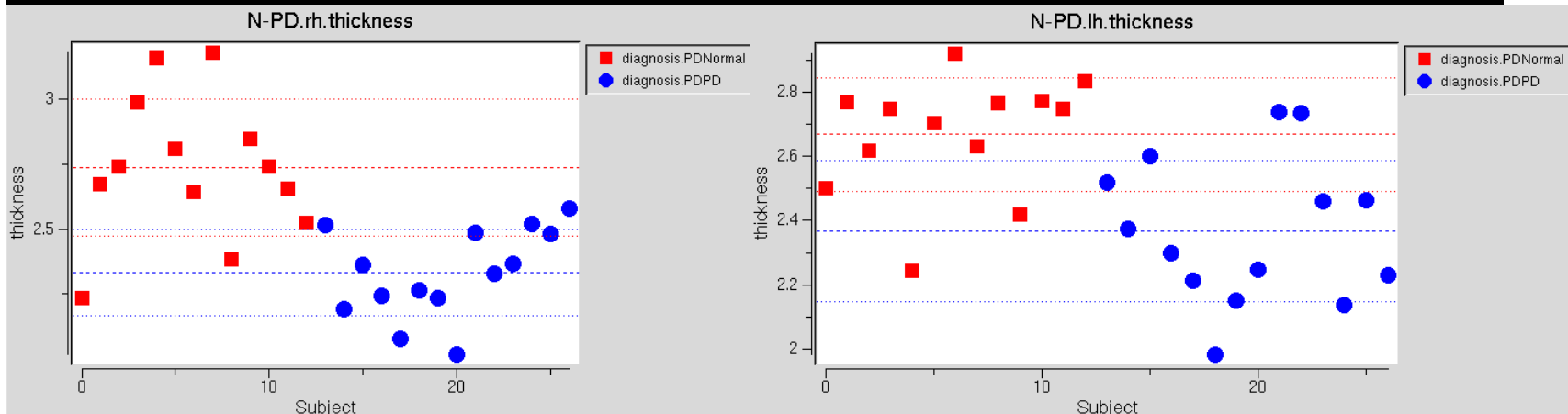
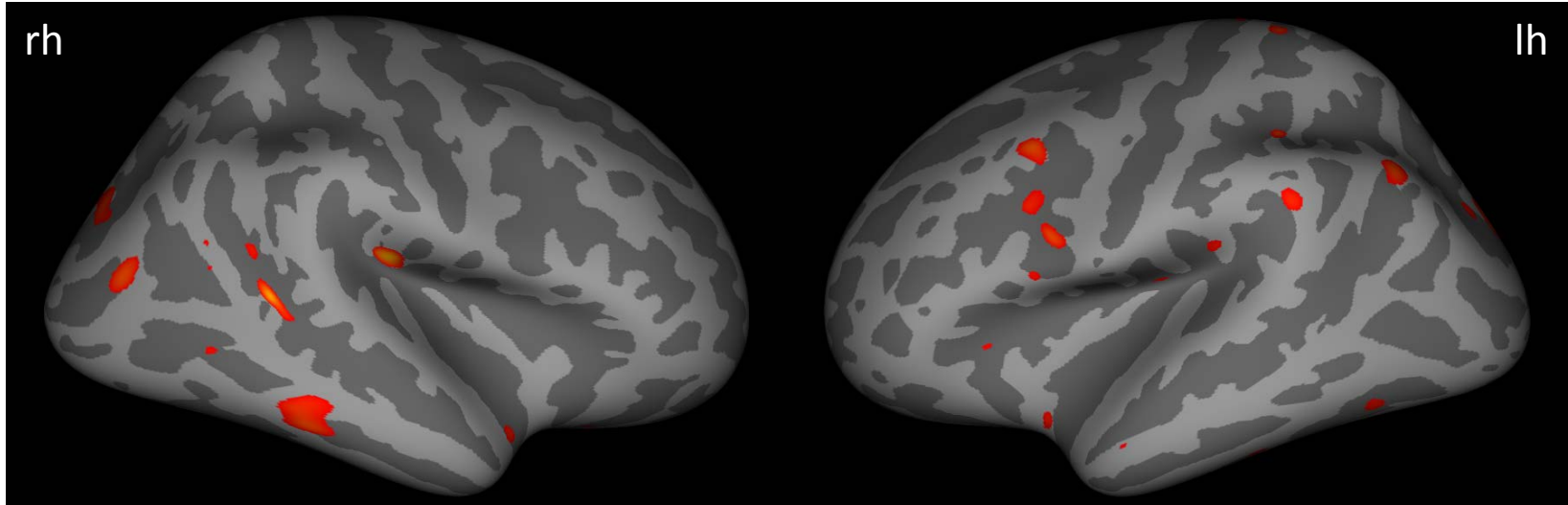
flat

- `$SUBJECTS_DIR/bert/surf`
- Number/Identity of vertices stays the same (except flat)
- XYZ Location Changes
- Flattening not done as part of standard reconstruction

