TRACING THE HIPPOCAMPAL WHITE MATTER: Manual segmentation of the fornix, fimbria and alveus on high-resolution 3T MRI

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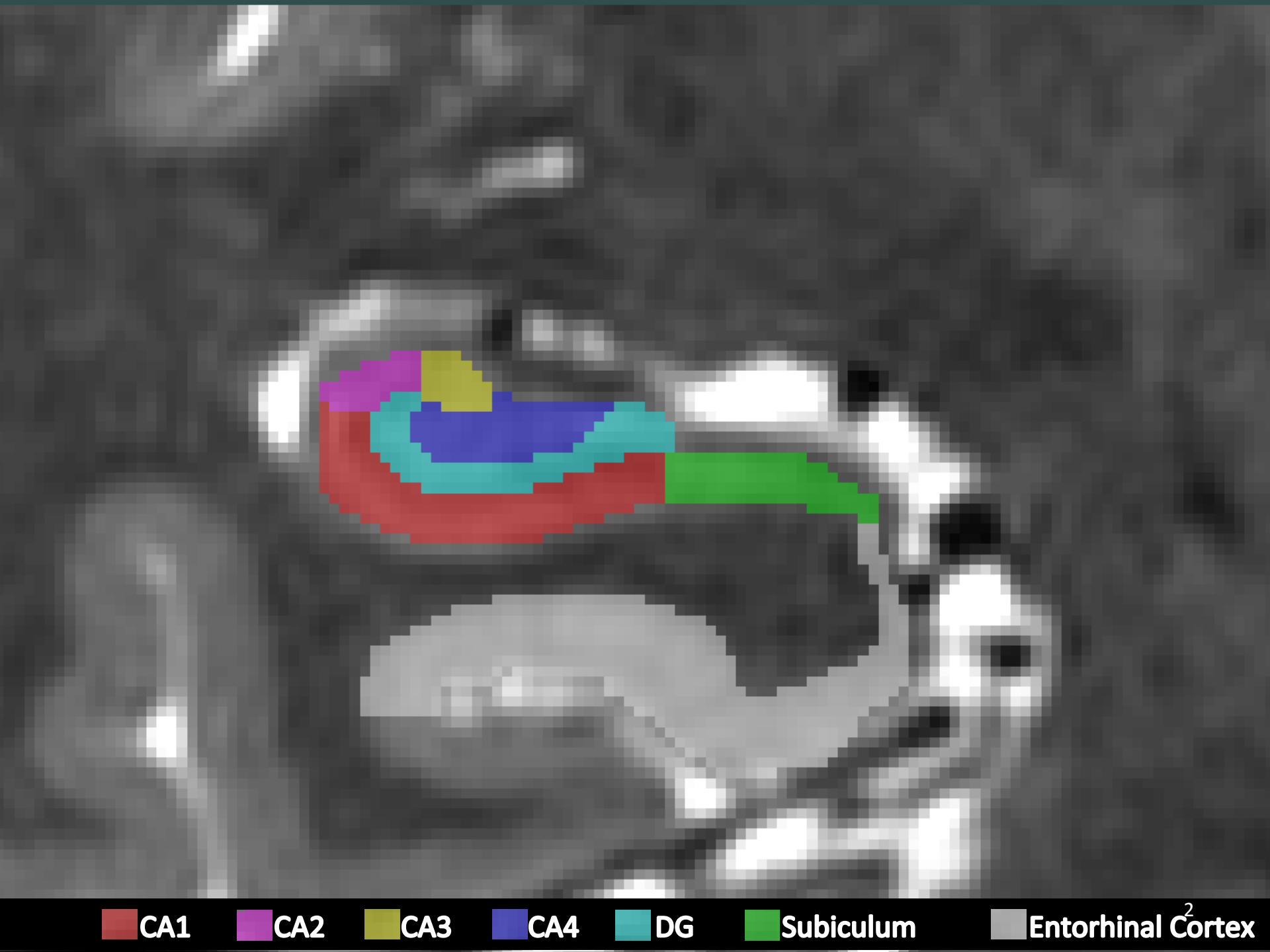
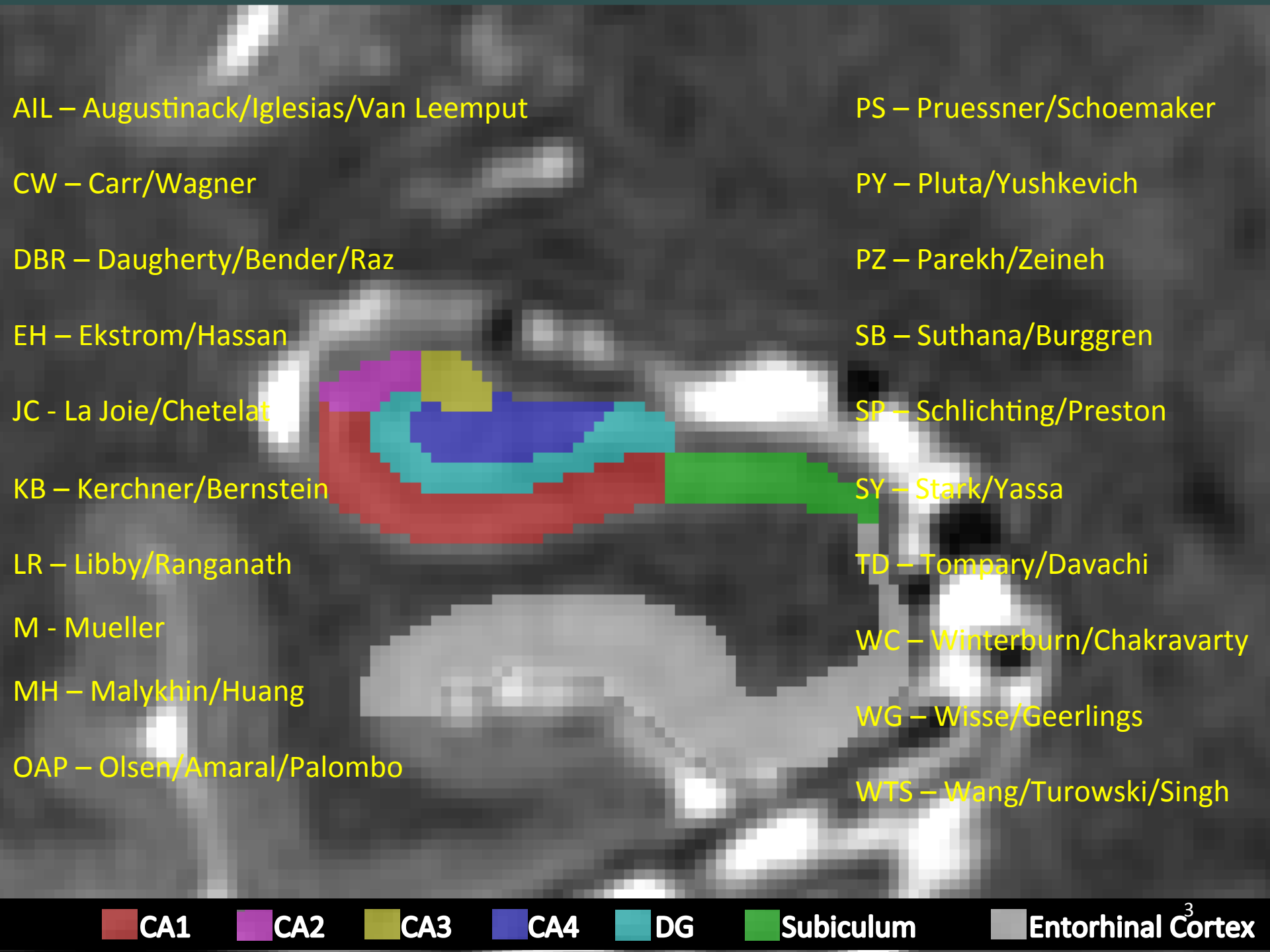
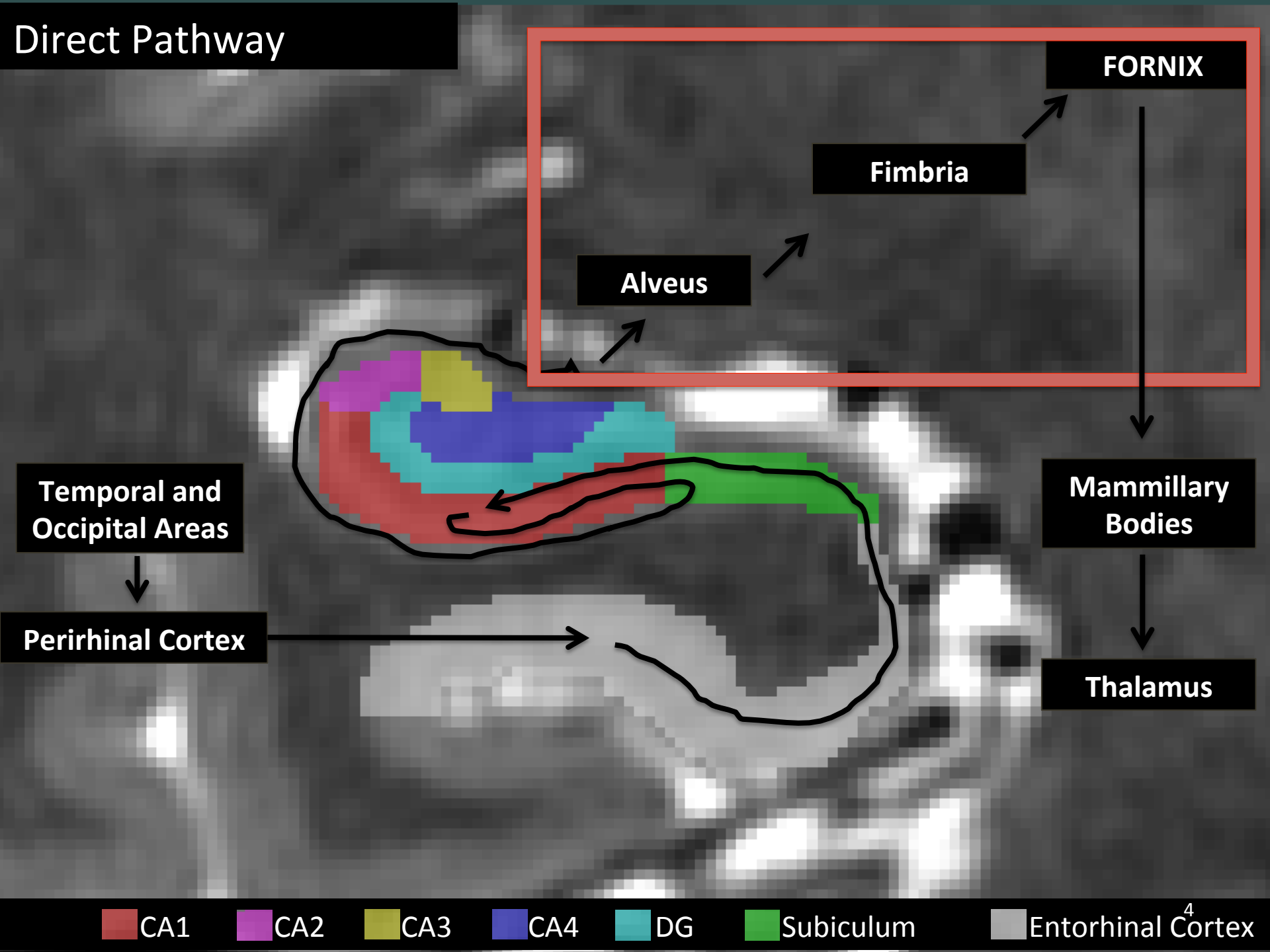

