MRI 를 이용한 치매 질환 예측

2018.6.28

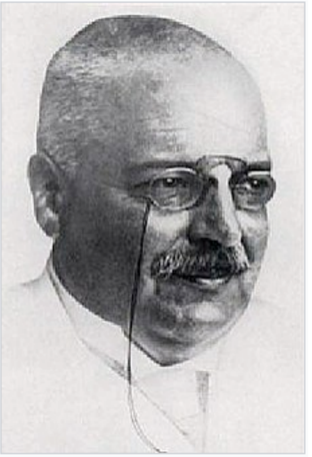
박세진

VUNO Inc.

Contents

- 왜 치매 관련 연구를 하는가?
- 어떤 문제에 집중할 것인가?
- 작은 문제정의, 어려움들
- 접근방법들.

Dementia vs Alzheimer



알츠하이머병을 발견한 알로이스 알츠하이머(Alois Alzheimer)

- Alzheimer : 치매의 가장 흔한 형태. 75% 치매환자. 치료 불가. (발견자의 이름)
  - 증상 : 단기기억 상실, 혼란, 격한 행동, 조울증, 언어장애, 장기기억상실
  - 원인 : 신경변성 (Neurodegeneration). 아밀로이드 플라크가 정상 알츠하이머 단백질을 변형시켜 플라크 덩어리를 형성해 고유기능 파괴하는 것으로 추정.
  - 조직병리학적 특징 : 뇌위축 (Atrophy), 뉴론의 다발성 병변, 초로성 반점
  - 신경병리학적 특징 : 대뇌피질 (Cerebral cortex) 및 특정 피질 아래 영역에서의 뉴런과 시냅스 소실.
- Dementia (Alzheimer 에 의한) : 알츠하이머에 의해 인지능력이 저하된 상태
  - 아밀로이드베타의 축적 -> 시냅스 이상 -> 뉴론 파괴 -> 뇌 구조 이상 -> 인지 저하 -> 임상 증상

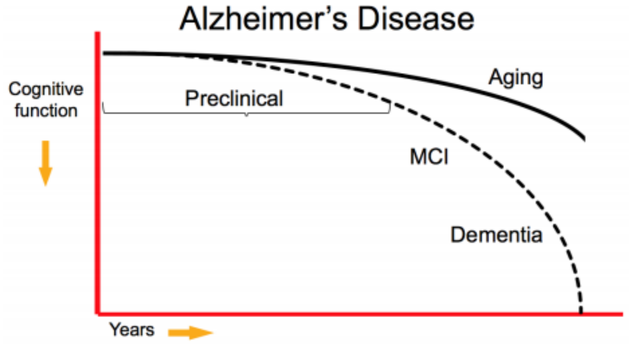


Figure 1. Model of the clinical trajectory of AD. The stage of preclinical AD precedes MCI and encompasses both asymptomatic individuals in whom the pathophysiological process has already begun but who are clinically indistinguishable from the profile of normal or "typical" aging, as well as individuals who have demonstrated subtle decline from their own baseline that exceeds that expected in typical aging, but would not yet meet criteria for MCI.

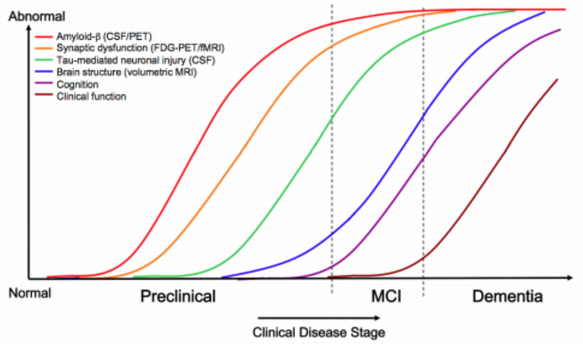


Figure 3: Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade, expanded in the preclinical phase. Aβ as identified by CSF $A\beta_{42}$ assay or PET amyloid imaging. Synaptic dysfunction evidenced by FDG PET or functional MRI. Tau-mediated neuron injury by CSF tau or phospho-tau. Brain structure by structural MRI. Biomarkers change from maximally normal to maximally abnormal (y axis) as a function of disease stage (x axis). The temporal trajectory of two key indicators used to stage the disease

Alzheimer Diagnosis

- 신경학 (Neurology)
  - 뇌 및 신경계의 질환 분석
  - 반사, 균형, 눈움직임, 말 및 감각도
  - MR, CT, PET 촬영
- 정신 분석학 (Psychoanalysis)
  - 마음이 어떻게 작동하는지 또는 기분에 영향을 미치는 장애 검사
  - 신경 심리 검사
- 심리학 (Psychology)
  - 기억력, 집중력, 문제해결력, 언어 및 기타 정신 기능검사
  - 신경 심리 검사

Neuroimaging for AD Prediction

- Objectives : 뇌 구조 이상을 MR 로 인식하여, 인지저하가 예상되는 환자 (MCI) 를 판별
  - 신경심리검사를 동반하거나, MR only
  - MCI (Mild cognitive impairment) : 경미한 인지기능저하, 일상생활에 방해.
  - 즉, 인지기능이상이 없거나 경미하지만 뇌 구조 이상이 관찰되는 환자를 조기에 발견하는 것이 목표

- Methodology
  - AD 에 연관되는 뇌 부위들을 정교하게 영역 분류 (Parcellation)
  - Parcellation 과정|결과를 이용하여 정상인 대비한 특이도 (dissimilarity | distance | percentile) 측정

Previous Approach

Neuroimaging research survey

- ML 을 기반으로 한 치매 진단 연구들을 조사
- 2006 ~ 2016 까지의 111개 연구들을 치매질환의 종류, 성능차이 등 관점에서 분석
  - AD vs CN 분류 : 76 %
  - AD|MCI vs CN : 42 %
  - AD vs MCI : 9 %
- Dataset
  - 대부분 연구에서 ADNI 공개 데이터를 사용 (T1, FAIR, PET)
  - Non-imaging feature 추가 사용 (신경 심리 검사 등)
- Methodology
  - Freesurfer 활용한 regional volume 측정
  - Visual feature 기반 (Voxel wise, Local/Nonlocal image patch)
  - Cortical thickness 측정
  - Gray matter, white matter, CSF 측정
  - Relevant pathologies keywords
    - microvascular change, cognitive impairment, cognitive decline, MCI, Lewy bod*, LBD, frontotemporal, FTD, lacun*, white matter hyperintens*, white matter lesion*, WMH, leukoaraiosis, periventricular, microbleed*, microhaemorr*, microhemorr*, stroke, cerebrovascular, CVA, perivascular space*, PVS, Virchow–Robin space*, pathological aging, pathological ageing, brain, cerebr*, medial temporal, mesial temporal, volume loss, atrophy

Previous Approach

Data sources	HC v AD	HC v MCI	MCInc v MCIc	MCI v AD	Total
ADNI	54	24	34	7	119
ADNI + Bdx-3C	0	0	1	0	1
AddNeuroMed	1	0	2	0	3
AddNeuroMed + ADNI	2	1	1	0	4
Local	4	3	0	0	7
OASIS	7	2	0	1	10
Total	68*	30	38	8	144
Machine learning method					
AdaBoost	1	0	1	0	2
Deep Learning	2	2	0	0	4
Gaussian Process	0	0	1	0	1
LDA	5	0	5	1	11
Logistic Regression	4	0	2	0	6
OPLS	2	1	1	0	4
QDA	0	0	1	0	1
RBF-NN	0	0	1	0	1
Random Forest	3	1	3	0	7
SRC	2	1	2	0	5
SVM	39	22	17	7	85
SVM + MKL	3	1	1	0	5
SVM + OPLS	1	0	1	0	2
SVM + Random Forest	2	1	2	0	5
SVM + SRC	1	1	0	0	2
kNN	3	0	0	0	3

