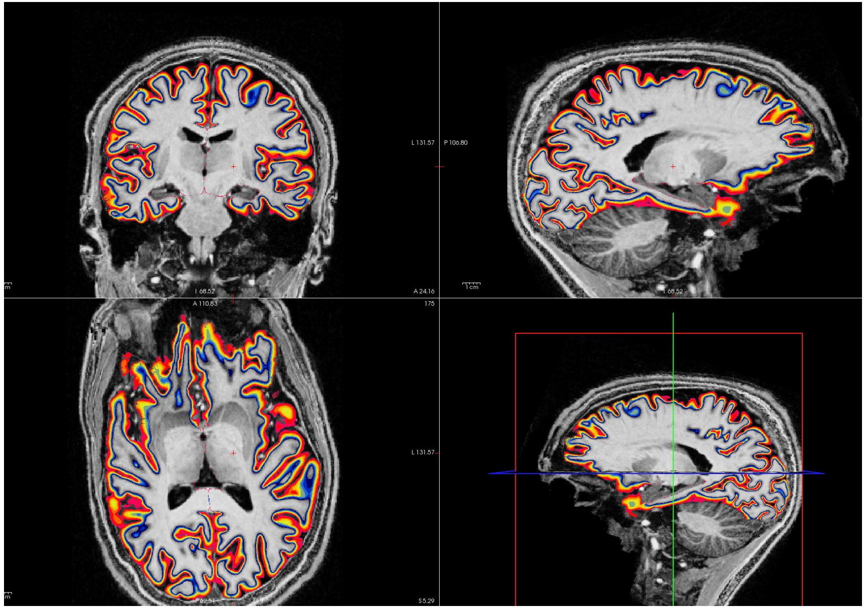
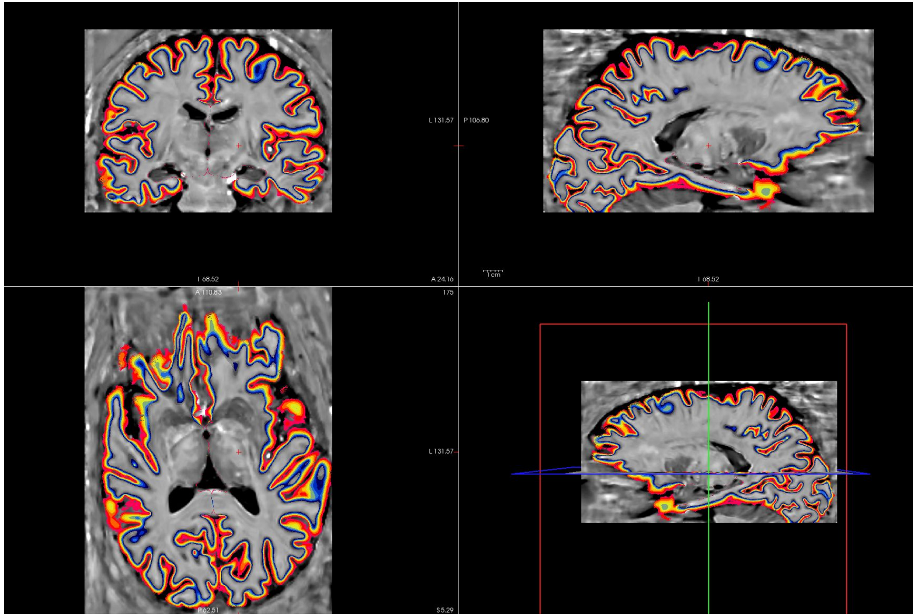
# Layers

