

## **Supplementary Figures**

# **Linking human brain functional connectivity to underlying neurotransmission**

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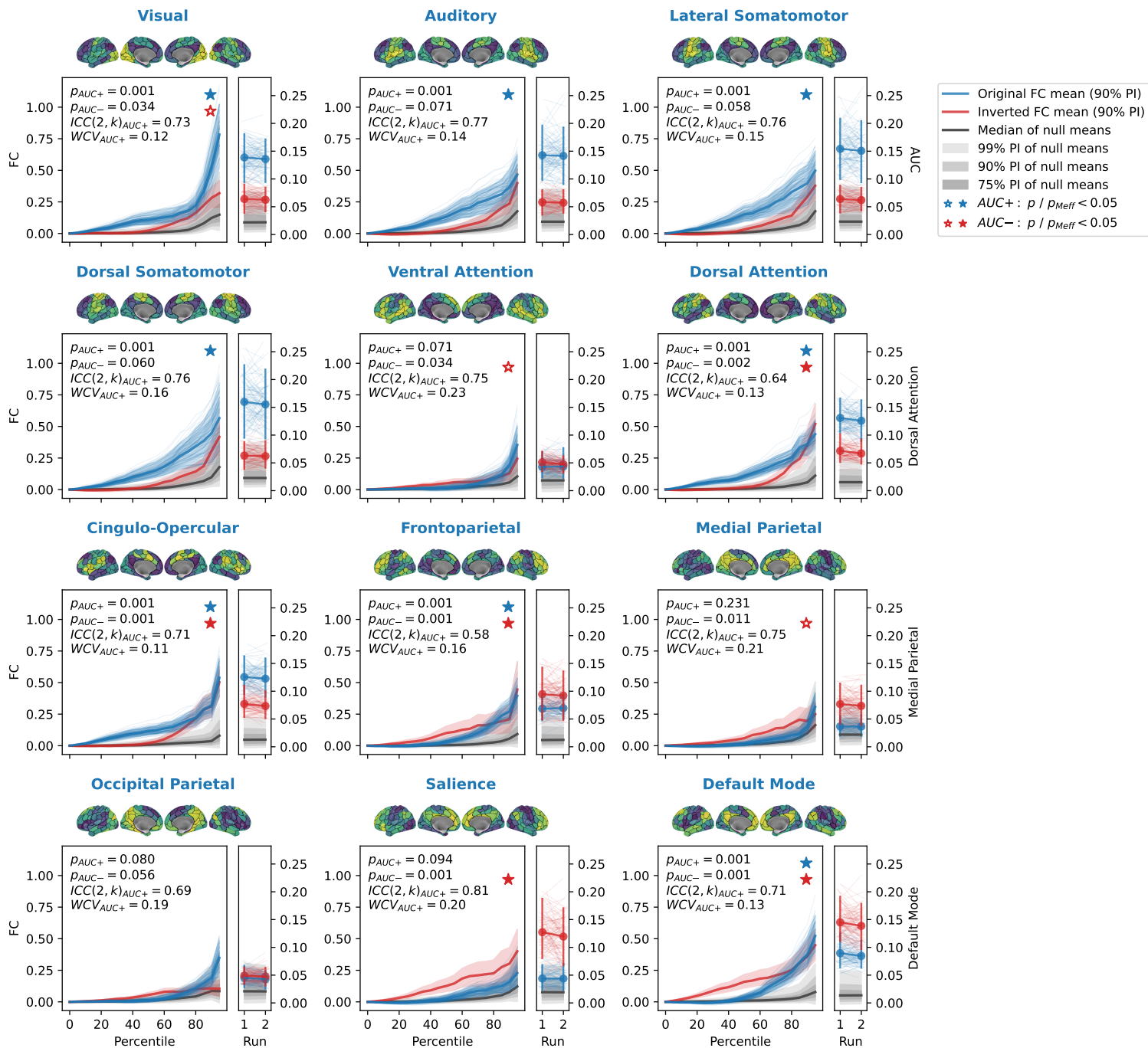
**Fig. S15:** Quality control of HCP-YA physiological data (heart-rate variability)

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**Fig. S1**

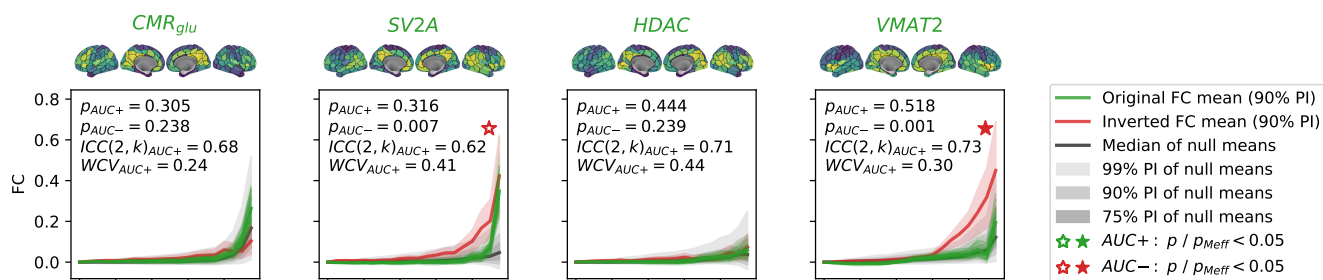


## **Fig. S1:** NEOFC curves derived from resting-state network probability

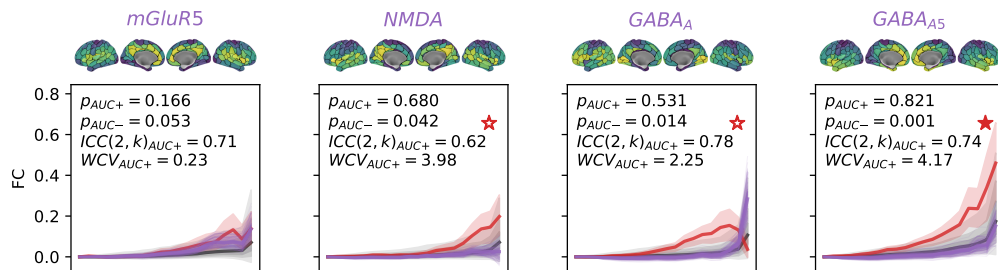
NEOFC curves for all 12 RSN probability atlases used as positive controls (Schaefer200 parcellation). Each panel shows mean rsFC as a function of the density percentile threshold for the original atlas (blue) and its spatially inverted reference (dark red). Colored shaded area: 90% PI across individuals; grey shaded area: null distribution. Right inset: individual AUC+ and AUC− scores (each dot: one participant). Displayed as in **Fig. 2b**. Brain maps indicate the parcellated RSN probability atlas, converted to percentiles. Abbreviations: rsFC: resting-state functional connectivity; AUC: area under the curve; RSN: resting-state network; PI: percentile interval.

**Fig. S2**

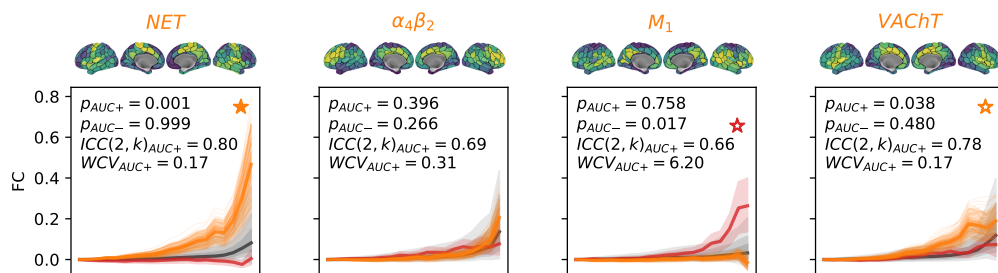
### General & Metabolic



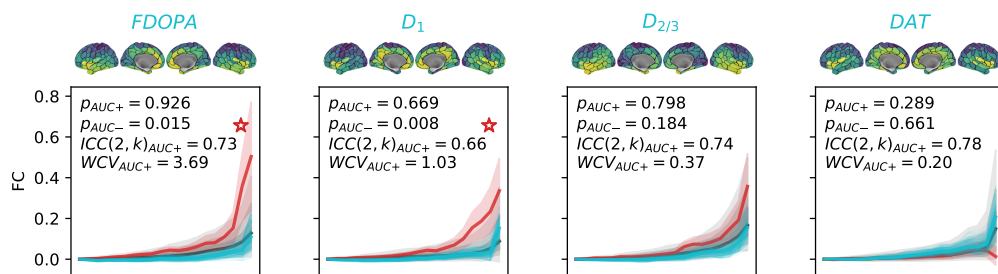
### Glutamate & GABA



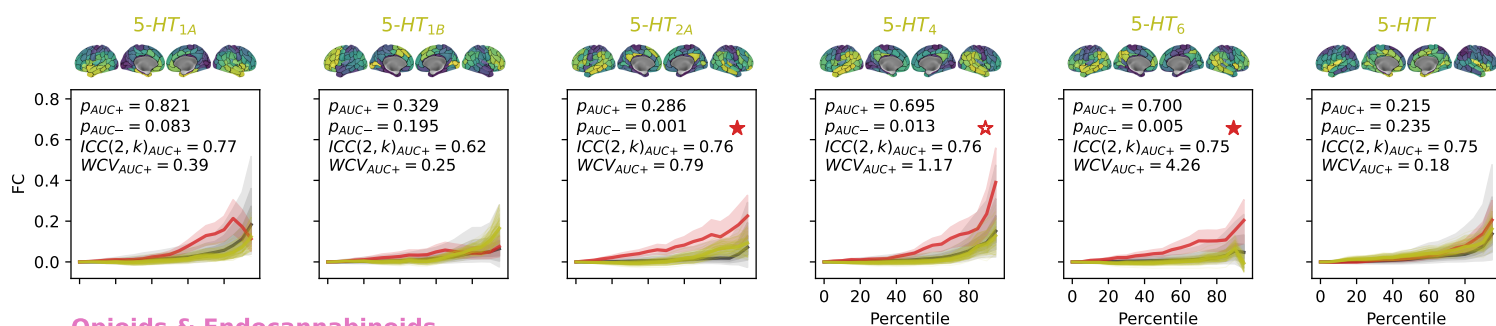
### Noradrenaline & Acetylcholine



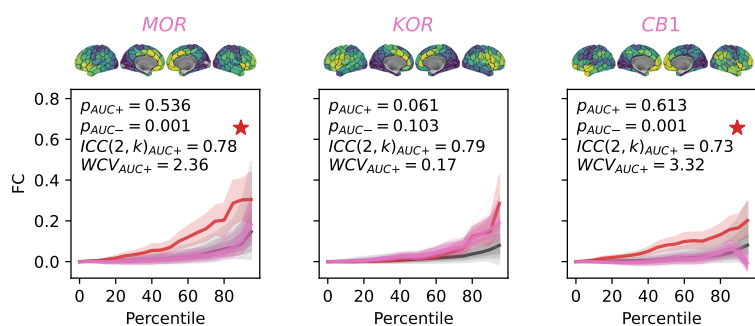
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### Serotonin