Total	68*	30	38	8	144
Types of Imaging and imaging plus non-imaging data used					
T1w only	46	13	26	6	91
T1w & other imaging data	8	8	2	0	18
T1w & other types of data	8	3	8	1	20
T1w & both other imaging & types of data	6	6	2	1	15
Total	68*	30	38	8	144
Size of dataset (range from 100 to 902 participants).					
150 and under	30	4	9	2	45
151 to 200	4	10	6	0	20
201 to 250	9	4	6	0	19
251 to 300	4	2	3	0	9
Over 300	21	10	14	6	51
Total	68*	30	38	8	144

HC=healthy control;
AD=Alzheimer's disease;
MCI=mild cognitive impairment;
nc=non converter to AD;
c=converter to AD

Evaluation

Reference	Dataset	Classification tasks (n)	Image features (FS and representation)	Additional imaging sequences and features	Classifiers	Results
(Aggarwal, Rana et al. 2015)	OASIS	HC vs AD (99 / 99)	3D-DWT (symmlet) of 7 ROI's: hippocampus, amygdalae, ventricles, anterior and posterior cingulate (FS by FDR and mRMR)	n.a.	kNN	Sen = 0.789 / Spe = 0.810
(Aguilar, Westman et al. 2013)	AddNeuroMed	HC vs AD (110 / 116) MCInc vs MCIc (98 / 21)	68 cortical thickness values and 50 regional volumes obtained with FreeSurfer.	Education. n.a.	SVM (non-lin) OPLS	Sen = 0.862 / Spe = 0.900 Sen = 0.810 / Spe = 0.684
(Ahmed, Mizotin et al. 2015)	ADNI	HC vs AD (162 / 137) HC vs MCI (162 / 210) AD vs MCI (210 / 137)	Circular harmonic features extracted from hippocampus and posterior cingulate cortex (FS by PCA; BoW representation)	n.a.	SVM (RBF)	Sen = 0.791 / Spe = 0.882 Sen = 0.626 / Spe = 0.748 Sen = 0.490 / Spe = 0.752
(Anagnostopoulos, Giannoukos et al. 2013)	AddNeuroMed	HC vs MCI vs AD (113 / 122 / 123)	Cortical volume and thickness for specific ROI's, manual volume measurement of the hippocampus.	T2w, demographics.	Ensemble of FF-NN, SVM, PESFAM, P-NN, kNN	Acc = 0.771
(Archana and Ramakrishnan 2014)	OASIS	HC vs AD (92 / 45) HC vs MCI (92 / 67) AD vs MCI (67 / 45)	Voxel-wise texture features from structure tensor analysis (FS by FDR).	n.a.	SVM	Sen = 0.877 / Spe = 0.849 Sen = 0.764 / Spe = 0.783 Sen = 0.747 / Spe = 0.767
(Babu, Suresh et al. 2013)	ADNI	HC vs MCIc (232 / 167) MCInc vs MCIc (236 / 167)	Voxel-wise GM probability values from VBM analysis (FS by t-test).	n.a.	RBF-NN	Sen = 0.730 / Spe = 0.840 Sen = 0.880 / Spe = 0.890
(Beheshti, Demirel et al. 2015)	ADNI	HC vs AD (130 / 130)	Voxel-wise GM probability values from VBM analysis (FS based on PDF of ROI's).	n.a.	SVM (RBF)	Sen = 0.908 / Spe = 0.908
(Casanova, Hsu et al. 2013)	ADNI	HC vs AD (188 / 171) HC vs MCInc (188 / 182) HC vs MCIc (188 / 153) MCInc vs MCIc (182 / 153)	Voxel-wise intensities from GM, WM and CSF maps.	n.a. n.a. n.a. Cognitive scores.	Regularized logistic regression	Sen = 0.843 / Spe = 0.890 Sen = 0.586 / Spe = 0.681 Sen = 0.740 / Spe = 0.881 Sen = 0.579 / Spe = 0.701
(Chaddad, Desrosiers et al. 2016)	OASIS	HC vs AD (62 / 62)	3D co-occurrence matrix.	n.a.	Random forest.	Sen = 0.742 / Spe = 0.759
(Chen and Pham 2013)	OASIS	HC vs AD (75 / 75)	2D regularity information from semi-variogram analysis of GM maps.	n.a.	HMM	Sen = 0.800 / Spe = 0.800
(Chen, Wei et al. 2015)	ADNI	MCInc vs MCIc (167 / 236)	GM volumes in 93 ROI's (sparse representation).	n.a.	SRC	Sen = 0.581 / Spe = 0.763
(Chincarini, Bosco et al. 2011)	ADNI	HC vs AD (189 / 144) HC vs MCIc (189 / 136) MCInc vs MCIc (166 / 136)	Voxel intensities of filtered masks in 9 ROI's: hippocampi, amygdalae. middle and inf temp gyri, rolandic.	n.a.	Random forest + SVM	Sen = 0.890 / Spe = 0.940 Sen = 0.890 / Spe = 0.800 Sen = 0.720 / Spe = 0.650
(Cho, Seong et al. 2012)	ADNI	HC vs AD (80 / 66) HC vs MCIc (80 / 35) MCInc vs MCIc (66 / 35)	Cortical thickness values (FS by PCA).	n.a.	LDA	Sen = 0.820 / Spe = 0.930 Sen = 0.660 / Spe = 0.890 Sen = 0.630 / Spe = 0.760
(Costafreda, Dinov et al. 2011)	AddNeuroMed	MCInc vs MCIc (81 / 22)	Thickness values of hippocampi.	n.a.	SVM (RBF)	Sen = 0.770 / Spe = 0.800
(Coupé, Fonov et al. 2015)	ADNI	MCInc vs MCIc (309 / 37)	SNIPE (Scoring by Nonlocal Image Patch Estimator) hippocampal features.	n.a.	LDA	Sen = 0.649 / Spe = 0.735