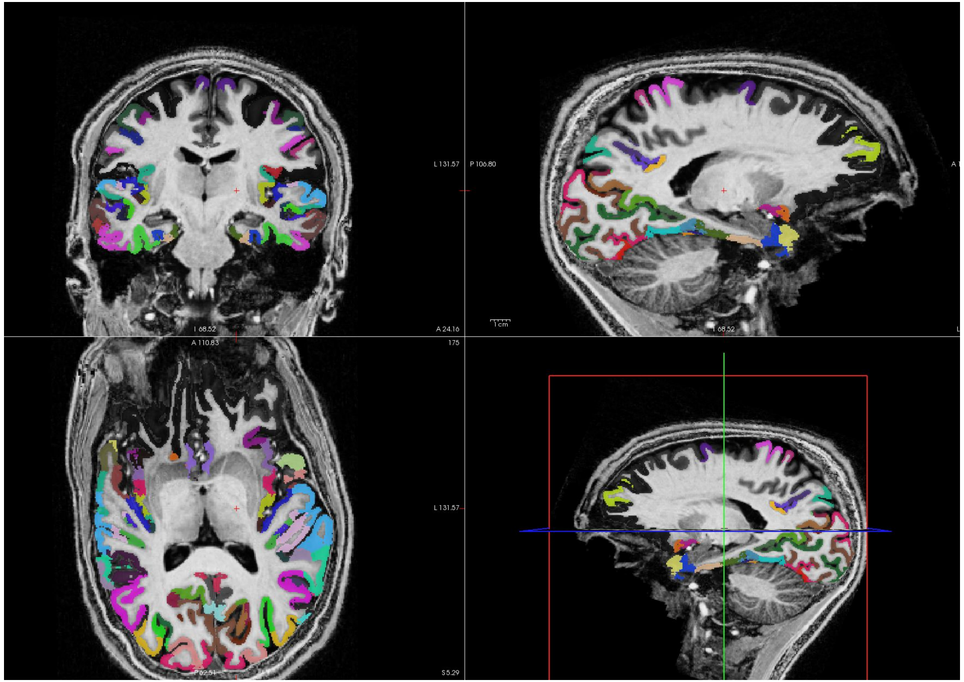
T1



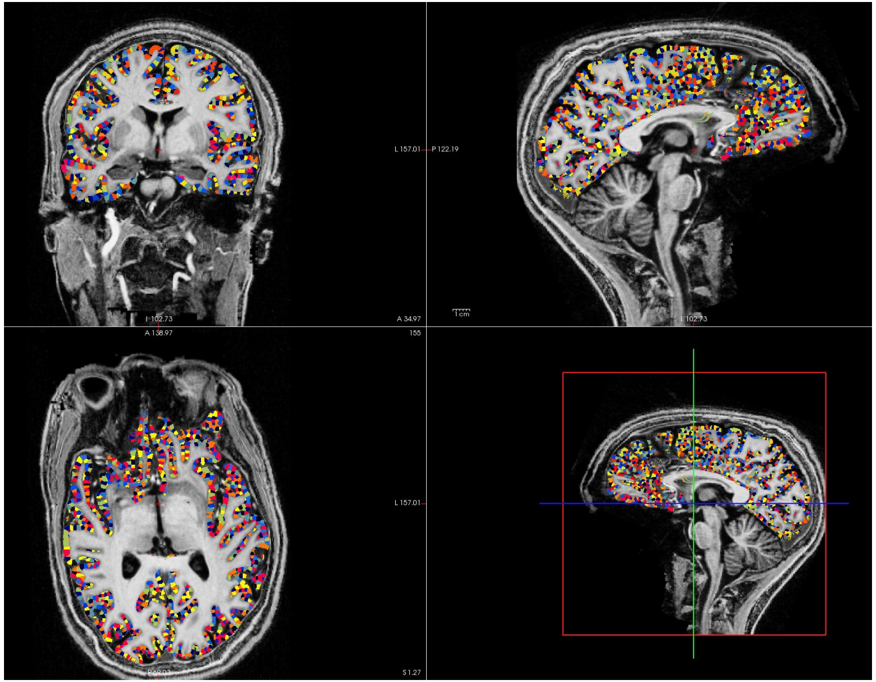
EPI



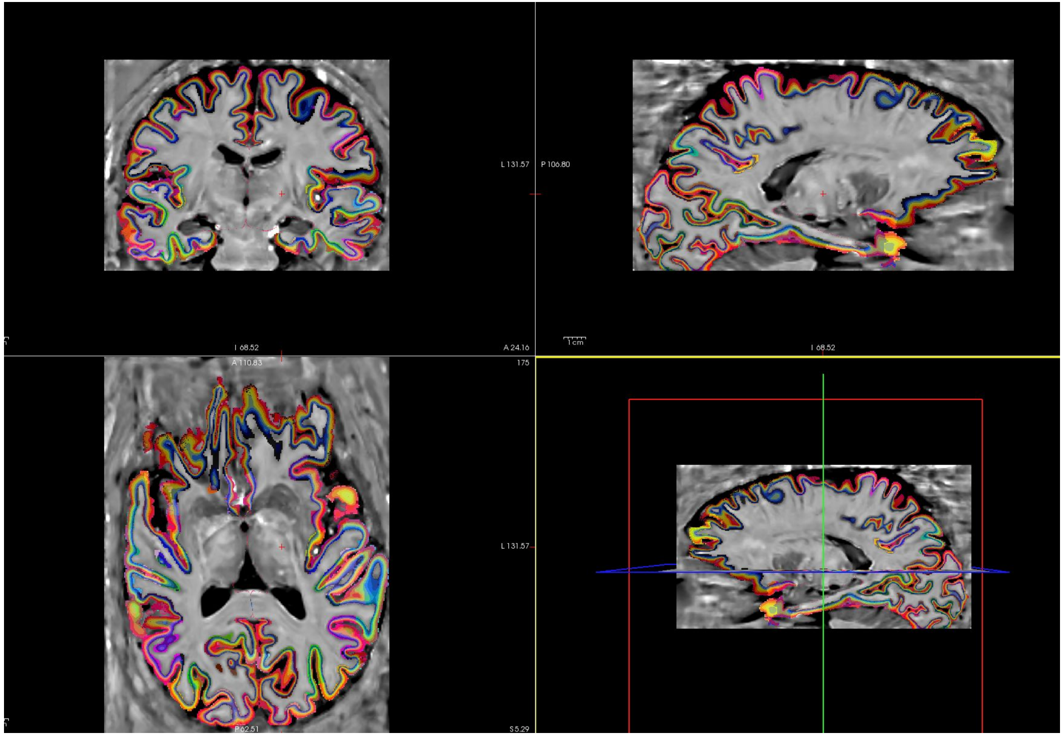
HCP-multimodal parellation



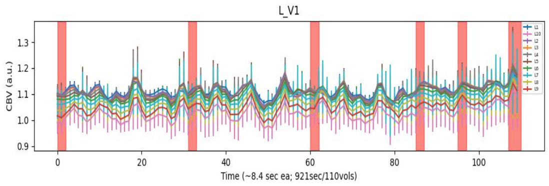
equidist_columns_38000

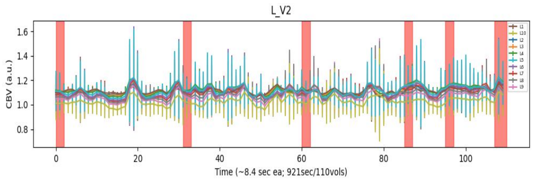


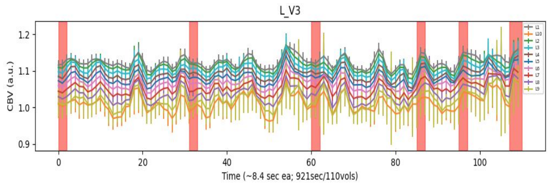
# Layers + Atlas

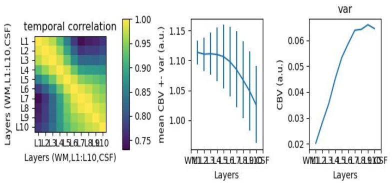


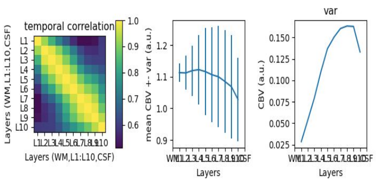
# Layer profiles

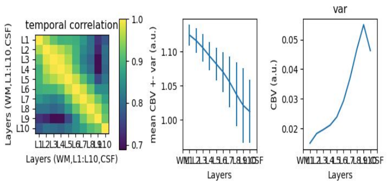


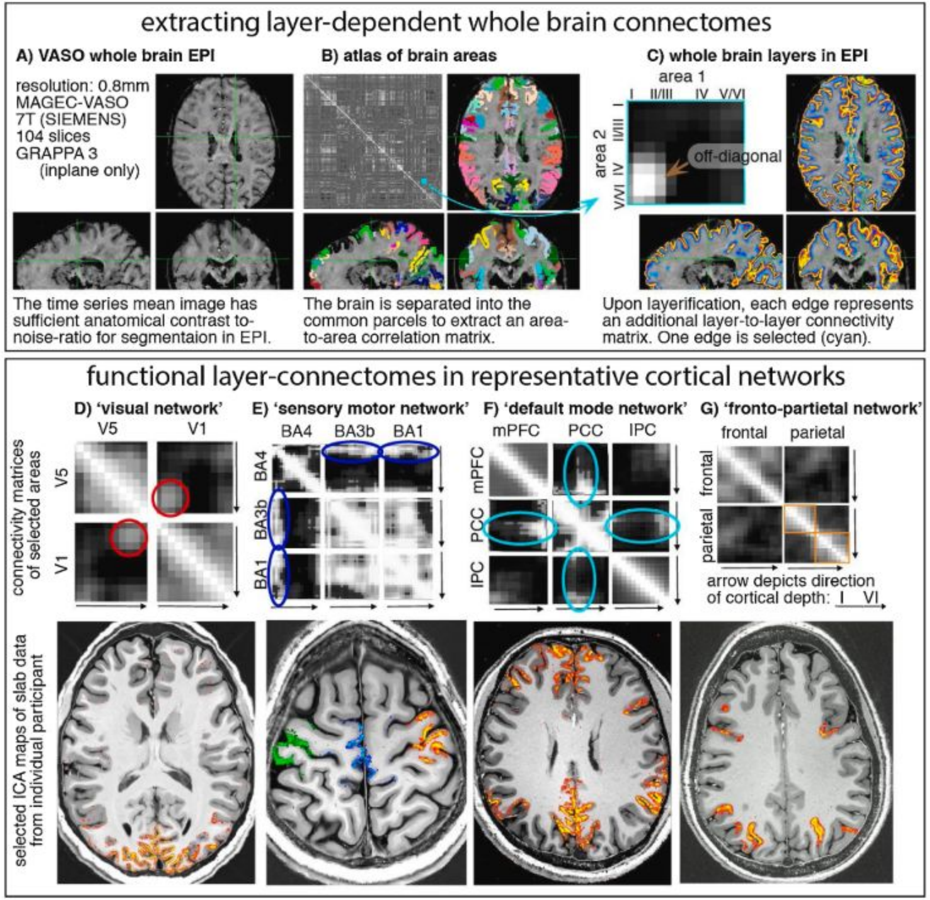



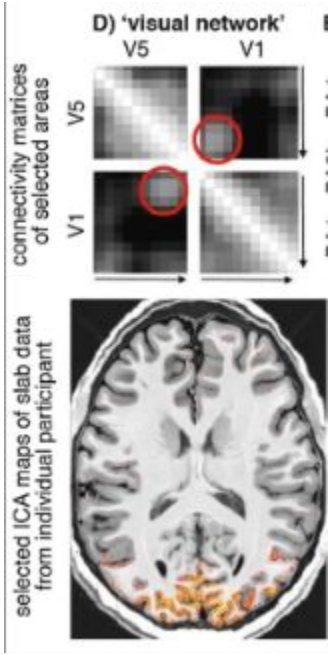



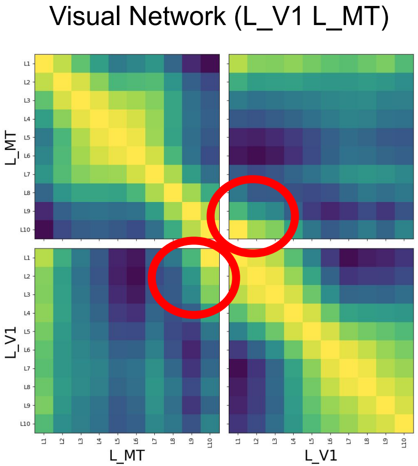

1. Calculate %change CBV (Finn et al. 2019)
2. Average across sessions (9 sessions total)?
3. Other layer metrics



extracting layer-dependent whole brain connectomes
A) VASO whole brain EPI
resolution: 0.8mm
MAGEC-VASO
7T (SIEMENS)
104 slices
GRAPPA 3
(inplane only)
B) atlas of brain areas
C) whole brain layers in EPI
area 1
I II/III IV V/VI
area 2
off-diagonal
The time series mean image has sufficient anatomical contrast to-noise-ratio for segmentaion in EPI.
The brain is separated into the common parcels to extract an area-to-area correlation matrix.
Upon layerification, each edge represents an additional layer-to-layer connectivity matrix. One edge is selected (cyan).
functional layer-connectomes in representative cortical networks
D) 'visual network'
V5
V1
E) 'sensory motor network'
BA4
BA3b
BA1
F) 'default mode network'
mPFC
PCC
IPC
G) 'fronto-partietal network'
frontal
parietal
connectivity matrices of selected areas
arrow depicts direction of cortical depth: I VI
selected ICA maps of slab data from individual participant

# Visual Network

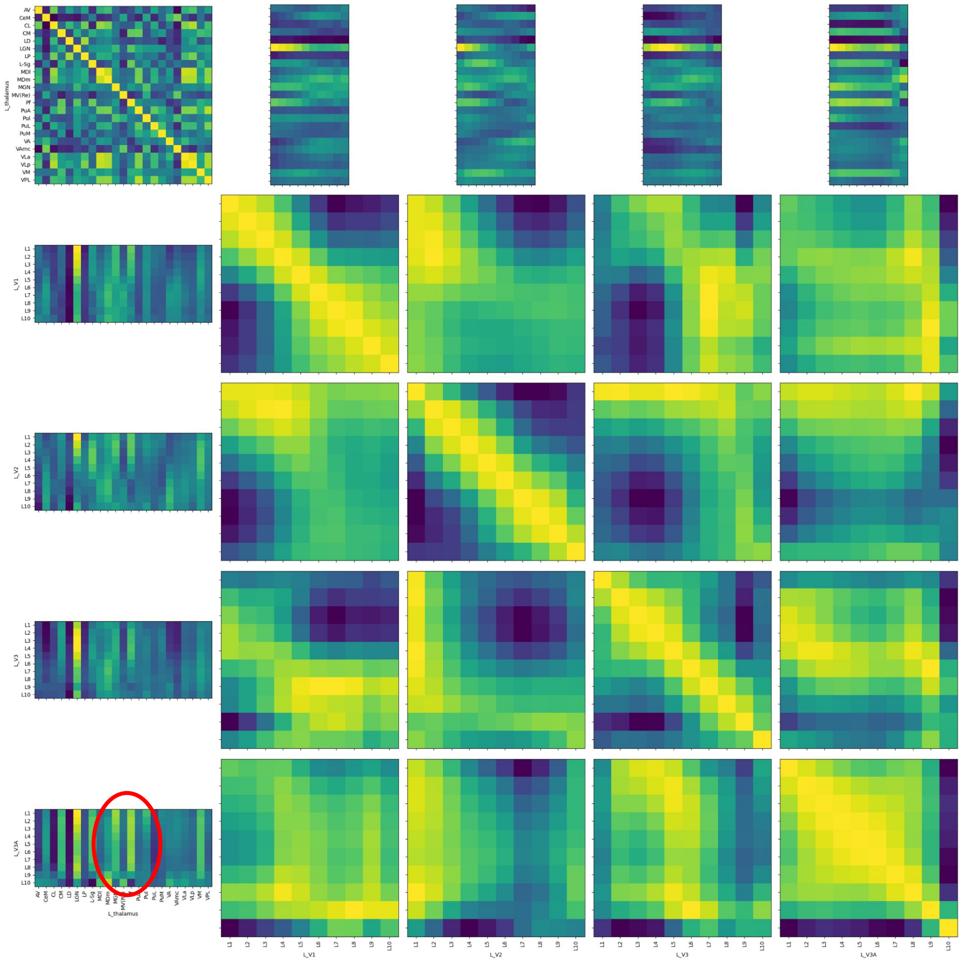


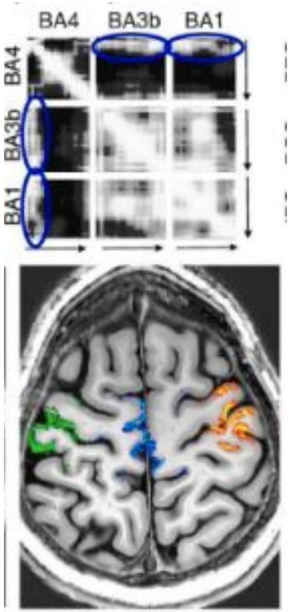

Panel **D–G)** depict representative layer-dependent connectivities of common large networks.
Panel **D)** depicts the 'visual network'. Selected correlation diagrams between V1 and V5/hMT + confirm data from Fig. 4D. Namely, V1 receives top-down feedback in superficial layers from V5, while V5 receives bottom-up input in the middle/deeper layers (red circles).

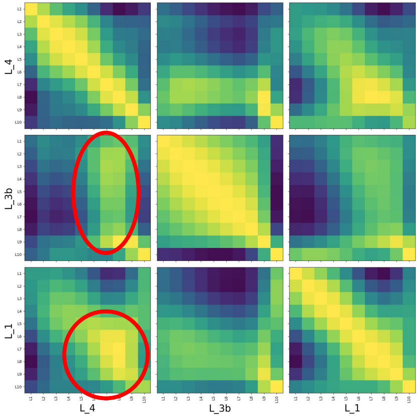
# Visual Network

It would be interesting if we could find connectivity between early visual and auditory areas.



# Sensory Motor Network



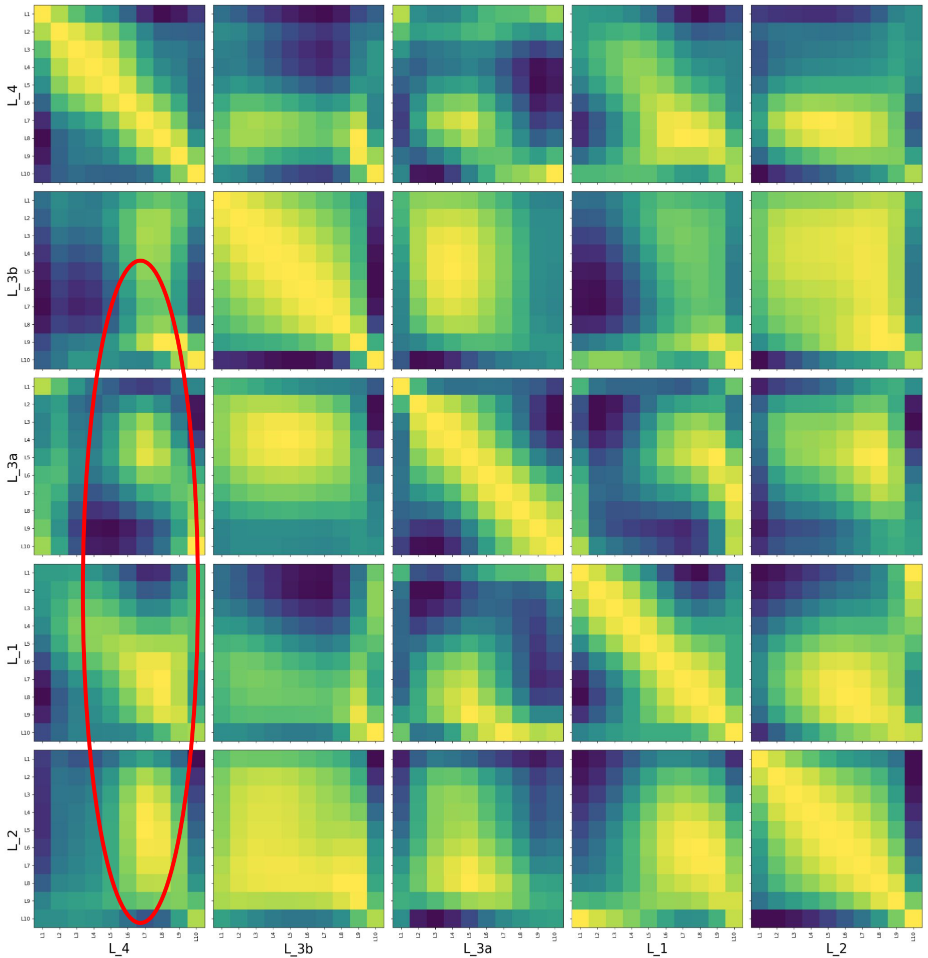




Don't quite see the same same results.

