

Manual SEGMENTATION PROTOCOL medial temporal lobes

Abbreviations:

AC: Anterior Commissure
AG: Amygdala
ARG: Andreas-Retzius gyrus
CFX: Crus of the fornix
CS: Collateral Sulcus
FG: Fasciolar Gyrus
GM: Grey matter
GSW: Gyri of Schwalbe
HC: Hippocampus
IHLV: Inferior horn lateral ventricle
ILG: Intralimbic gyrus
ITG: Inferior temporal gyrus
LI: Limen Insulae
MR: Magnetic resonance
MTL: Medial temporal lobes
PHC: Parahippocampal cortex
PRC: Perirhinal cortex
SSA: Sulcus semiannularis
THLV: Temporal horn lateral ventricle
TLV: Temporal horn of the lateral ventricle
TPC: Temporopolar cortex
URIHLV: Uncal recess of the inferior horn of the lateral ventricle
WM: White matter

GENERAL RECOMMENDATIONS:

- Draw the structures mainly on the coronal plane (except for HC, which is better recognizable on the sagittal), correct them on the sagittal (or coronal for the HC) and try to touch as less as possible the axial plane. (Insausti recommendation)
- Correct for magnetic field non-uniformities and use that image to localize the Limen Insulae. To find the LI, you have to select a threshold to equal a value that is below 10% below the highest MR signal found in the medial part of the anterior commissure (AC). The correction for field-nonuniformities applied to all images prior to segmentation guaranteed the exclusion of interhemispheric differences due to signal drift in this approach. (Pruessner, 2002).
- A suggestion from Ricardo Insausti was to take approximately the 3rd first mm of the GSW as TPC and the following ones, as PRC. Although GSW are not very well recognised in most of the scans.

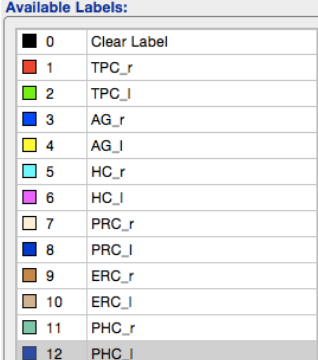
PRE-PROCESSING:

- Use spm to reorient the scan to the AC-PC line (you can also use another software if you prefer as long as no other processes are being applied beyond reorientation. In spm, use the 'display' button, reorient the scan and save it with the .mat file.
- In matlab, apply to restore12.m to your scan
- In the terminal run, fast -B scan.nii
- Use the scan_restore.nii file for segmenting in itk snap, keeping the ROI labels as mentioned in a previous email.

MASK HIPPOCAMPUS TO SUB-SEGMENT:

- To create a mask go to FSL: fslmaths and define the thresholds in which your regions are.
- In our case: 5 and 6. Define thresholds:
'fslmaths x_seg.nii.gz -thr 5 -uthr 6 x_seg_HC.nii.gz'

***VERY IMPORTANT:** Don't forget to rename the second file (I mean 'x_seg_ **HC**.nii.gz', rather than 'x_seg.nii.gz' as otherwise you will rewrite your whole segmentation and you will lose everything!!)



Available Labels:	
0	Clear Label
1	TPC_r
2	TPC_l
3	AG_r
4	AG_l
5	HC_r
6	HC_l
7	PRC_r
8	PRC_l
9	ERC_r
10	ERC_l
11	PHC_r
12	PHC_l

1st _ TEMPOROPOLAR CORTEX:

Start from the rostral end to the temporal pole and proceed caudally.

- The coronal MR image contains the most rostral portion of the temporal pole. The entire cortex has to be selected caudally until the appearance of the WM. (Fig.1)

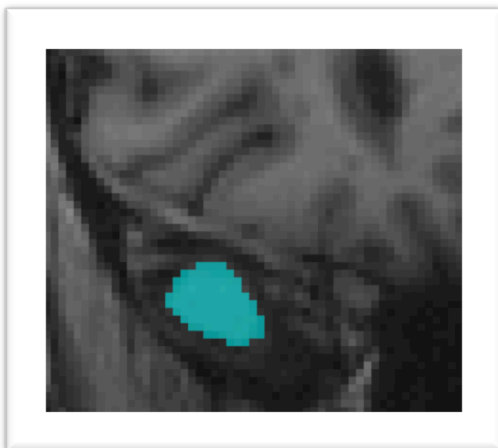
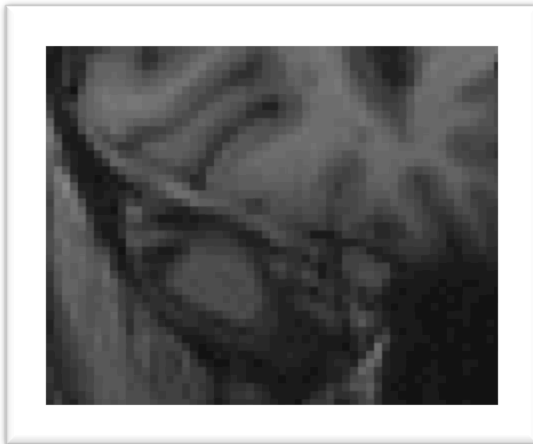
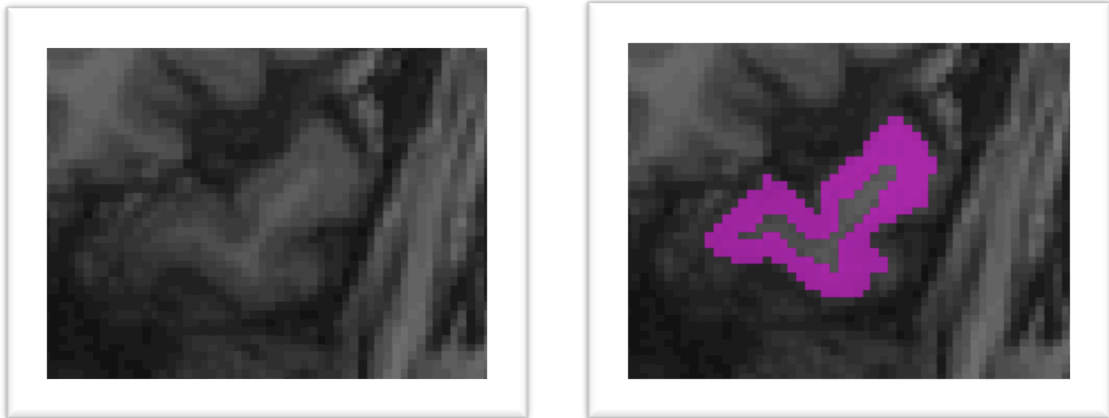


Fig. 1

- When the WM appears, draw only the TPC (more or less, a ring shape). Proceed caudally until the first appearance of the GSW and the ITG. (Fig.2)



- In the first slice in which the GSW and the ITG are identifiable, you should trace a line from the first GSW to the ITG end. And start to draw only the ventral part of the TPC. Proceed caudally until the appearance of the CS. (Fig.3)

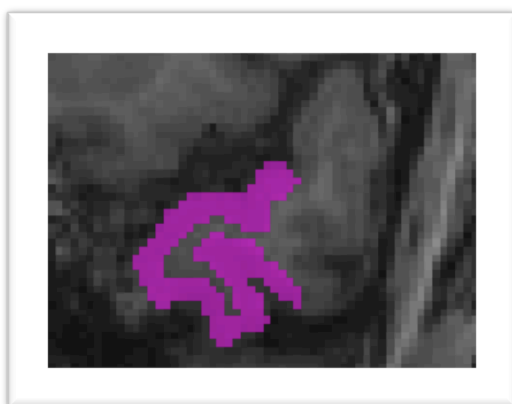
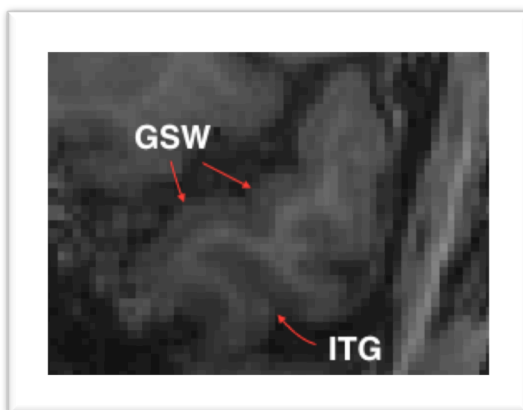


Fig.3

- d
- ❖ There are cases in which the brain is very damaged, or due to the brain characteristics, the GSW are not well identified. My recommendation is

that if you are not sure about that, you should follow the plan B (Insausti recommendation): count 8 mm since the first appearance of the GSW and then trace a line from ITG up until where the GSW should appear. And start to draw only the ventral part of the TPC. Proceed caudally until the appearance of the CS.