MKL : Multiple Kernel Learning

Evaluation

Reference	Dataset	Classification tasks (n)	Image features (FS and representation)	Additional imaging sequences and features	Classifiers	Results
(Jiang and Shi 2014)	ADNI	HC vs AD (52 / 51)	83 ROI volumes from GM maps (FS by sparse kernel entropy component analysis).	n.a.	kNN	Sen = 0.920 / Spe = 0.904
(Jie, Zhang et al. 2014)	ADNI	HC vs AD (52 / 51) HC vs MCI (52 / 99)	GM volumes and PET intensity values in 93 ROI's(FS by manifold regularized multitask learning method).	PET, CSF biomarkers.	MKL	Sen = 0.947 / Spe = 0.958 Sen = 0.894 / Spe = 0.708
(Khedher, Ramirez et al. 2015)	ADNI	HC vs AD (229 / 188) HC vs MCI (229 / 401) MCI vs AD (401 / 188)	Voxel intensities in GM and WM maps (FS by partial least square).	n.a.	SVM (linear)	Sen = 0.913 / Spe = 0.851 Sen = 0.822 / Spe = 0.816 Sen = 0.870 / Spe = 0.838
(Komlagan, Ta et al. 2014)	ADNI	MCInc vs MCIc (236 / 166)	SNIPE (Scoring by Nonlocal Image Patch Estimator) hippocampal features (FS by sparse logistic regression).	n.a.	SVM (linear)	Sen = 0.615 / Spe = 0.856
(Korolev, Symonds et al. 2016)	ADNI	MCInc vs MCIc (139 / 120)	Cortical thickness, volumes, curvature and surface area of 180 ROI's (FS by joint mutual information criterion).	Risk factors, cognitive scores, proteomic data.	MKL	Sen = 0.834 / Spe = 0.764
(Krashenyi, Ramirez et al. 2016)	ADNI	HC vs AD (229 / 188) HC vs MCI (229 / 401) MCI vs AD (401 / 188)	Mean ROI intensity values of GM and WM maps from T1w and mean intensity from PET (FS by t-test).	PET.	Fuzzy inference system.	Sen = 0.933 / Spe = 0.922 Sen = 0.759 / Spe = 0.861 Sen = 0.749 / Spe = 0.820
(Lebedev, Westman et al. 2014)	ADNI	HC vs AD (75 / 35) MCInc vs MCIc (130 / 35)	Volumes from 41 ROI's and cortical thickness values (FS by PCA and RFE).	APOE3, demographics.	Random forest.	Sen = 0.920 / Spe = 0.886 Sen = 0.833 / Spe = 0.813
(Li, Wang et al. 2010)	OASIS	HC vs MCI (80 / 89)	GM values in 19 ROI's (FS by t-test and feature ranking).	MMSE.	SVM (RBF)	Sen = 0.919 / Spe = 0.880
(Li, Liu et al. 2014)	ADNI	MCIc vs MCInc (161 / 132)	Cortical thickness values, volumes of cortical ROI's, volumes of WM in ROI's, total surface area of the cortex (FS by hierarchical Lasso method).	Demographics, genetic data, cognitive scores, lab tests.	Random forest	Sen = 0.667 / Spe = 0.814
(Li, Oishi et al. 2014)	ADNI	HC vs AD (142 / 80) MCInc vs MCIc (142 / 141)	Voxel-wise combination of 2D-LBP from axial, coronal and sagittal orientations (FS by t-test and a priori knowledge).	n.a.	SVM	Sen = 0.804 / Spe = 0.827 Sen = 0.615 / Spe = 0.635
(Li, Yan et al. 2015)	ADNI	HC vs AD (60 / 60) HC vs MCI (60 / 60)	Volume and 15 texture features from 4 structures (GM, WM, CSF, hippocampus) in L / R hemispheres (FS by chain-like agent genetic algorithm).	n.a.	SVM (RBF)	Sen = 0.927 / Spe = 0.973 Sen = 0.804 / Spe = 0.864

Neuro Computing 2015

Evaluation

(Martinez-Murcia, Gorriz et al. 2016)	ADNI	HC vs AD (180 / 180)	LBP features from GM and WM maps (2D representation of the brain and FS by t-test).	n.a.	SVM (linear)	Sen = 0.899 / Spe = 0.919
(McEvoy, Fennema-Notestine et al. 2009)	ADNI	HC vs AD (139 / 84)	Morphometric measures from 58 ROI's.	n.a.	LDA	Sen = 0.830 / Spe = 0.930
(Moradi, Pepe et al. 2015)	ADNI	MCInc vs MCIc (100 / 164)	Voxel-wise GM density values (FS by regularized logistic regression).	Age, RAVLT, ADAS-Cog, MMSE, CDR-SB, FAQ.	Random forest + SVM (RBF)	Sen = 0.870 / Spe = 0.740
(Morgado and Silveira 2015)	ADNI	HC vs AD (75 / 59) HC vs MCI (75 / 135)	Voxel-wise GM density values (FS by Minimal Neighborhood Redundancy Maximal Relevance).	n.a.	SVM	Sen = 0.869 / Spe = 0.872 Sen = 0.688 / Spe = 0.670
(Nho, Shen et al. 2010)	ADNI	HC vs AD (226 / 182) HC vs MCI (226 / 355)	GM density values from 86 ROI's, cortical thickness values from 56 ROI's (FS by SVM-RFE).	APOE3, family history.	SVM (RBF)	Sen = 0.850 / Spe = 0.948 Sen = 0.694 / Spe = 0.698
(Plocharski and Østergaard 2016)	ADNI	HC vs AD (96 / 109)	Depth, length, curvature and surface area of 24 sulci (FS by forward selection).	n.a.	SVM (linear)	Sen = 0.900 / Spe = 0.867
(Rao, Lee et al. 2011)	Local	HC vs AD (60 / 69)	Voxel-wise GM density values (FS by spatially regularized formulation).	n.a.	Logistic regression	Sen = 0.904 / Spe = 0.803
(Rueda, Gonzalez et al. 2014)	OASIS	HC vs MCI + AD (98 / 100)	Voxel intensities (graph-based saliency map representation).	n.a.	MKL	Sen = 0.670 / Spe = 0.735
(Zhou, Goryawala et al. 2014)	ADNI	HC vs AD (127 / 59) HC vs MCIc (127 / 67) HC vs MCInc (127 / 56)	41 regional and 10 morphometric volumes (FS by t-test).	MMSE.	SVM (RBF)	Sen = 0.840 / Spe = 0.961 Sen = 0.611 / Spe = 0.834 Sen = 0.552 / Spe = 0.823
(Zhu, Suk et al. 2014)	ADNI	HC vs AD (52 / 51) HC vs MCI (52 / 99)	GM volumes and PET intensity values in 93 ROI's (FS by regularized least square regression).	n.a.	SVM	Sen = 0.886 / Spe = 0.978 Sen = 0.948 / Spe = 0.569
(Zhu and Shi 2014)	ADNI	HC vs AD (52 / 51)	GM volumes in 93 ROI's (co-training semi-supervised learning approach).	n.a.	SVM (linear)	Sen = 0.869 / Spe = 0.904
(Zhu, Shi et al. 2014)	ADNI	HC vs AD (52 / 51)	GM volumes and PET intensity values in 93 ROI's (FS by Hessian regularization semi-supervised approach).	n.a.	SVM (linear)	Sen = 0.952 / Spe = 0.907