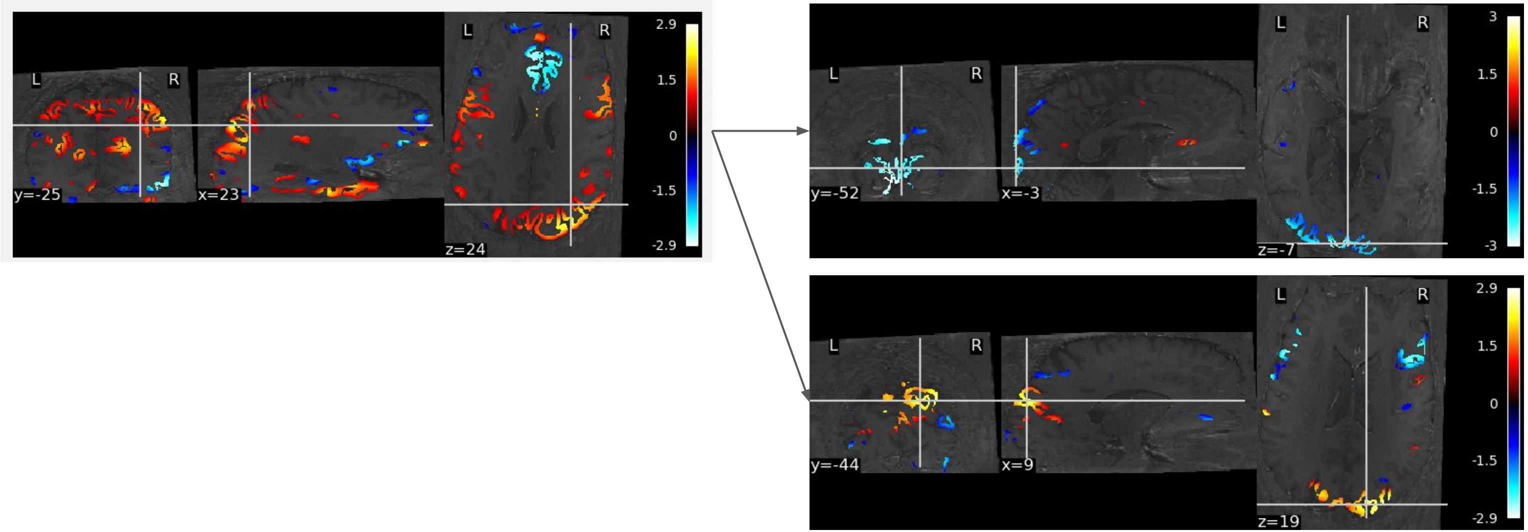
- Preprocessing?
- HCP vs shen ROIs?

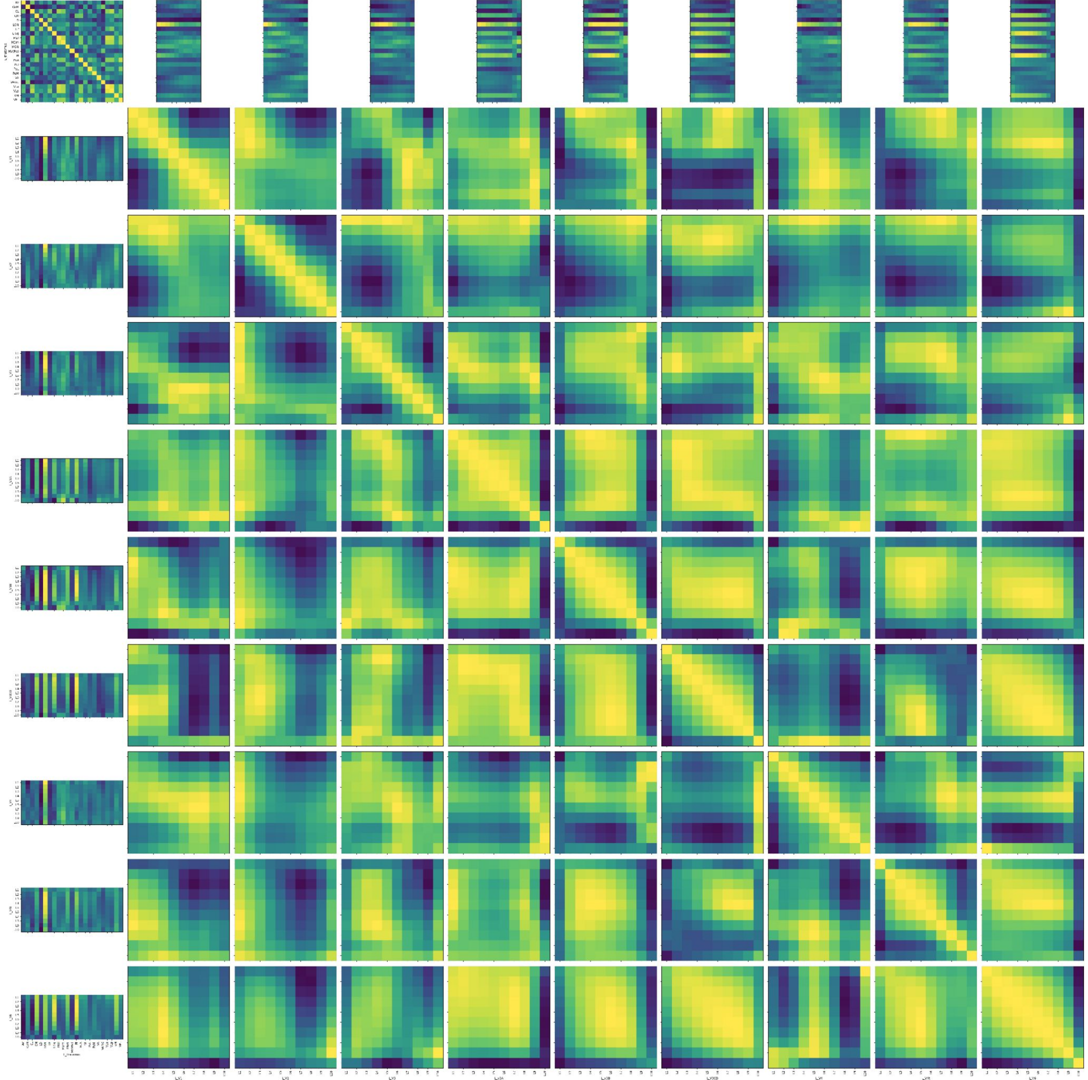
Panel E) depicts the 'sensory motor network'. As expected from previous layer-fMRI studies (Huber et al., 2017), the primary motor cortex receives input from the sensory areas solely in superficial layers (dark blue ellipses).