2nd _ PERIRHINAL AND ENTORHINAL CORTEX:

- The rostral end of the PRC was identified at the rostral end of the CS. Often the same slice is the first appearance of the amygdala as well (1st appearance of LI). (Pruessner, 2002). However, the CS is sometimes unusually long and extended as far as rostral as the inferior temporal sulcus. In these cases, the identity of the presumed collateral sulcus was made certain in a section in which all five of the temporal lobe gyri could be identified. (Insausti, 1998). (Fig.4 see note below) Kivisaari et al (2013) define the PRC as 2mm anterior to the most anterior coronal slice containing grey matter in the limen insulae. I've been using Kivisaari recommendation in brains where the structures were damaged, as LI is always clearly identifiable. (Fig. 5)

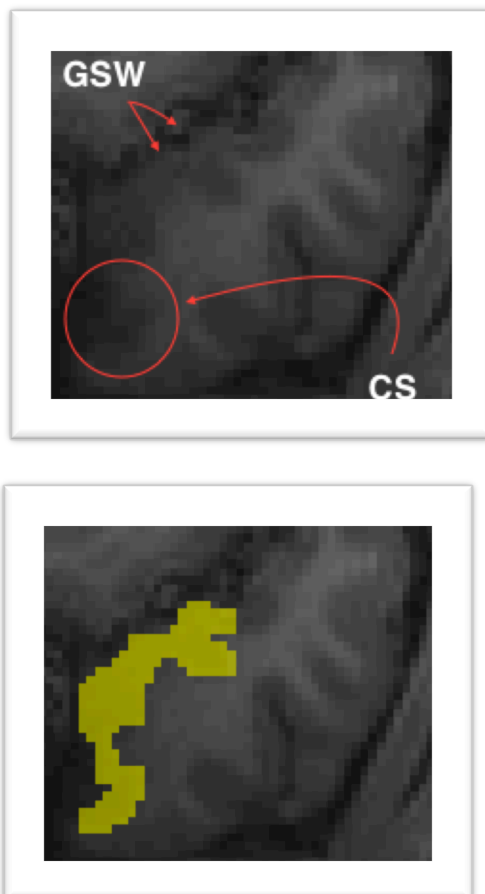


Fig.4

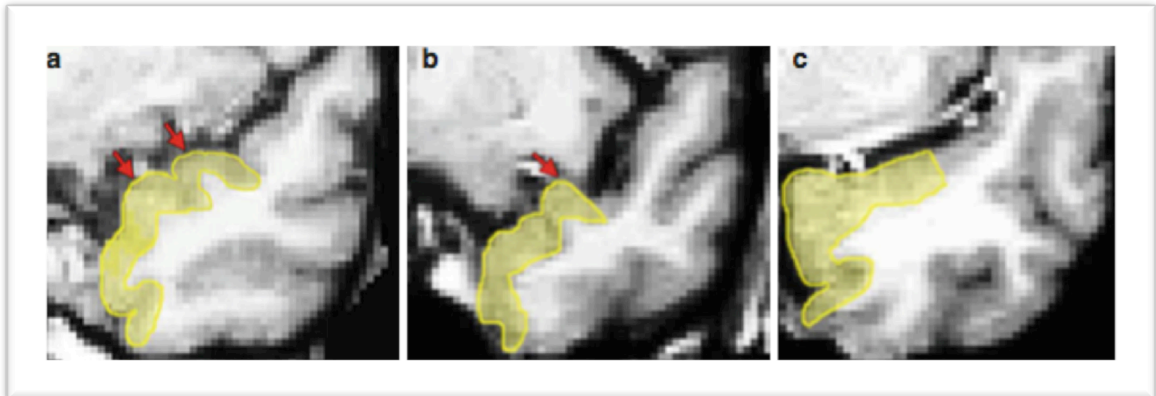
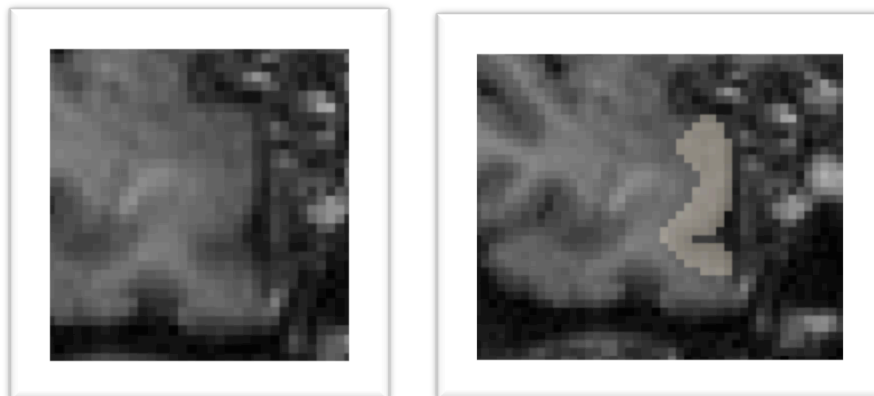


Fig.5 Native space coronal slices of the right hemisphere temporal pole area 1-2mm anterior to the limen insulae. The figure illustrates the three variants of the gyri of Schwalbe (red arrows) and corresponding locations of the PRC (yellow outlines): (a) a case with two gyri of Schwalbe, (b) a case with one gyrus of Schwalbe, and (c) a case whose superior aspect of the temporal pole is relatively flat, indicating no gyri of Schwalbe. (Pic and text from: Kivisaari et al. 2013)



*Plan B for difficult brains: In this figure you can see that sometimes is difficult to recognize the gyri, but it is essential to do it to recognize the PRC. If the CS starts to rostral, Insausti recommends to count 2mm since its first appearance to start with the PRC, at the same time, if you are not able to well recognize the ERC, you should count 4mm since the first appearance of the CS to start to draw it, although you always should count on the “real landmarks” as much as you can. Even if you are using the plan B, double check, try to identify markers, check and double check. Maybe going to other plane could help as well.