CA1
CA2
CA3
CA4
DG
Subiculum
Entorhinal Cortex


AIL – Augustinack/Iglesias/Van Leemput
CW – Carr/Wagner
DBR – Daugherty/Bender/Raz
EH – Ekstrom/Hassan
JC - La Joie/Chetelat
KB – Kerchner/Bernstein
LR – Libby/Ranganath
M - Mueller
MH – Malykhin/Huang
OAP – Olsen/Amaral/Palombo
PS – Pruessner/Schoemaker
PY – Pluta/Yushkevich
PZ – Parekh/Zeineh
SB – Suthana/Burggren
SP – Schlichting/Preston
SY – Stark/Yassa
TD – Tompary/Davachi
WC – Winterburn/Chakravarty
WG – Wisse/Geerlings
WTS – Wang/Turowski/Singh
CA1
CA2
CA3
CA4
DG
Subiculum
Entorhinal Cortex


Direct Pathway
FORNIX
Fimbria
Alveus
Temporal and Occipital Areas
Perirhinal Cortex
Mammillary Bodies
Thalamus
CA1
CA2
CA3
CA4
DG
Subiculum
Entorhinal Cortex

Why Segmentation?

1. A different measure of tract integrity
2. Can obtain volume estimates and perform shape analysis
3. Unexplored areas in disease and healthy states
4. Mapping and measurement of the entire circuit

Previous Protocol for the Alveus/Fimbria/Fornix

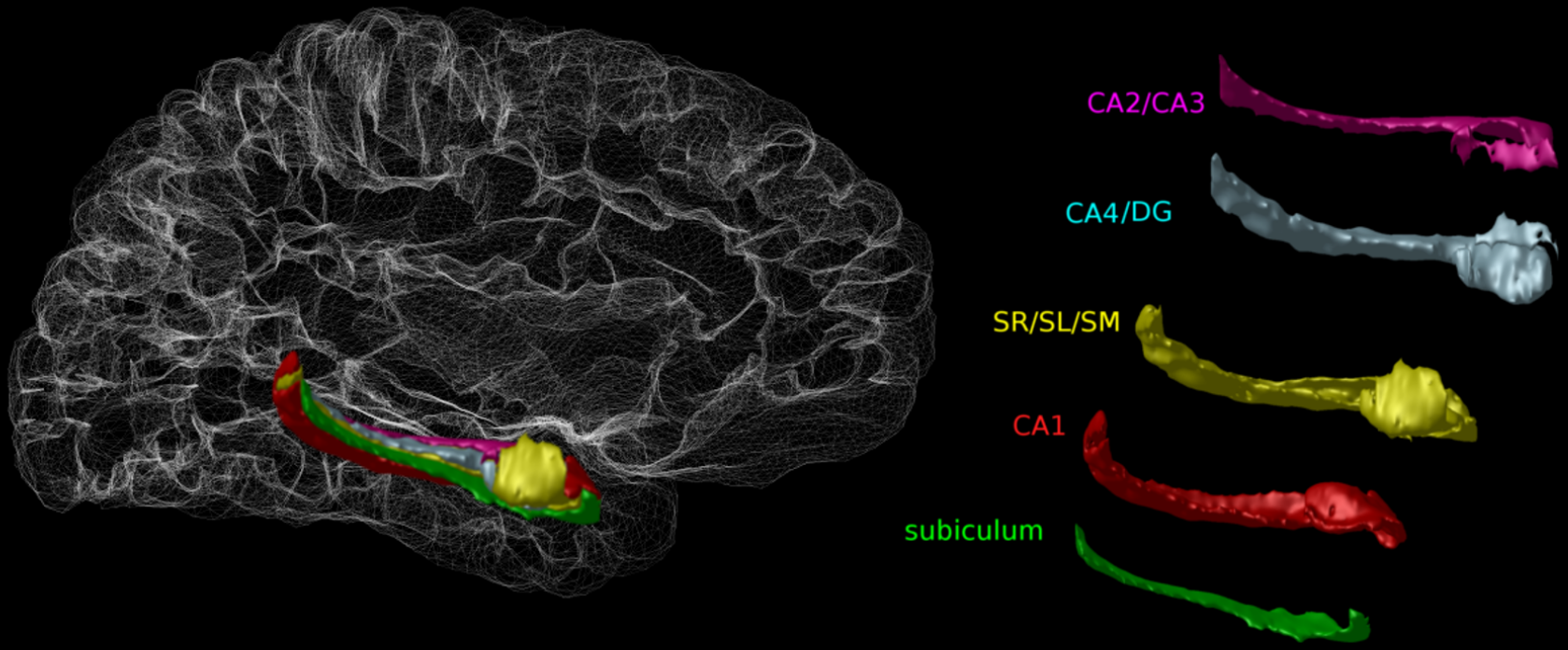
Fornix only:

- Copenhaver et al., 2006
- Zahajszky et al., 2001
- Kuzniecky et al., 1999
- Bilir et al., 1998
- Gale et al., 1993