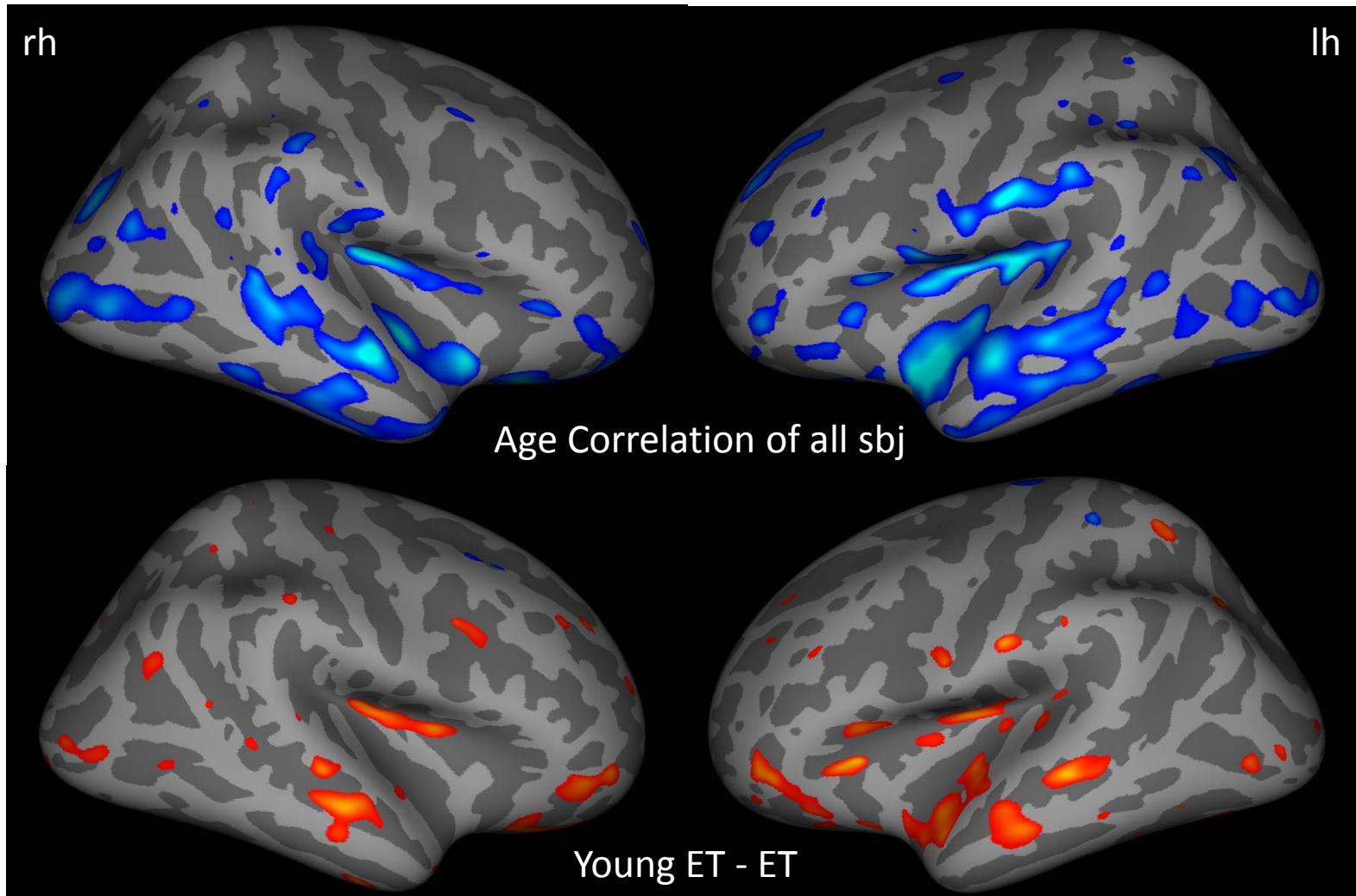
Surface Viewer:
tksurfer

Normal > PD (cortical thickness)

N=13
PD=14
P<0.01



Aging (cortical thickness)