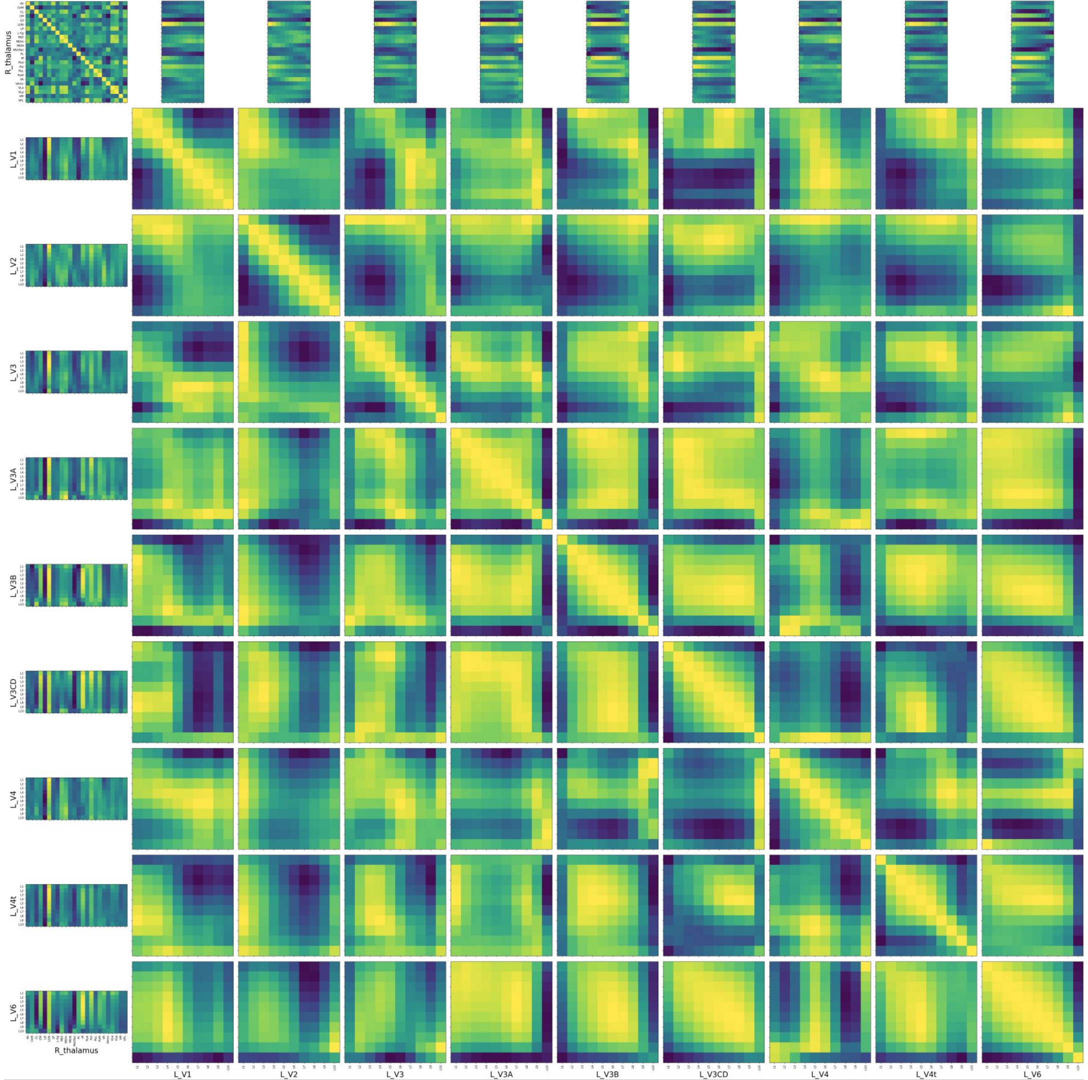
# Sensory Motor Network

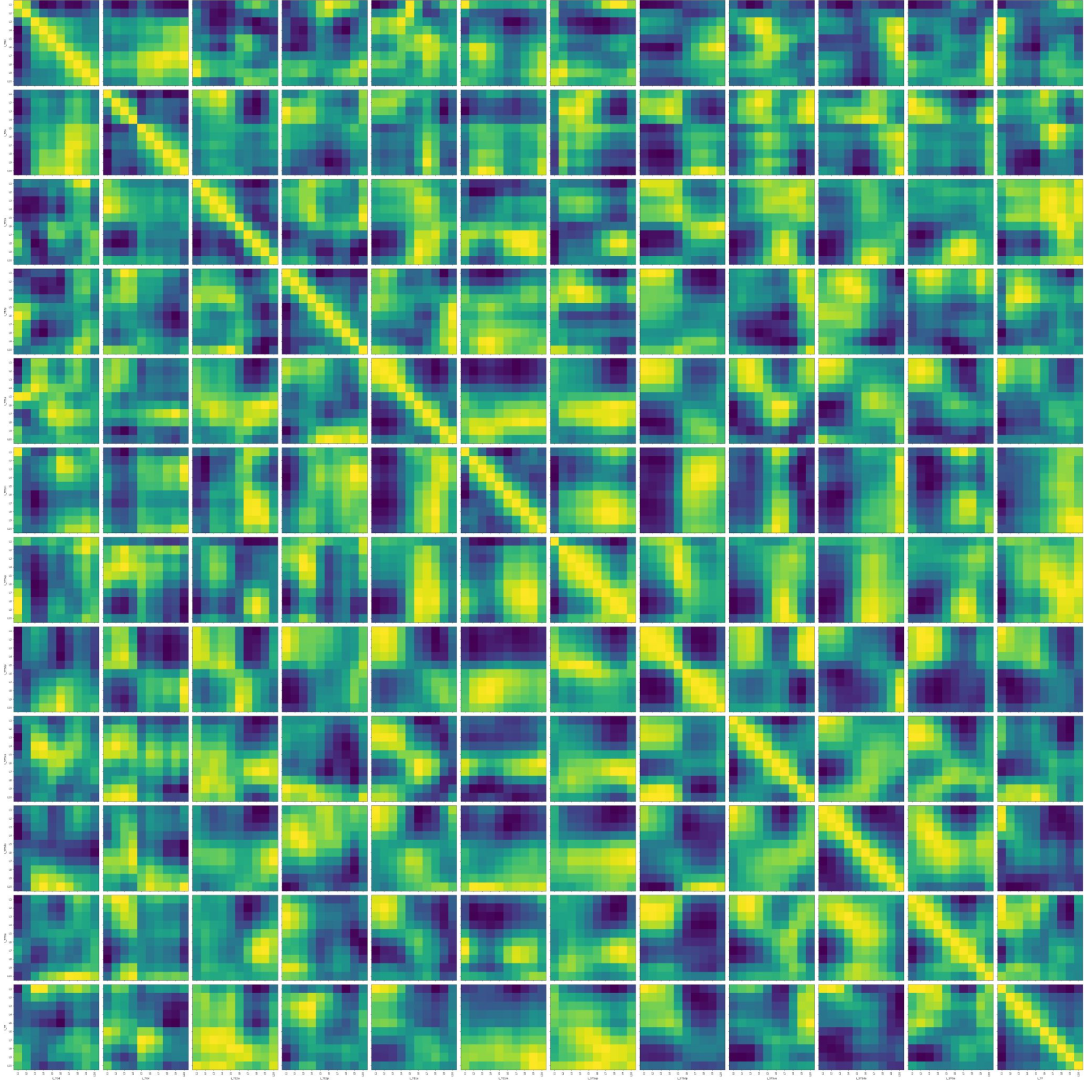


# Iterative ICA






R_thalamus
L_V1
L_V2
L_V3
L_V3A
L_V3B
L_V3CD
L_V4
L_V4t
L_V6
R_thalamus
L_V1
L_V2
L_V3
L_V3A
L_V3B
L_V3CD
L_V4
L_V4t
L_V6



# Extra

I'm using the Glasser (hcp-mmp) ROIs to limit the memory overhead. Using nibabel I can load specific voxel time courses without loading the whole file (120 gb). I used 10 layers, but I also have 3 layer version--plots not included here.

The "layer profiles" need some more work, but I intend to duplicate some of the plots Renzo includes in his paper. Red horizontal bars in the layer profiles are "rest" periods, but I haven't used this to calculate the %CBV change yet across layers.

The correlation analysis is going well. I have some different distance measures (cosine, pearson). I also have some code for building "neural dissimilarity matrices" and calculating the correlation between ROIs/layers using a kind of multivariate variation. I haven't included these plots. The main issue here is that I don't have a good way to visualize these results--too many plots. I was thinking that using 3 layers would simplify things and then using a circular graph to visualize significant ROI1-output to ROI2-input connections, but I haven't done this yet.

The ROIs I did include in the plots are:

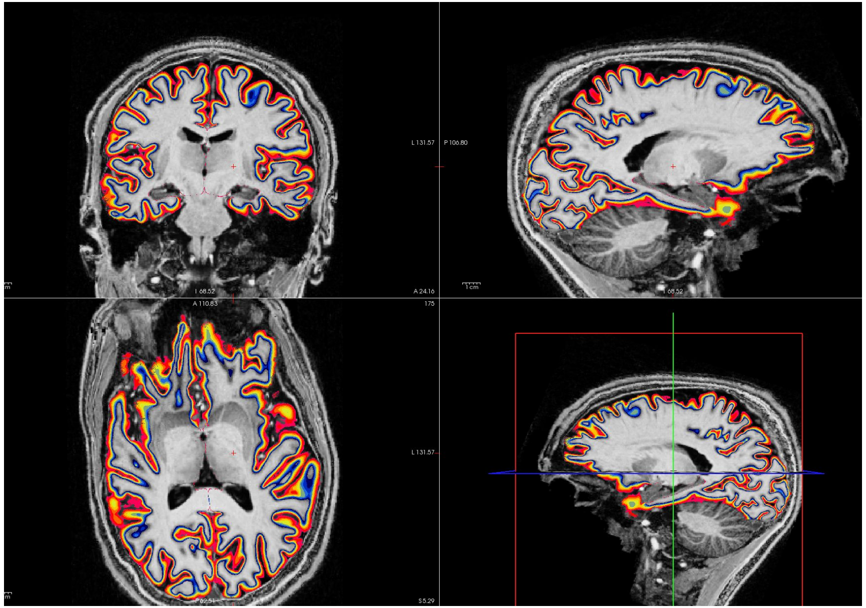
- an early visual (L_thalamus L_V1 L_V2 L_V3 L_V3A)
- thalamus parcellation+early visual (L_thalamus L_V1 L_V2 L_V3 L_V3A L_V3B L_V3CD L_V4 L_V4t L_V6)
- thalamus+temporal lobe ROIs ( L_TGd L_TGv L_TE2a L_TE2p L_TE1a L_TE1m L_STSvp L_STSdp L_STSva L_STSda L_STGa L_TF)

I did start looking into downloading hcp data to identify networks and to help constrain the VASO layer analysis, but I haven't made too much progress on this.

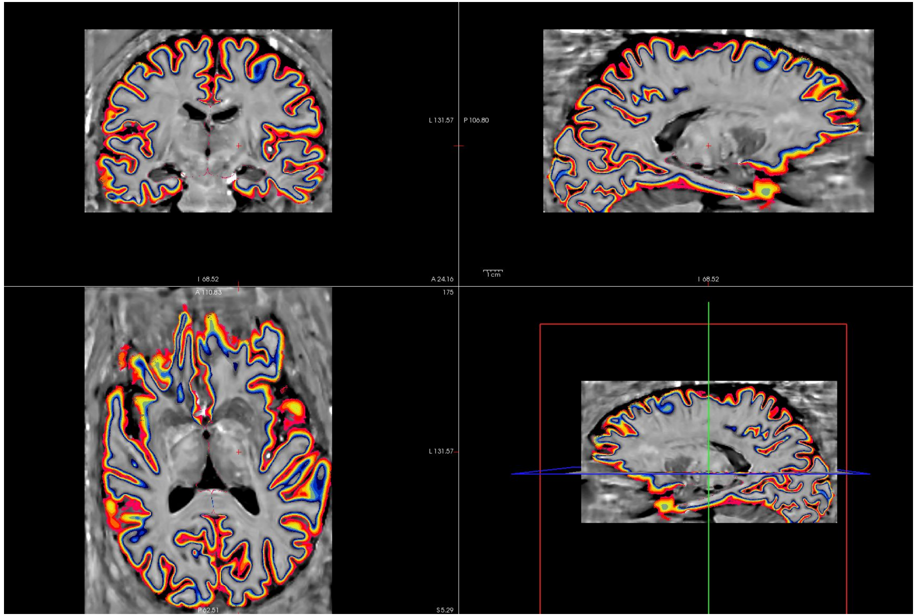
Right now, I'm thinking that I should be working with the hcp data to find a candidate network that we can then evaluate using the VASO data. Does this sound good? Here is the github for the code ([https://github.com/rlk41/laminar_fmri](https://github.com/rlk41/laminar_fmri)) and I can upload extracted time courses to Box if you'd like.