- Draw the PRC as was described in the last step until the appearance of SSA, at this moment, from the SSA to the rostral end of the CS you will find the ERC. The PRC will be restricted only to the CS. (Pruessner, 2002) (Fig. 6). Proceed caudally with these instructions with special careful on the depth of the CS. (Fig. 7. Insausti et al.,1998)

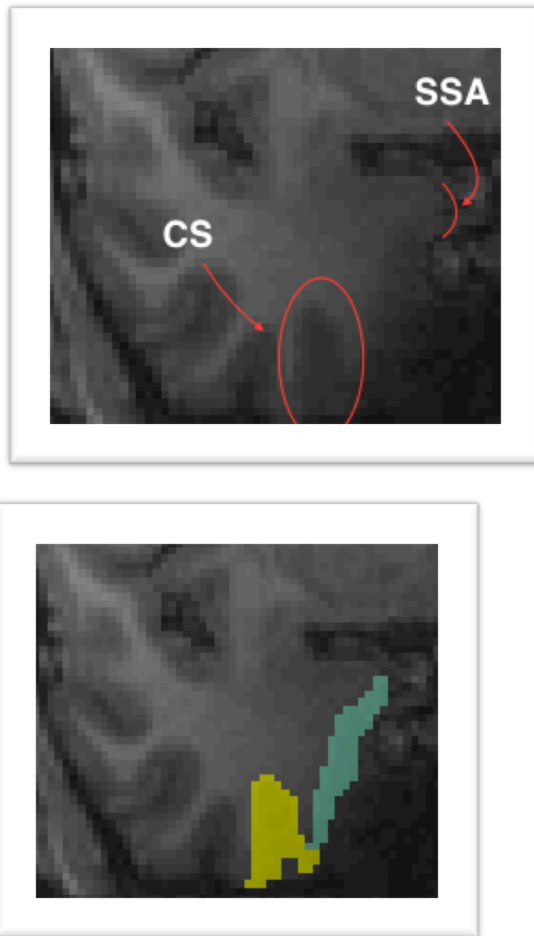
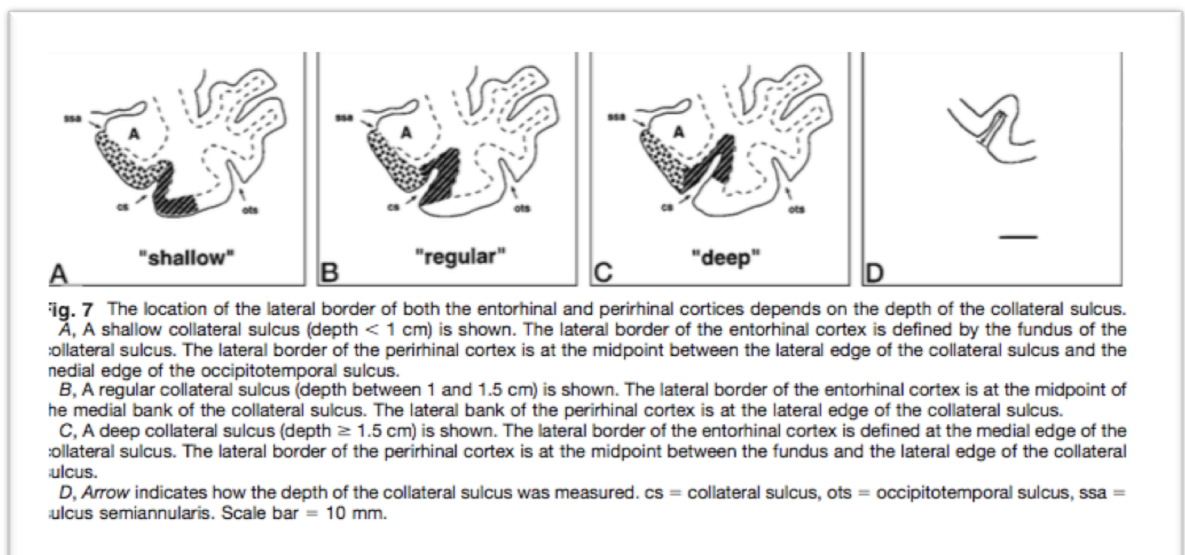


Fig. 6 (first slice where ERC and PRC appear together)



- When you can see the fimbria above the HC, and you are not longer able to see the TLV will be the first slice in where the EC is not visible caudally. You will have to draw the PRC still a few more slices caudally. (Kivisaari et al.,

2013; Insausti, phone) (Fig. 8) The PRC will extend only around 2mm since the ERC disappear (Insausti phone).

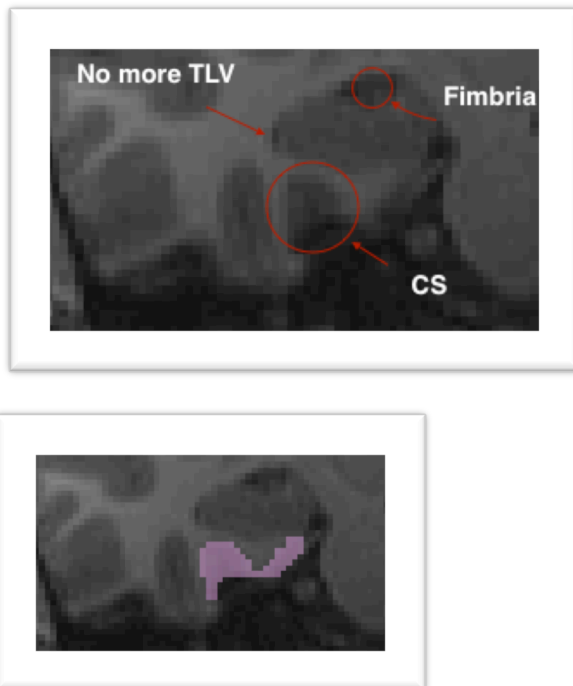


Fig. 8

3rd _ PARAHIPPOCAMPAL CORTEX:

- The coronal limit between PRC and PHC will be the ILG, as Insausti has explained to us, this ILG is the final part of the medial portion in the HC (whole CA3). The first coronal slice in where you are able to see the fimbria as a dot of hiperintensity, and another hiperintense dot just close, you will define the ILG. Examples below (fig. 9).
These two dots of hiperintensity will define the first slice in where the PHC is seen for the first time on the coronal view. (Fig. 10)

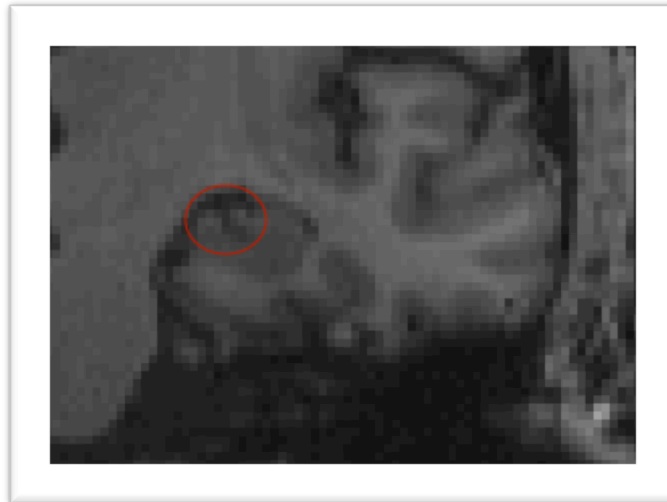
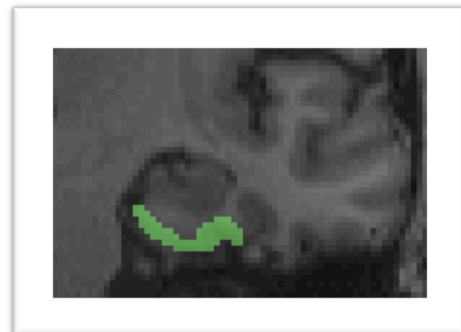


Fig. 9



Figs. 10

- The PRC will extend from the point that we described in the last point, until the moment in which you can see the last part of the thalamus, this is the best way to determine it as the thalamus is always well preserved.