Thicker cortical regions in MDD

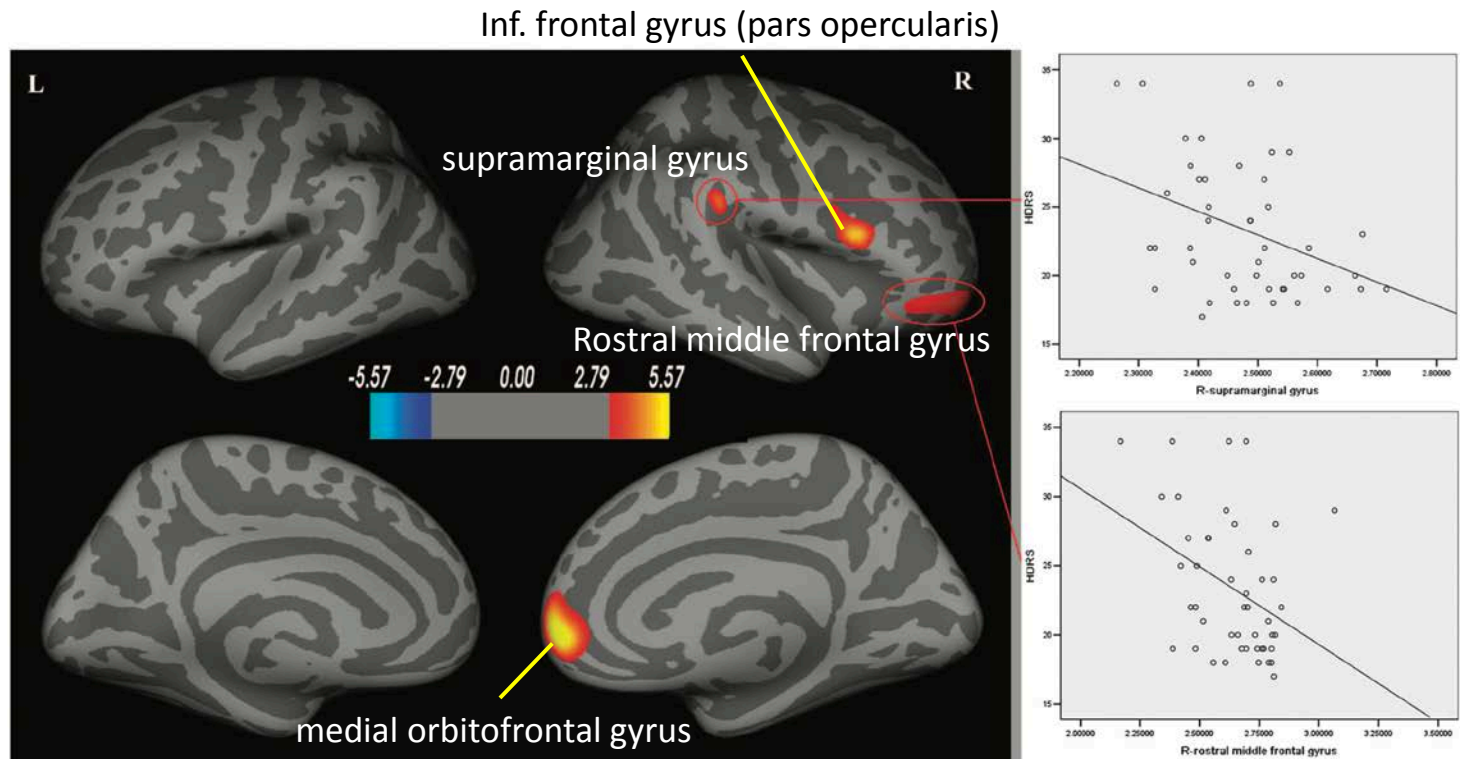
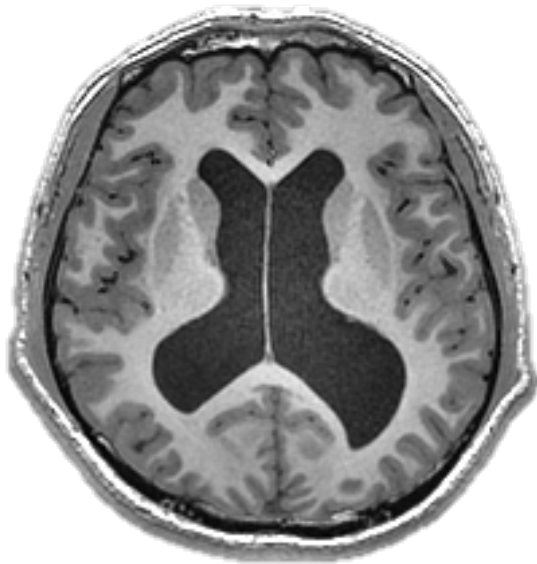


Figure 1. Areas with cortical thickness differences between healthy controls and patients with major depression (left) after FDR correction. Scatterplots show the negative correlation between HDRS with right rostral middle frontal gyrus and right supramarginal gyrus (right). Warmer colors (positive values) represent cortical thickening; cooler colors (negative values) represent significant cortical thinning in MDD patients. The color-coding for P -values is on a logarithmic scale of 1–6. L, left hemisphere; R, right hemisphere.

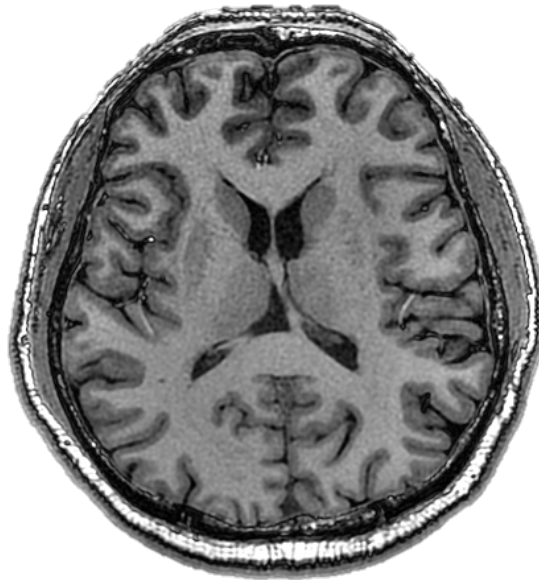
How old are they?