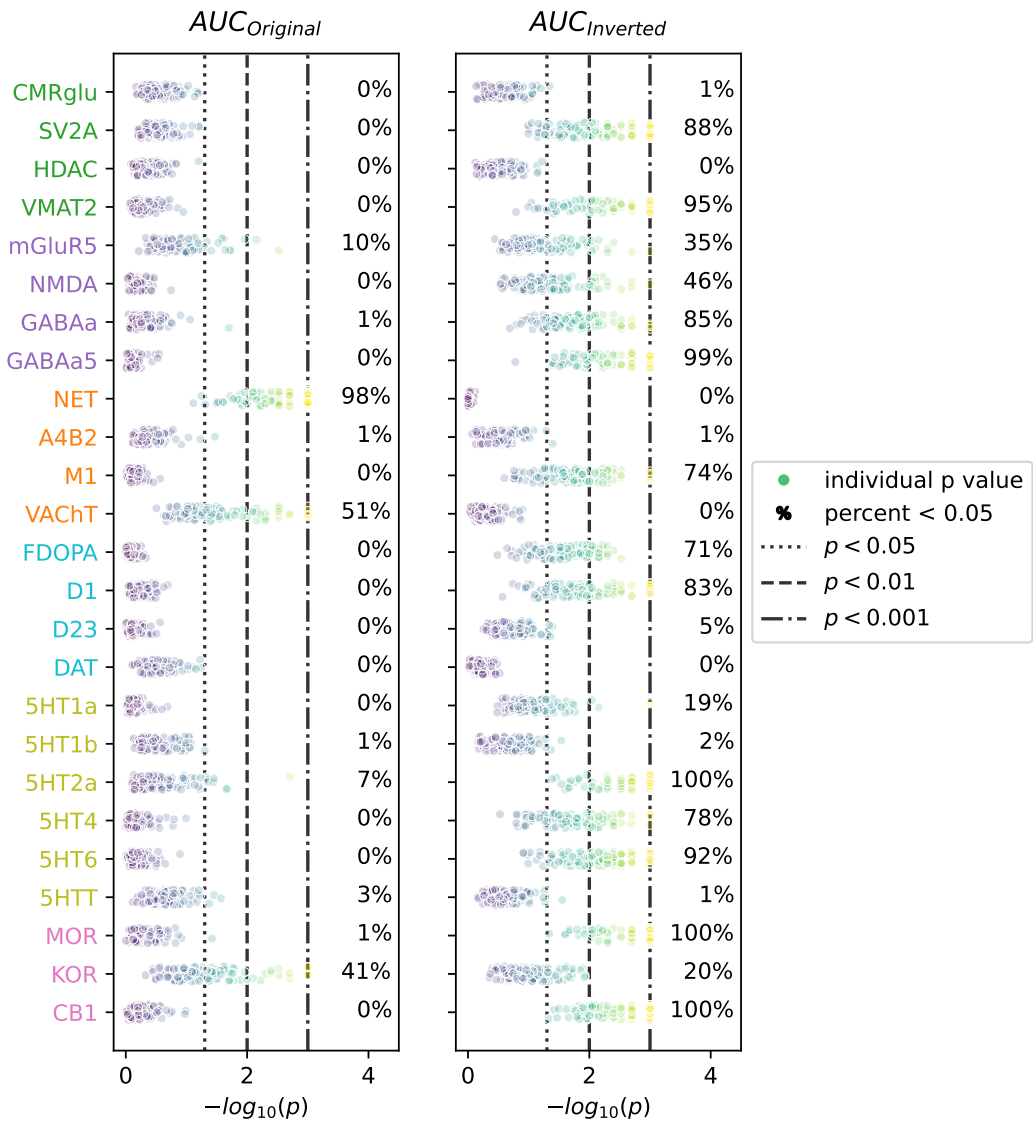
### Opioids & Endocannabinoids



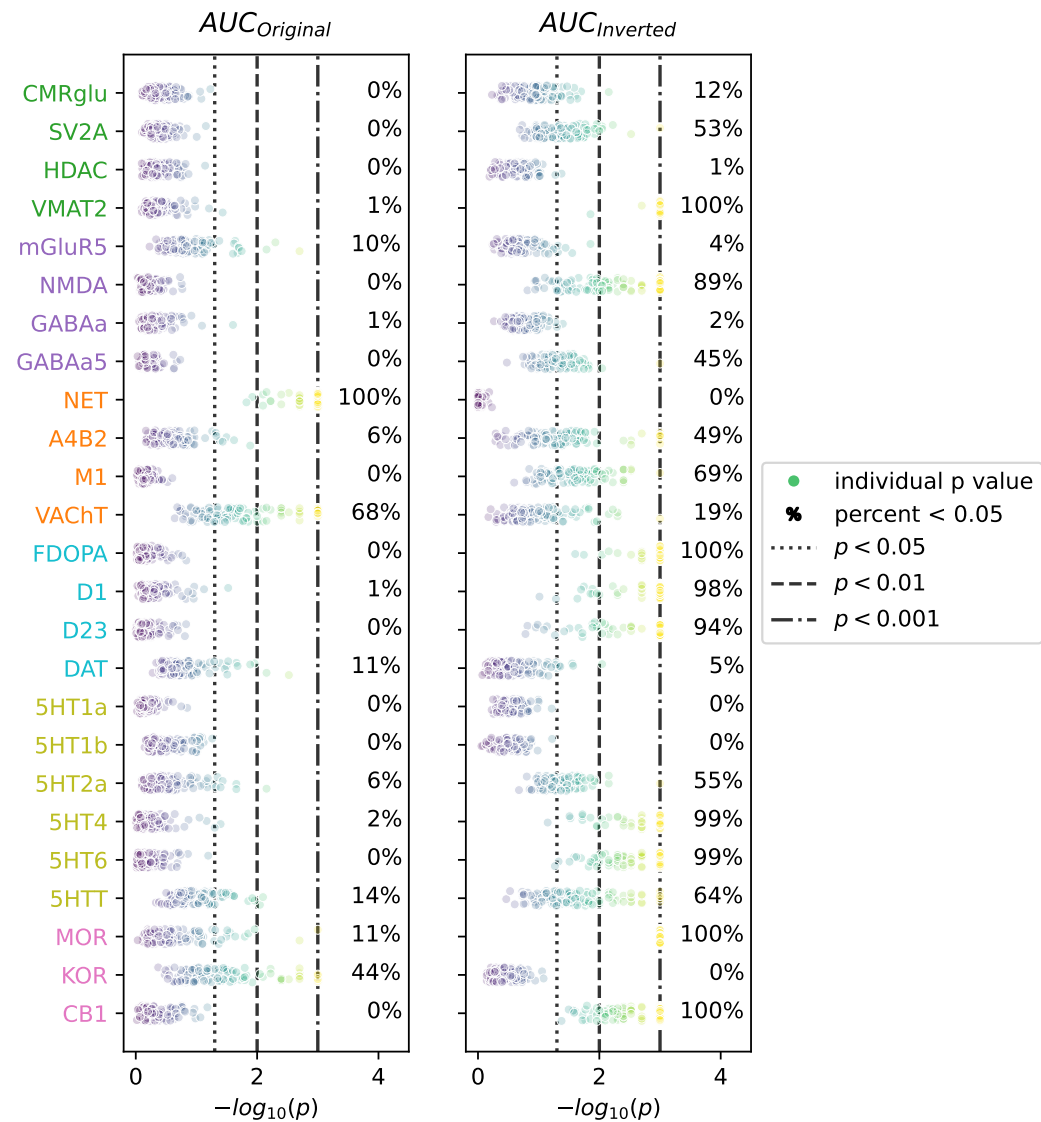
## **Fig. S2:** NEOFC curves derived from neurobiological atlases

NEOFC curves for all 25 nuclear imaging reference maps, organized by broad neurotransmitter systems (Schaefer200 and Schaefer200 + subcortex parcellation). Each panel shows mean rsFC as a function of the density percentile threshold for the original atlas (colored by neurotransmitter system) and its spatially inverted reference (dark red). Colored shaded area: 90% PI across individuals; grey shaded area: null distribution. Brain maps indicate the parcellated reference atlas, converted to percentiles. Statistics printed in each plot include the raw p values for AUC+ and AUC−, the ICC(2,k), and the WCV for AUC+. Displayed as in **Fig. 2d**. Abbreviations: rsFC: resting-state functional connectivity; PI: percentile interval; ICC: intraclass correlation coefficient; WCV: within-subject coefficient of variability; see **Fig. 2** for reference map abbreviations.

**Fig. S3a: Schaefer200**



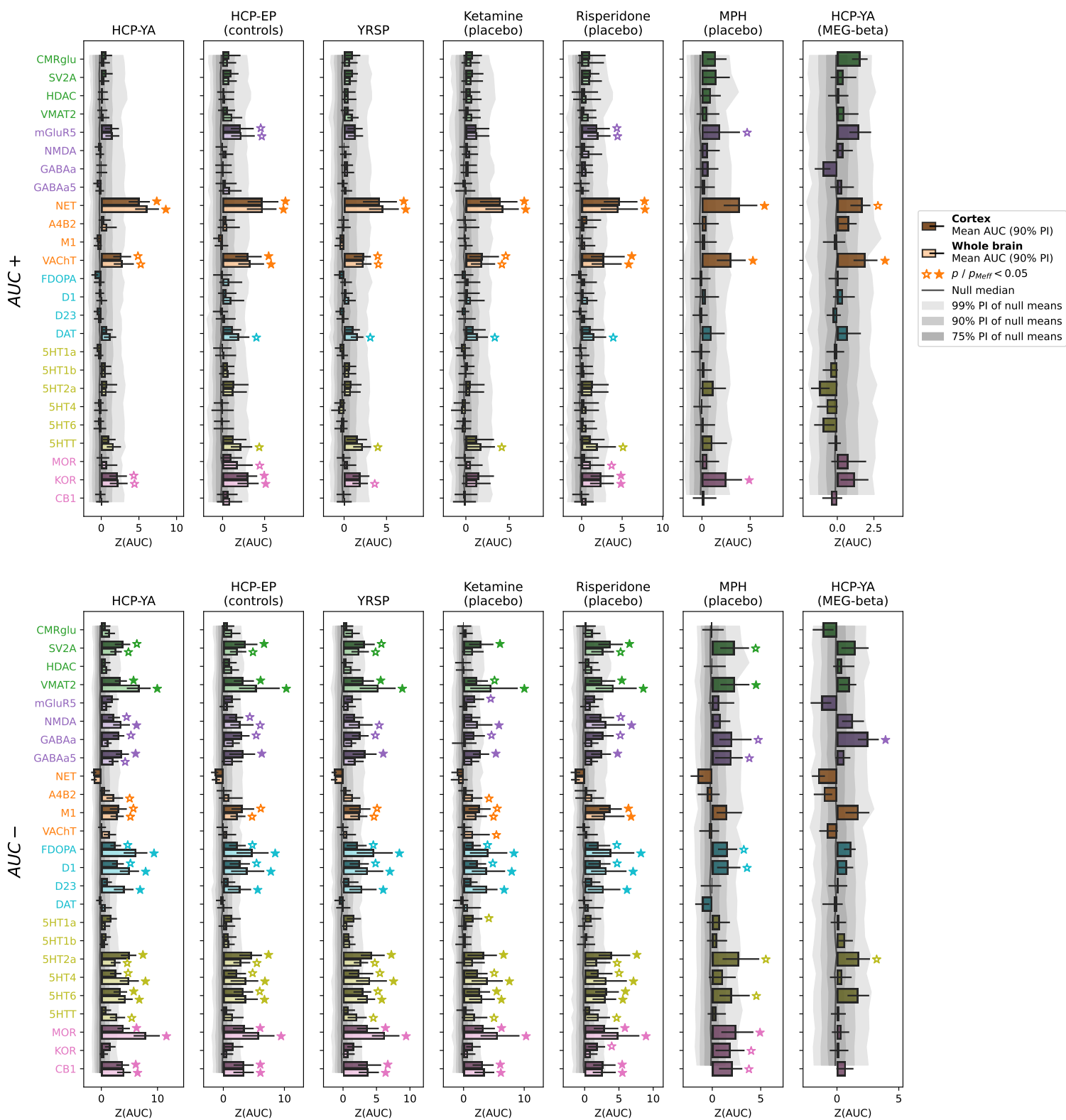
**Fig. S3b: Schaefer200+Subcortical**



**Fig. S3:** Individual-level p values associated to AUC scores

Distribution of individual-level  $-\log_{10}(p)$  values for AUC+ (left) and AUC- (right) across 25 nuclear imaging reference maps. **a:** Schaefer200 parcellation; **b:** Schaefer200 + subcortex parcellation. Each dot represents one participant; color indicates  $-\log_{10}(p)$ . Vertical lines indicate significance thresholds at  $p < 0.05$  (dotted),  $p < 0.01$  (dashed), and  $p < 0.001$  (dot-dashed). Abbreviations: AUC: area under the curve; see **Fig. 2** for reference map abbreviations.