4th_ AMYGDALA:

- The first slice where the AG appears is the same as the LI. (Adriana's recommendation: Draw first the PRC and the ERC. Even the HC before, could be helpful). (Fig. 11)

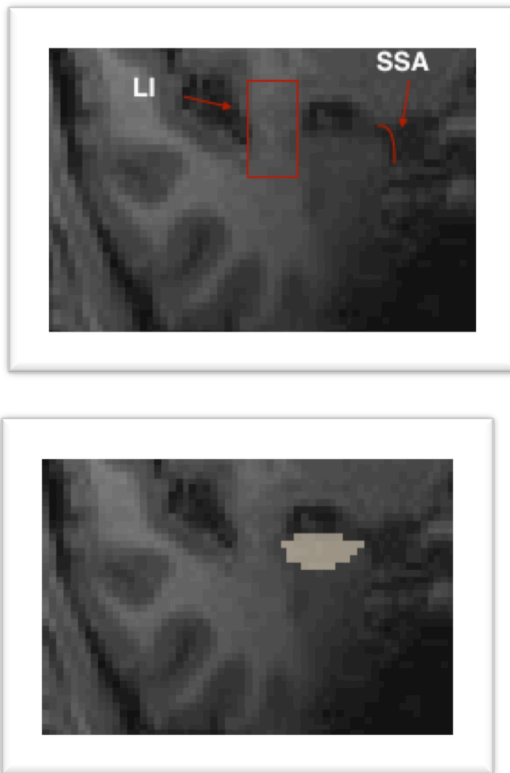


Fig.11

- Laterally, the GM of the AG blends together with the ventral putamen. (Pruessner et al, 2000) (Fig. 12)

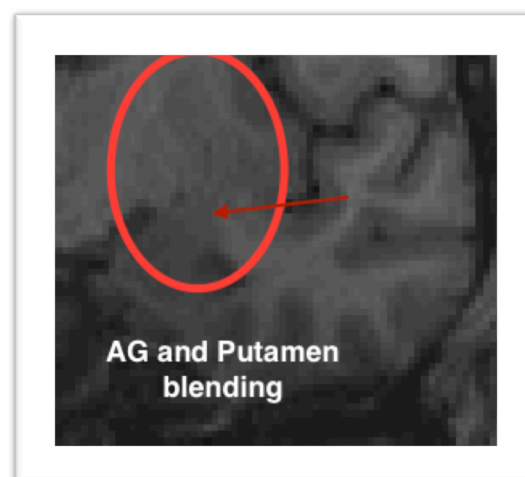


Fig.12

- Inferolaterally, the THLV separates the AG from adjacent structures. And to define the posterior end of the AG, the IHLV must be used. The medial border is easily identifiable since it is attached to the border of the ambient cistern at this point. (Pruessner, 2000) (Fig. 13). Further anterior and inferior, EC blends into the AG medially (Pruessner et al, 2000; Insausti et al, 1998)(Fig. 14).

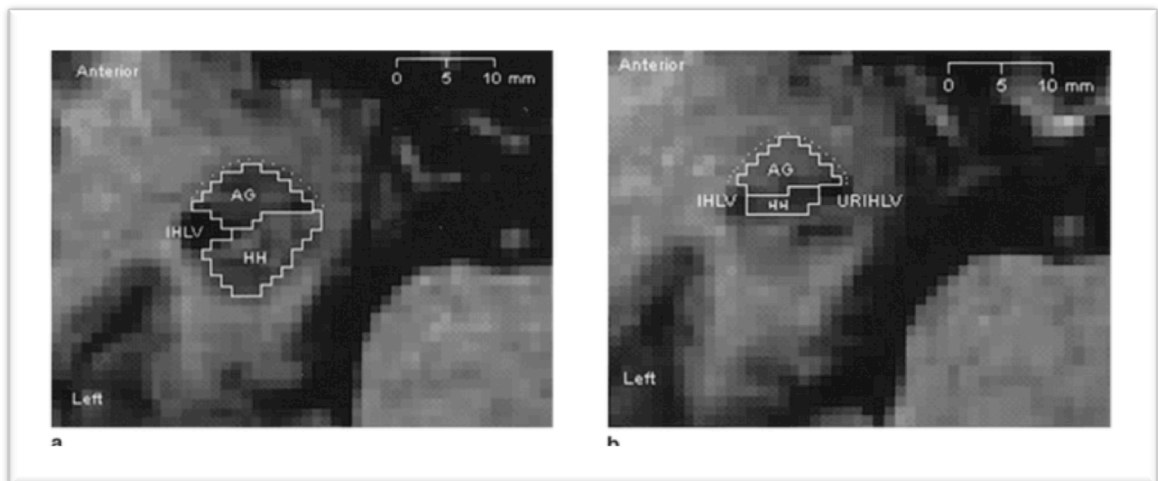


Fig. 13. (a) Horizontal section of the MTL; delineation of AG and HC by IHLV and URIHLV. (b) Horizontal section of the MTL; inferior portion of HC and AG; delineation of AG and HC by IHLV and URIHLV. (Pruessner et al., 2000)

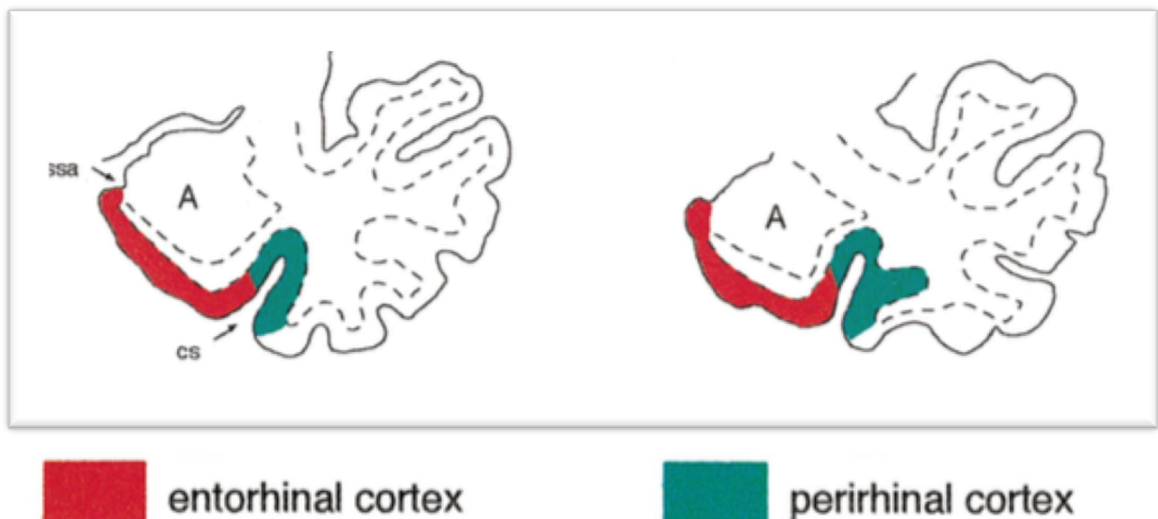


Fig. 14. (Insausti et al. 1998)

- The suggestion is to draw the HC head first on the sagittal view to define the landmark between AG and HC. In the coronal view, must be well defined with a WM band. Then, is possible to come back in the coronal view and draw the AG until its disappearance. (Fig. 15, 16, 17)