A



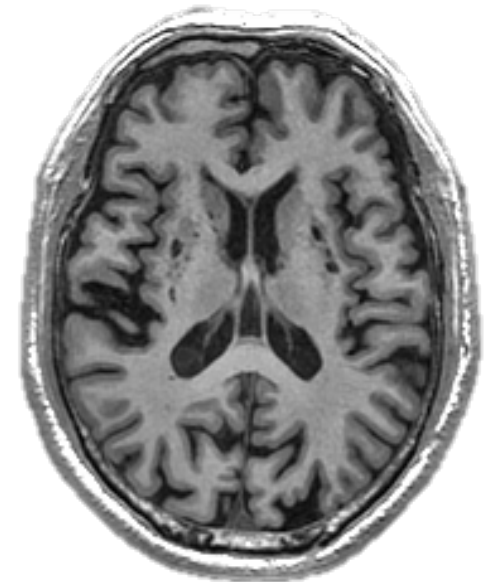
28y

B



55y

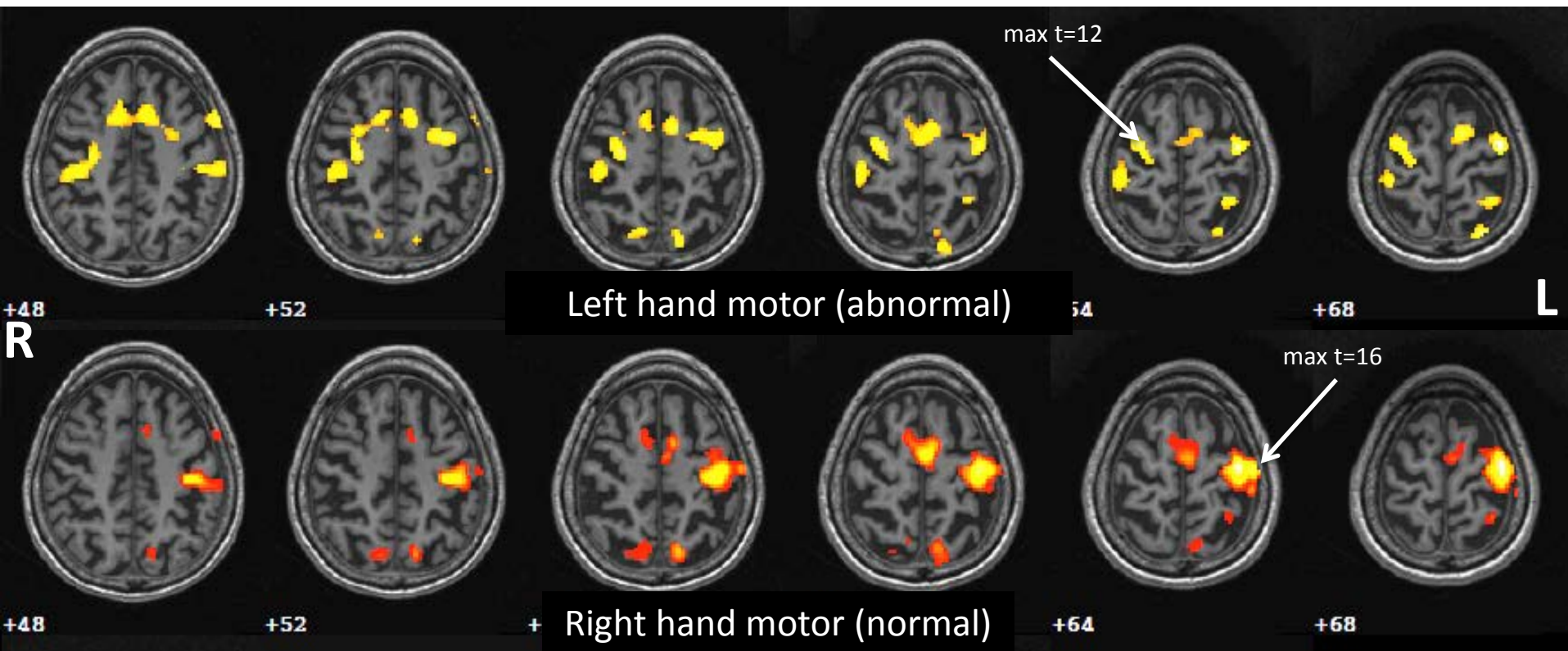
C



71y

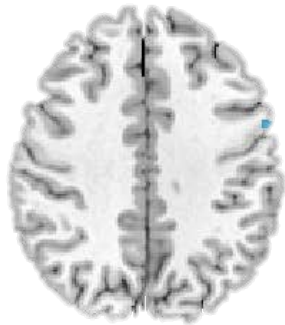
Movement Disorder - fMRI

- F67y, acute left hand motor abnormality

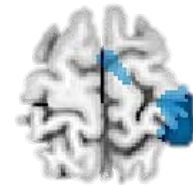
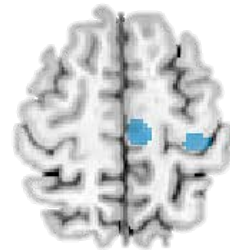
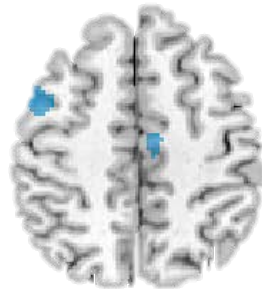