# Layers

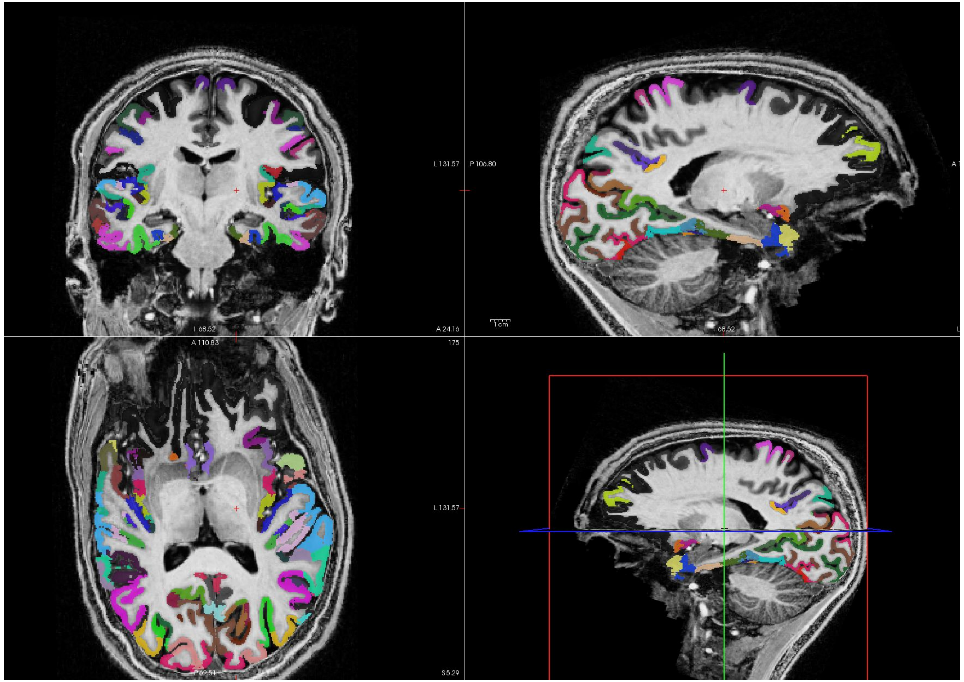
T1



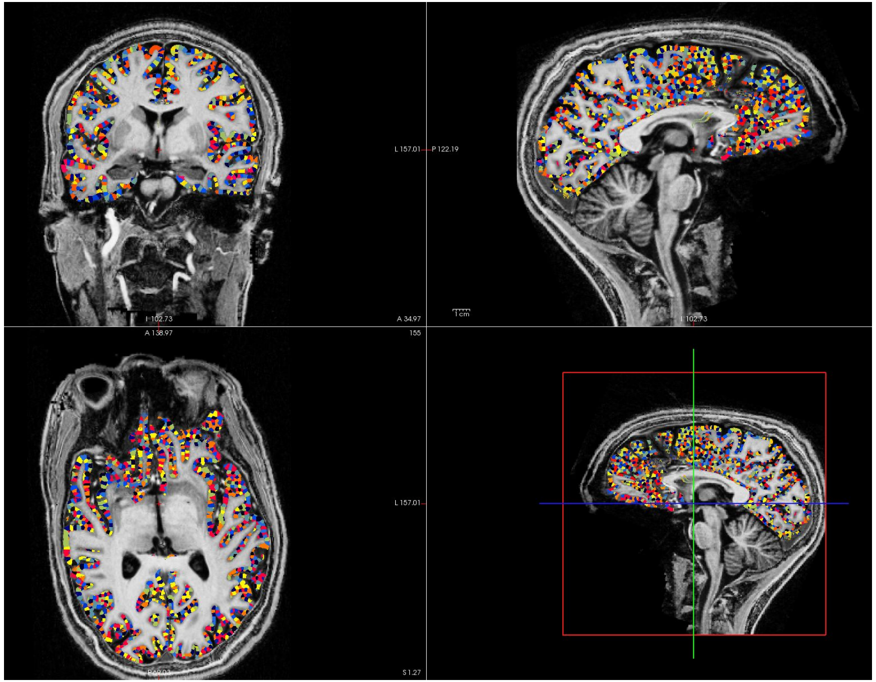
EPI



hcp-mmp



equidist_columns_38000



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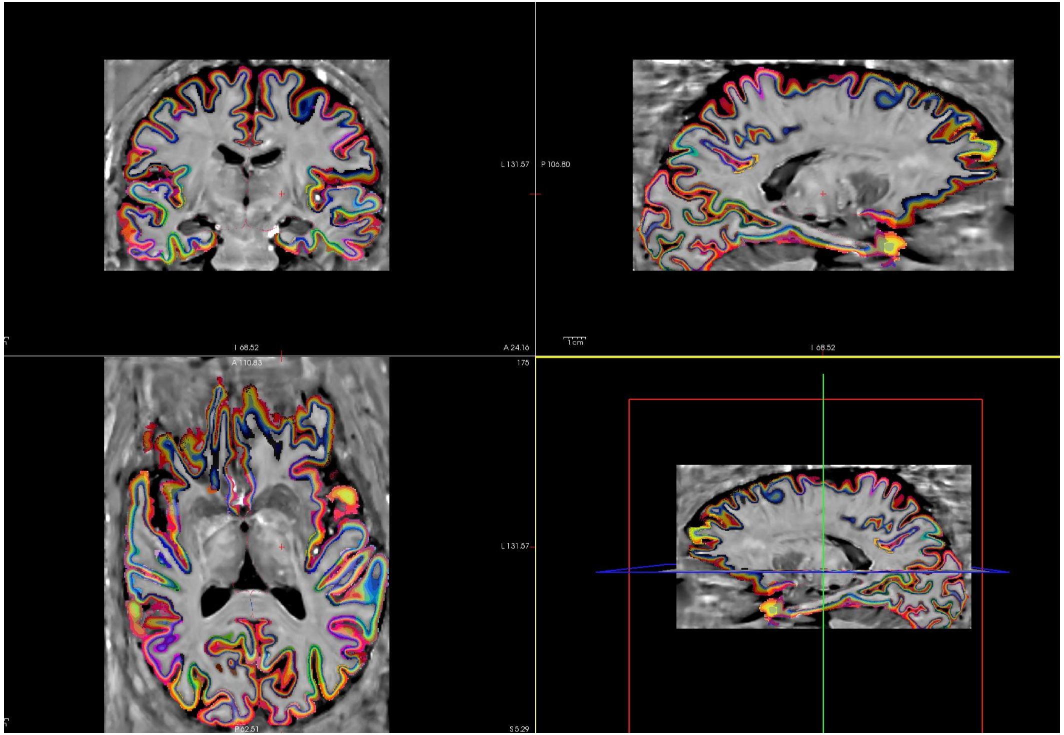
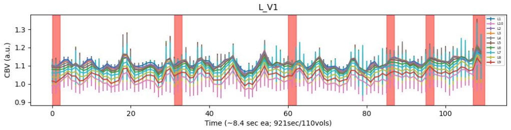
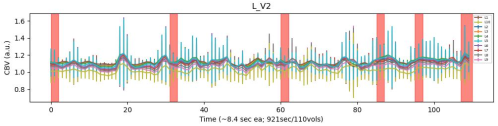
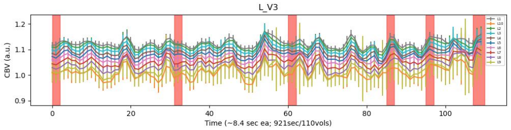
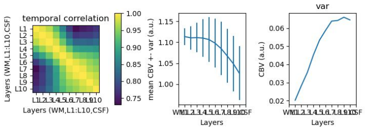


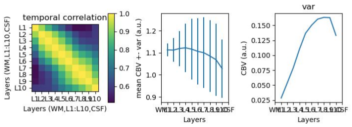
# Layer profiles

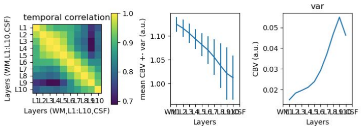
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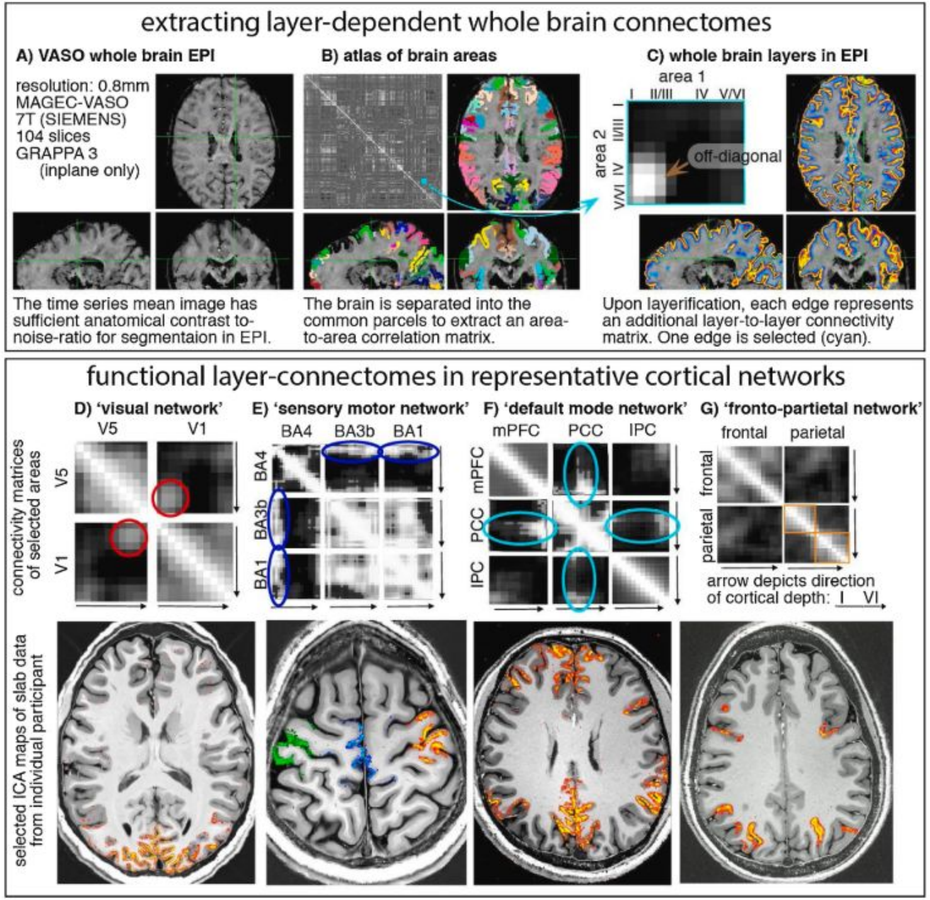
3. Other layer metrics



extracting layer-dependent whole brain connectomes
A) VASO whole brain EPI
resolution: 0.8mm
MAGEC-VASO
7T (SIEMENS)
104 slices
GRAPPA 3
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The time series mean image has sufficient anatomical contrast to-noise-ratio for segmentaion in EPI.
B) atlas of brain areas
The brain is separated into the common parcels to extract an area-to-area correlation matrix.
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I II/III IV V/VI
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Upon layerification, each edge represents an additional layer-to-layer connectivity matrix. One edge is selected (cyan).
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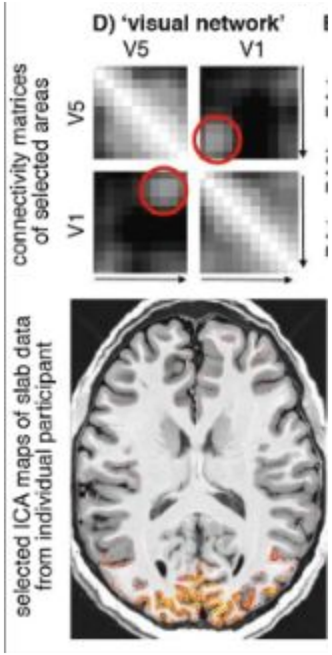
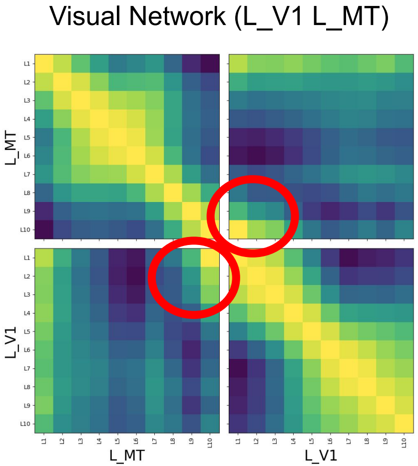
D) 'visual network'
V5 V1
connectivity matrices of selected areas
E) 'sensory motor network'
BA4 BA3b BA1
F) 'default mode network'
mPFC PCC IPC
G) 'fronto-partietal network'
frontal parietal
arrow depicts direction of cortical depth: I VI
selected ICA maps of slab data from individual participant

# Visual Network

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# Visual Network

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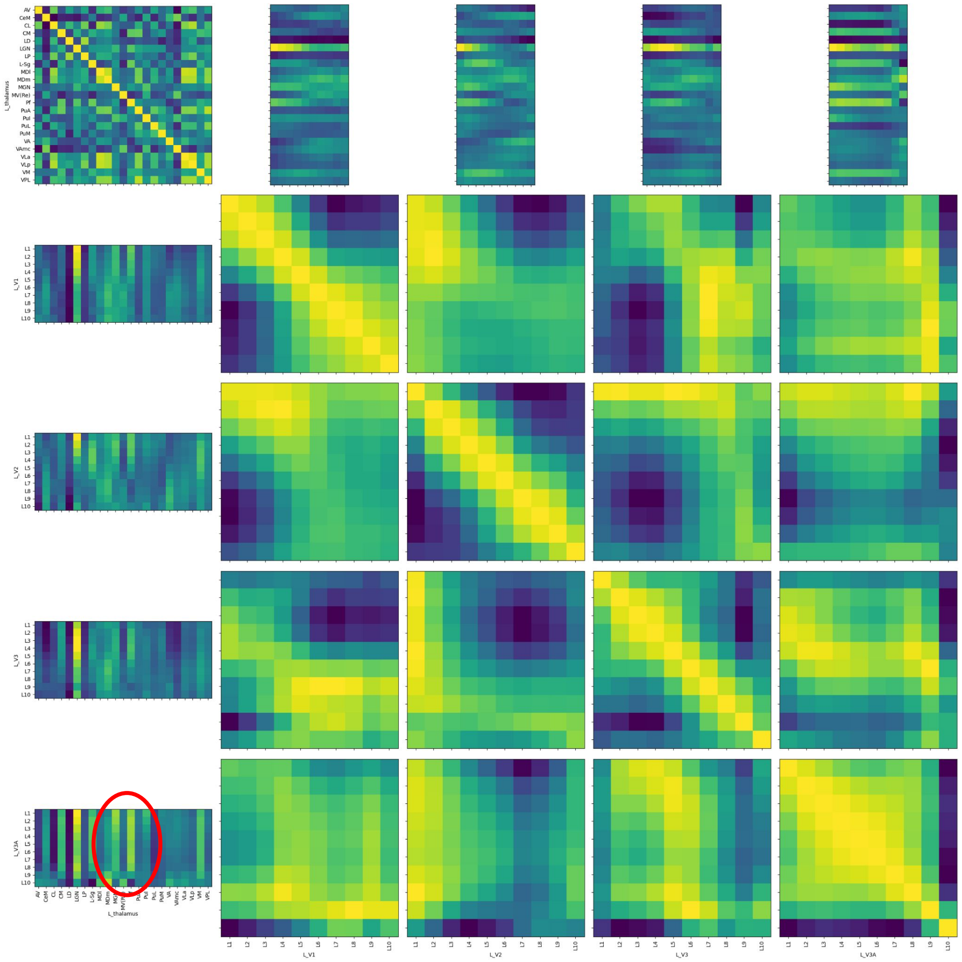
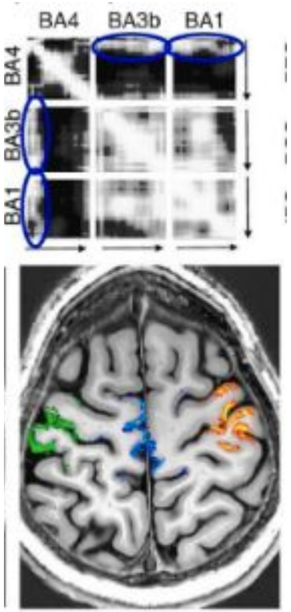
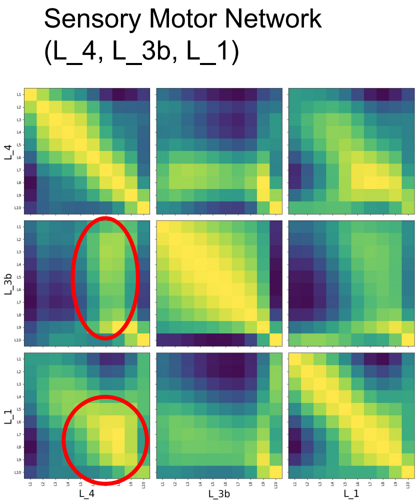


# Sensory Motor Network




Don't quite see the same same results.