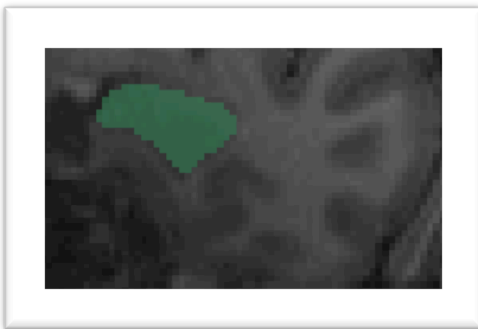


Fig. 15

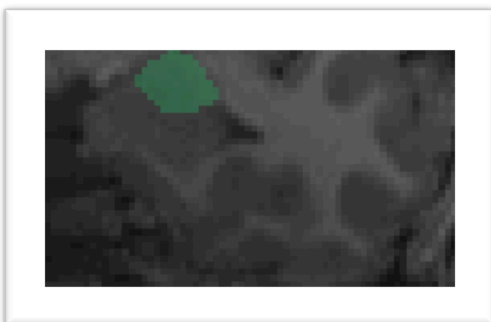


Fig. 16

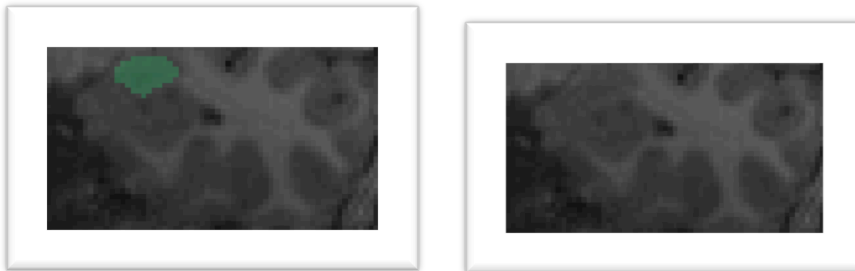


Fig. 17

5th_ HIPPOCAMPUS:

- This structure must be drawn in the sagittal view. This structure is well distinguishable, so the best option may be to draw on the sagittal following the differences between tissues. See bellow to see examples (Fig. 18, 19, 20, 21, 22, 23). And to learn more about the Hippocampus anatomy, these terms could help your segmentation. (Fig.24, 25)



Fig. 18



Fig. 19

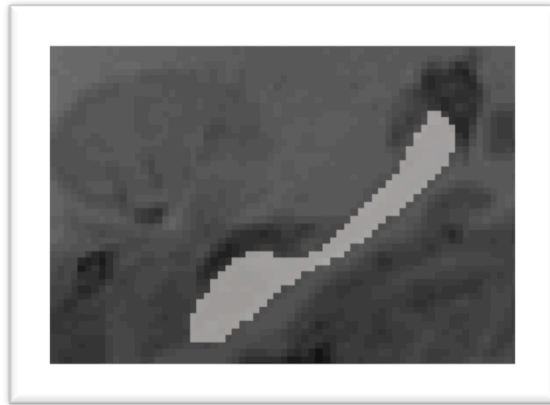


Fig. 20

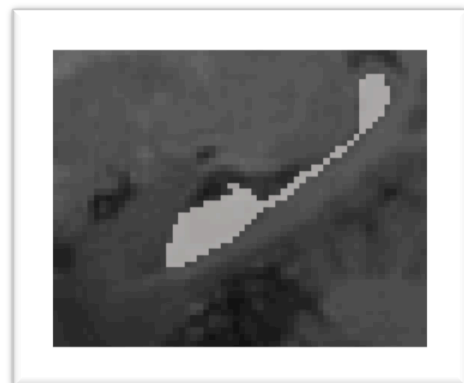
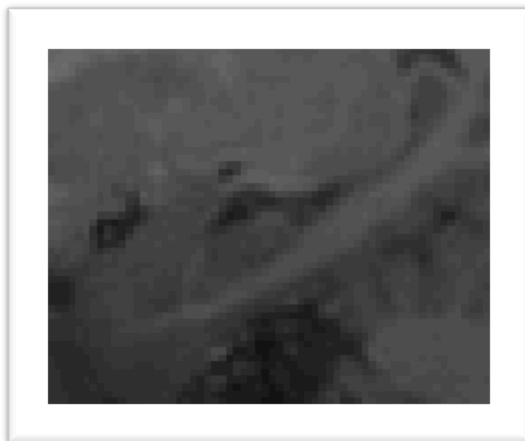


Fig. 21

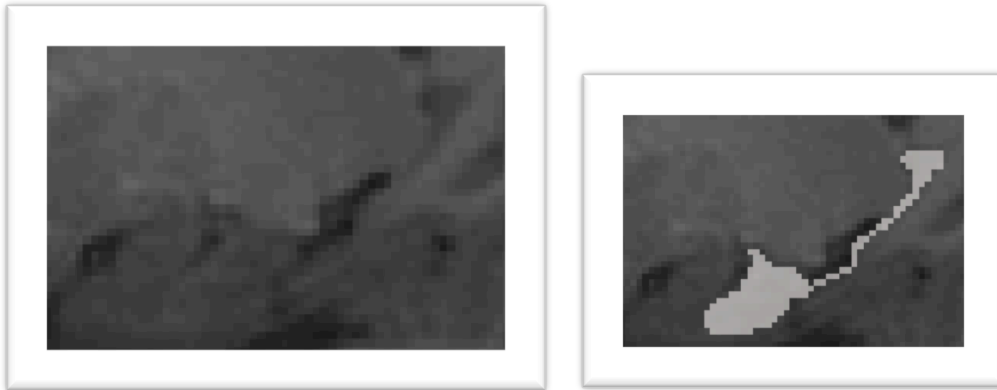


Fig. 22

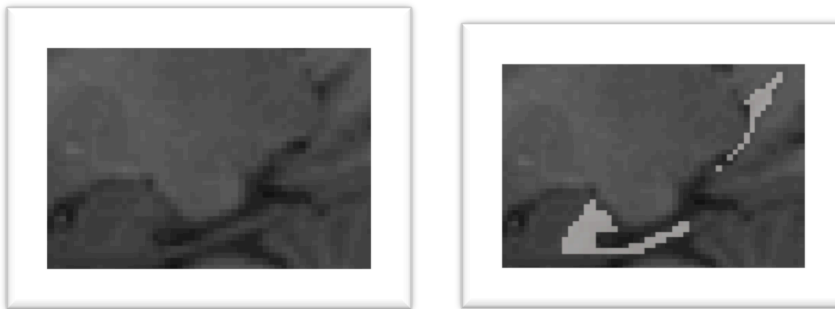


Fig. 23

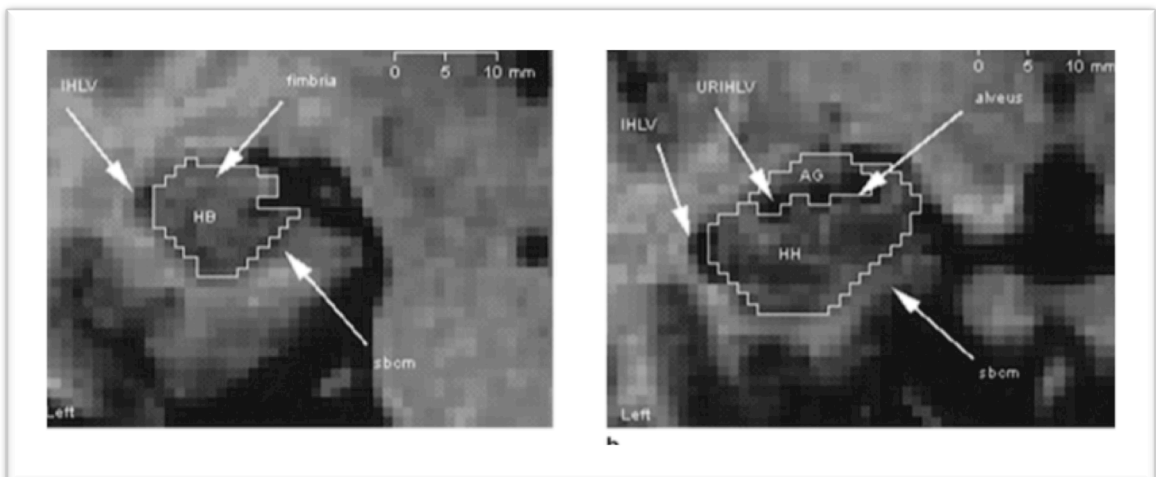


Fig. 24 (a) Coronal section of the MTL; discrimination of Hippocampal tail from ARG and FG and cfx by employing arbitrary borders. (b) Sagittal section of the MTL; the Hippocampal tail and its superior and inferior borders. Note the clearly visible white matter inferior to the Hippocampal tail. (Figure and text from: Pruessner et al. 2000)