Movement Disorder - fMRI

- F27y, bilateral movement disorder
- Red/Blue: Patient/Normal

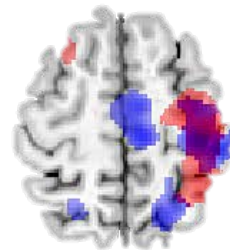
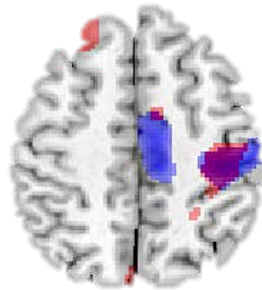
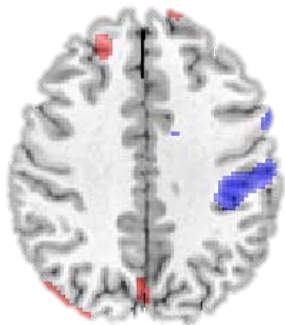


L



R

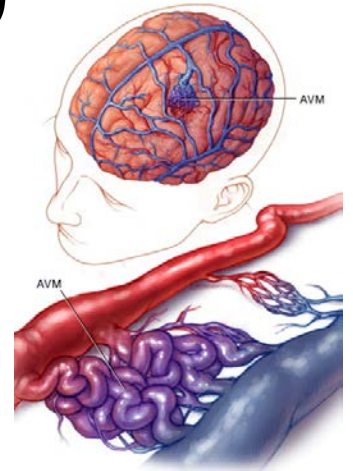
Left motor imagery



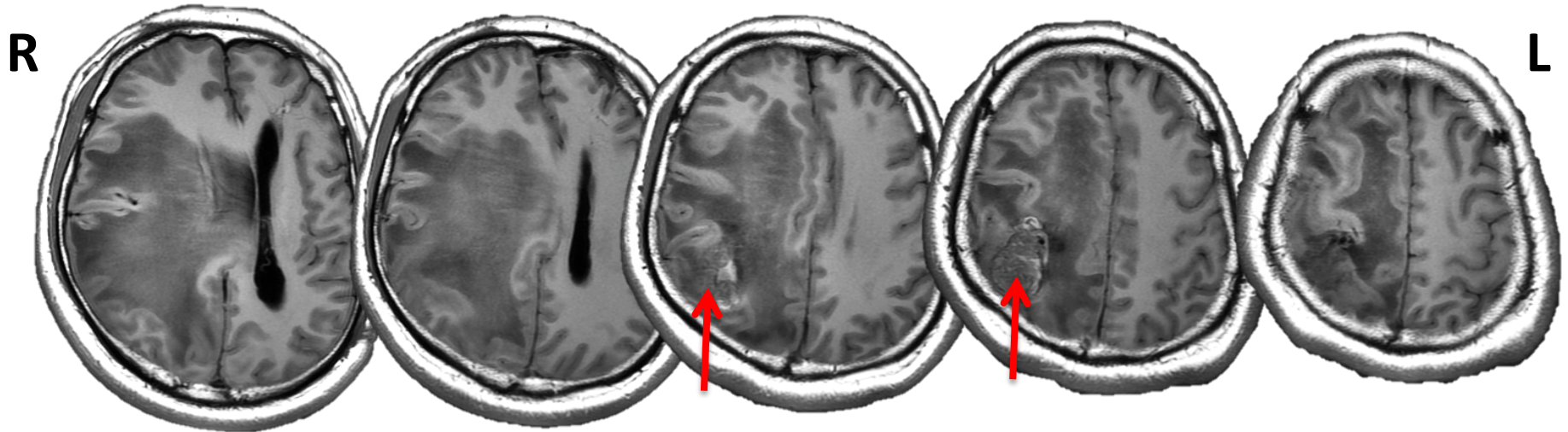
Left real motor