MICCAI 2014

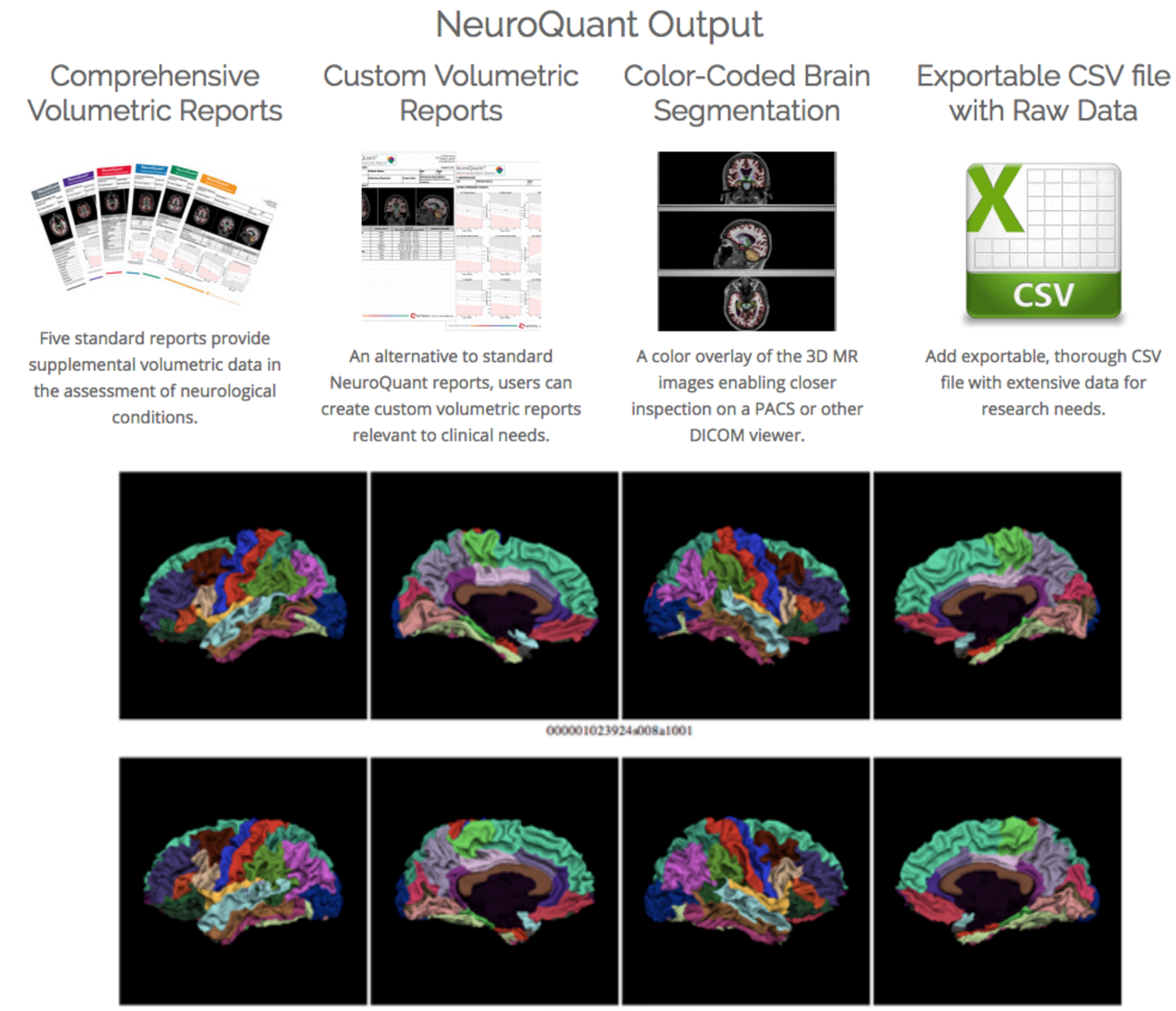
Our Approach

Neuroimaging to Diagnose AD

- Bio marker extraction
  - Whole brain parcellation 으로 atrophy 측정
  - Multi center | multi device | multi sequence adaptation
- AD prediction
  - AD | MCI | CN 환자의 age-sex-volume-biomarker 를 이용한 분류
- WMH, CSF, Cortical thickness
- Non-imaging data
  - Cognitive test scores, CDR

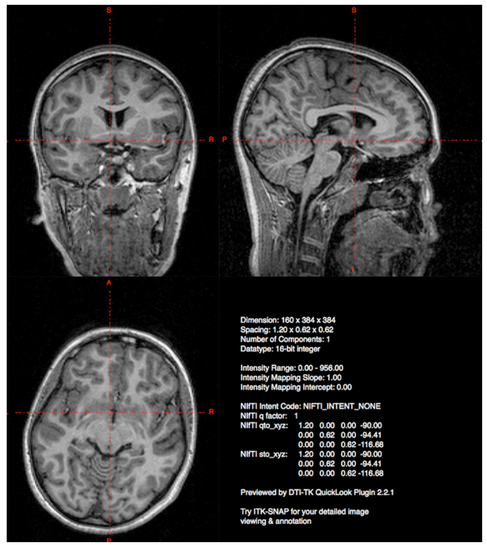
Whole Brain Parcellation

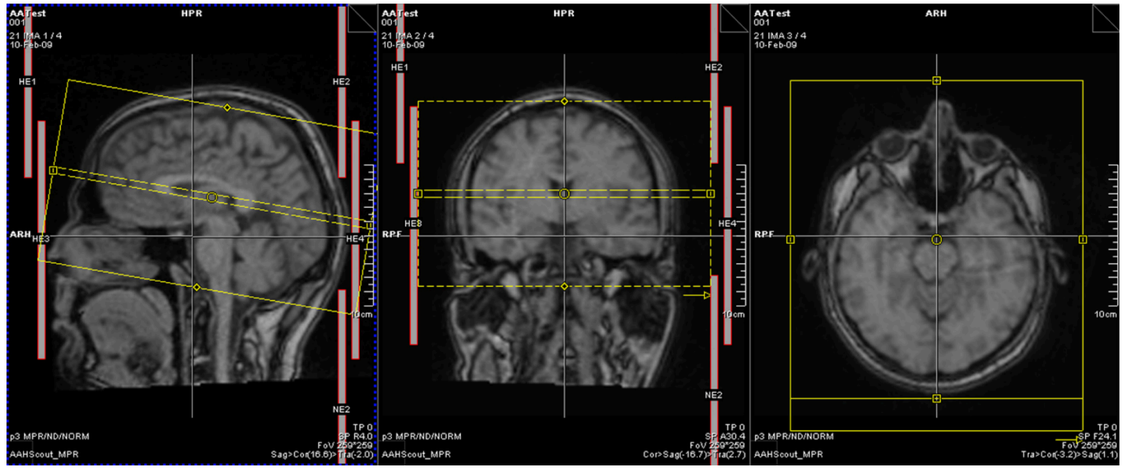
- Neuroquant
  - 상용
  - 다양한 분석 툴, 리포트, 시각화
  - 빠른 분석 시간 (10분)
- Freesurfer
  - 공개소프트웨어
  - 분석시간 6시간 (full parcellation)



Brain MR Preprocessing

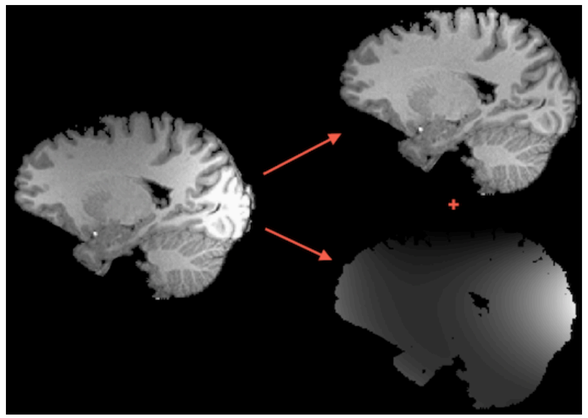
Dcm to nii (nifti format) → Reorientation → AC-PC Alignment