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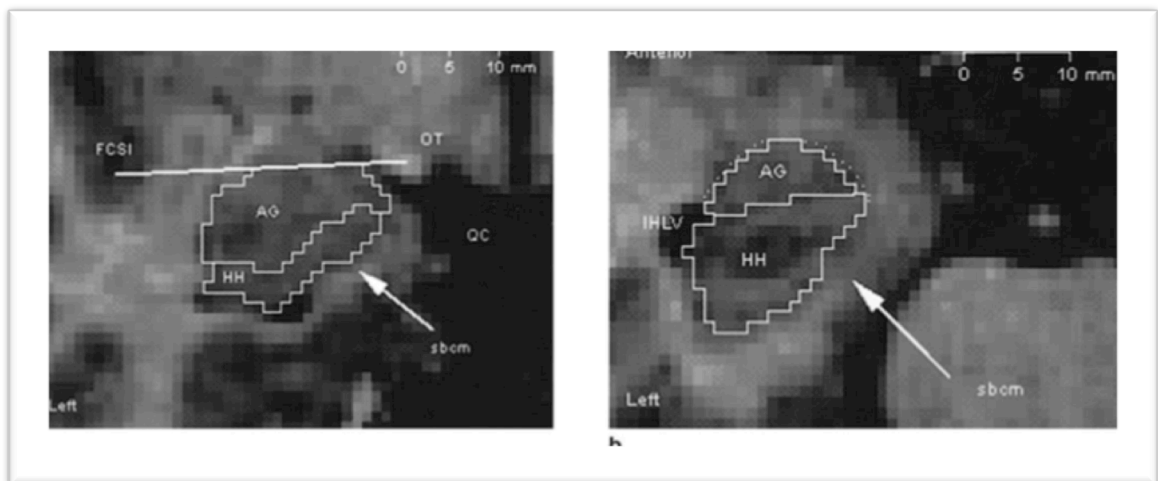


Fig. 25 (a) Coronal section of the MTL; segmentation of the Hippocampal body.
(b) Sagittal section of the MTL; delineation of the fimbria as superior border
(Figure and text from: Pruessner et al. 2000)

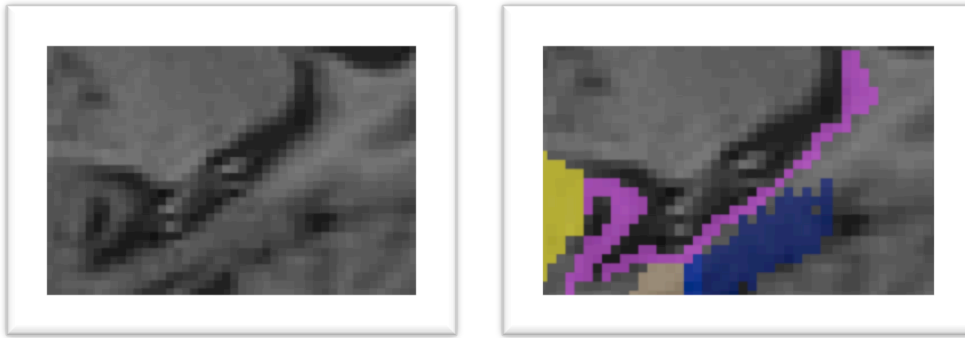


Fig 26

Fig26: Sometimes HC is very damaged. In these cases more than ever, you have to define the HC in the sagittal. Same rules you would follow for the Healthy brains. It is not very difficult to recognize the HC even if it is damaged.

Manual SEGMENTATION PROTOCOL hippocampus

HEAD: From the most anterior slice to the first appearance of the uncal apex (where the uncal apex is clearly present)

BODY: As the Fig 9 defines above, The coronal limit between PRC and PHC will be the ILG, this ILG is the final part of the medial portion in the HC (whole CA3). The first coronal slice in where you are able to see the fimbria as a dot of hiperintensity, and another hiperintense dot just close, you will define the ILG. So we will define the fist slice of the Body of the HC as the slice before the two hiperintensities. That means, the first slice before the Fig. 9 you can find above in this procol . From here, the body of the HC will extend to the slice before the cirstern ambiens appers.

TAIL: Identify the cistern ambiens, this will be the first slice of the hippocampus' tail, from there to the end of the HC.



ATTACHED USEFUL FIGURES

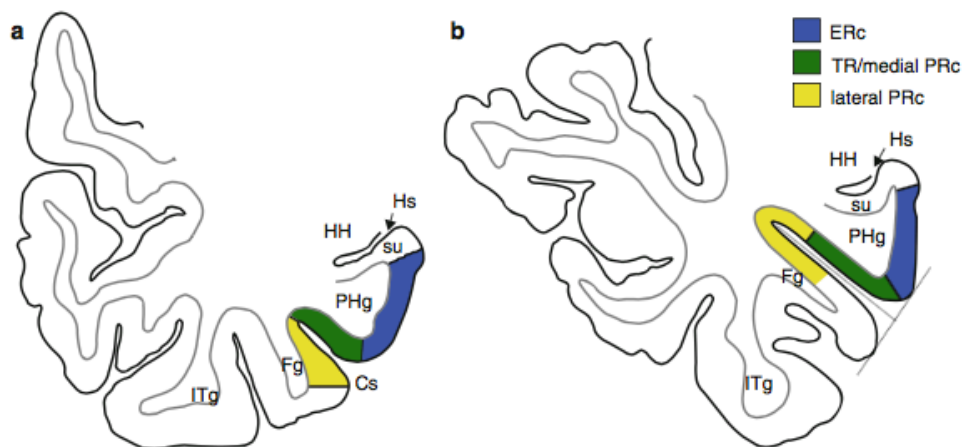


Fig. 19.4 Coronal view of the medial temporal lobe at the level of the hippocampal sulcus (similar coronal level as Fig. 19.8k). The locations of the PRC and TR depend on the depth of the collateral sulcus (*Cs*; see text): (a) borders when the collateral sulcus is of regular depth (i.e., 1–1.5 cm) and (b) when the collateral sulcus is deep (i.e., > 1.5 cm). *Abbreviations:* *Fg* fusiform gyrus, *HH* hippocampal head, *Hs* hippocampal sulcus, *ITg* inferotemporal gyrus, *PHg* parahippocampal gyrus, *su* subiculum of the hippocampus