**Fig. S4**

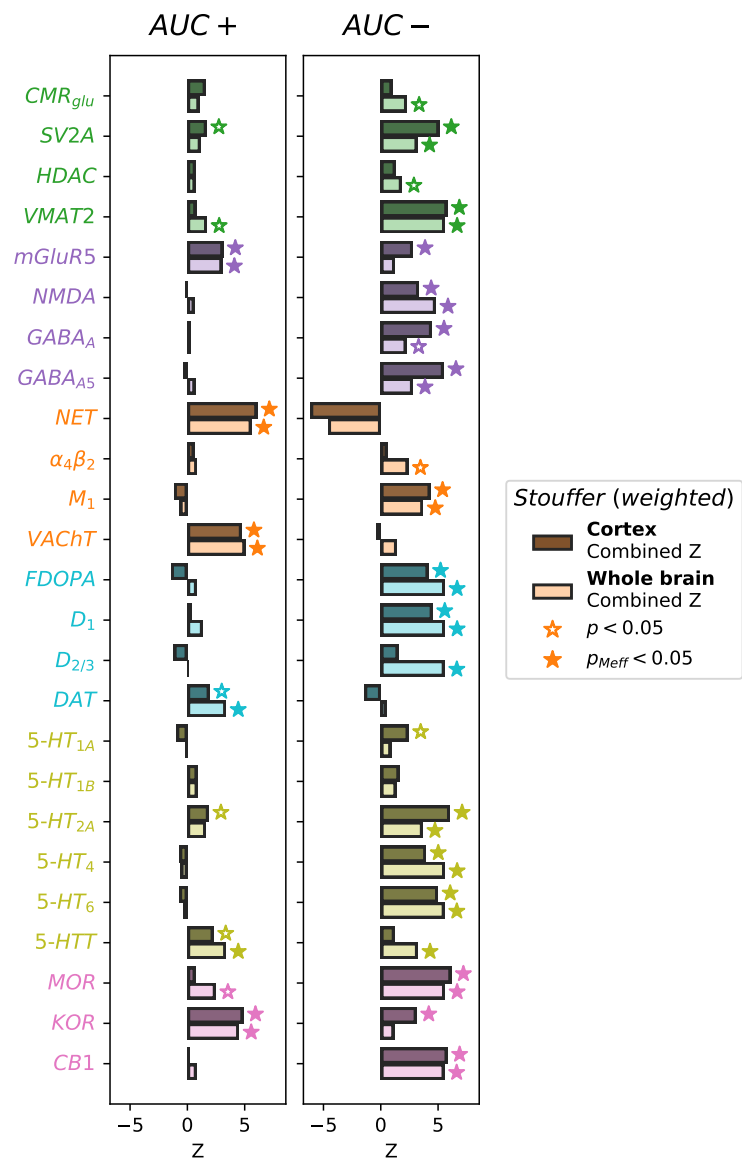




## **Fig. S4:** Replication of AUC profiles in adult control samples

AUC+ and AUC− scores (z-scored against a null distribution of spatially matched reference maps) for 25 nuclear imaging reference maps, shown separately for six independent adult control samples. Displayed as in **Fig. 2c** (Schaefer200 and Schaefer200 + subcortex parcellations). Abbreviations: AUC: area under the curve; PI: percentile interval; WCV: within-subject coefficient of variability; see **Fig. 2** for reference map abbreviations.

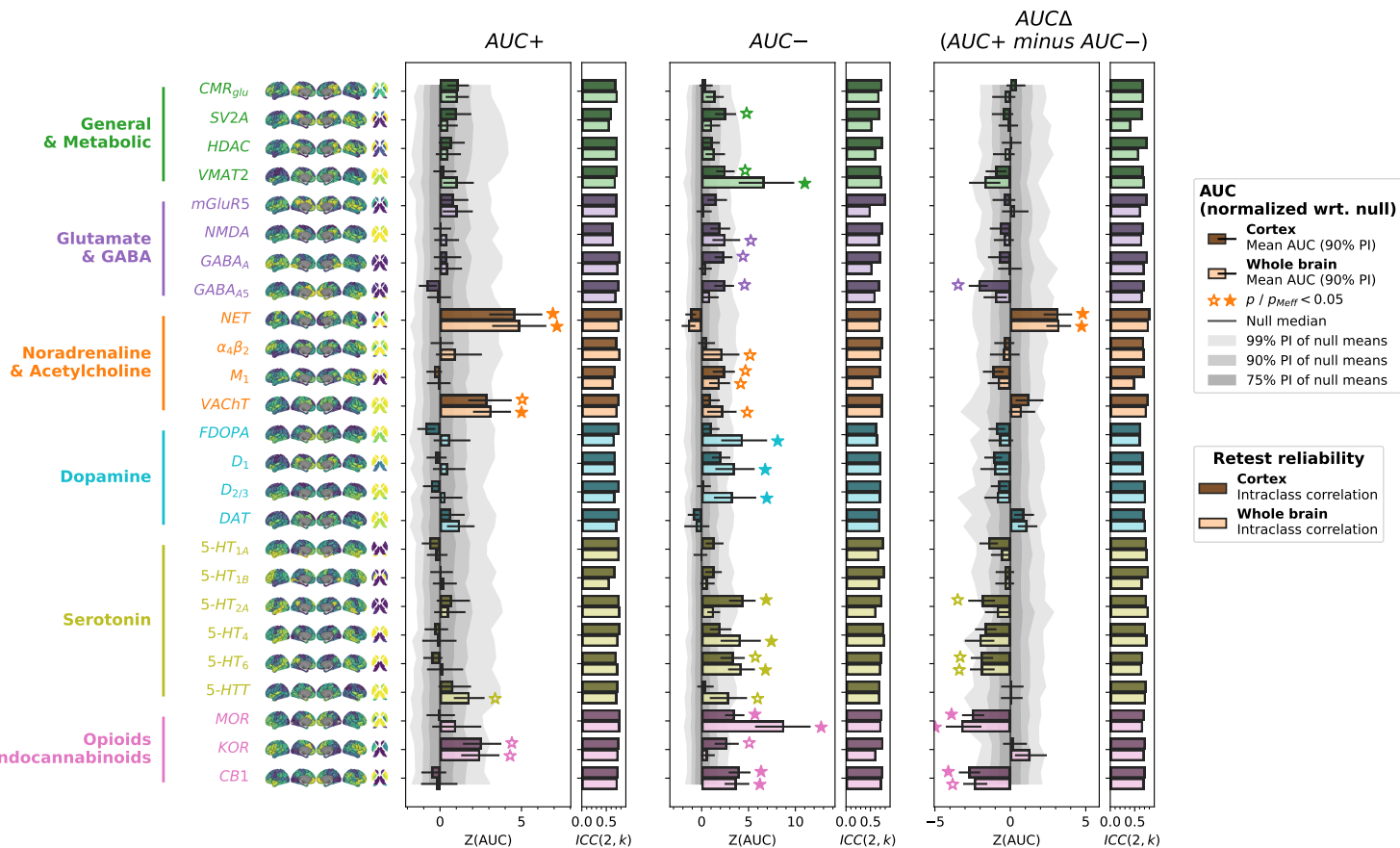
**Fig. S5**



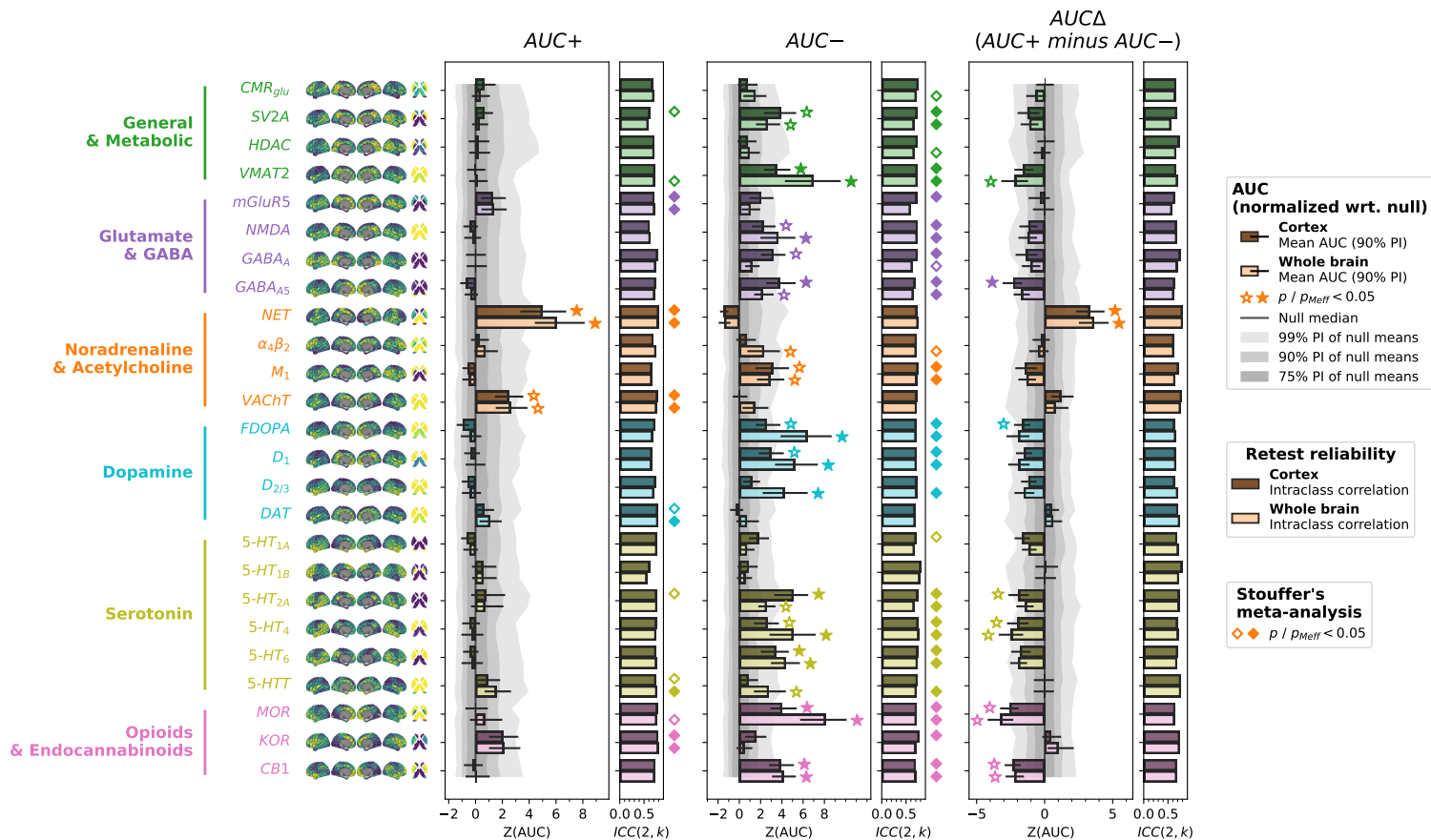
## **Fig. S5:** Meta-Analysis of AUC p values from six MRI datasets

Meta-analytic Z scores (weighted Stouffer's method) for AUC+ and AUC− across 25 nuclear imaging reference maps, combining raw p values from six independent fMRI cohorts weighted by sample size. Darker bars: Schaefer200; brighter bars: Schaefer200 + subcortex; significance markers indicate pMeff. Abbreviations: AUC: area under the curve; pMeff: p-value corrected for effective number of comparisons; see **Fig. 2** for reference map abbreviations.