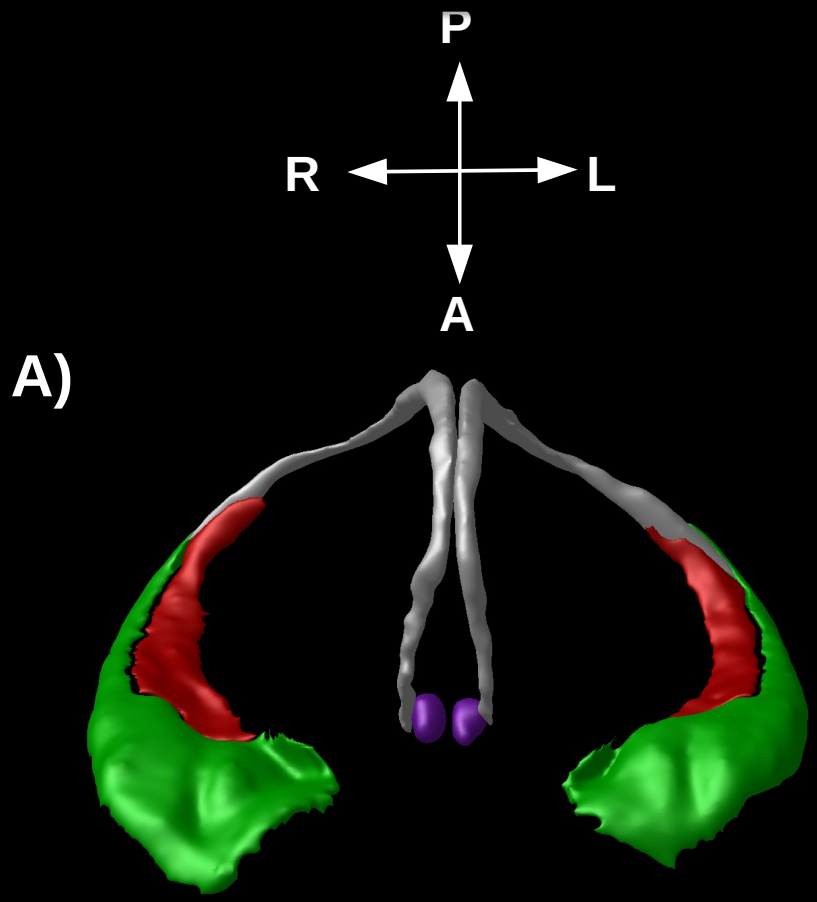
Alveus/Fimbria:

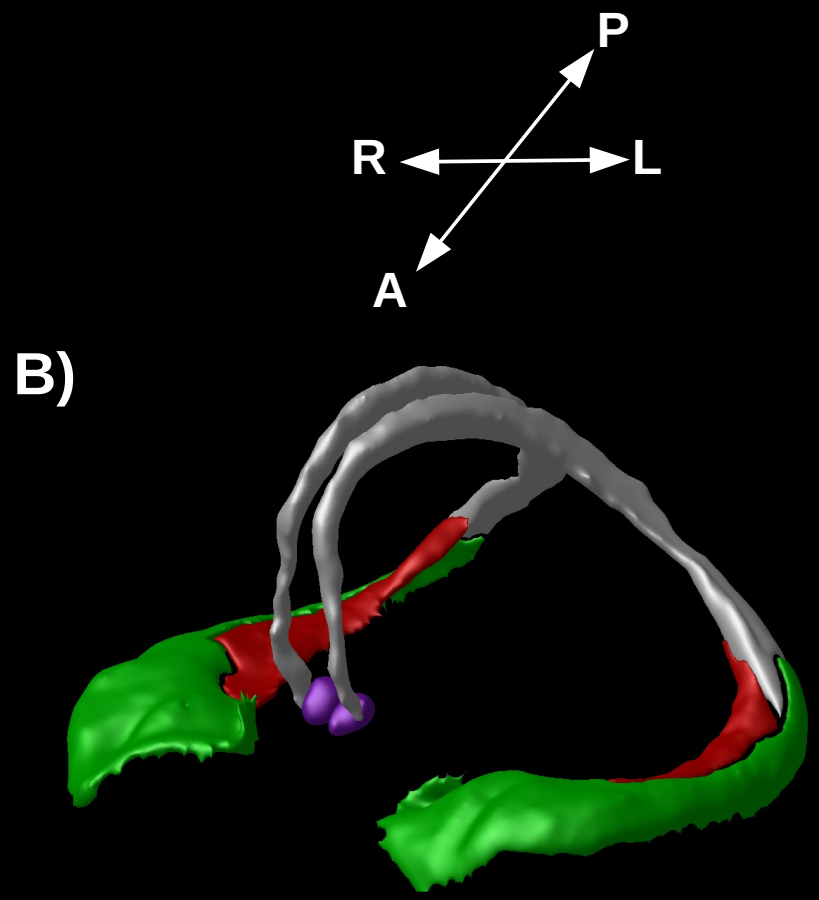
- Wang, Turowski & Singh (Wang et al., 2003)
- Parekh & Zeineh (Zeineh et al., 2012)

Winterburn et al. 2013



Final Protocol Product



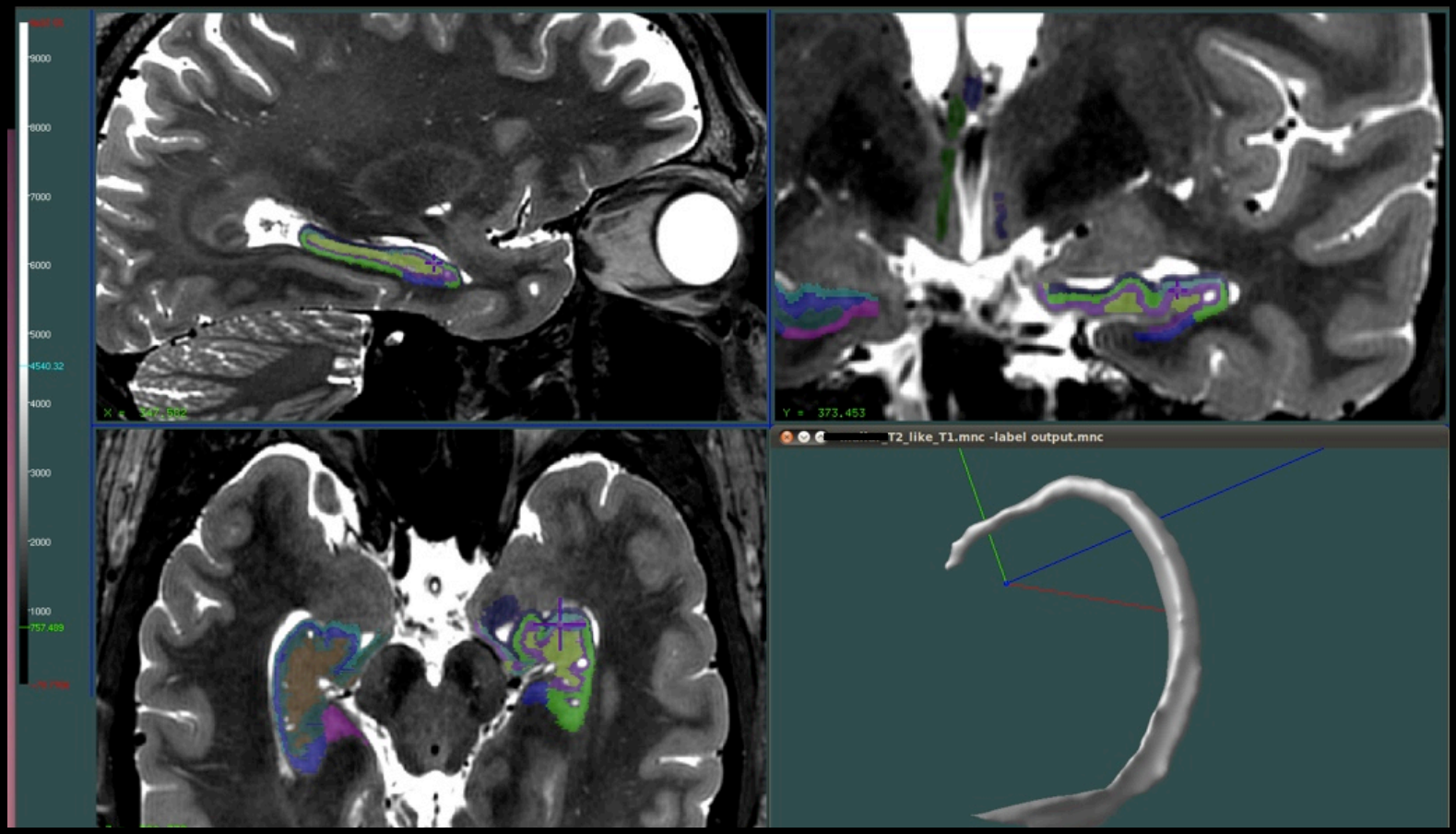


Acquisition

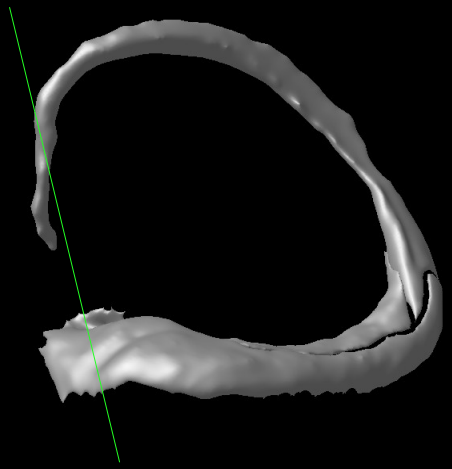
- Same data as Winterburn et al. 2013
- 3T GE Discovery MR 750 (8-channel head coil)
- 3 T1-weighted images averaged (FSPGR-BRAVO, ~20min each)
- 3 T2-weighted images averaged (FSE-CUBE, ~20min each)
- T1/T2 images rigidly co-aligned
- Final voxel dimensions of 0.3 mm isotropic
- Corrected for RF inhomogeneity non-uniformity

- 5 healthy volunteers (age range 29-57, average 37)