Fig. 28 Kivisaari et al, 2013

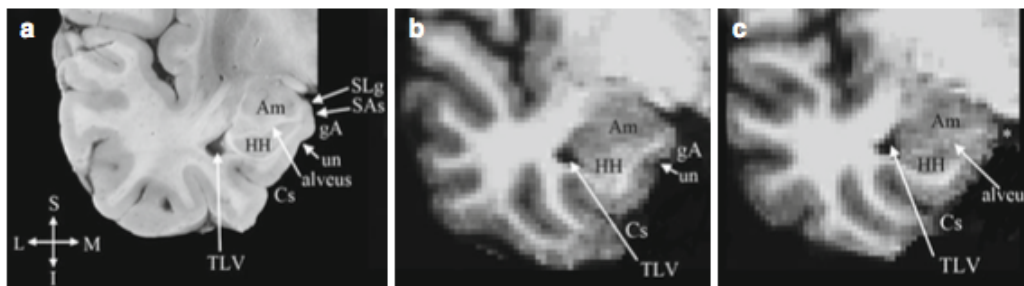


Fig. 19.5 Sections of the temporal lobe at the level of the uncus (approximate MNI $y=-5$): (a) a histological section and (b) an MRI slice at a similar coronal level where the gyrus ambiens (*gA*) and uncus (*un*) are visible. (c) An MRI slice at a similar coronal level where the *gA* and *un* are not visible. In these instances, the medial apex of the parahippocampal gyrus (*asterisk*) is defined as the medial ERc border. *Abbreviations:* *Am* amygdala, *Cs* collateral sulcus, *gA* gyrus ambiens, *HH* hippocampal head, *SAs* semiannular sulcus, *SLg* semilunar gyrus and *TLV* temporal horn of the lateral ventricle, *un* uncus notch. Anatomical directions: *S* superior, *M* medial, *I* inferior, *L* lateral

Fig. 29 Kivisaari et al, 2013

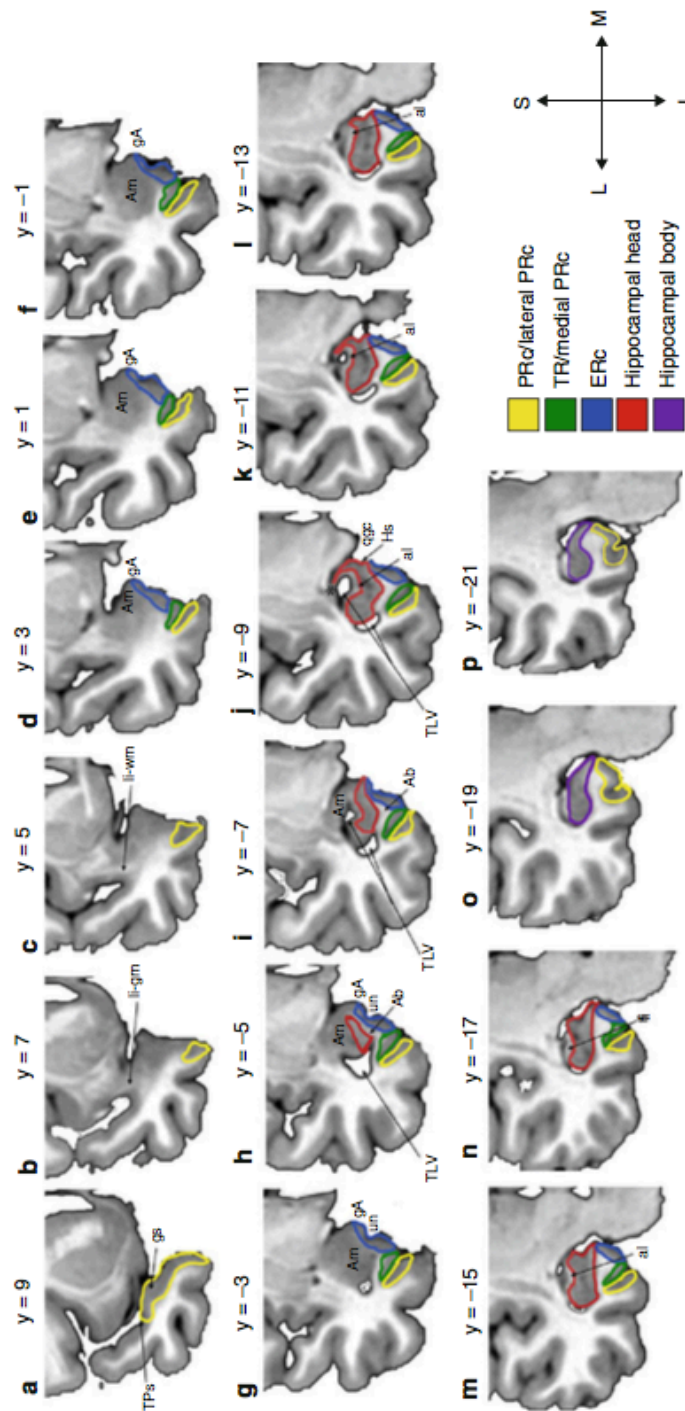


Fig. 19.8 Coronal sections of the temporal lobe at anterior to posterior levels every 2 mm. The coronal level is identified in MNI coordinates. The asterisk represents the most anterior slice where the TLV is continuous with the quadrigeminal cistern (i.e., where ventricular slit is present). The structures are drawn on an MRIcron template (<http://www.mccauslandcenter.sc.edu/mricron/mricron/>). Note that a part of the medial surface in (b, c) is unsegmented due to the unreliability of tracing the oblique anterior end of the ERc (see text). The fimbria begins only at the level of posterior hippocampal head. *Abbreviations:* Ab angular bundle (parahippocampal gyrus white matter), al alveus, Am amygdala, fi fimbria, gA gyrus ambiens, Hs hippocampal sulcus, li-gm intralimbic gyrus (the apex is located at y=-18), qgc quadrigeminal cistern, li-wm limen insulae gray matter, li-wm limen insulae white matter, TLV temporal horn of the lateral ventricle, and un uncus notch. Anatomical directions: S superior, M medial, I inferior, and L lateral

Fig. 30 Kivisaari et al, 2013

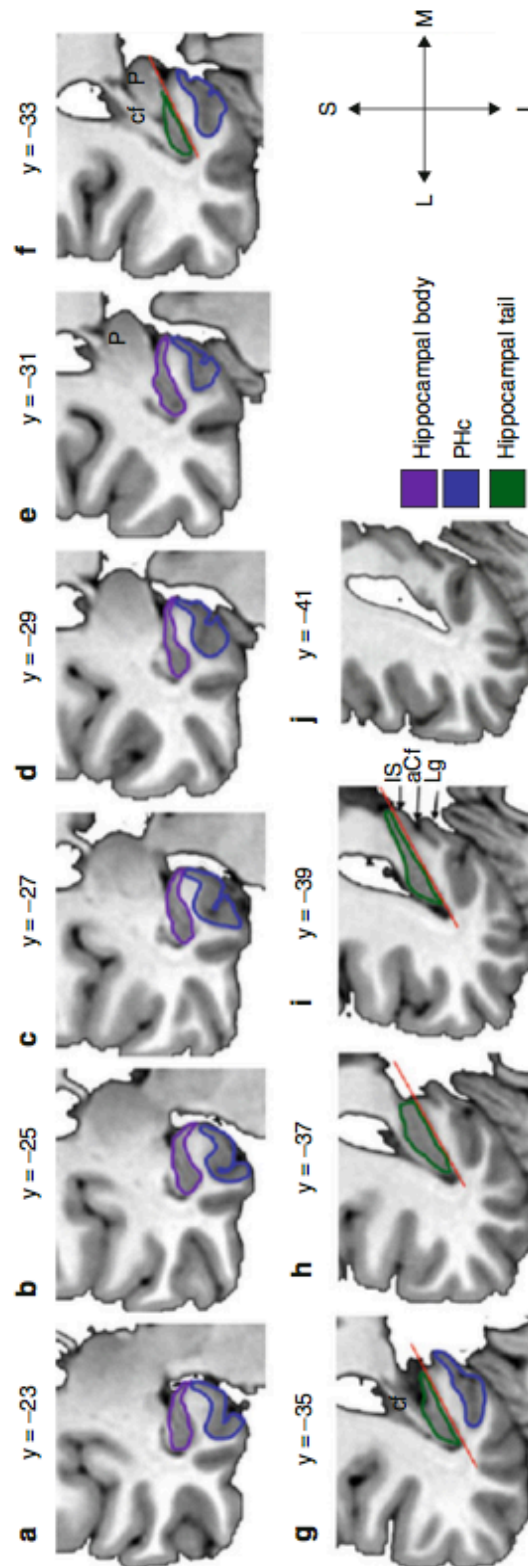


Fig. 19.9 Coronal sections of the temporal lobe at anterior to posterior levels every 2 mm. The numbers represent different coronal levels in MNI (y) coordinates. The structures are drawn on an MriCron template (<http://www.mccauslandcenter.sc.edu/micro/mcron/>). The red line illustrates the arbitrary border used as the inferomedial limit of the hippocampal tail. *Abbreviations:* *aCf* anterior calcarine fissure, *cf* crus of the fornix, *Is* isthmus, *Lg* lingual gyrus, and *P* pulvinar. Anatomical directions: *S* superior, *M* medial, *I* inferior, and *L* lateral