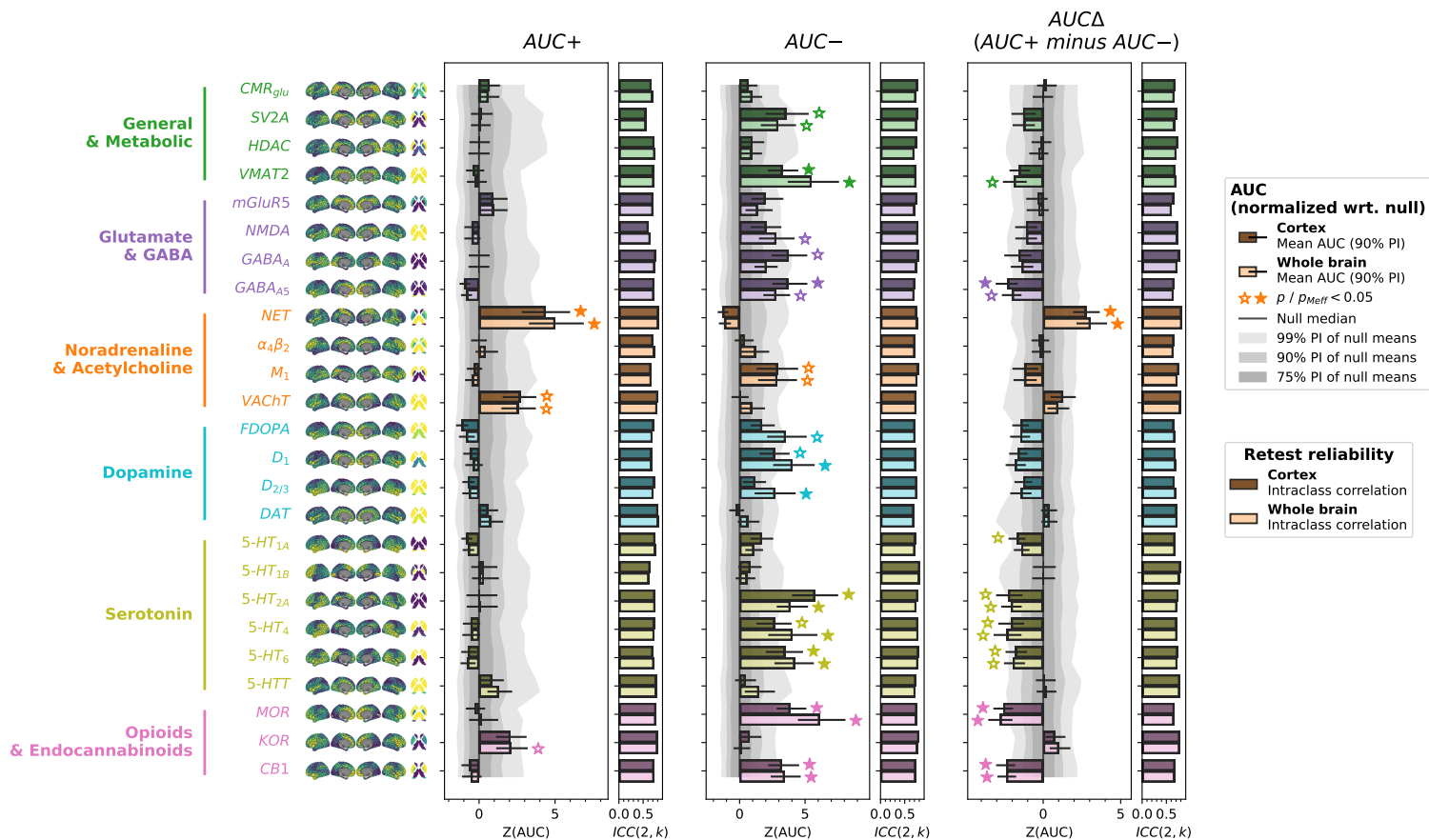
**Fig. S6a: Schaefer100(+Subcortical)**



**Fig. S6b: Schaefer200(+Subcortical)**



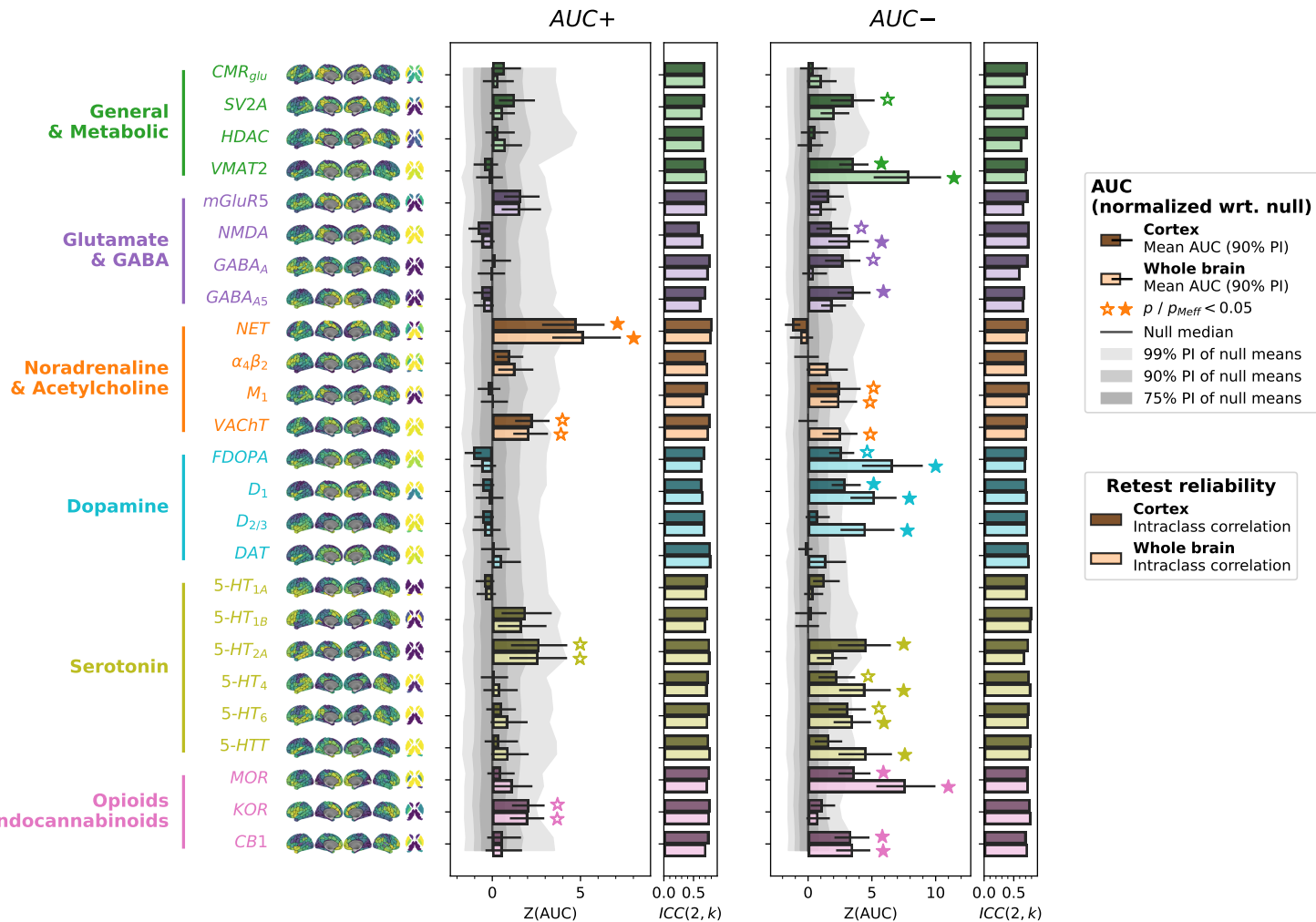
**Fig. S6c: Schaefer400(+Subcortical)**



**Fig. S6:** AUC results including AUC-delta for different parcellation resolutions

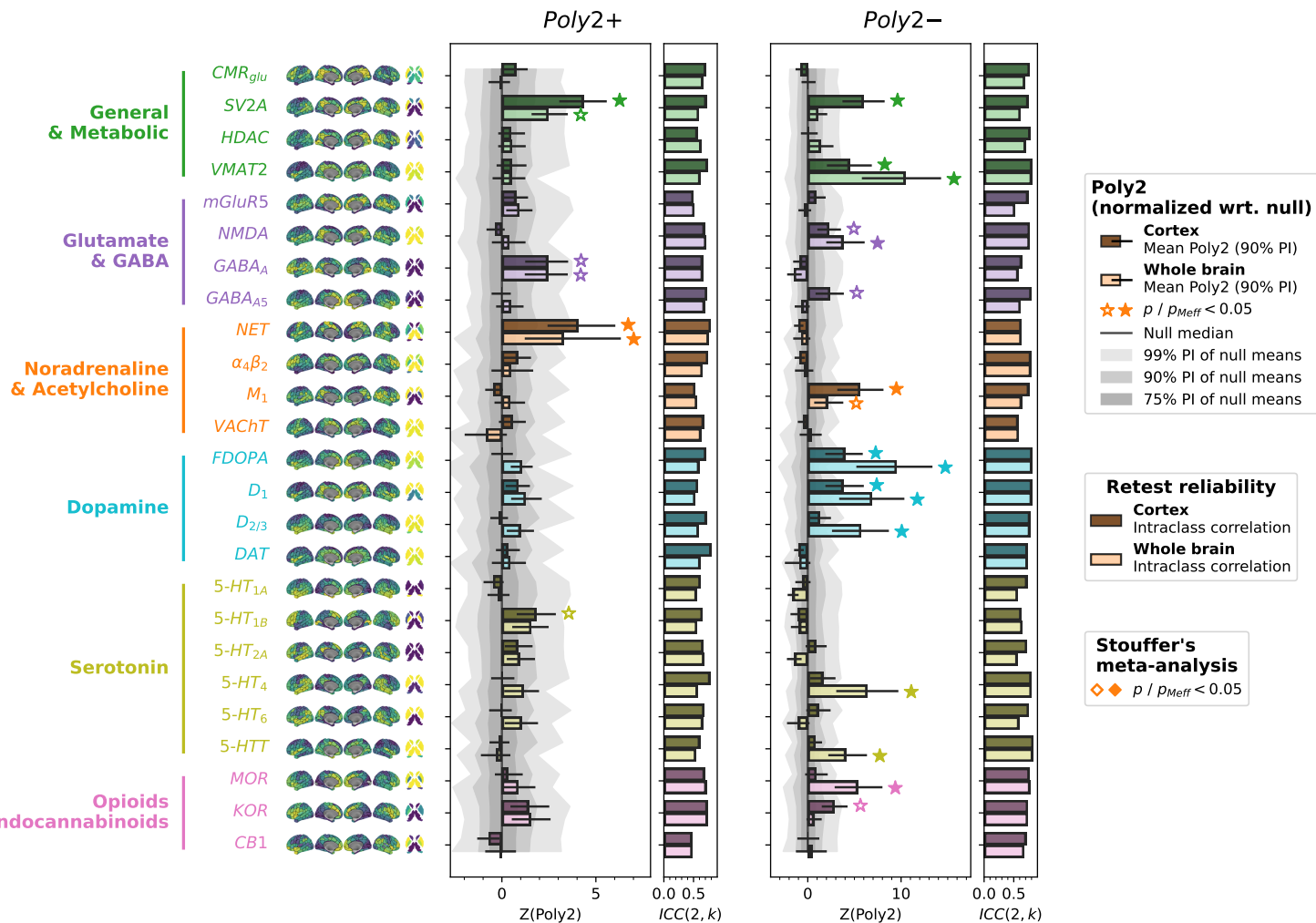
AUC+, AUC−, and AUCΔ (AUC+ minus AUC−) scores for 25 nuclear imaging reference maps, shown for three parcellation resolutions: **a** Schaefer100 (+subcortex), **b** Schaefer200 (+subcortex), **c** Schaefer400 (+subcortex). Displayed as in **Fig. 2c**. Abbreviations: AUC: area under the curve; PI: percentile interval; ICC: intraclass correlation coefficient; see **Fig. 2** for reference map abbreviations.