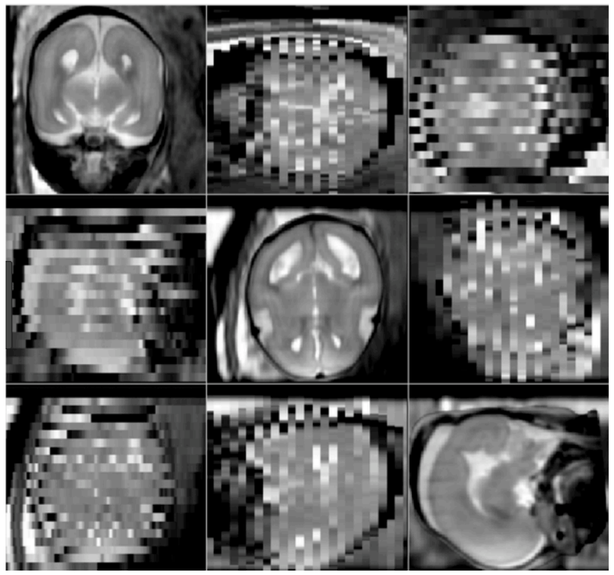


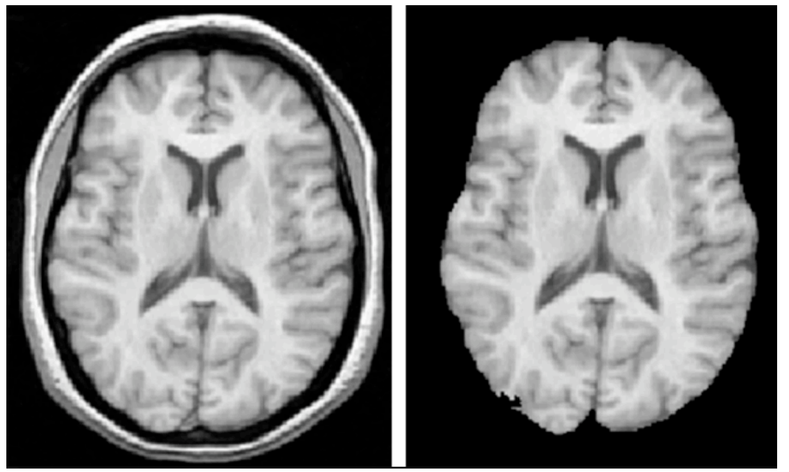


Brain MR Preprocessing

Bias field correction → Resample to 1mm Isotropic → AC-PC Alignment







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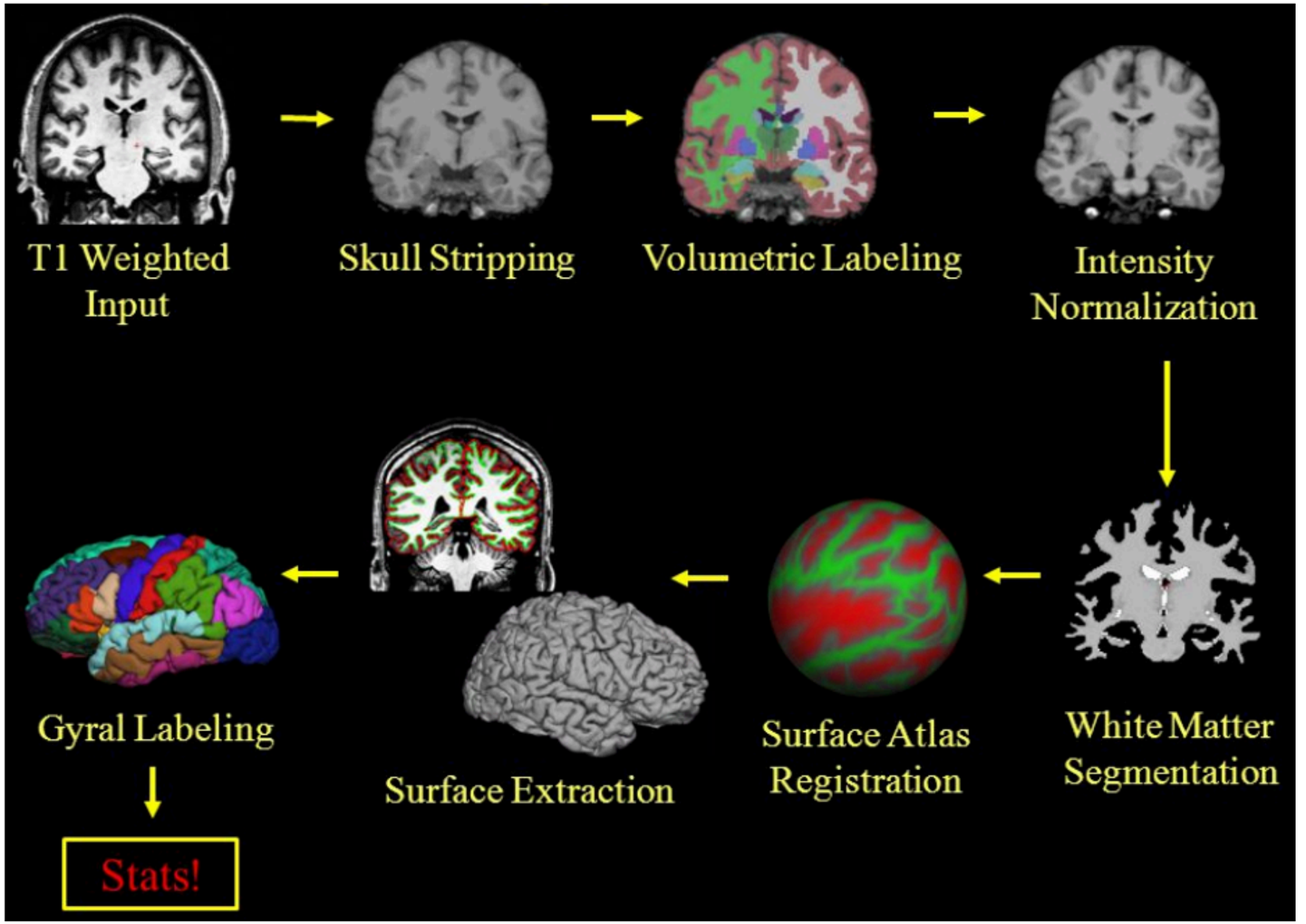
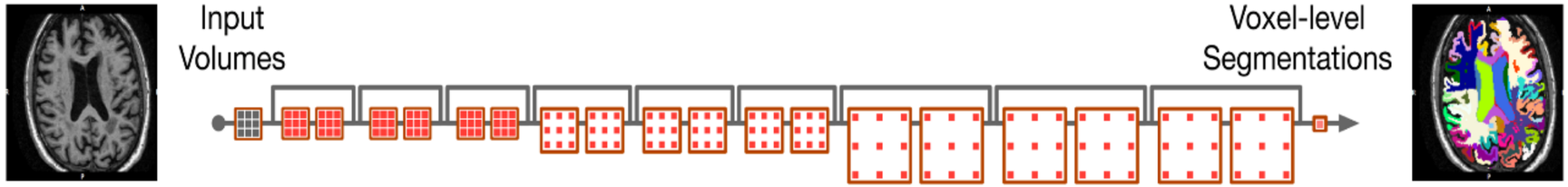
Parcellation Algorithms