Fig. 31 Kivisaari et al, 2013

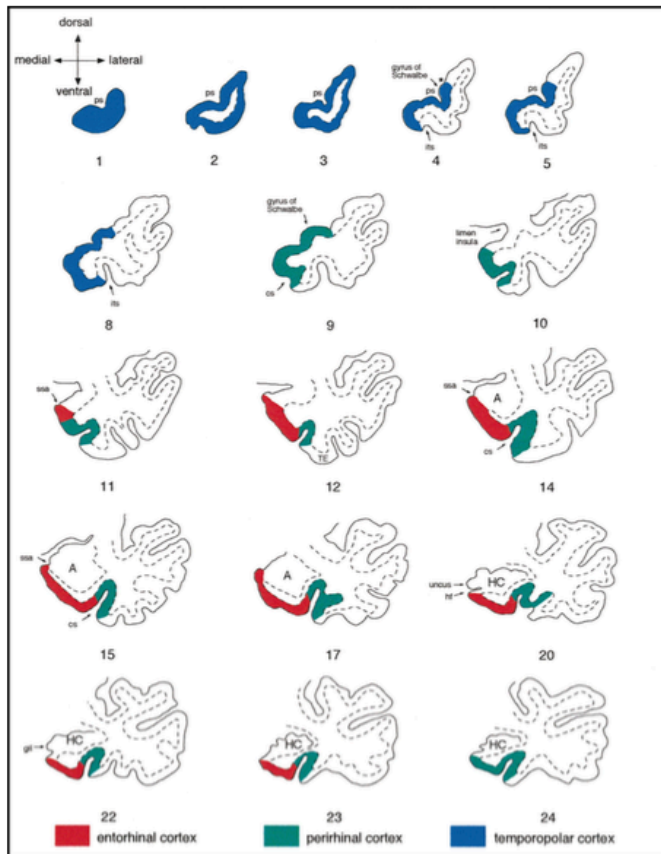


FIG 5. Schematic drawings summarize the anatomic landmarks used to draw the outlines of the temporopolar, perirhinal, and entorhinal cortices on coronal MR images. Sections were outlined from a series of 2-mm-thick coronal MR images from one healthy subject (section numbers 1–24). Only the MR images displaying critical landmarks are shown (therefore, some section numbers are missing). *Red* indicates the entorhinal cortex, *green* the perirhinal cortex, and *blue* the temporopolar cortex. Note that in section 4, the temporopolar cortex recedes and the superior temporal gyrus and inferotemporal cortex appear associated with the most rostral portions of the superior temporal sulcus (sts) and the inferior temporal sulcus (its), respectively. A single temporopolar sulcus (ps) is present in the first five sections, the lateral edge of which demarcates the dorsal limit of the temporopolar cortex (*asterisk*). The appearance of the collateral sulcus (cs) in section 9 marks the transition between the temporopolar and perirhinal cortices (the latter shown in *green*). At the level of the limen insulae in section 10, the dorsomedial border of the perirhinal cortex is at the most medial point of the parahippocampal gyrus (note that we have included the piriform cortex into the perirhinal cortex). Section 11 (one section behind the limen insulae) marks the beginning of the entorhinal cortex (*red*), which extends medially to the sulcus semiannularis (ssa). In this case, the depth of the collateral sulcus is regular, and therefore, the border between the entorhinal and perirhinal cortices is at the midpoint of the medial bank of the collateral sulcus. The boundary between the perirhinal and inferotemporal (TE) cortices is at the lateral edge of the sulcus. Note how in sections 17 and 20, a small gyrus appears in the depth of the collateral sulcus owing to its noncontinuous course. These interruptions can most often be detected at the

level of the uncus. The gyrus intralimbicus (gil) located at the caudal end of the uncus can be seen in section 22. Note that the end of the entorhinal cortex is one section behind the end of the uncus (section 23). The perirhinal cortex extends one more section caudally (section 24). A = amygdala, cs = collateral sulcus, its = inferior temporal sulcus, gil = gyrus intralimbicus, HC = hippocampus, hf = hippocampal fissure, ssa = sulcus semiannularis, TE = area TE.

Fig. 32 Insausti et al. 1998

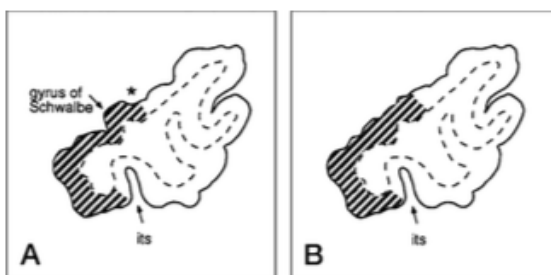


FIG 6. Criteria used to define the dorsolateral border of the temporopolar cortex.

A, When the gyrus of Schwalbe was present, the dorsolateral border of the temporopolar cortex was defined at the lateral border of the gyrus; that is, in the fundus of the temporopolar sulcus (*asterisk*).

B, If the gyrus of Schwalbe was not present, the dorsolateral border of the temporopolar cortex was located at the dorsal midpoint between the medial and lateral corners of the temporal pole. Ventrally, the temporopolar cortex extends to the medial edge of the inferior temporal sulcus (its). The temporopolar cortex is indicated with shading.

Fig. 33 Insausti et al. 1998

REFERENCES:

- Pruessner JC, Li LM, Serles W, Pruessner M, Collins DL, Kabani N, Lupien S, Evans AC (2000) Volumetry of hippocampus and amygdala with high-resolution MRI and three-dimensional analysis software: minimizing the discrepancies between laboratories. *Cereb Cortex* 10:433–442.
- Pruessner JC, Köhler S et al (2002) Volumetry of temporopolar, perirhinal, entorhinal and parahippocampal cortex from high-resolution MR images: considering the variability of the collateral sulcus. *Cereb Cortex* 12:1342-1353.
- Insausti R, Juottonen K et al (1998) MR volumetric analysis of the human entorhinal, perirhinal, and temporopolar cortices. *AJNR Am J Neuroradiol* 19:659–671.
- Kivisaari SL, Probst A, Taylor KI (2013) The perirhinal, Entorhinal, and Parahippocampal cortices and Hippocampus: An overview of functional anatomy and protocol for their segmentation in MR images. In the book: *fMRI: Basics and Clinical Applications*, Edition: 2nd, Chapter: 19, Publisher: Springer, Editors: S. Ulmer, O. Jansen, pp.239-267.

ADDITIONAL CONSULTATIONS:

- *The Human Nervous System*, 3rd Edition from Juergen Mai, George Paxinos. ISBN-9780080921303, Elsevier (2011).
- Duvernoy HM (1998) *The human hippocampus*, 2nd edn. Springer, Berlin.