**Fig. S7a: No interhemispheric connections**





**Fig. S7b: Polynomial fit aggregation**

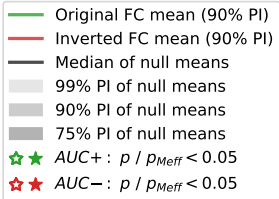
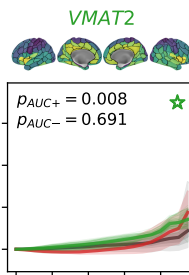
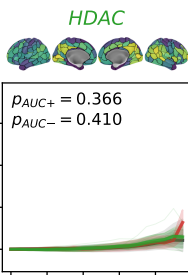
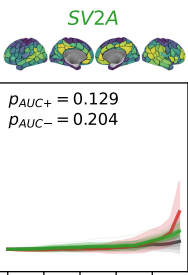
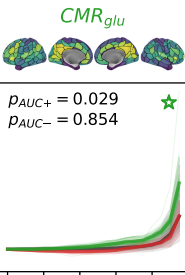


**Fig. S7:** AUC results without interhemispheric connections and an alternative aggregate metric

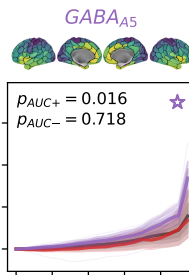
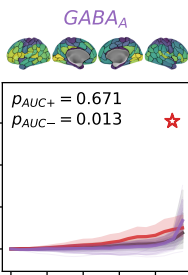
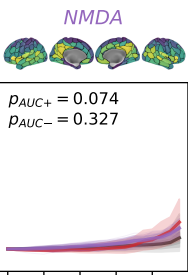
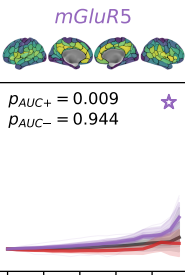
AUC+ and AUC− scores for 25 nuclear imaging reference maps under two methodological variants (Schaefer200 parcellation). **a** Replication of the main analysis excluding interhemispheric connections. **b** Replication using a 2nd-degree polynomial fit coefficient (Poly2) as an alternative to AUC as the aggregate metric. Displayed as in **Fig. 2c**. Abbreviations: AUC: area under the curve; Poly2: 2nd-degree polynomial fit coefficient; PI: percentile interval; ICC: intraclass correlation coefficient; see **Fig. 2** for reference map abbreviations.

**Fig. S8a: delta**

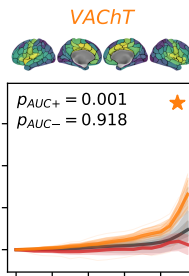
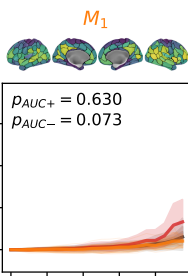
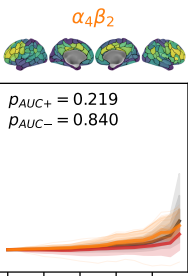
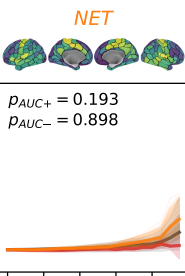
**General & Metabolic**



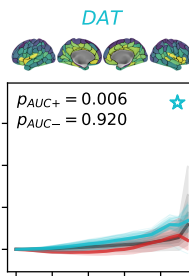
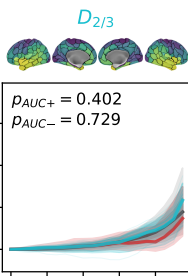
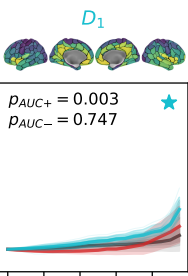
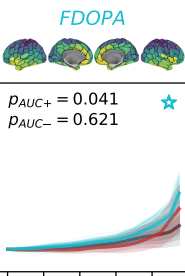
**Glutamate & GABA**



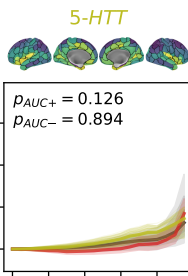
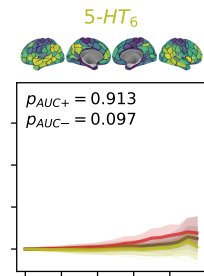
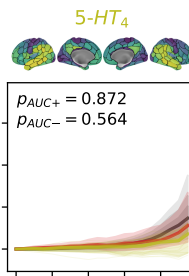
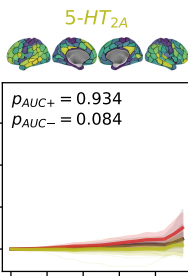
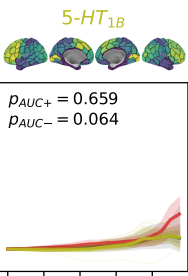
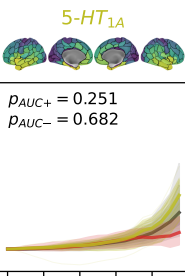
**Noradrenaline & Acetylcholine**



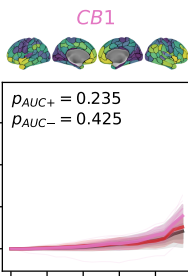
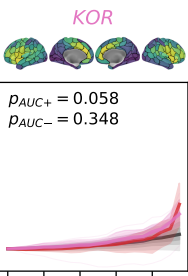
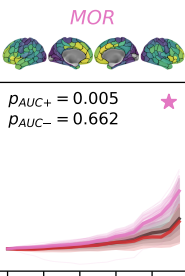
**Dopamine**



**Serotonin**

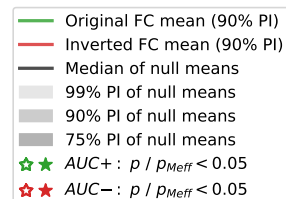
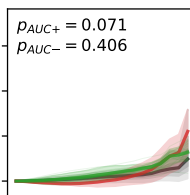
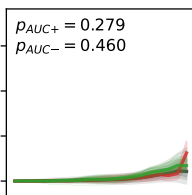
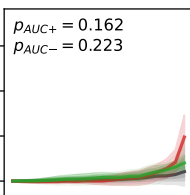
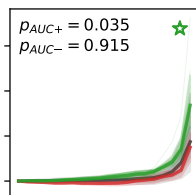
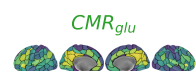


**Opioids & Endocannabinoids**

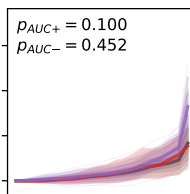
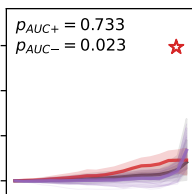
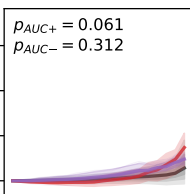
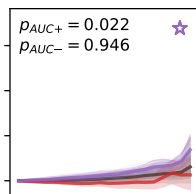


**Fig. S8b: theta**

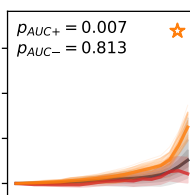
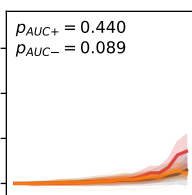
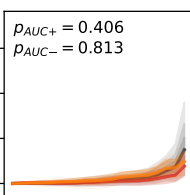
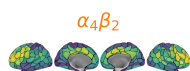
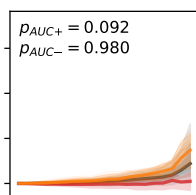
### General & Metabolic



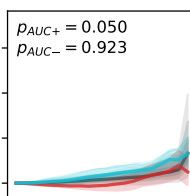
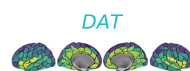
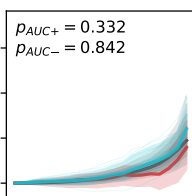
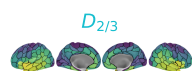
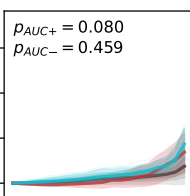
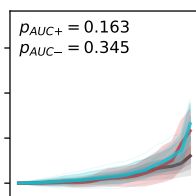
### Glutamate & GABA



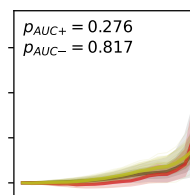
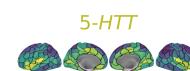
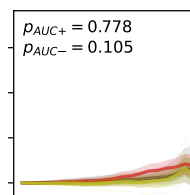
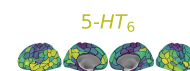
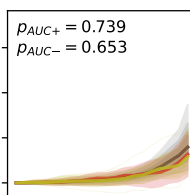
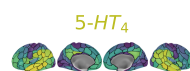
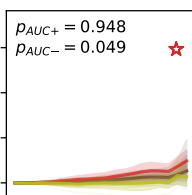
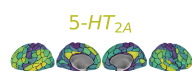
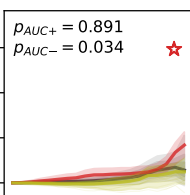
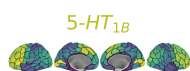
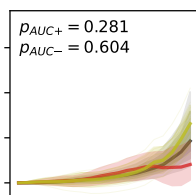
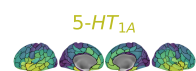
### Noradrenaline & Acetylcholine



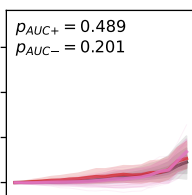
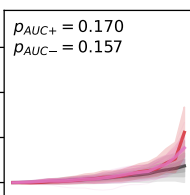
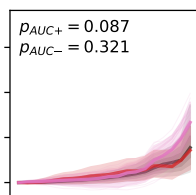
### Dopamine



### Serotonin

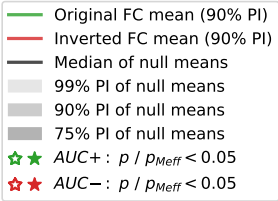
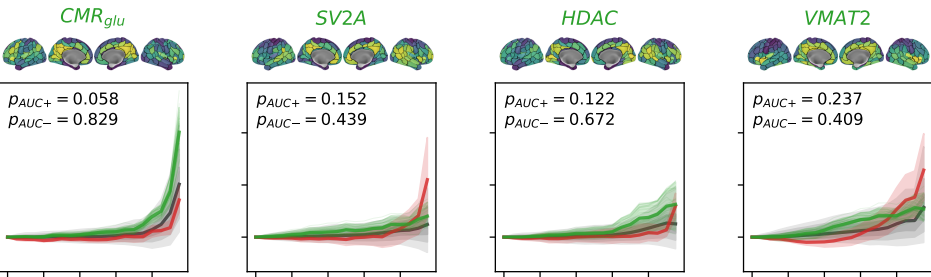


