A high-resolution in vivo atlas of the human brain’s serotonin system

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The serotonin (5-HT) system

- Involved in cognition, mood, social interaction, sexual behaviors, ...
- But also in disorders such as depression, anxiety, schizophrenia.
- The 5-HT system has 14 receptor subtypes and a transporter
5-HT autoradiography

Whole hemisphere autoradiograms comparing the distribution of the 5-HT transporter and receptor binding sites in human brain cryosections. The following information and the abbreviation list apply to all images: Total binding is shown for the different radioligands. A: Cresyl violet-stained section. B: $[^3H]A$Clonazepam binding to the 5-HT$_{1A}$ receptor. C: $[^3H]A$WAY-100635 binding to the 5-HT$_{1A}$ receptor. D: $[^3H]A$GR 125743 binding to the 5-HT$_{1B}$ receptor in the presence of the 5-HT$_{1D}$ antagonist PNU-142633 (800 nM). E: $[^3H]A$BMY14803 binding to the 5-HT$_{2A}$ receptor. F: $[^3S]A$B 207710 binding to the 5-HT$_{4}$ receptor.4

Positron Emission Tomography
Cimbi Database Demographics

Healthy controls from the Cimbi database aged between 18 and 45

Binding potential and autoradiography

A \[5 - \text{HTT} \quad \rho = 0.65 \quad \text{slope} = 7.52\]

B \[5 - \text{HT}_{1A} \quad \rho = 0.90 \quad \text{slope} = 18.3\]

C \[5 - \text{HT}_{1B} \quad \rho = 0.88 \quad \text{slope} = 11.73\]

D \[5 - \text{HT}_{2A} \quad \rho = 0.92 \quad \text{slope} = 32.78\]

E \[5 - \text{HT}_{4} \quad \rho = 0.97 \quad \text{slope} = 2.35\]

Cortical density maps

5-HTT

5-HT_{1A}R

5-HT_{1B}R

5-HT_{2A}R

5-HT_{4}R

(pmol/ml)

2 9

6 50

6 30

15 60

1 3
Subcortical density maps

![Subcortical density maps](image)

- **5-HTT**: 2 (pmol/ml) to 9 (pmol/ml)
- **5-HT1A R**: 6 (pmol/ml) to 50 (pmol/ml)
- **5-HT1B Rb**: 6 (pmol/ml) to 30 (pmol/ml)
- **5-HT2A R**: 15 (pmol/ml) to 60 (pmol/ml)
- **5-HT2C R**: 1 (pmol/ml) to 3 (pmol/ml)
Protein localization and mRNA
Density and mRNA

PET Surfer

by Doug

https://surfer.nmr.mgh.harvard.edu/fswiki/PetSurfer

(image inspired by Melanie Ganz)
FreeSurfer provides...

Surface smoothing

Multimodel registration

Individualized Automated Segmentations
Cortical surface-based analysis reduces bias and variance in kinetic modeling of brain PET data

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The PET pipeline

Individual PET frames → AIR → PET space → Realigned PET frames → Weighted average PET → PVC PET frames

bbregister → mri_gtmpvc

T1-weighted → recon-all → Anatomical/Subject Space → GTM segmentation → gtmseg

Standard volume space (MNI152)
- mri_glimfit
- mri_fwhm
- mri_vol2vol
- mri_vol2surf

Standard surface space (fsaverage)
- mri_glimfit

https://surfer.nmr.mgh.harvard.edu/fswiki/PetSurfer
Pial surface refinement with T2 images

New recon:
recon-all --all --s <subj> -i <img> -T2pial -T2 <T2img>

Old recon:
recon-all --all --s <subj> -T2pial -T2 <T2img> -autorecon3
Pial surface refinement with T2 images
T2 edit trick

- Parts of the T2 can be ignored if voxels are set to 110
- If the –T2 flag is reused in recon-all, changes will be overwritten
Thank you for your attention!

Collaborators

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