Tri-Planar + 3D Approach



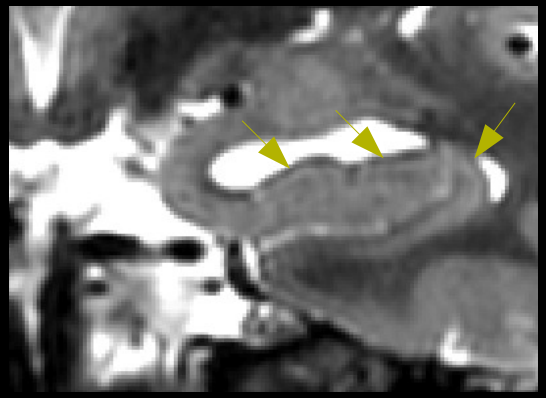
The Protocol



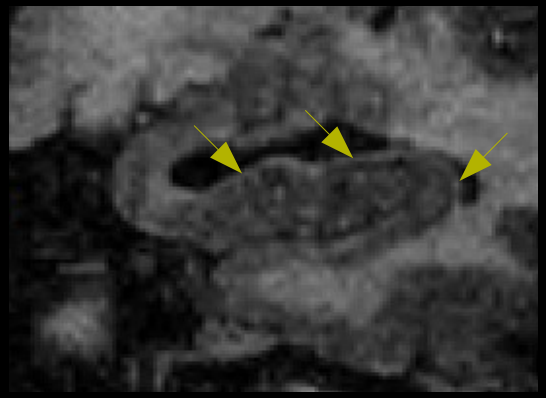
T2-Weighted

S

L

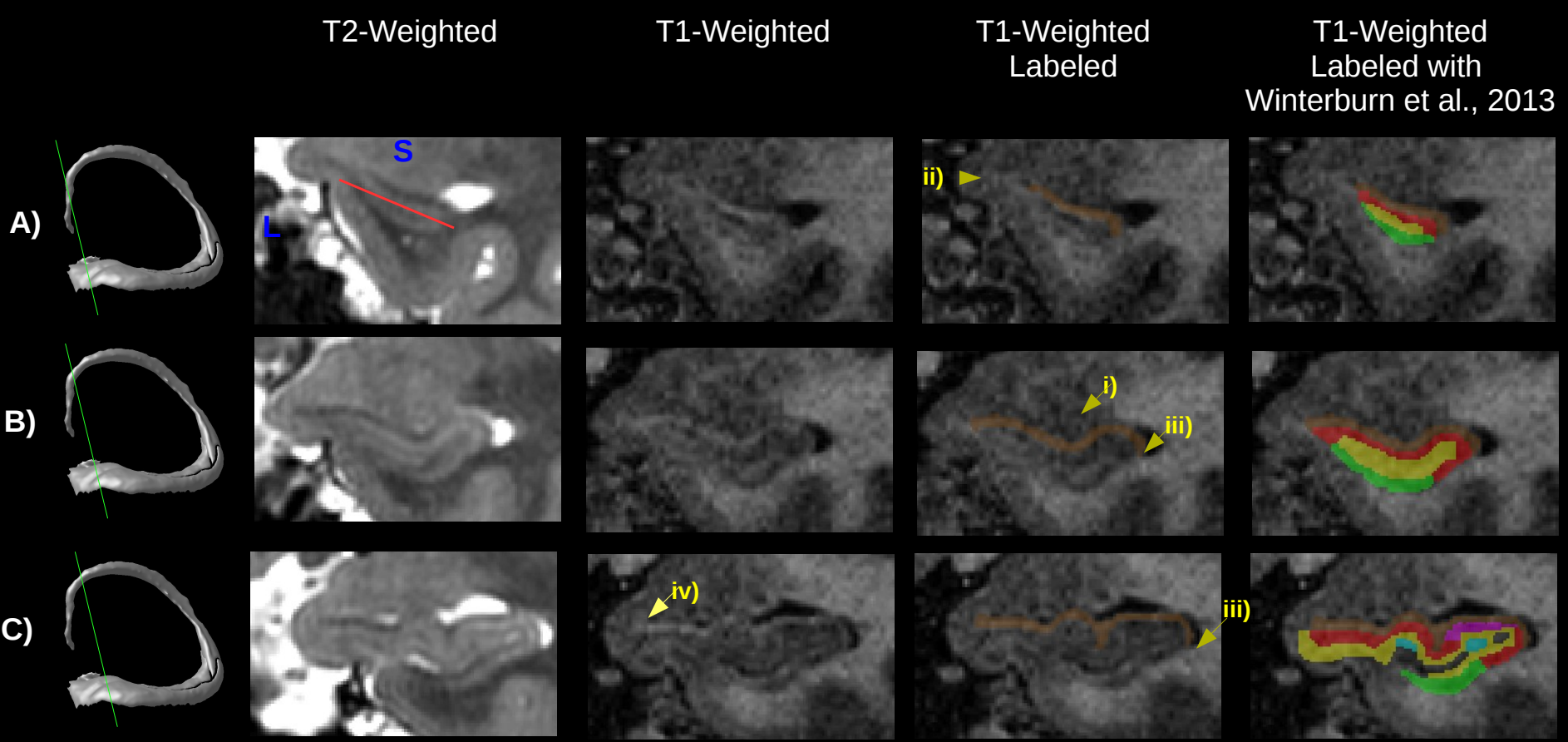


T1-Weighted

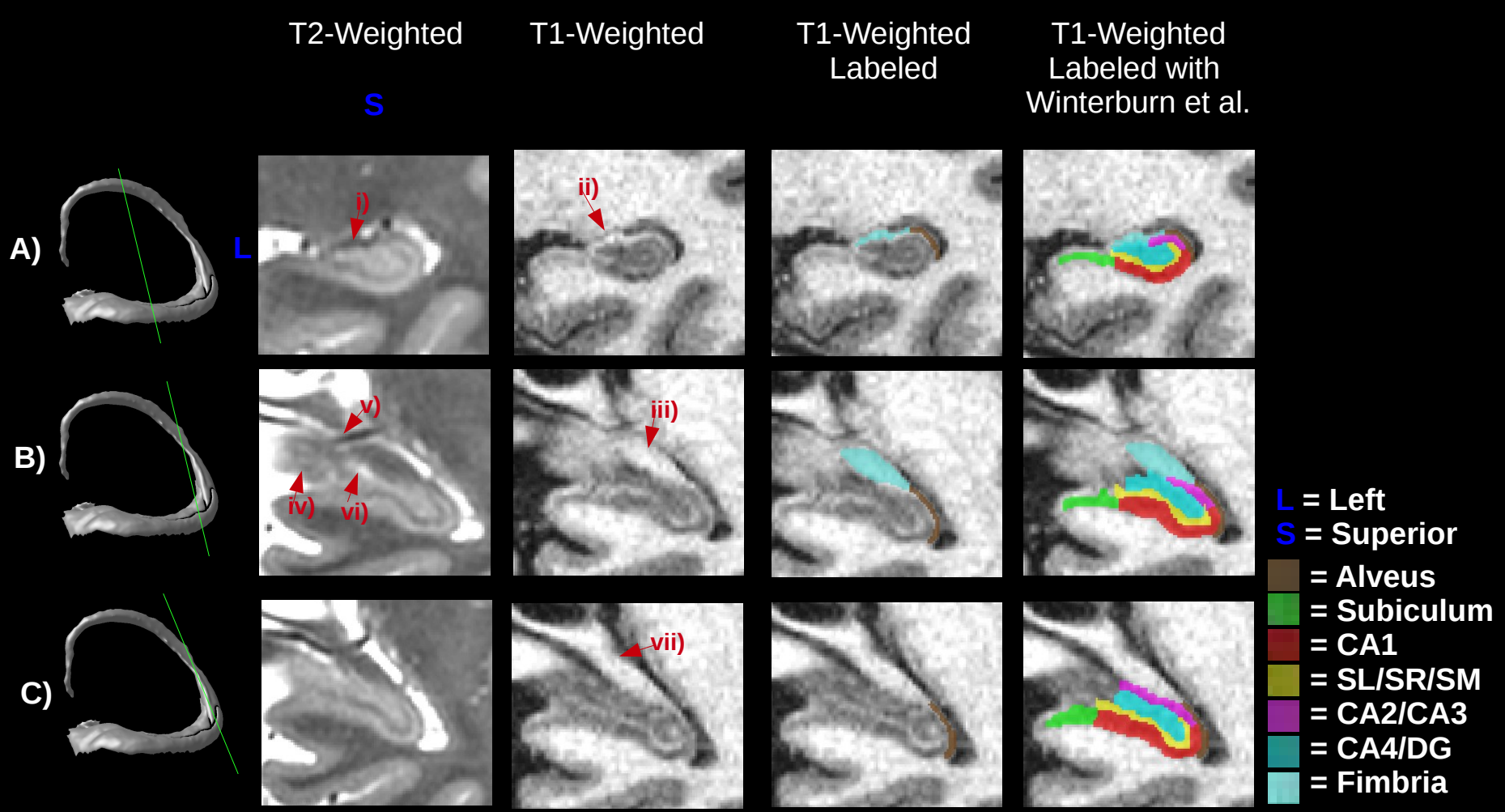


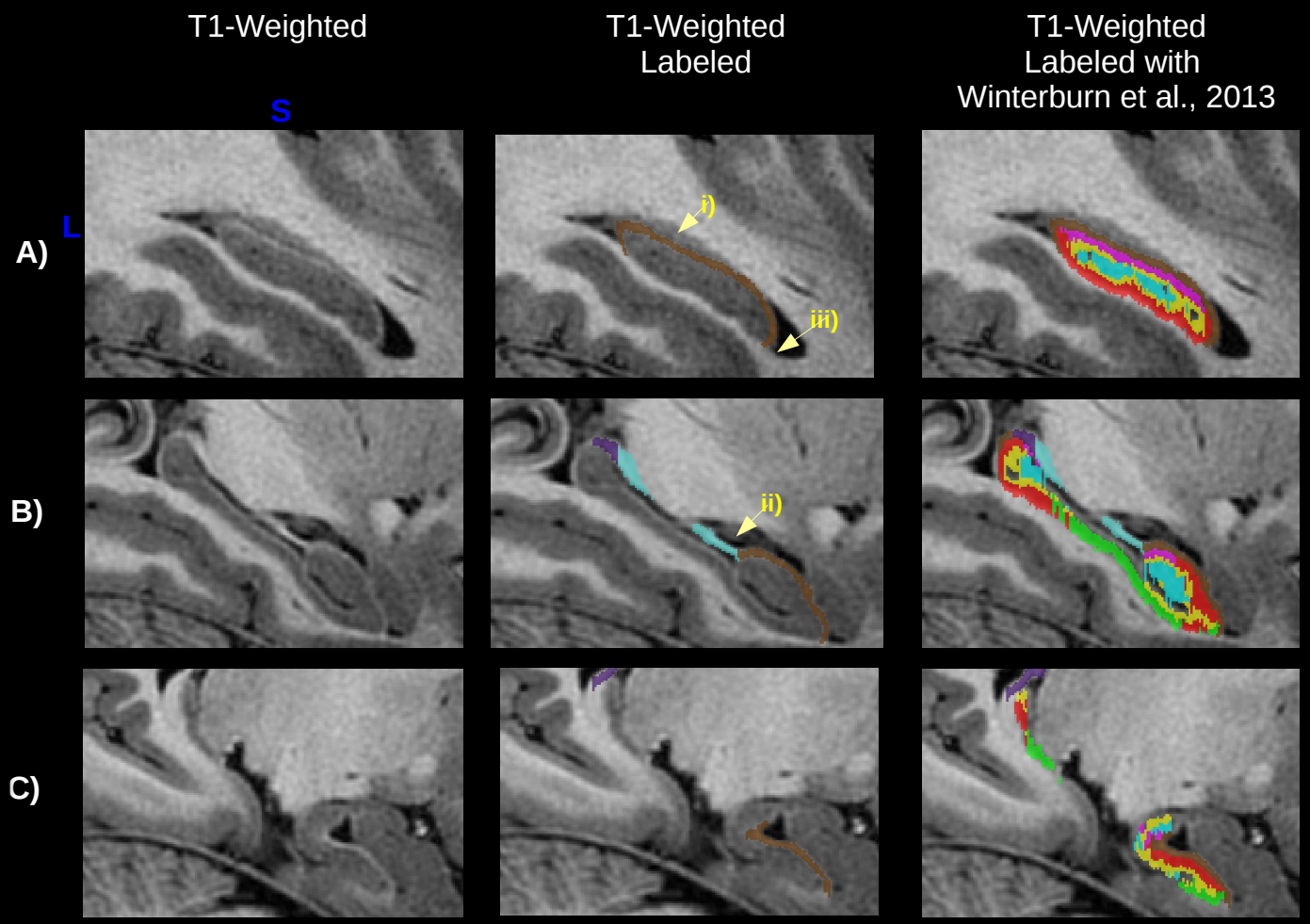