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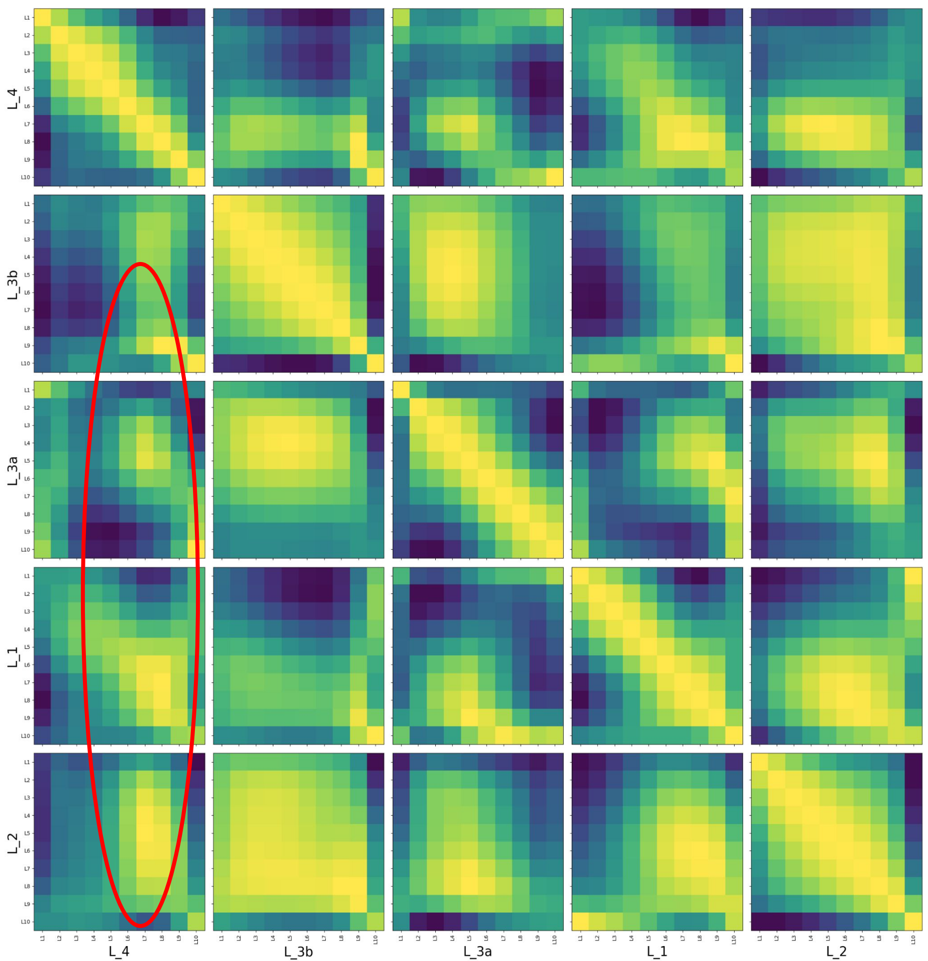
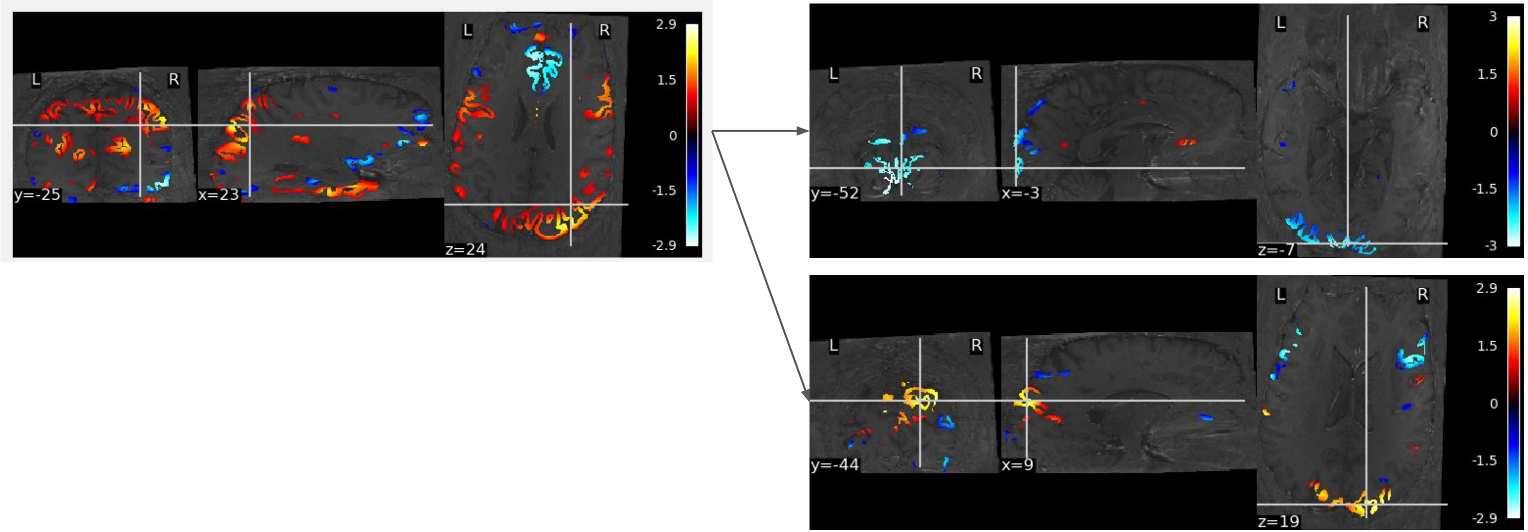
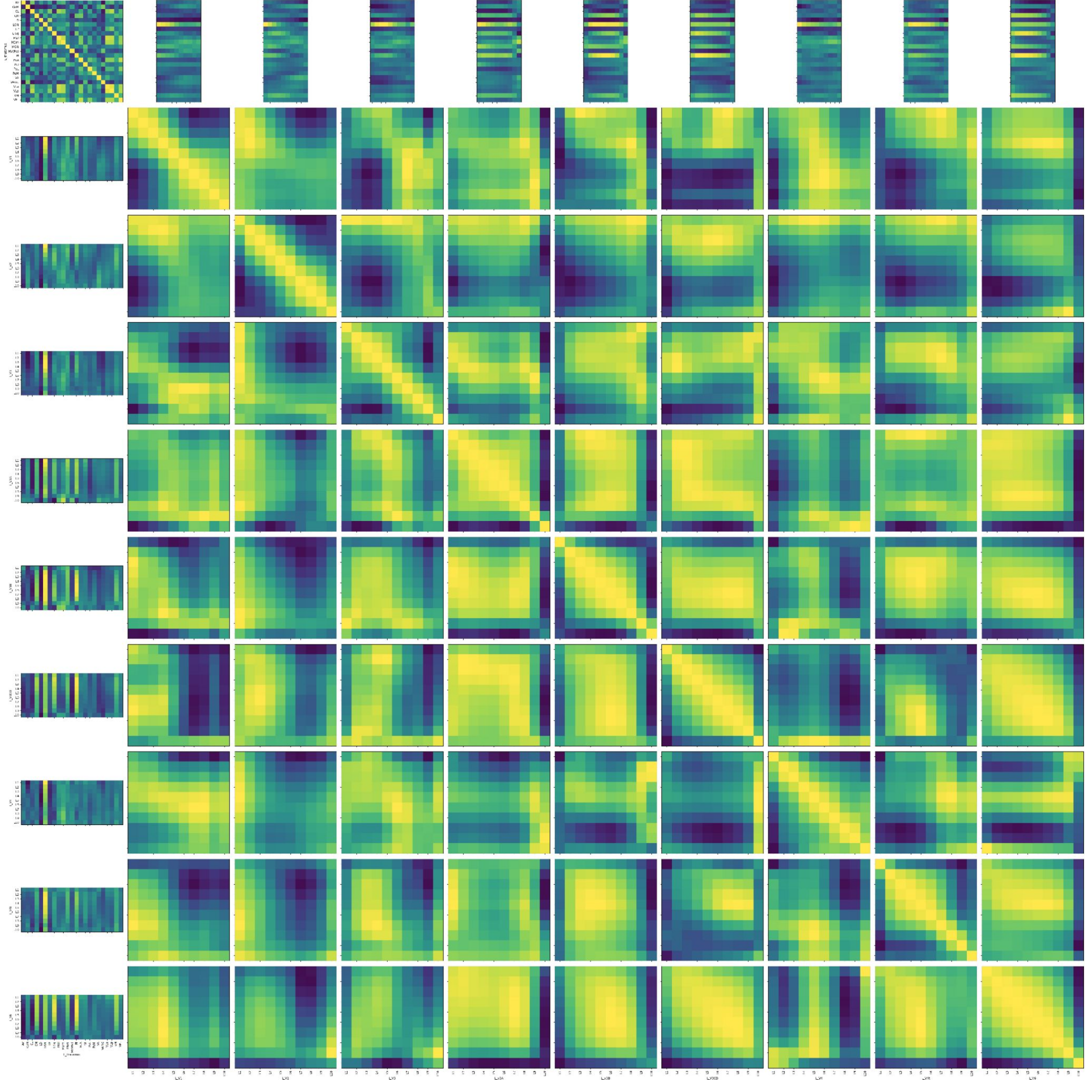
Panel E) depicts the 'sensory motor network'. As expected from previous layer-fMRI studies (Huber et al., 2017), the primary motor cortex receives input from the sensory areas solely in superficial layers (dark blue ellipses).