Whole Brain Parcellation with ML

- 2.5D HiResNet
  - Atrous convolution
  - ResNet
  - Dice loss

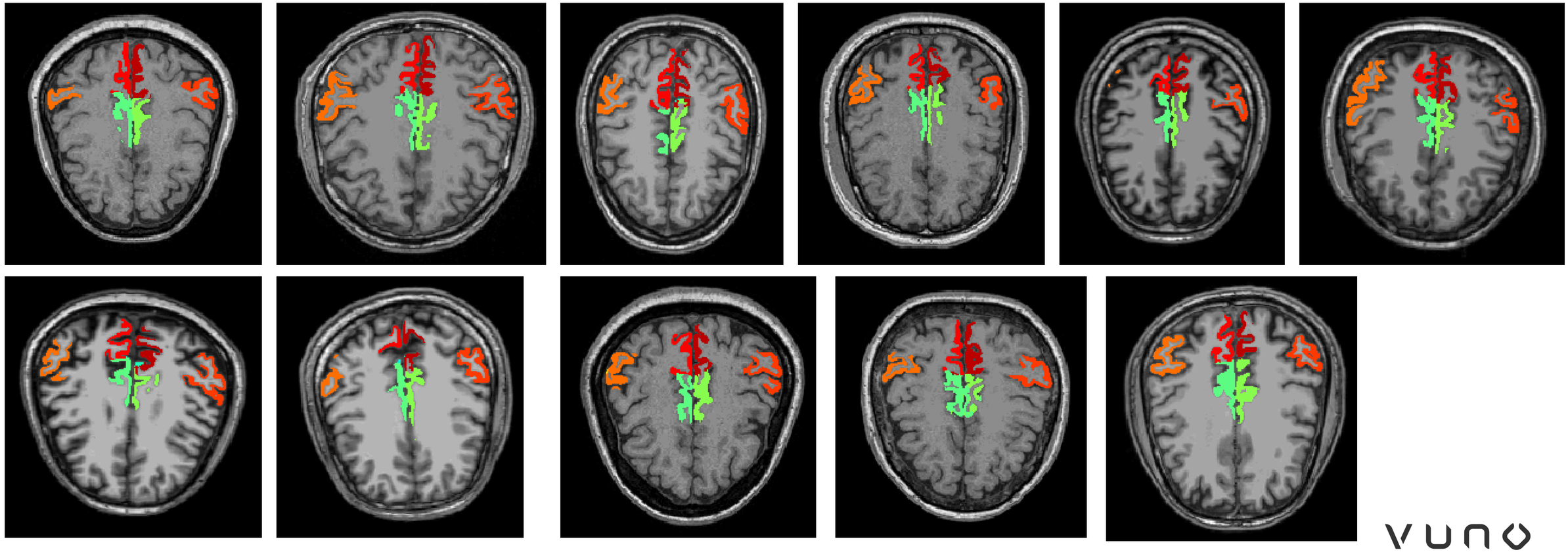


$$\mathcal{D}(\{x_n\},\{y_n\}) = \frac{1}{C}\sum_{c=1}^{C}\frac{2\sum_{n=1}^{N}\delta(y_n=c)F_c(x_n)}{\sum_{n=1}^{N}[\delta(y_n=c)]^2+\sum_{n=1}^{N}[F_c(x_n)]^2}.$$

Preprocessing

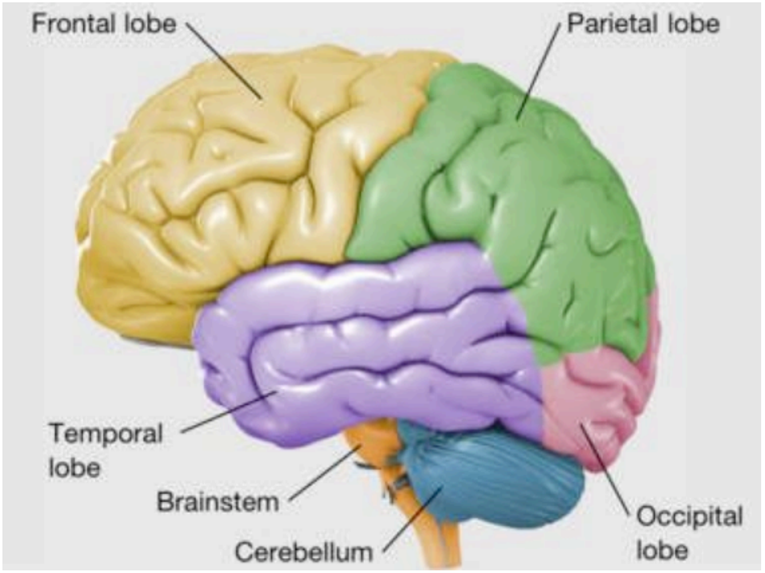
Image Quality Variation (Device, Sequence, Clinical center)

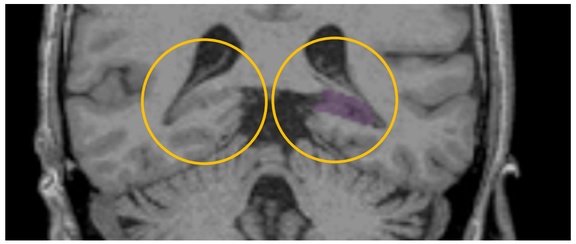
- Part based Normalization (Gray matter)
- Histogram matching
- Noise synthesis



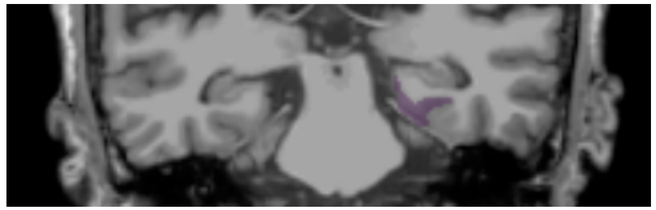
Location Aware

- 뇌 영역에서의 상대적 위치를 인식
- 기존방법 : Brain atlas mapping (사전지식)
  - Co-registration (정규화)
  - Atlas map 생성 (한국인)
  - Re-location
  - Segmentation
- 객체인식방법 :
  - No registration/standardization
  - No atlas map
  - Detection and segmentation 을 동시에 수행
  - 위치를 전체 뇌영역에 인접한 패턴으로 인식, 좌/우 위치도 같은 방식으로 위치에 대한 사전지식 없이
  - 뇌 영역간 상대적 연결성 문제 (Affinity map, relational… , geometric …)