L = Left
S = Superior

Alveus

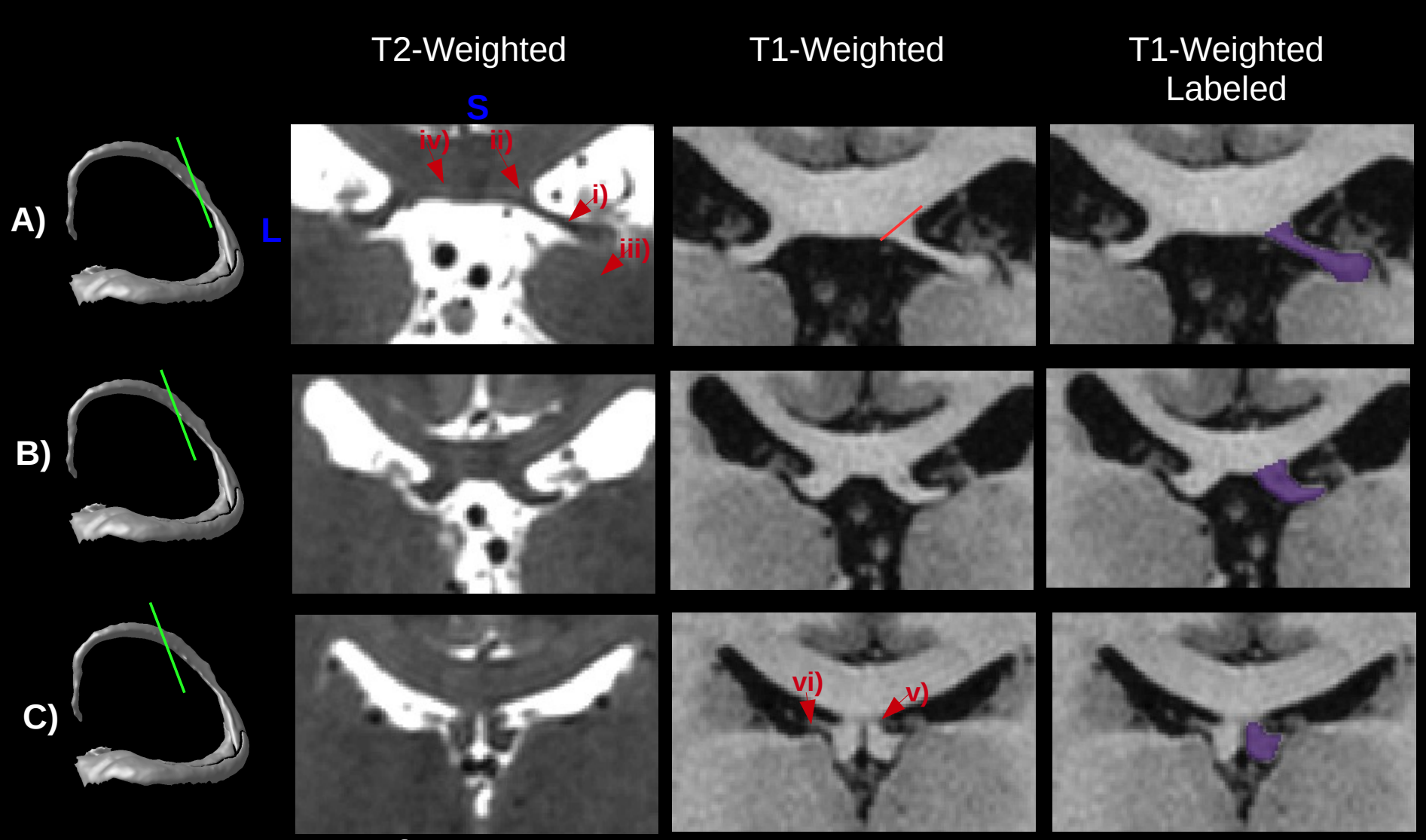

T2-Weighted
T1-Weighted
T1-Weighted Labeled
T1-Weighted Labeled with Winterburn et al., 2013
A)
B)
C)
S
L
ii)
i)
iii)
iv)
iii)
L = Left
S = Superior
= Alveus
= Subiculum
= CA1
= SL/SR/SM
= CA2/CA3
= CA4/DG