### Opioids & Endocannabinoids

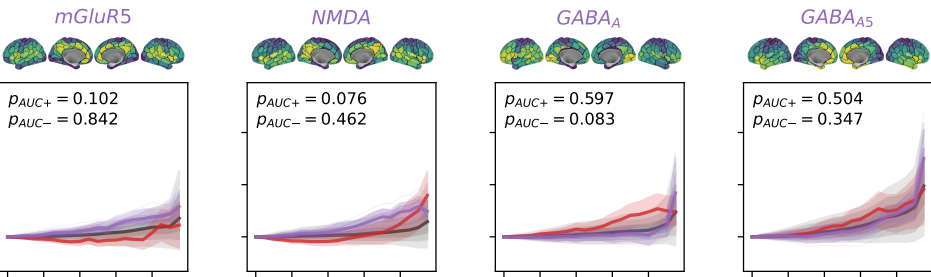


**Fig. S8c: alpha**

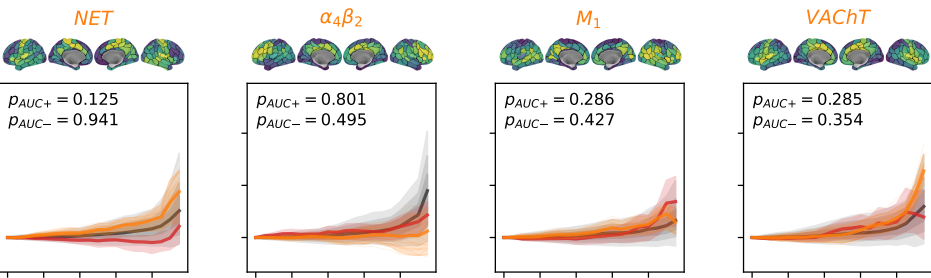
**General & Metabolic**



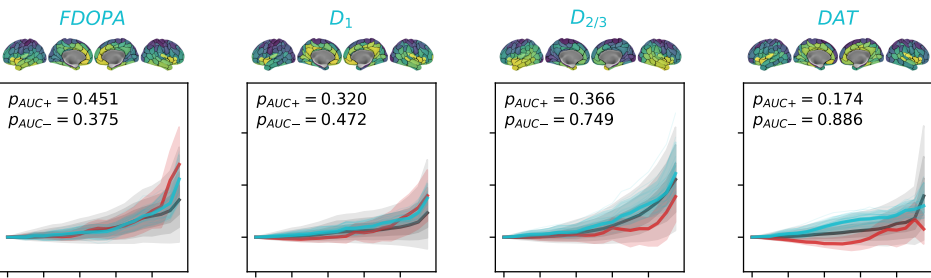
**Glutamate & GABA**



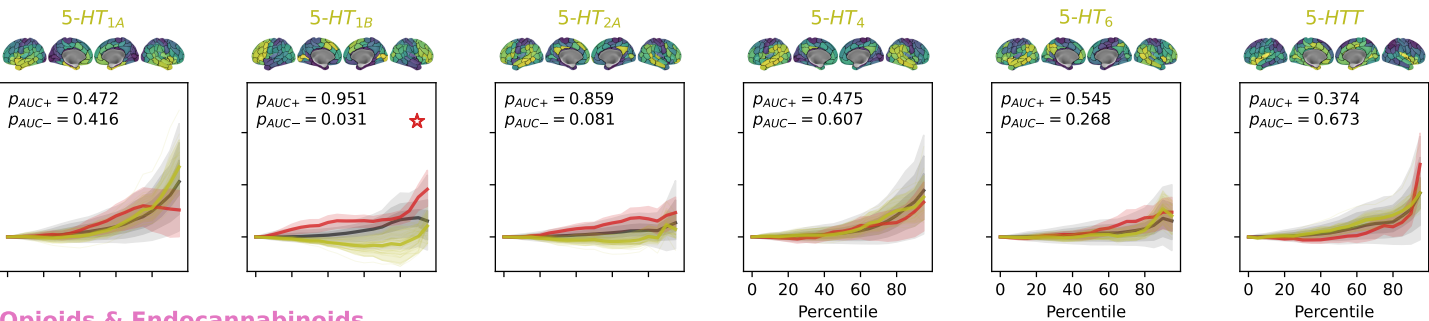
**Noradrenaline & Acetylcholine**



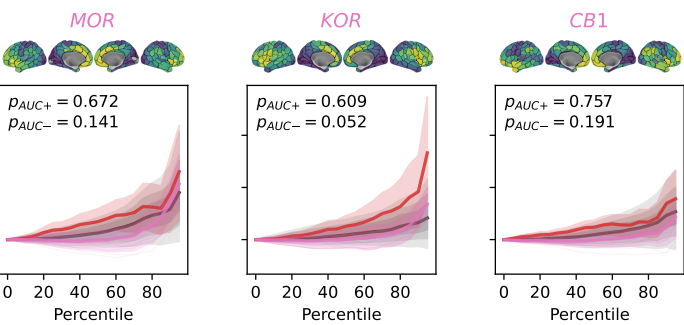
**Dopamine**



**Serotonin**



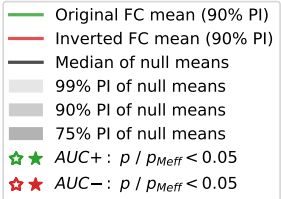
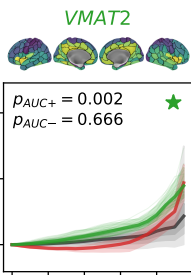
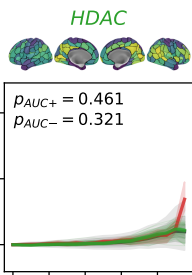
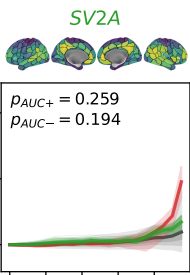
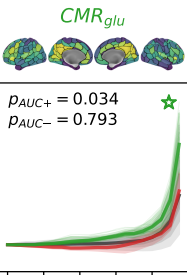
**Opioids & Endocannabinoids**



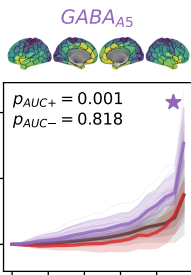
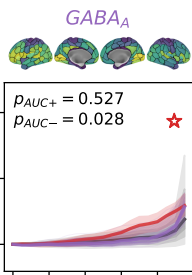
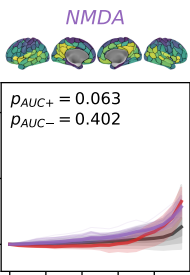
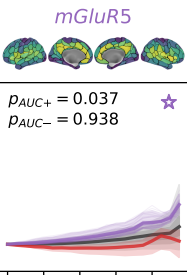


**Fig. S8e: lgamma**

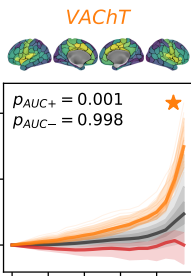
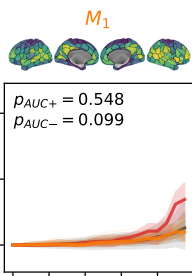
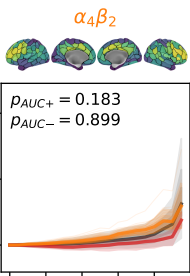
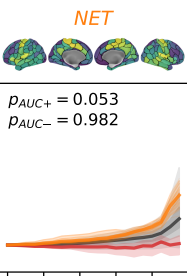
**General & Metabolic**



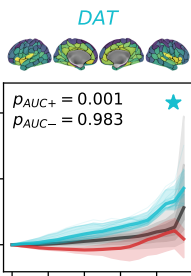
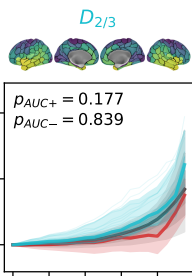
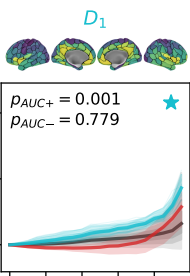
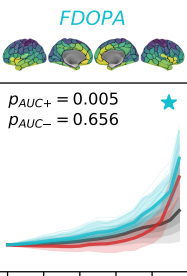
**Glutamate & GABA**



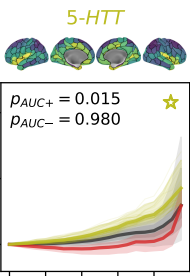
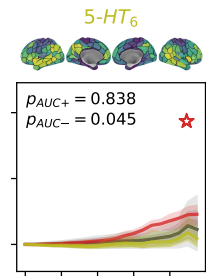
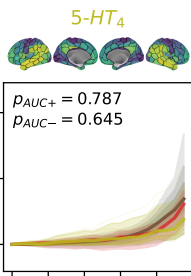
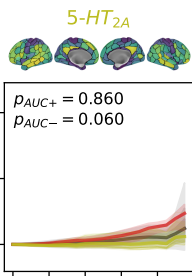
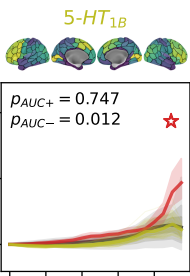
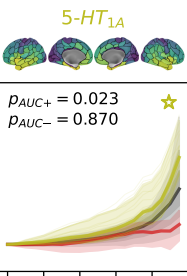
**Noradrenaline & Acetylcholine**



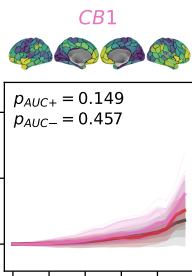
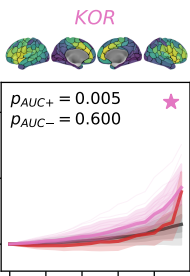
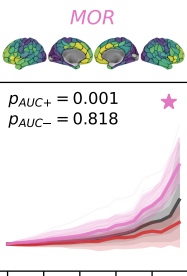
**Dopamine**