Hippocampus

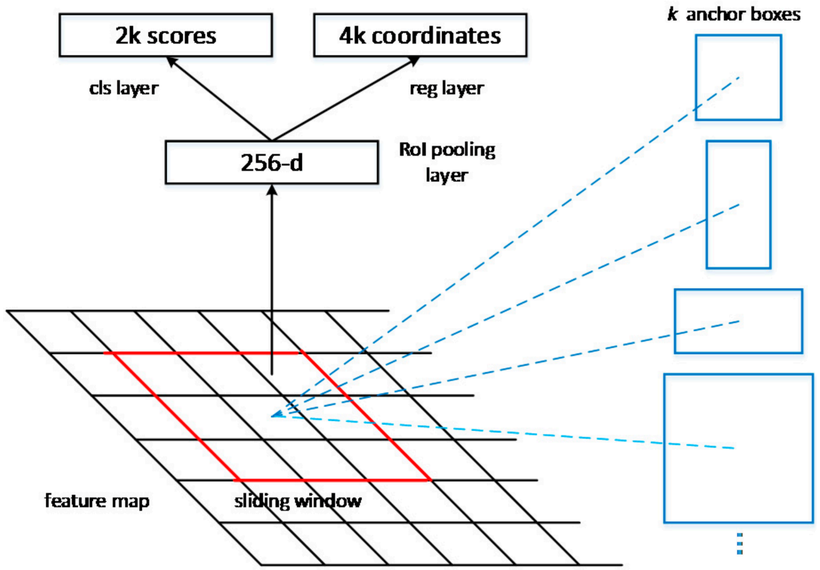


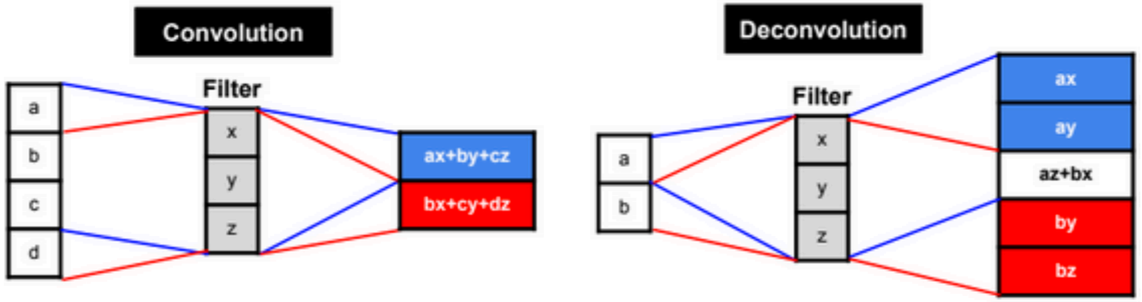
Parahippocampal

Entorhinal

Object Detection

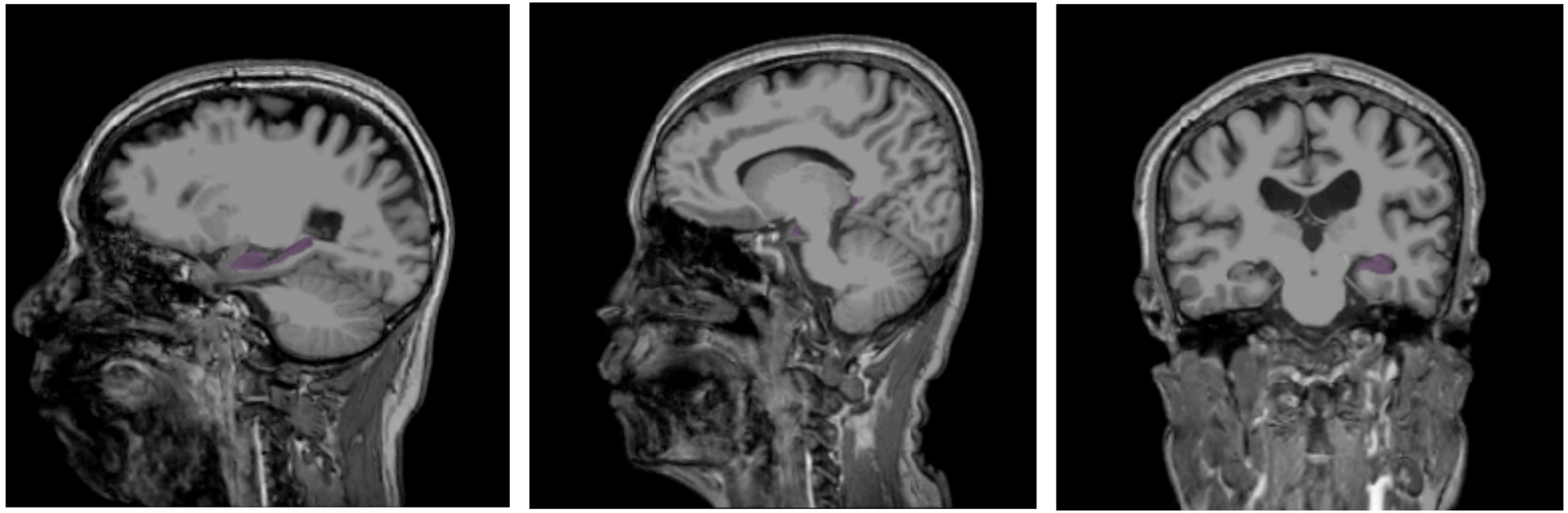
- Negative (background) 가 훨씬 많은 데이터, 객체의 위치 검출
- Faster RCNN vs Deconvolutional network
  - 위치 : class map + clustering | class map + deconvolution
  - 크기 : box regression | pixel classification
  - Negative 처리 : output selection | loss weighting
  - 특징 : instance detection | pixel level classification (≅ segmentation)





Pixel Classification

- Image Segmentation
  - 영상에서 물체의 경계를 찾는 기법
  - Histogram/edge based clustering
  - GraphCut
  - Segmentation by classification



Hippocampus

Data Imbalance

- Positive, negative, class imbalance
- Categorical weight balancing
  - Label 의 비율대로 class 별 loss 비율을 맞춤

$$L(y, \hat{y}) = -\sum_{nk} w_k y_{nk} \log \hat{y}_{nk}$$

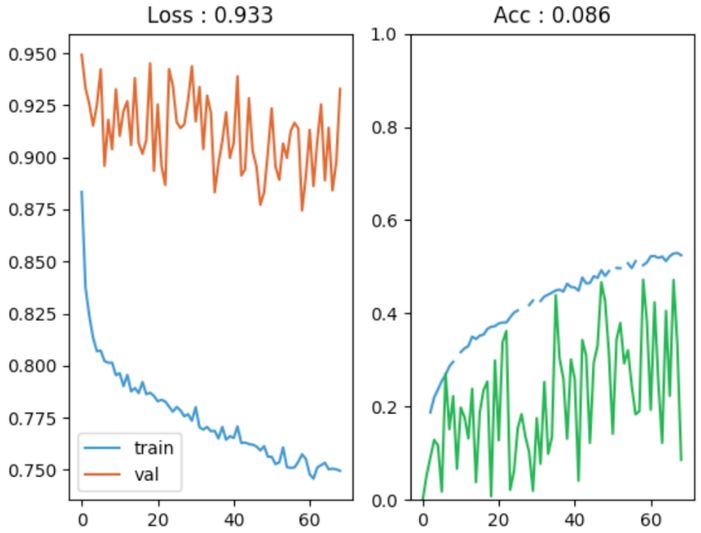
- Dice coefficient loss
  - Dice coefficient : $\frac{2pt}{p^2+t^2}$ (p : softmax output t : target)
  - Gradient : $\frac{2t^2}{(p+t)^2}$
  - P 와 t 가 작을 때 gradient 가 매우 커짐
  - t 에 따라 다른 loss function 을 사용 혹은 Gradient clipping

$$\text{dice}(X, Y) = \frac{2X \cap Y}{X + Y}$$

High ResNet

http://www.ucl.ac.uk/interventional-surgical-sciences/research/research-platforms/nifty-net

- No pooling
  - 객체 인식 문제 + 특정 데이터에서는 pooling 이 도움이 안됨
  - Pooling 이 도움이 되는 경우 : 크기의 변화가 심하고, 객체의 상대 데이터 수가 적으며, 배경 변화가 심한 경우
  - 해상도 유지가 중요한 문제 (영상 복원)
- Network depth
  - GPU 메모리가 허용하는 최대
  - 1 batch : oscillation 문제. Group norm 이 도움이 됨.




```python
def GroupNorm(x, gamma, beta, G, eps=1e-5):
    # x: input features with shape [N,C,H,W]
    # gamma, beta: scale and offset, with shape [1,C,1,1]
    # G: number of groups for GN

    N, C, H, W = x.shape
    x = tf.reshape(x, [N, G, C // G, H, W])

    mean, var = tf.nn.moments(x, [2, 3, 4], keep_dims=True)
    x = (x - mean) / tf.sqrt(var + eps)

    x = tf.reshape(x, [N, C, H, W])

    return x * gamma + beta
```

Figure 3. Python code of Group Norm based on TensorFlow.