Fimbria

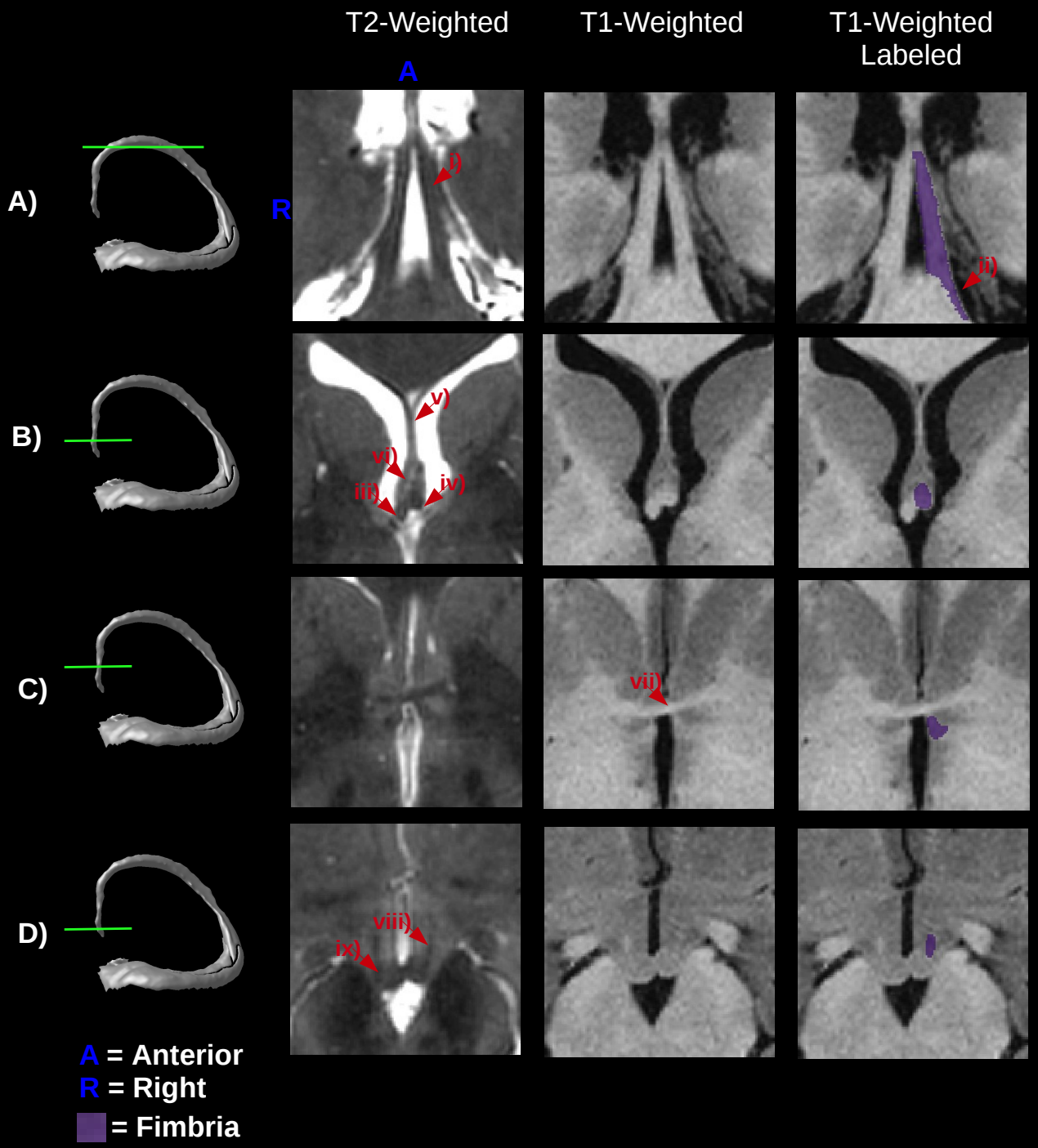

T2-Weighted
T1-Weighted
T1-Weighted Labeled
T1-Weighted Labeled with Winterburn et al.
S
A)
B)
C)
L
i)
ii)
iii)
iv)
v)
vi)
vii)
L = Left
S = Superior
= Alveus
= Subiculum
= CA1
= SL/SR/SM
= CA2/CA3
= CA4/DG
= Fimbria


T1-Weighted
T1-Weighted Labeled
T1-Weighted Labeled with Winterburn et al., 2013
S
L
A)
B)
C)
i)
ii)
iii)
L = Left
S = Superior
= Alveus
= Fimbria
= Fornix
= Subiculum
= CA1
= SL/SR/SM
= CA2/CA3
= CA4/DG

Fornix



L = Left
S = Superior


T2-Weighted
T1-Weighted
T1-Weighted Labeled
A
R
A)
B)
C)
D)
i)
ii)
iii)
iv)
v)
vi)
vii)
viii)
ix)
A = Anterior
R = Right
= Fimbria

Consistency

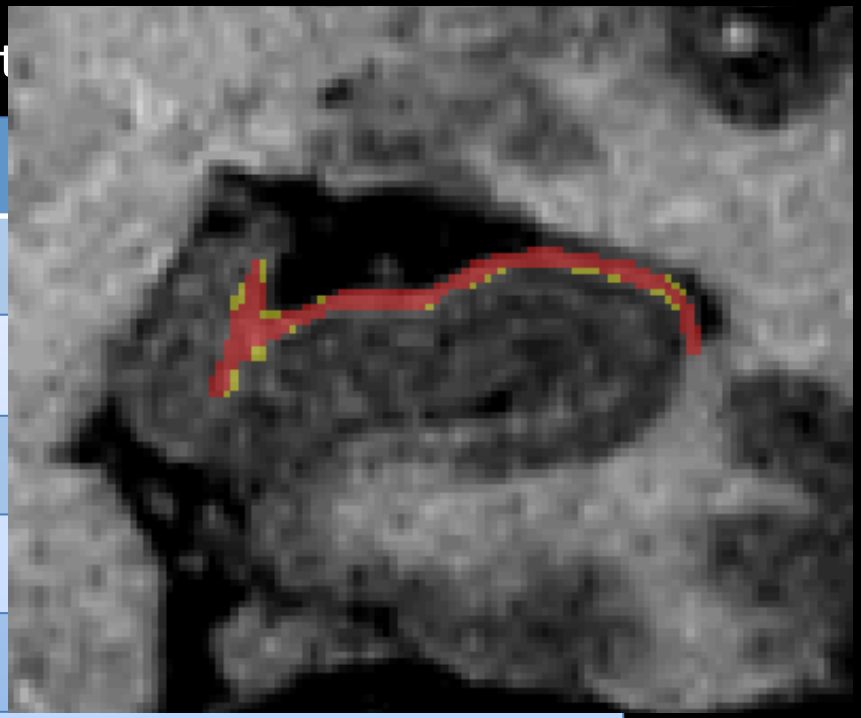
- Two hemispheres traced (1 Male, 1 Female) for test-retest intra-rater reliability
- Dice overlap metric
  where: 0=no overlap and 1=complete overlap

Summary of Intra-rater Reliability		
Structure	**Left**	**Right**
Alveus	0.90	0.90
Fimbria	0.90	0.86
Fornix	0.87	0.87
Total White Matter	0.90	0.89

Average intra-rater reliability was calculated using Dice's volumetric Kappa. A score of 0 represents no overlap between test and retest labels, whereas a value of 1 represents a complete overlap.

Consistency

- Two hemispheres traced (1 Male, 1 Female) for test-retest intra-rater reliability
- Dice overlap metric
  where: 0=no overlap and 1=complet



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Application 1: ADNI Dataset

- Healthy Controls Vs. Alzheimer's Disease?

- 151 individuals from the ADNI 3T baseline dataset
  - 47 normal controls
  - 69 MCI
  - 47 AD

- MAGeT Brain to automatically segment WM using the high resolution atlases
- MAGeT Brain validated for use in whole-hippocampus/ subfield segmentation – Pipitone et al., 2014. Neuroimage.

Quality Control

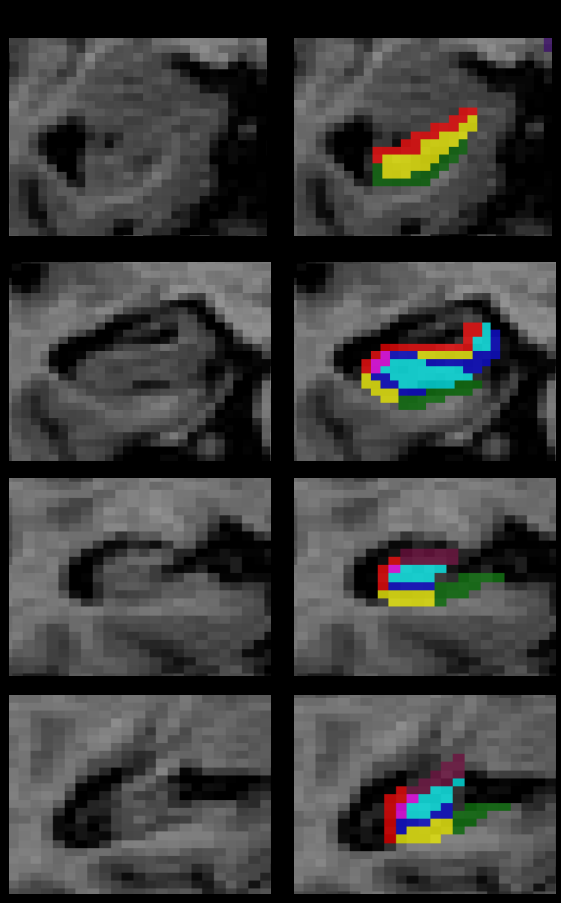
- All images inspected manually using MINC Display
- ROI results rated based on their quality:
  - 1 = Pass
  - 0.5 = Pass (low quality)
  - 0 = Fail