Pre-surgical Planning

- M36y, right side AVM
- (arteriovenous malformation)
- pre-surgical planning

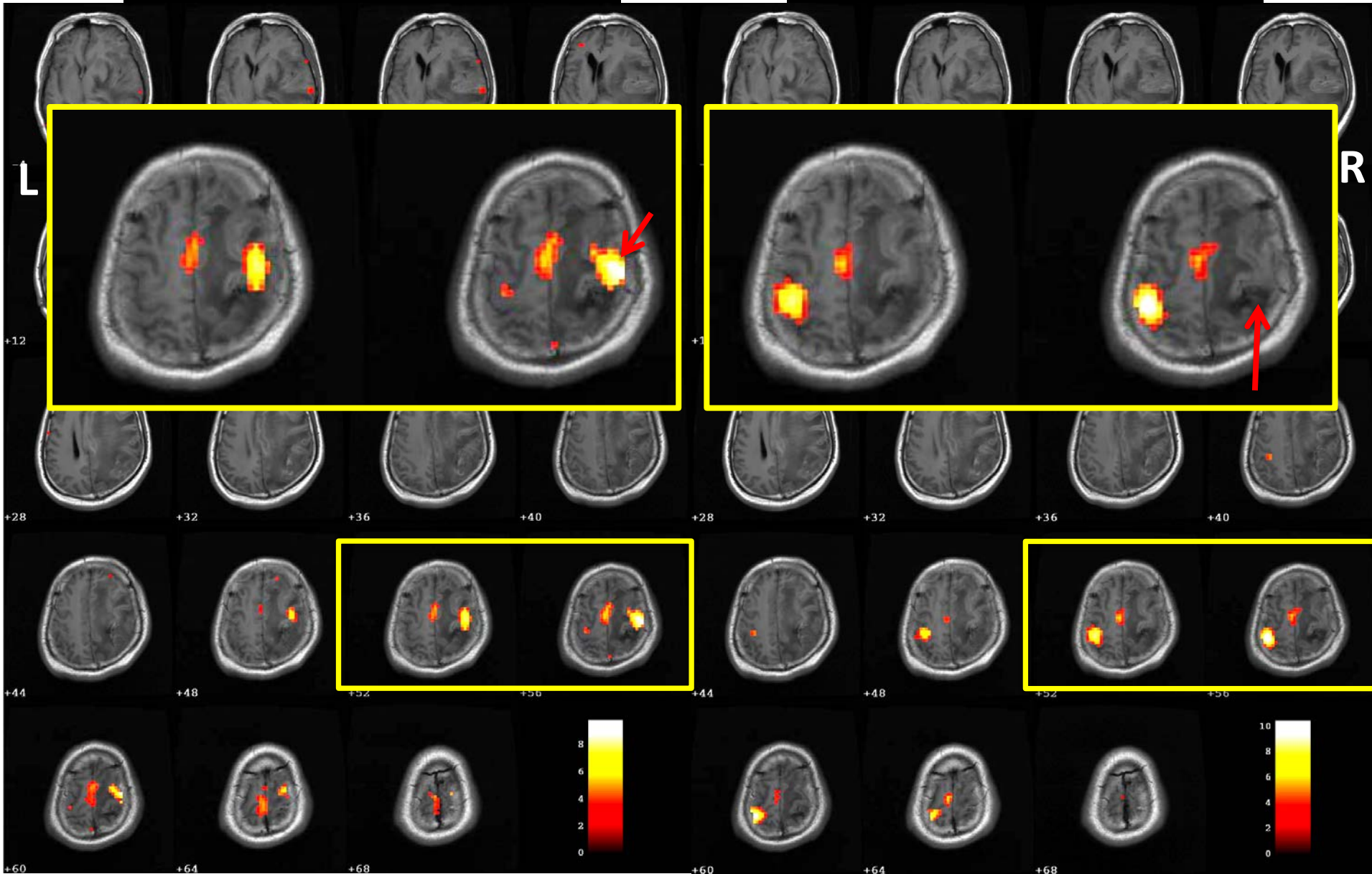


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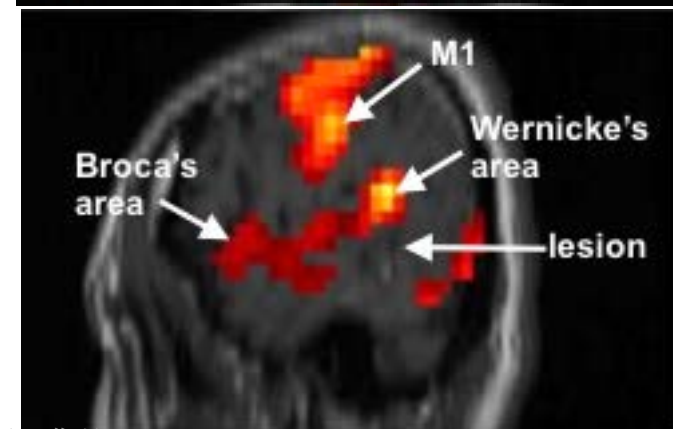
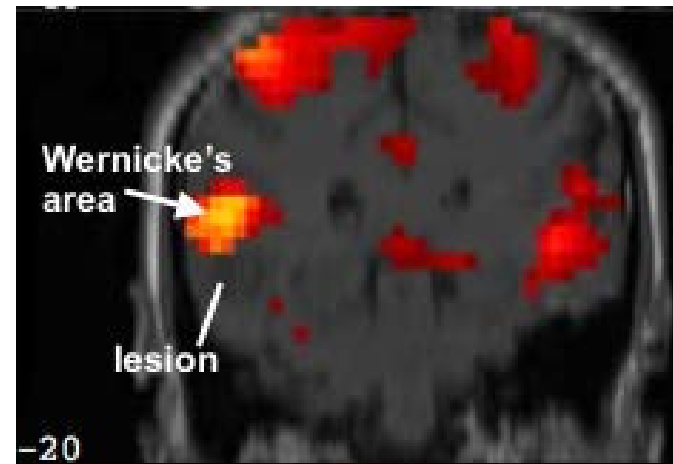
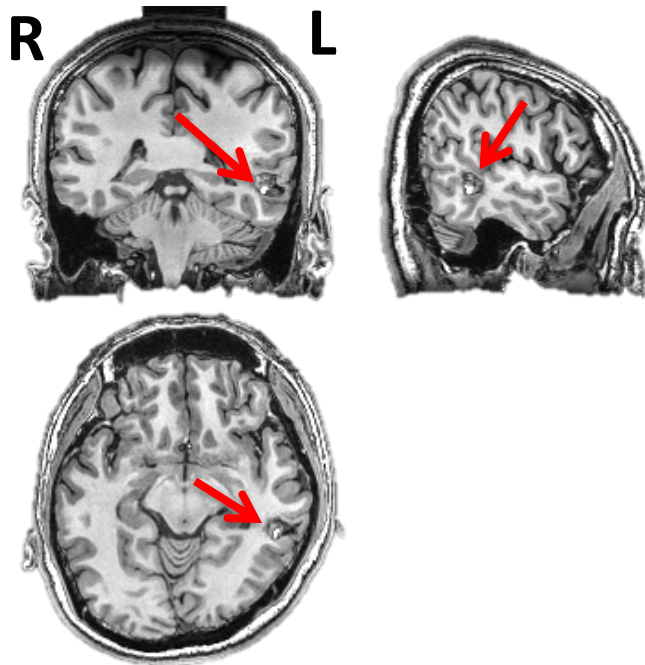
Left hand motor (tumor side)