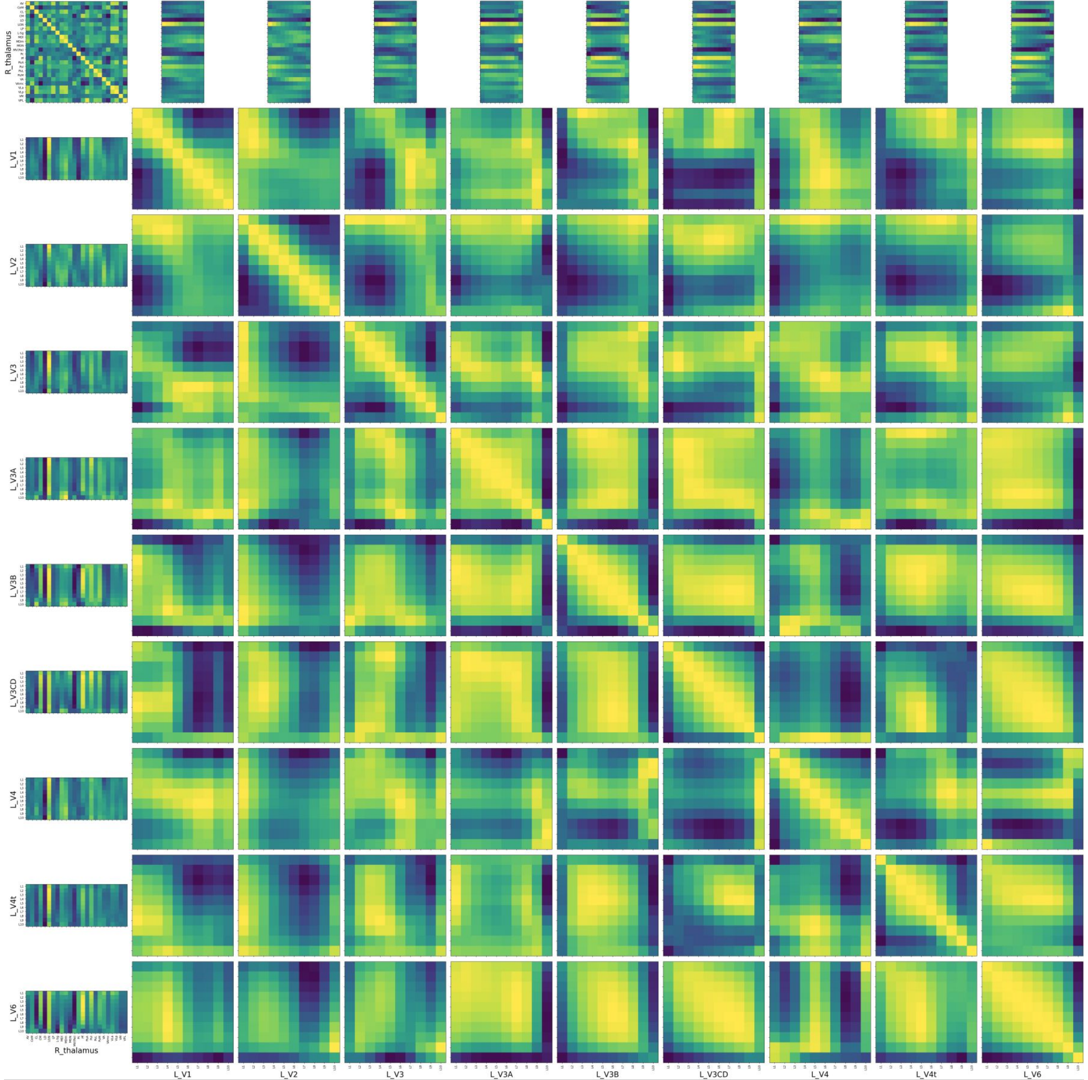
# Sensory Motor Network

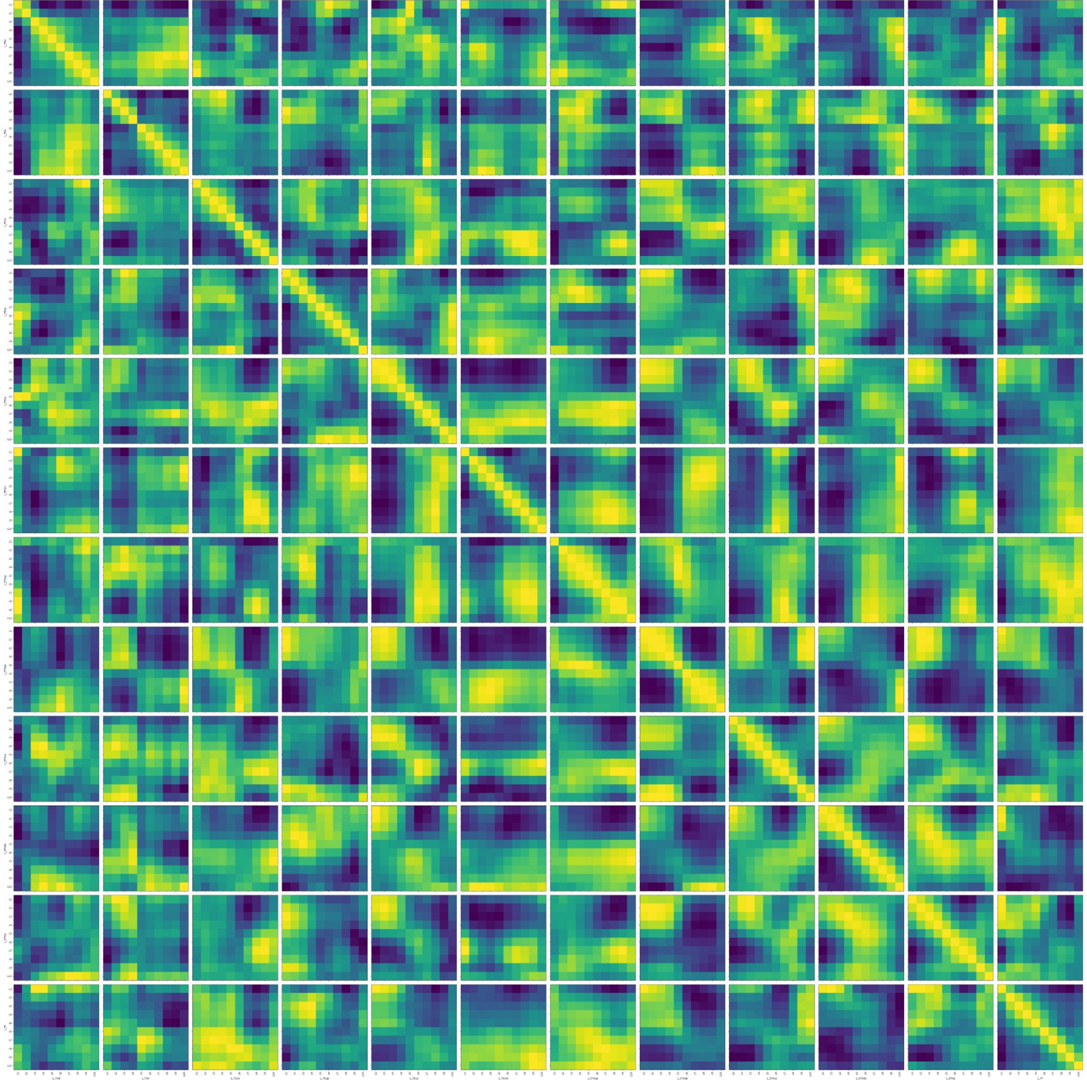


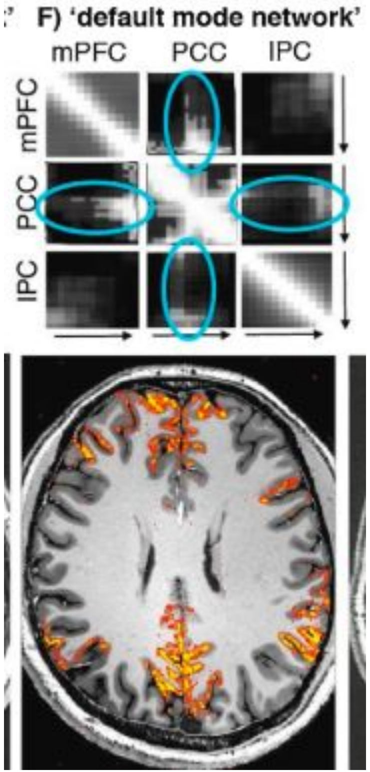
# Iterative ICA



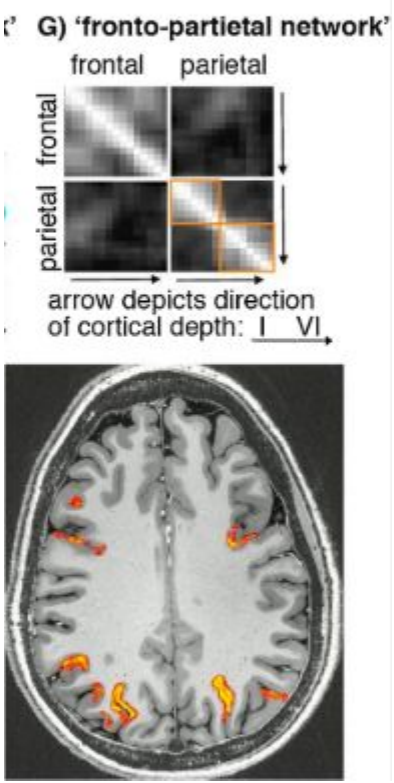


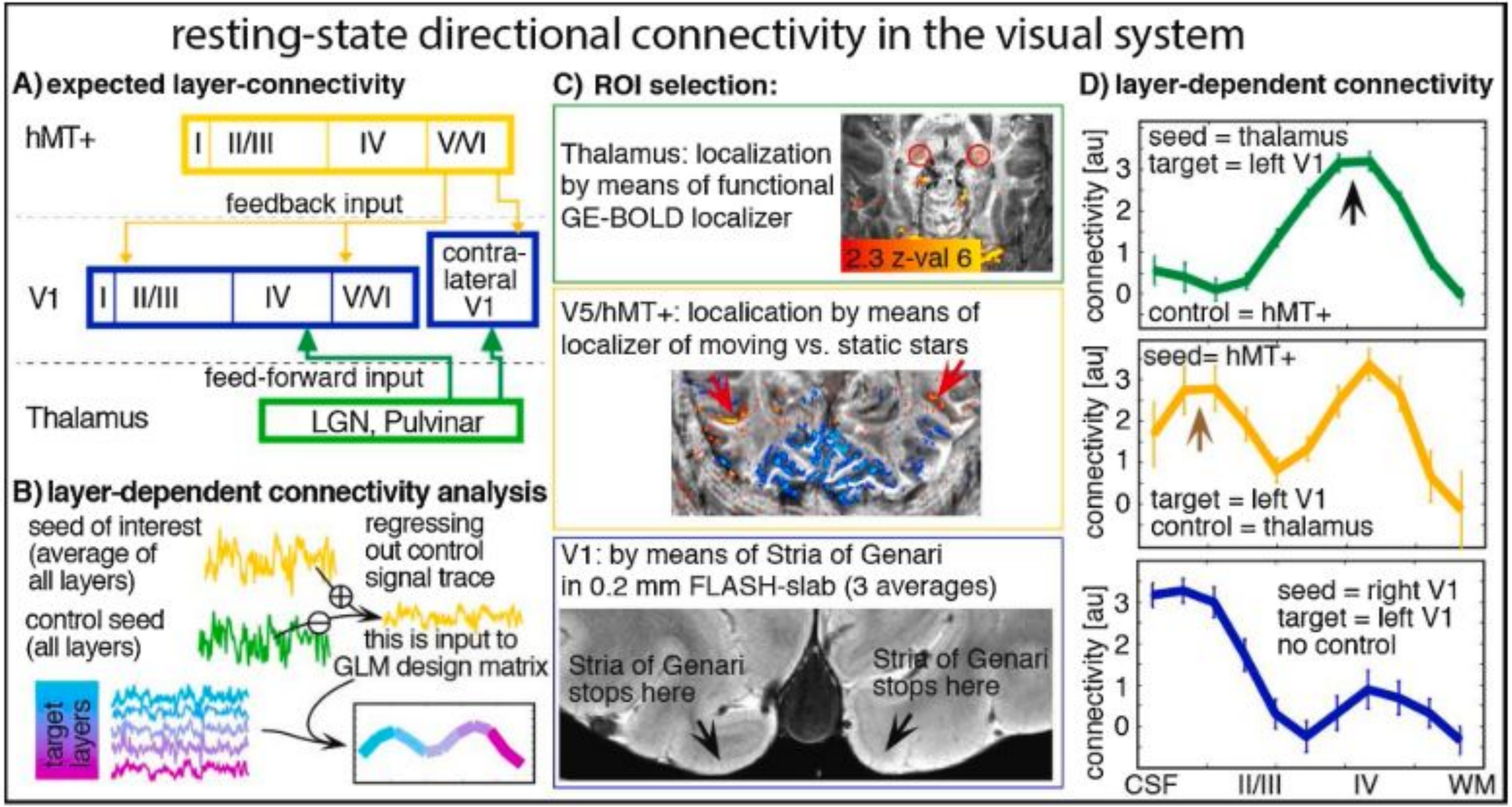

R_thalamus
L_V1
L_V2
L_V3
L_V3A
L_V3B
L_V3CD
L_V4
L_V4t
L_V6
R_thalamus
L_V1
L_V2
L_V3
L_V3A
L_V3B
L_V3CD
L_V4
L_V4t
L_V6





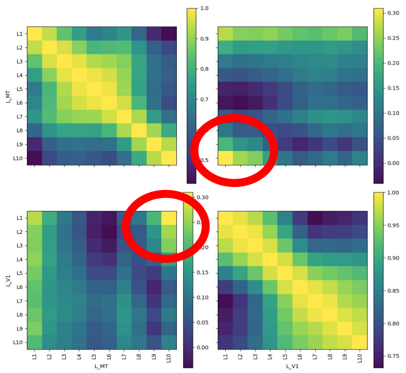

Panel **F)** shows an example of the 'default mode network'. Cyan ellipses highlight that the PCC is the only middle-layer dominated ROI. The other ROIs seem to be more feedback driven. This can be taken as an indication that the PCC is the major hub of the 'default mode network', while the other areas are being passively driven perhaps by PCC activity.