L = Left
S = Superior

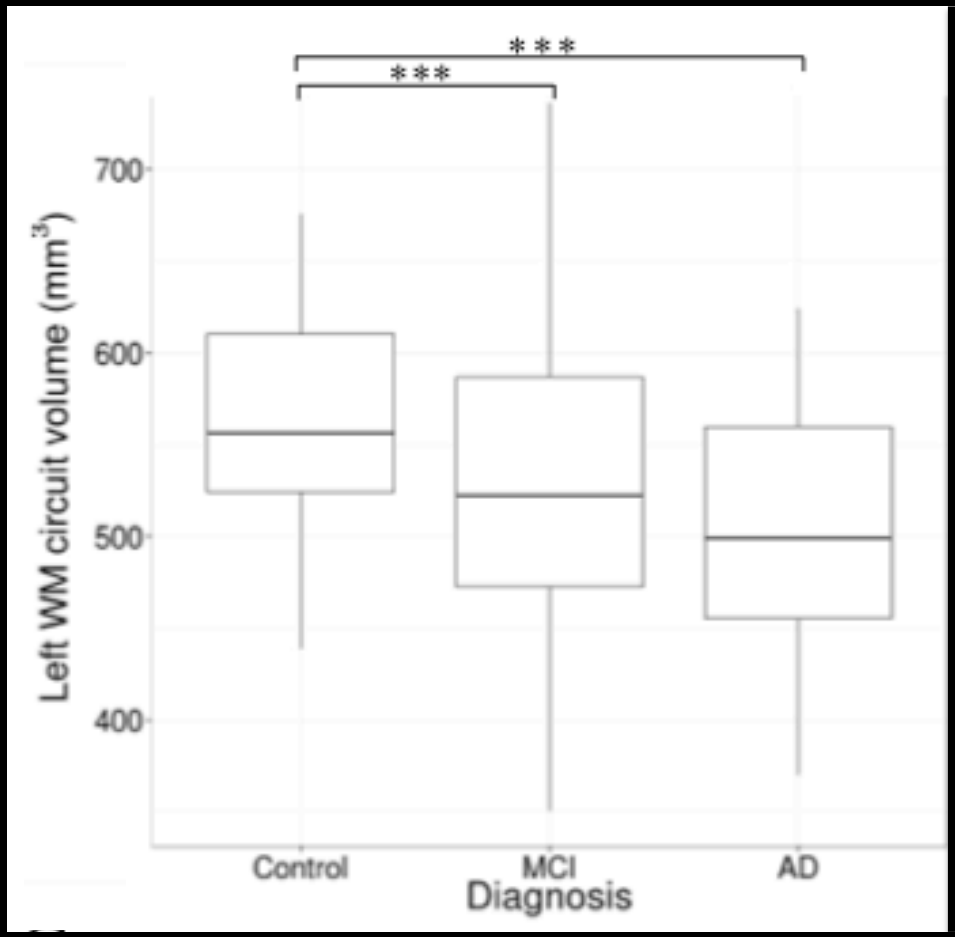
Alveus
Fimbria
Fornix

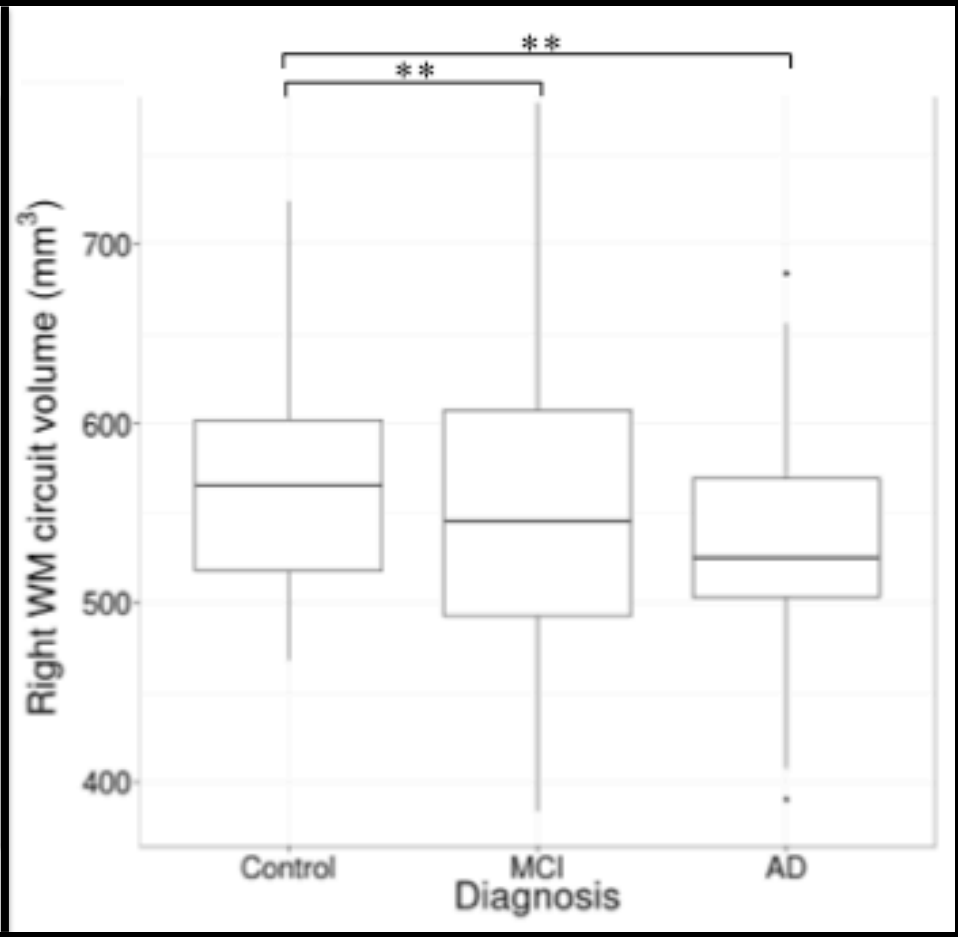
CA1
CA2/3
CA4/DG
SR/SL/SM
Subiculum

Sample Output of Automatic Segmentation (MAGeT Brain)