https://arxiv.org/abs/1803.08494

High ResNet

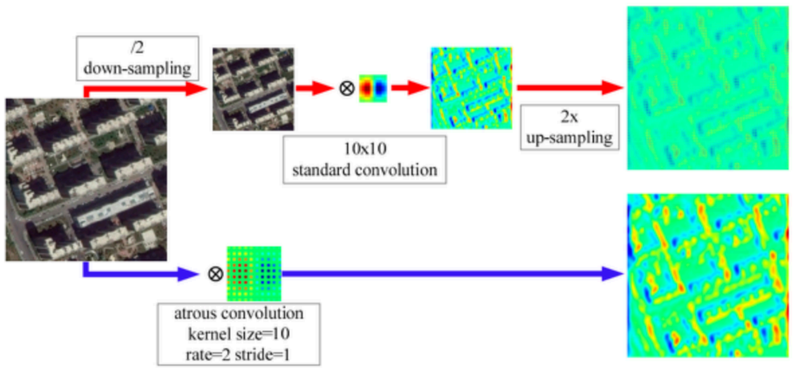
- Atrous convolution
  - Convolution 의 횟수, stride size, kernel size 를 늘리면 Receptive field 가 커짐

n : number of features
r : receptive field size
j : jump (distance between two consecutive features)
$start$: center coordinate of the first feature

k : convolution kernel size
p : convolution padding size
s : convolution stride size

$$n_{out} = \left\lfloor \frac{n_{in} + 2p - k}{s} \right\rfloor + 1$$
$$j_{out} = j_{in} * s$$
$$r_{out} = r_{in} + (k-1) * j_{in}$$
$$start_{out} = start_{in} + \left(\frac{k-1}{2} - p\right) * j_{in}$$

  - 깊이와 파라미터 수를 동시에 줄이면서 Receptive field 와 성능 개선



https://medium.com/mlreview/a-guide-to-receptive-field-arithmetic-for-convolutional-neural-networks-e0f514068807

2D vs 3D

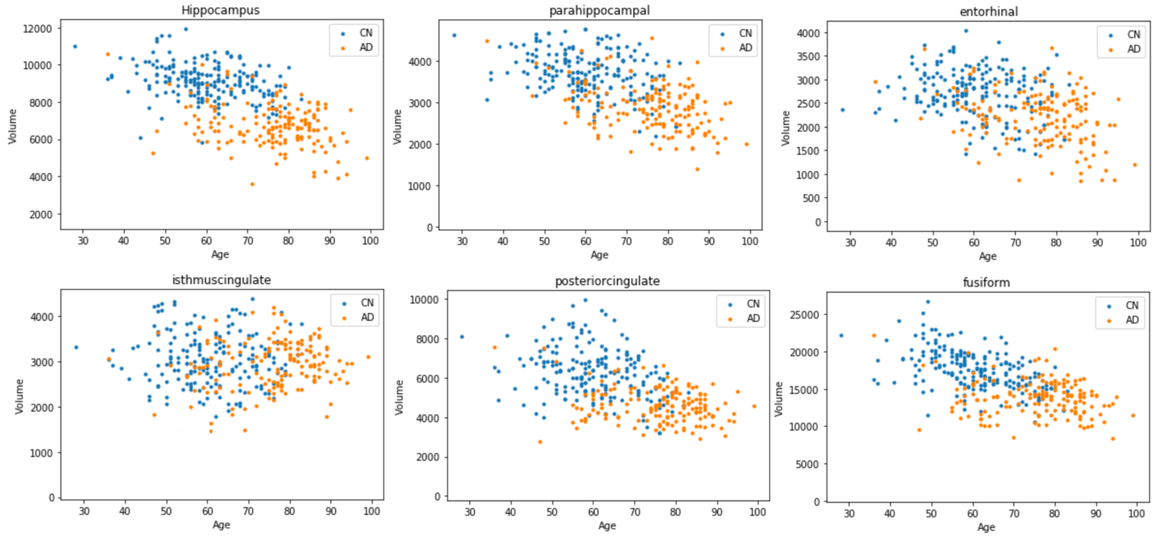
- 3D voxel classification
  - Vanilla 3D CNN 의 성능 한계
  - 3D convolution 의 파라미터 수
  - 3D voxel data 의 구조적 문제 (surface/volume texture)
- 3D object detection
  - 3D FCN : 이상적이지만 현실적으로 어려움
    - GPU 메모리 문제
    - Voxel sliding window
  - 2.5D : n 개 slice 를 2D channel 로 구성
    - 3D 로의 확장
      - FCN 은 kernel 을 모든 영역에서 share 하므로, slice 단위 batch learning 도 slice 축 FCN 을 적용한 것과 유사한 효과
      - Slice 를 shuffling 함으로써 인접한 slice correlation 을 깨트리는 효과
      - 학습이 용이한 것들 먼저 샘플링

Algorithm	ModelNet40 Classification (Accuracy)	ModelNet40 Retrieval (mAP)	ModelNet10 Classification (Accuracy)	ModelNet10 Retrieval (mAP)
SO-Net[34]	93.4%		95.7%	
Minto et al.[33]	89.3%		93.6%	
RotationNet[32]	97.37%		98.46%	
LonchaNet[31]			94.37	
Achlioptas et al. [30]	84.5%		95.4%	
PANORAMA-ENN [29]	95.56%	86.34%	96.85%	93.28%
3D-A-Nets [28]	90.5%	80.1%		
Soltani et al. [27]	82.10%			
Arvind et al. [26]	86.50%			
LonchaNet [25]			94.37%	
3DmFV-Net [24]	91.6%		95.2%	
Zanuttigh and Minto [23]	87.8%		91.5%	
Wang et al. [22]	93.8%			
ECC [21]	83.2%		90.0%	
PANORAMA-NN [20]	90.7%	83.5%	91.1%	87.4%
MVCNN-MultiRes [19]	91.4%			
FPNN [18]	88.4%			
PointNet[17]	89.2%			
Klokov and Lempitsky[16]	91.8%		94.0%	
LightNet[15]	88.93%		93.94%	
Xu and Todorovic[14]	81.26%		88.00%	
Geometry Image [13]	83.9%	51.3%	88.4%	74.9%
Set-convolution [11]	90%			
PointNet [12]			77.6%	
3D-GAN [10]	83.3%		91.0%	
VRN Ensemble [9]	95.54%		97.14%	
ORION [8]			93.8%	
FusionNet [7]	90.8%		93.11%	
Pairwise [6]	90.7%		92.8%	
MVCNN [3]	90.1%	79.5%		
GIFT [5]	83.10%	81.94%	92.35%	91.12%
VoxNet [2]	83%		92%	
DeepPano [4]	77.63%	76.81%	85.45%	84.18%
3DShapeNets [1]	77%	49.2%	83.5%	68.3%

http://modelnet.cs.princeton.edu/

AD Prediction

- Volume, ICV Percentile
  - Atrophy 를 volume 등의 수치로 표현하고, 정상/비정상 환자 분포에서의 percentile 계산



- Biomarker base
  - Parcellation 된 biomarker 를 이용하여 ML 로 분류
  - 임상 검증이 관건
  - 정상/비정상 군과의 거리 측정도 한 방법

Conclusion

- 왜 치매 관련 연구를 하는가?
  - MR 영상으로 AD 의심환자를 조기에 예측
- 어떤 문제에 집중할 것인가?
  - Atrophy 를 측정/분석, 정상환자와의 차이를 인식
- 작은 문제정의, 어려움들
  - 의료 데이터의 불규칙성은 다양한 데이터 수집과 기존 영상처리 기법들을 사용하여 극복
  - 뇌영역 위치인식과 영역 분류를 위해 객체 인식 기법 사용
  - 정교한 영역 분할을 위한 CNN 구조
  - 3D 데이터 학습을 위한 부분적인 해결책
  - 뇌영역간 연결성 문제는 숙제
  - Atrophy 측정, parcellation 기반의 AD 예측

Putting the world’s medical data to work

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