**Serotonin**



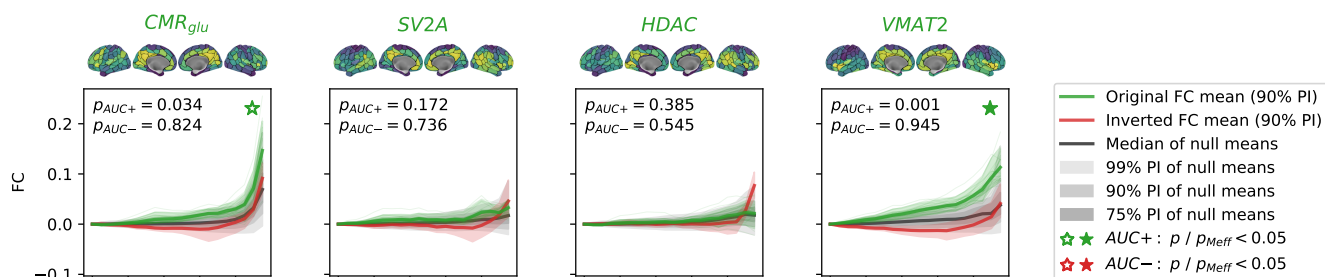
**Opioids & Endocannabinoids**



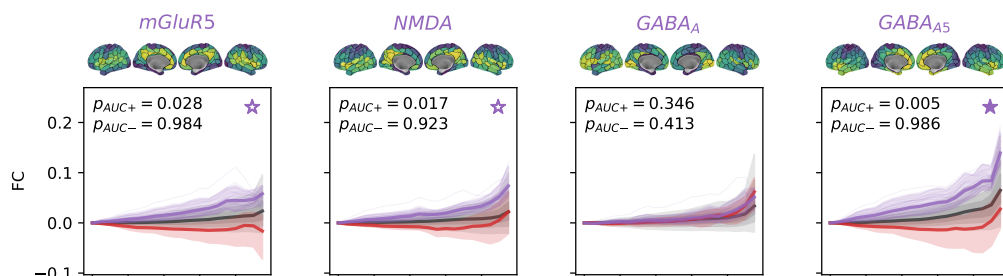


**Fig. S8f: hgamma**

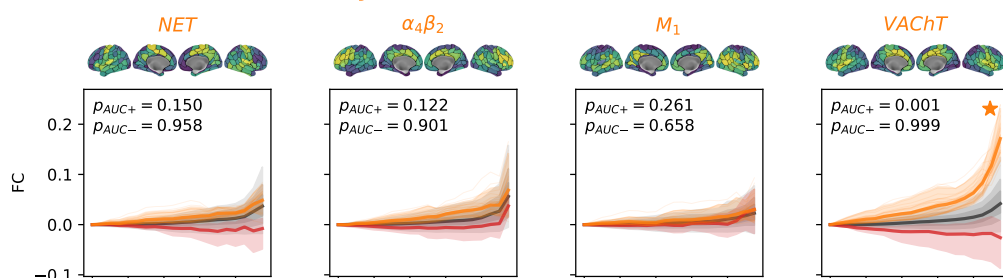
### General & Metabolic



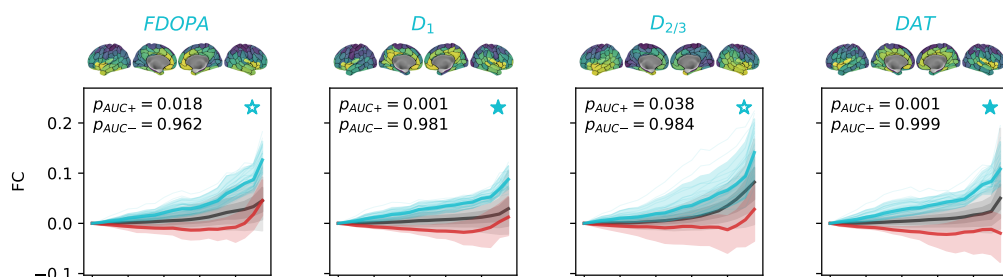
### Glutamate & GABA



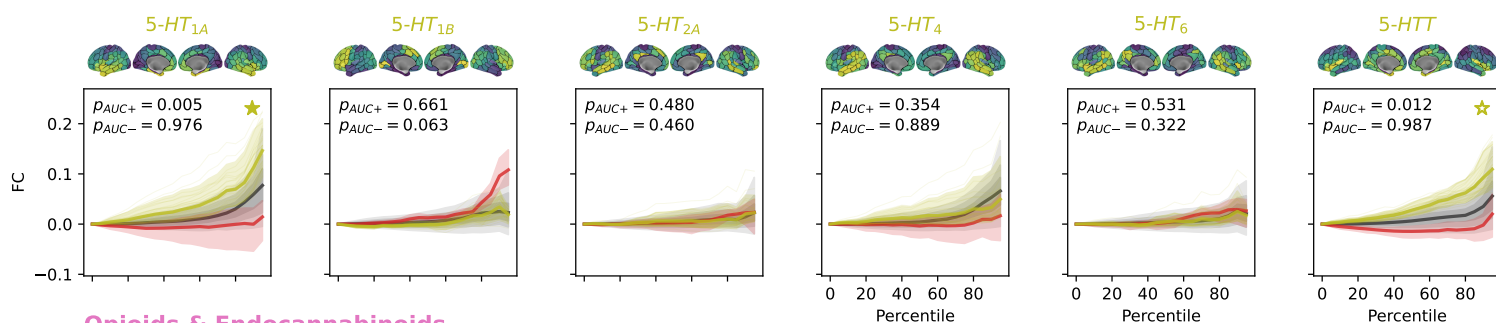
### Noradrenaline & Acetylcholine



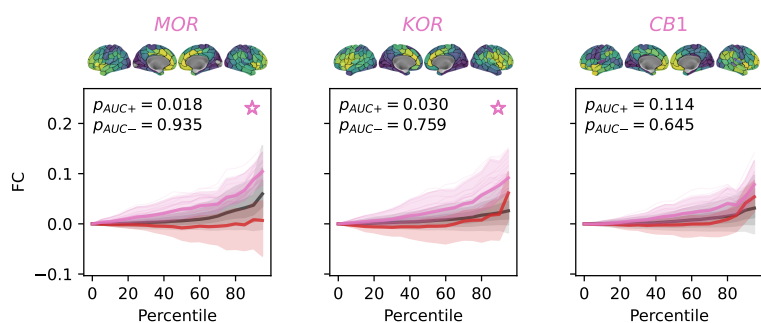
### Dopamine



### Serotonin



### Opioids & Endocannabinoids

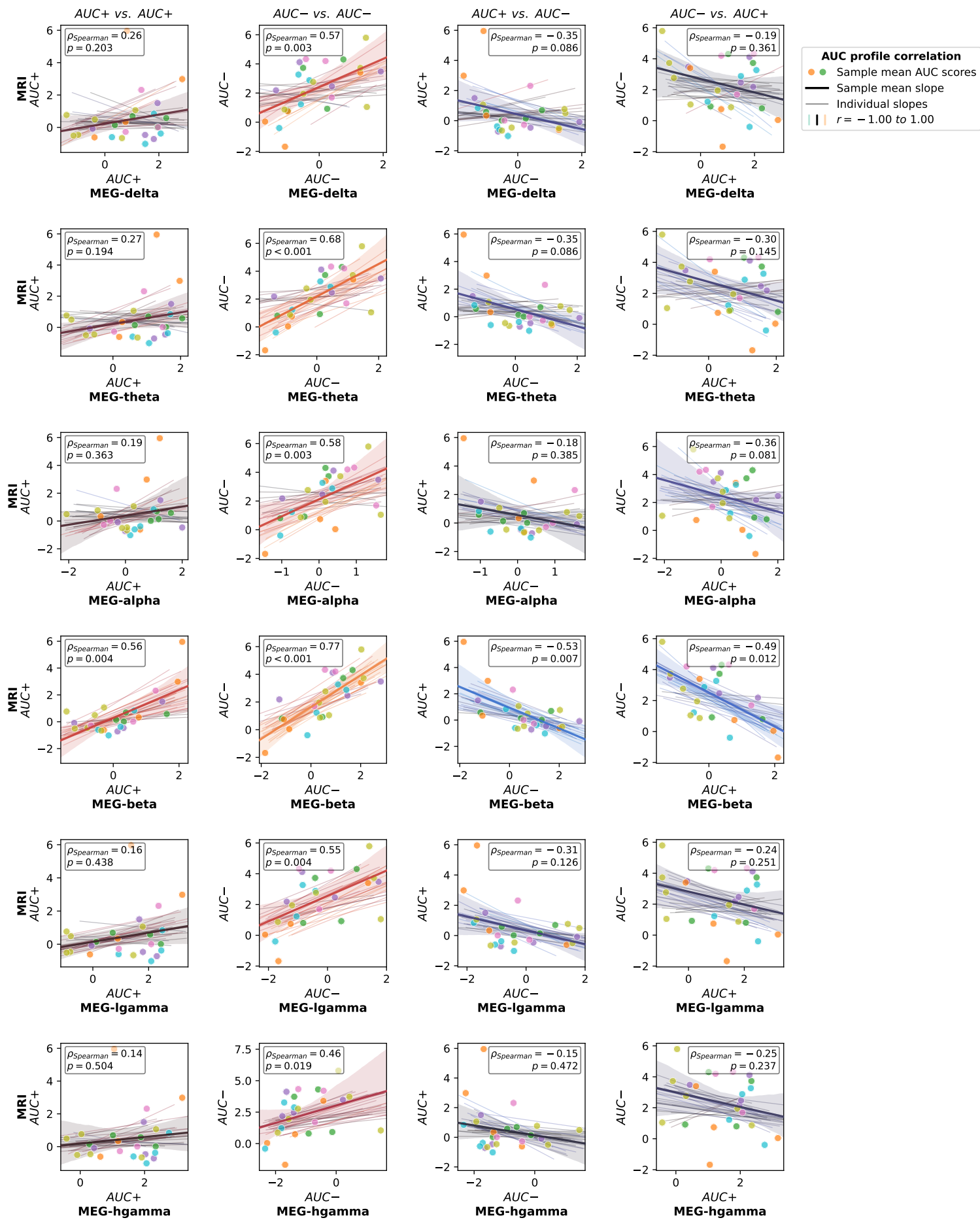




## **Fig. S8:** NEOFC curves across MEG frequency bands

NEOFC curves for all 25 nuclear imaging reference maps derived from MEG AEC FC matrices, shown for six frequency bands: **a** delta, **b** theta, **c** alpha, **d** beta, **e** low gamma, **f** high gamma. Displayed as in **Fig. S2** (Schaefer200 parcellation). Abbreviations: AEC: amplitude envelope correlation; FC: functional connectivity; PI: percentile interval; see **Fig. 2** for reference map abbreviations.