Right hand motor (normal side)

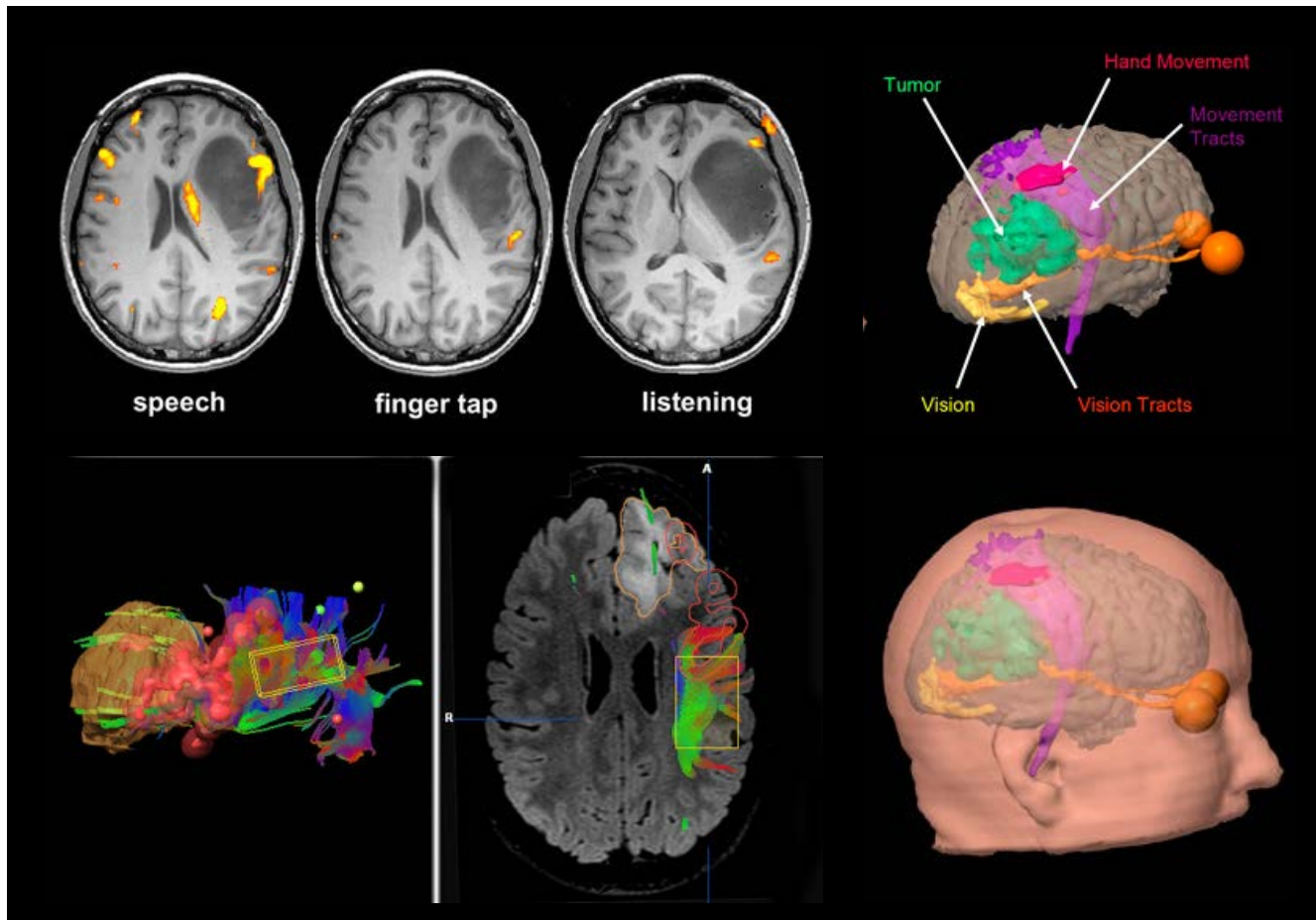


Pre-surgical Planning

- M28y, brain tumor, pre-surgical planning



Pre-surgical Planning

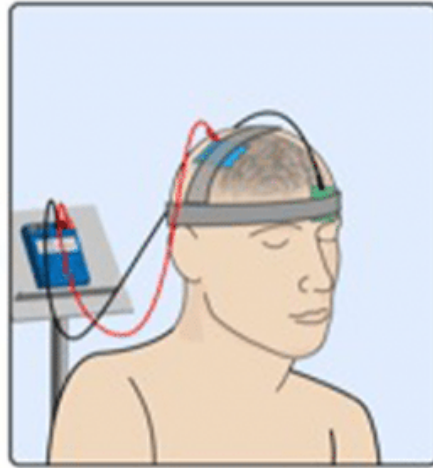


Data from University of Cincinnati Dep. of Radiology

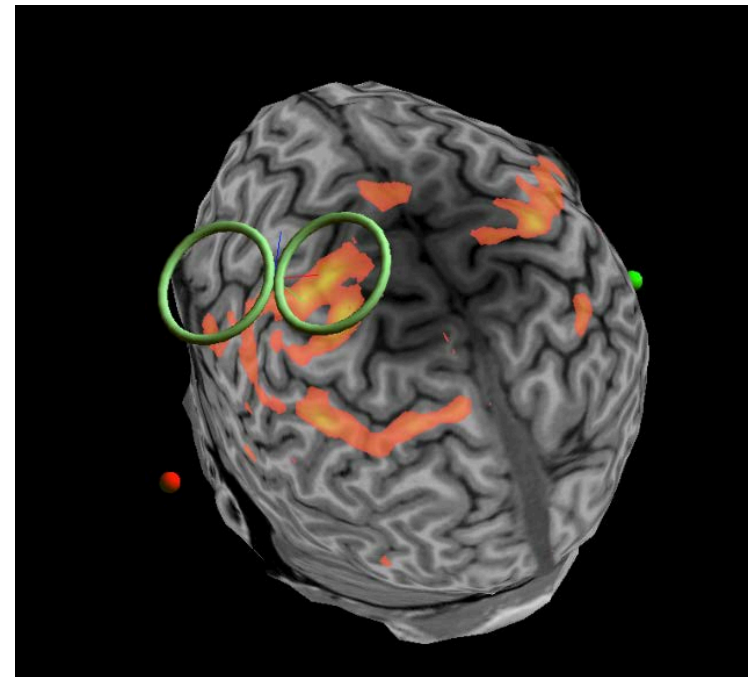
Active stimulators



TMS



tDCS



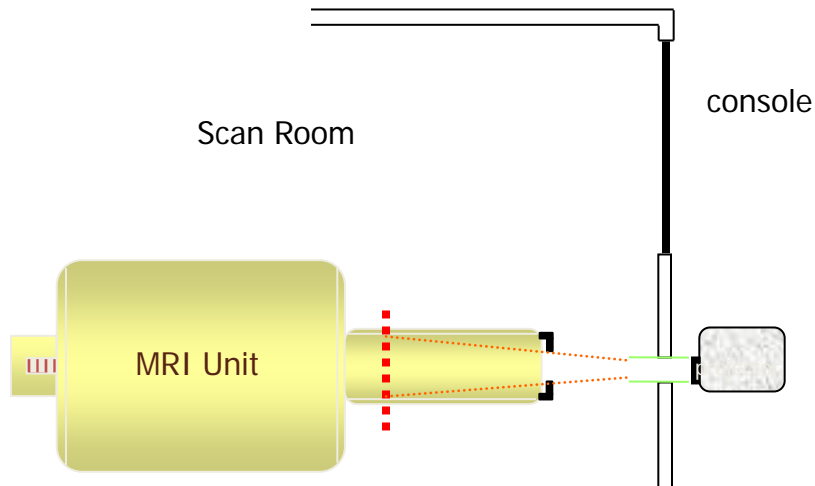
fMRI guided TMS

Limitation to become routine

- High field scanner (3T) (15% in Taiwan)
- fMRI equipment
- Preparation time (functional task)
- Scanning time
- Data processing
- Explanation



fMRI environment (UCSD)



Clinical fMRI



fMRI compatible equipments



Current limitation

- Currently, neuroimaging can't be used in diagnosis directly.
- Difference is too small to be observed in single case.
- The results remain inconsistency.
 - Image quality, parameters
 - Statistic method
 - heterogeneous of patients
 - Disease progresses
 - Treatment

Current limitation

- But can play an important role in understanding more about:
 - etiology, pathophysiology
 - treatment response
 - Prognosis

Future works

- Worldwide image pool.
- Meta-analysis.
- Machine/ Deep learning
- Biomarkers
- Diagnosis and treatment prediction (single subject)



大家以為的科學家：

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Thank you for your attention!

THE END