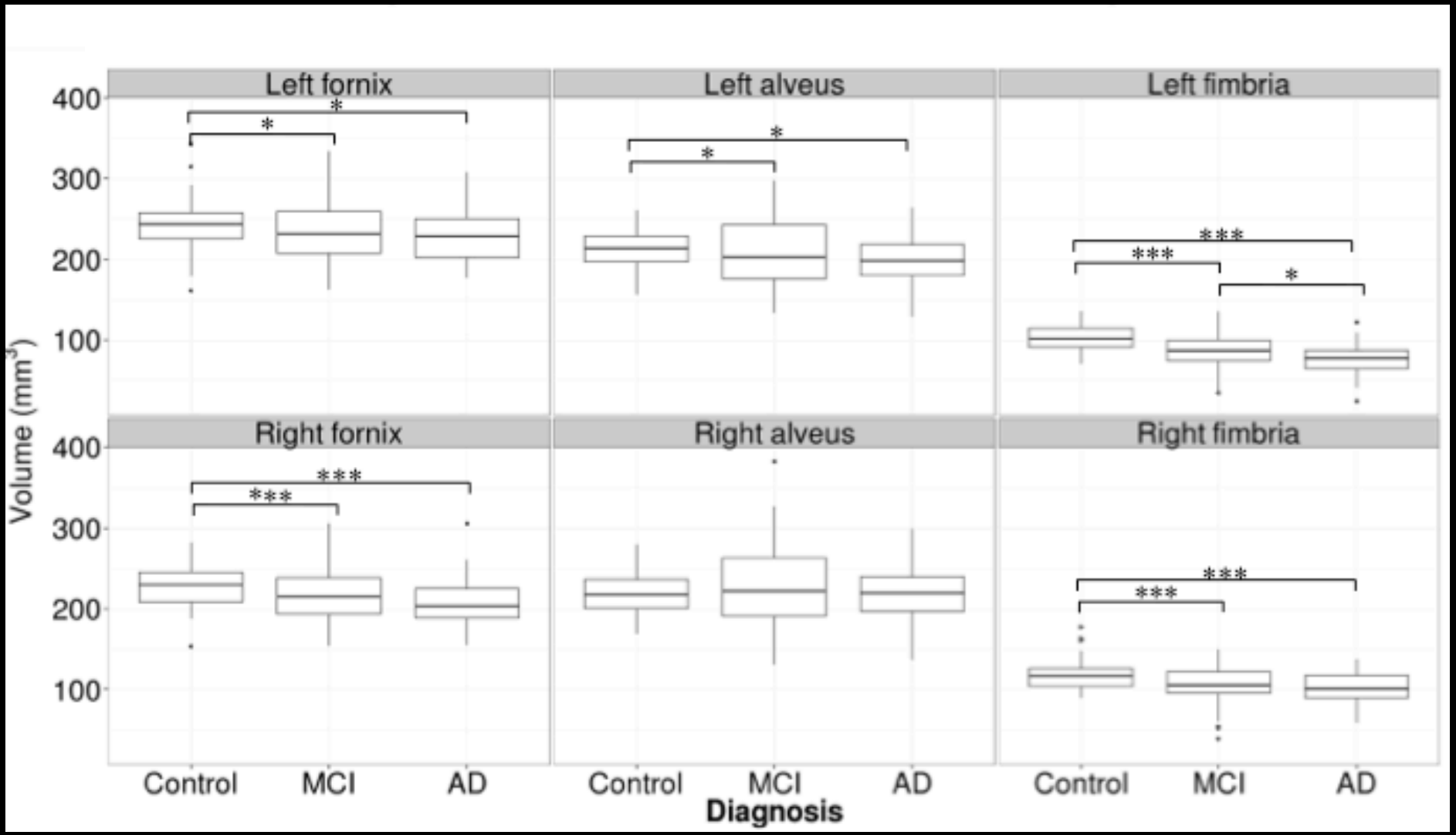
Results: Whole WM





*p<.05, **p<0.01, ***p<0.001

Results: Individual WM Regions



GLM controlling for Age, Sex, and TIC; *p<.05, **p<0.01, ***p<0.001

Acknowledgements

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Toronto, Canada

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- Dr. Aristotle Voineskos

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McGill University
Montreal, Canada

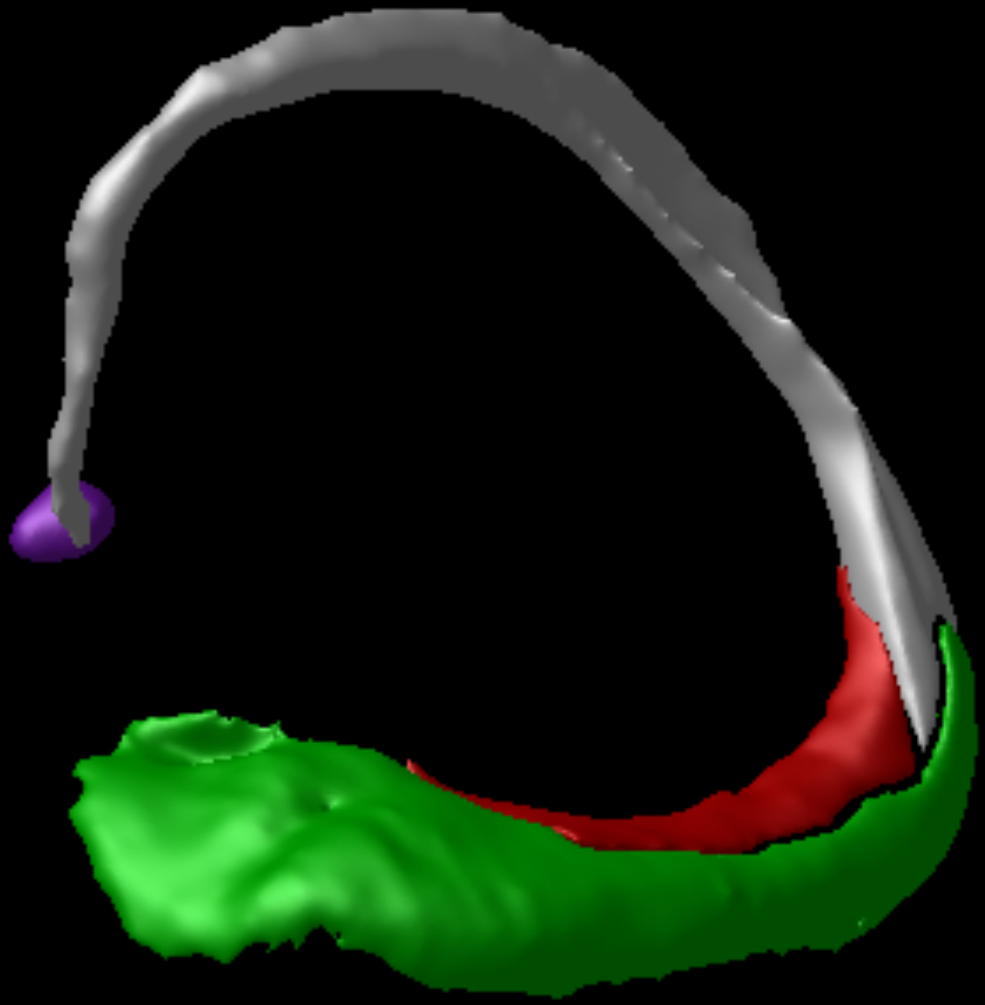
- Jens Pruessner

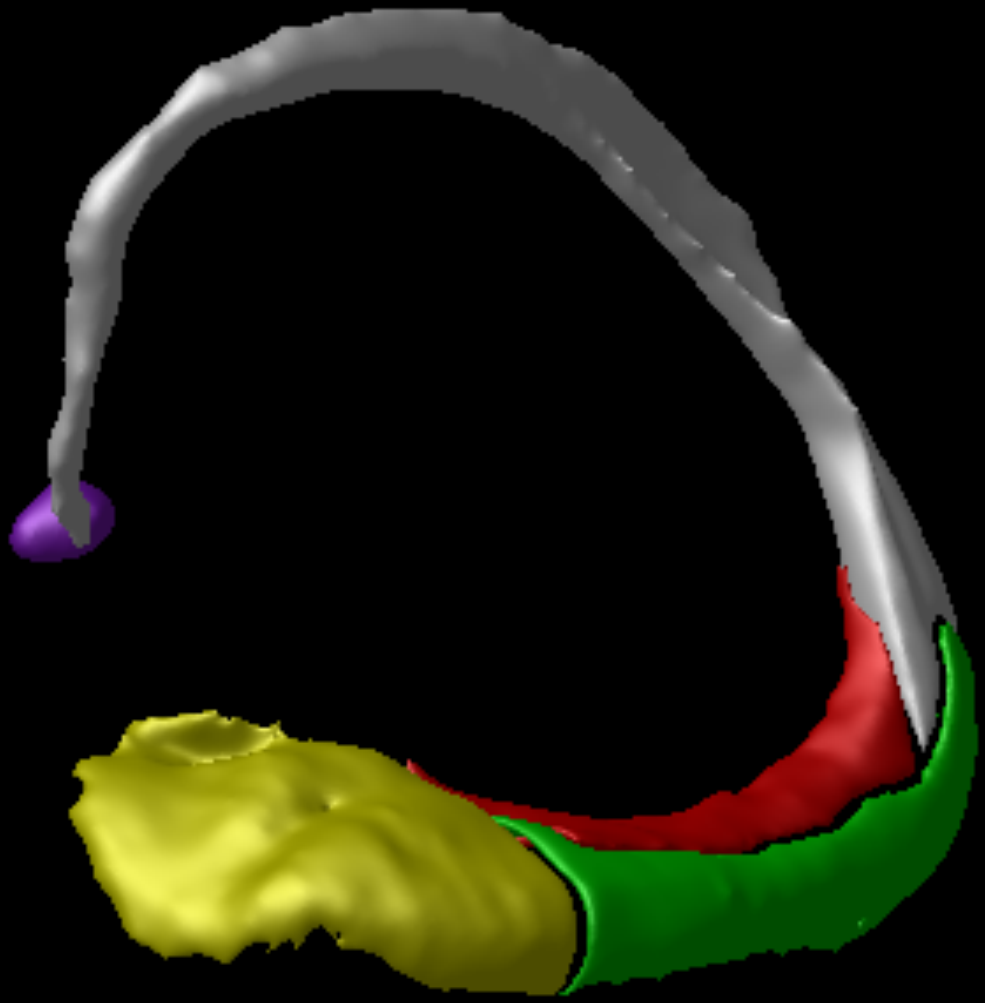
University of Wollongong
Wollongong, NSW, Australia

- Mark Schira

Resources

- MAGeT Brain Pipeline available at:
  - https://github.com/pipitone/MAGeTbrain
- Atlases available at:
  - http://imaging-genetics.camh.ca/Hippocampus





The problem with DTI

Why segmentation?

1. A different measure of tract integrity
2. Can obtain volume estimates and perform shape analysis
3. Unexplored areas in disease and healthy states
4. Mapping and measurement of the entire circuit

DTI WM LIMITATIONS:

1. Fornix is surrounded by CSF, which has high diffusivity
2. Since diffusion coefficients of the CSF are larger than the fornix white matter CSF may cause overestimation of diffusion coefficients in periventricular regions and therefore underestimation of FA
3. FLAIR can be used to eliminate the CSF partial volume effect, but lowers SNR and downgrades fiber tracking results
4. Resolution contraints