G) 'fronto-partietal network'
frontal
parietal
frontal
parietal
arrow depicts direction
of cortical depth: I VI

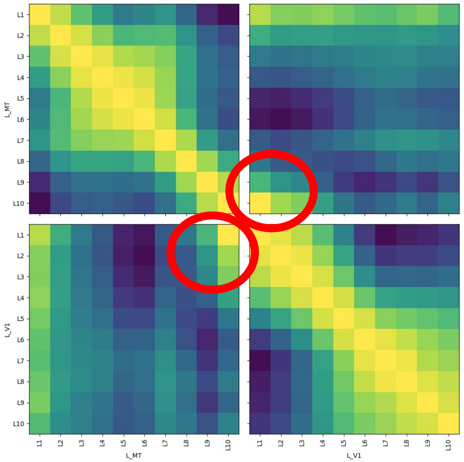


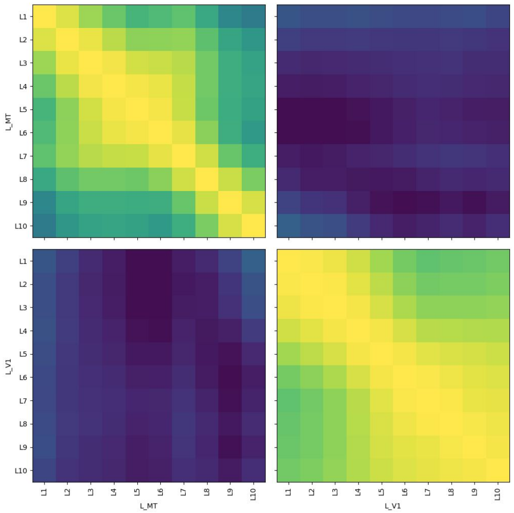
resting-state directional connectivity in the visual system
A) expected layer-connectivity
hMT+
I
II/III
IV
V/VI
feedback input
V1
contra-lateral V1
feed-forward input
Thalamus
LGN, Pulvinar
B) layer-dependent connectivity analysis
seed of interest (average of all layers)
regressing out control signal trace
control seed (all layers)
this is input to GLM design matrix
target layers
C) ROI selection:
Thalamus: localization by means of functional GE-BOLD localizer
2.3 z-val 6
V5/hMT+: localication by means of localizer of moving vs. static stars
V1: by means of Stria of Genari in 0.2 mm FLASH-slab (3 averages)
Stria of Genari stops here
Stria of Genari stops here
D) layer-dependent connectivity
seed = thalamus
target = left V1
control = hMT+
seed= hMT+
target = left V1
control = thalamus
seed = right V1
target = left V1
no control
connectivity [au]
CSF
II/III
IV
WM

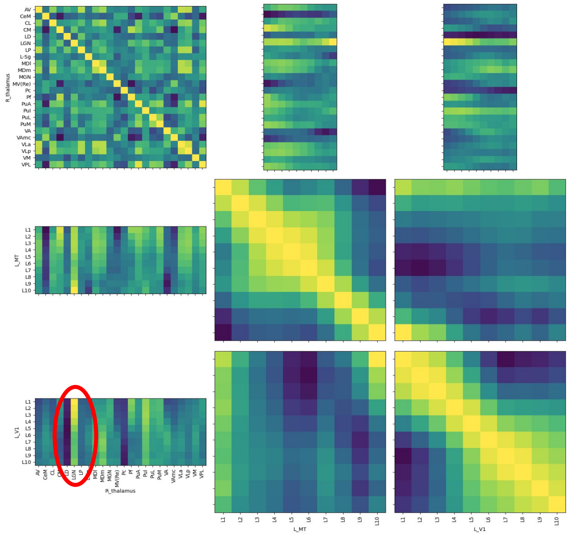
# Visual Network (L_V1 L_MT)

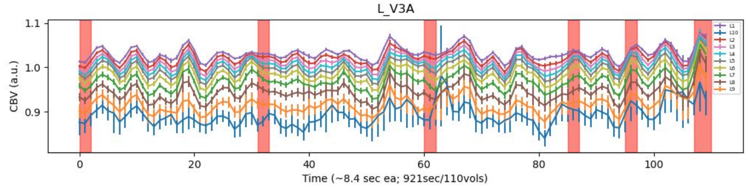


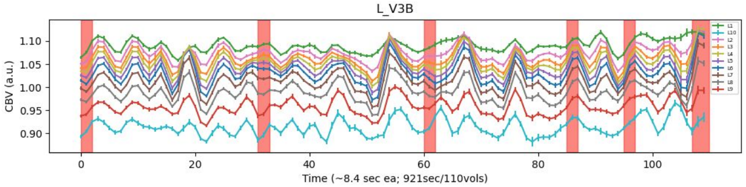

# Visual Network (L_V1 L_MT)

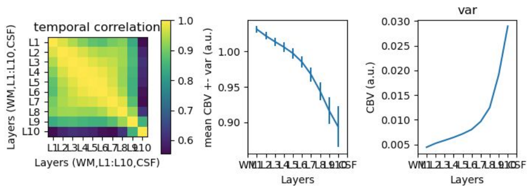


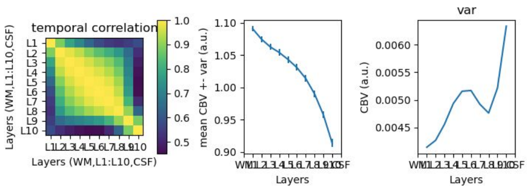



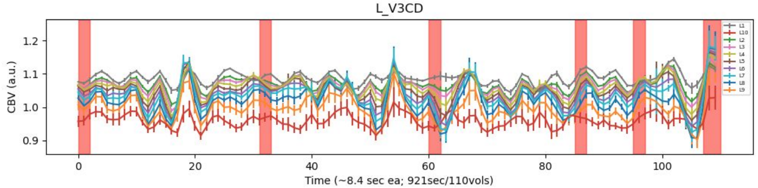



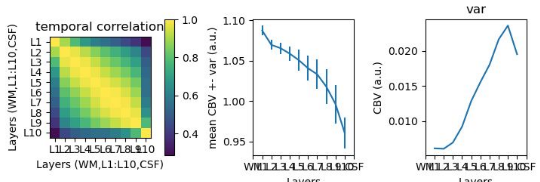

L_V3A
CBV (a.u.)
Time (~8.4 sec ea; 921sec/110vols)


L_V3B
CBV (a.u.)
Time (~8.4 sec ea; 921sec/110vols)


temporal correlation
Layers (WM,L1:L10,CSF)
mean CBV +- var (a.u.)
Layers
var
CBV (a.u.)
Layers


temporal correlation
Layers (WM,L1:L10,CSF)
mean CBV +- var (a.u.)
Layers
var
CBV (a.u.)
Layers


L_V3CD
CBV (a.u.)
Time (~8.4 sec ea; 921sec/110vols)


temporal correlation
Layers (WM,L1:L10,CSF)
mean CBV +- var (a.u.)
var
CBV (a.u.)

# Notes

- Background noise - https://layerfmri.com/2019/06/22/mp2rage/
- Smoothing - https://layerfmri.com/2018/03/15/smoothing-within-layers/
  - https://layerfmri.com/2018/11/03/anatomically-informed-spatial-smoothing/

# Multisensory integration

In the cortex, sensory areas may interact through several possible pathways, which are not mutually exclusive. For example, auditory stimulation can elicit specific activation patterns in human early visual cortex (Petro et al., 2017; Vetter et al., 2014). Influences from one sensory area to the other may arrive in form of feedback projections from multisensory areas (Felleman and Van Essen, 1991) or projected through nonspecific thalamic afferents, which are essentially feedforward projections (Van Atteveldt et al., 2014). In addition, there is accumulating evidence that early sensory cortices interact via direct cortico-cortical pathways. Recently, Ibrahim et al. (2016) were able to trace, in the mouse, the direct axonal projections from the primary auditory cortex, A1, to V1 (but not the reciprocal connections, i.e. from V1 to A1). The strength of the A1 to V1 projection was maximum in layer 1 of V1 and originated mostly from layer 5 of A1. This same study showed that neurons in V1 layer 1 are activated either by sound or by optogenetic stimulation of A1-V1 axons and that - as a consequence of the inhibitory effects of layer 1 neurons - the orientation tuning of layer 2/3 pyramidal neurons was sharpened (Ibrahim et al., 2016). That influences from other senses affect especially supragranular layers of the receiving area is also consistent with findings outside V1. For example, in awake macaque monkeys, Lakatos et al. (2007) found a strong influence of somatosensory inputs in the supragranular layers of A1. However, other reports are inconsistent with this hypothesis. For instance, laminar recordings in rats localized the correlates of a learned audiovisual association (tones and light) in infragranular V1 layers (layers 5 and 6; Headley and Weinberger, 2015). With laminar fMRI, these fundamental mechanisms and the neuronal pathways underlying multisensory interaction and interareal communication can be investigated in the human brain. This is highly relevant as predictions from animal models are not unequivocal and prominent differences between species may exist. It will be important to combine laminar fMRI with psychophysical paradigms that enable the online measurement of behavior. If indeed the supragranular layers of V1 do mediate the integration of information from other senses (e.g. A1), the modulation of fMRI activity in supragranular V1 should scale, trial-by-trial, with the facilitatory effects of, for example, informative auditory stimuli on visual target detection (e.g. Vroomen and de Gelder, 2000).

[http://dx.doi.org/10.1016/j.neuroimage.2017.07.004](http://dx.doi.org/10.1016/j.neuroimage.2017.07.004) - Laminar fMRI: Applications for cognitive neuroscience

- Carpet plots
- VASO signal normalization
- Average across sessions?
-

Note that unlike BOLD, VASO is a quantitative measure that is proportional to a physical unit (mL per 100 mL tissue volume), meaning units can be directly interpreted and it is not necessary to convert to percent signal change. VASO data were instead transformed as follows. First, to facilitate interpretation, each subject's VASO signal $v$ at each timepoint $t$ was transformed from a negative to a positive contrast as:

$$v_t = v_t{}^* - 100$$

Following this, VASO signals were normalized within subjects by calculating a per-layer mean baseline VASO signal ($\bar{v}_y$) by averaging signal during baseline timepoints (same timepoints as for BOLD above) across all four trial types. This mean baseline signal was subtracted from each timepoint as follows:

$$v_{y,t}{}' = v_{y,t} - \bar{v}_y$$