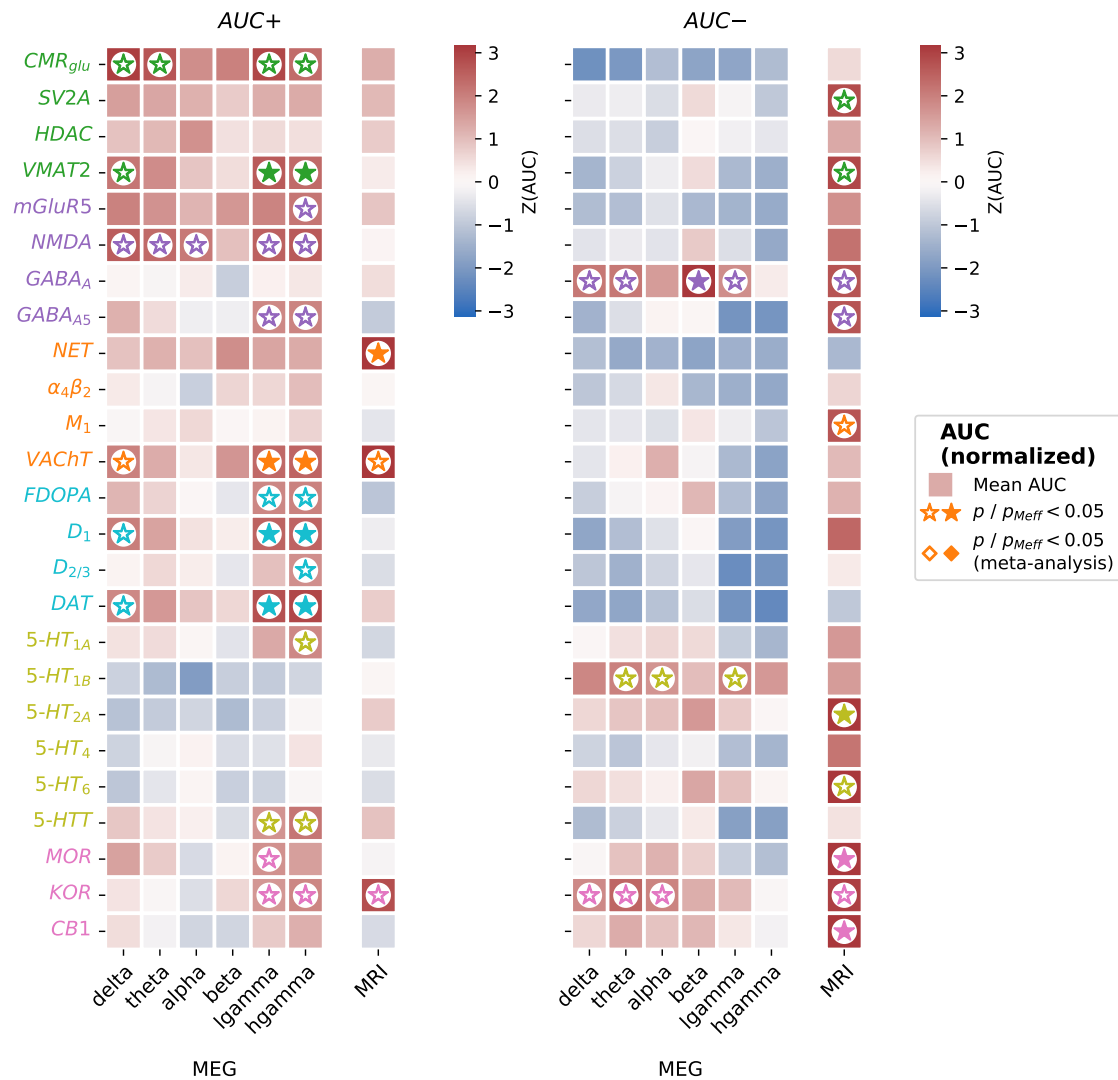
**Fig. S9**



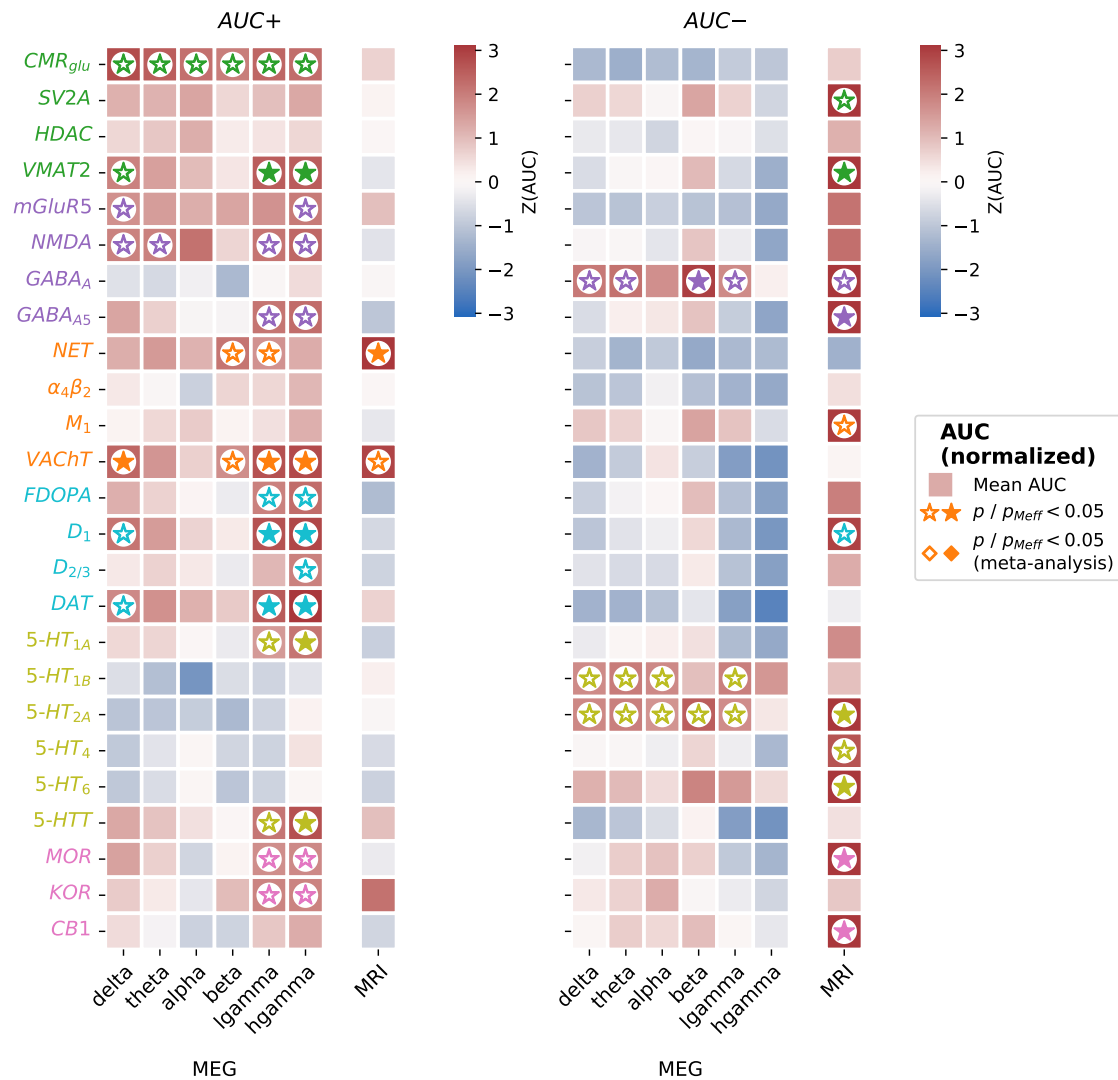
## **Fig. S9:** Correspondence of fMRI and MEG AUC profiles across all frequency bands

Correspondence between fMRI and MEG AUC profiles (z-scored against null) across 25 reference maps, shown for all six MEG frequency bands (rows) and four AUC combinations (columns): fMRI AUC+ vs. MEG AUC+, fMRI AUC− vs. MEG AUC−, fMRI AUC+ vs. MEG AUC−, fMRI AUC− vs. MEG AUC+. Displayed as in **Fig. 3c** (Schaefer200 parcellation). Abbreviations: AUC: area under the curve; fMRI: functional magnetic resonance imaging; MEG: magnetoencephalography; CI: confidence interval; see **Fig. 2** for reference map abbreviations.

**Fig. S10a: Schaefer100**



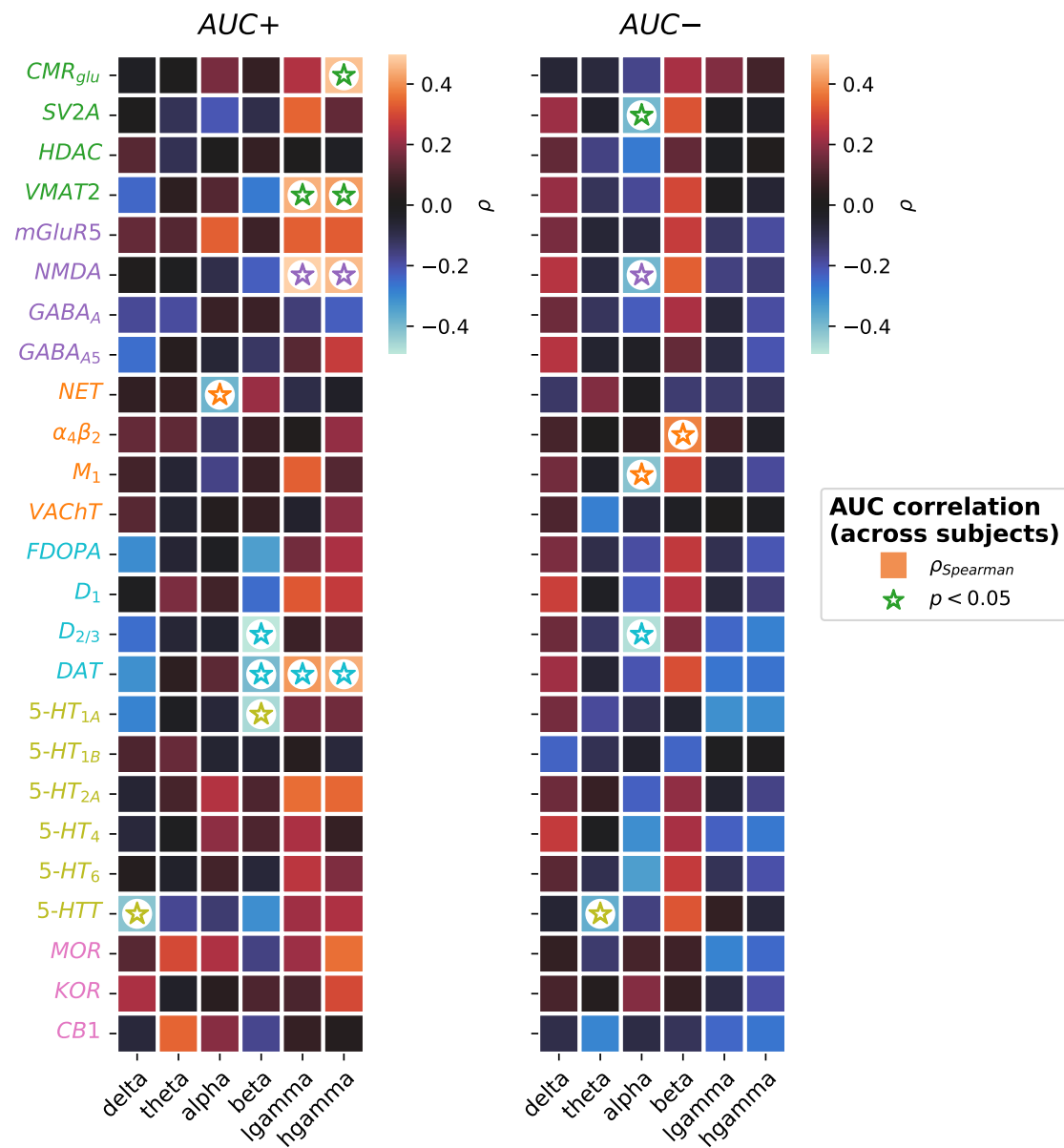
**Fig. S10b: Schaefer400**



**Fig. S10:** MEG AUC results with different parcellation resolutions

AUC+ and AUC− scores for 25 nuclear imaging reference maps derived from MEG AEC FC matrices, shown for two alternative parcellation resolutions: **a** Schaefer100, **b** Schaefer400. Displayed as in **Fig. 3b**. Abbreviations: AUC: area under the curve; AEC: amplitude envelope correlation; FC: functional connectivity; see **Fig. 2** for reference map abbreviations.

**Fig. S11**



## **Fig. S11:** Correlation of atlas-wise AUC scores between MRI and MEG

Spearman's rho between individual fMRI and MEG AUC profiles for 25 nuclear imaging reference maps and six MEG frequency bands, shown for AUC+ (left) and AUC- (right) (Schaefer200 parcellation). Color: Spearman's rho; markers indicate  $p < 0.05$ . Abbreviations: AUC: area under the curve; fMRI: functional magnetic resonance imaging; MEG: magnetoencephalography; see **Fig. 2** for reference map abbreviations.



**Fig. S12a: AUC+**

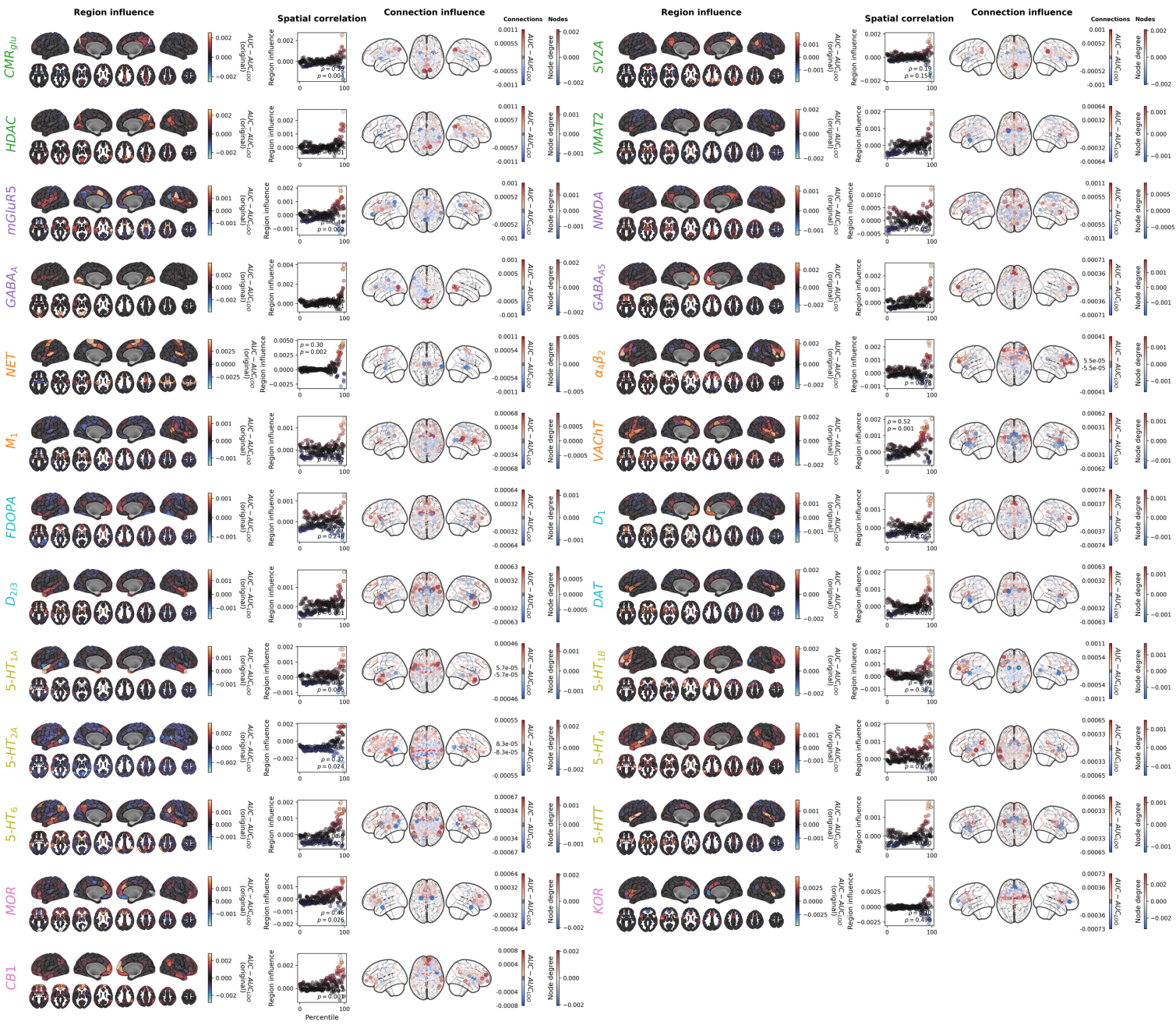
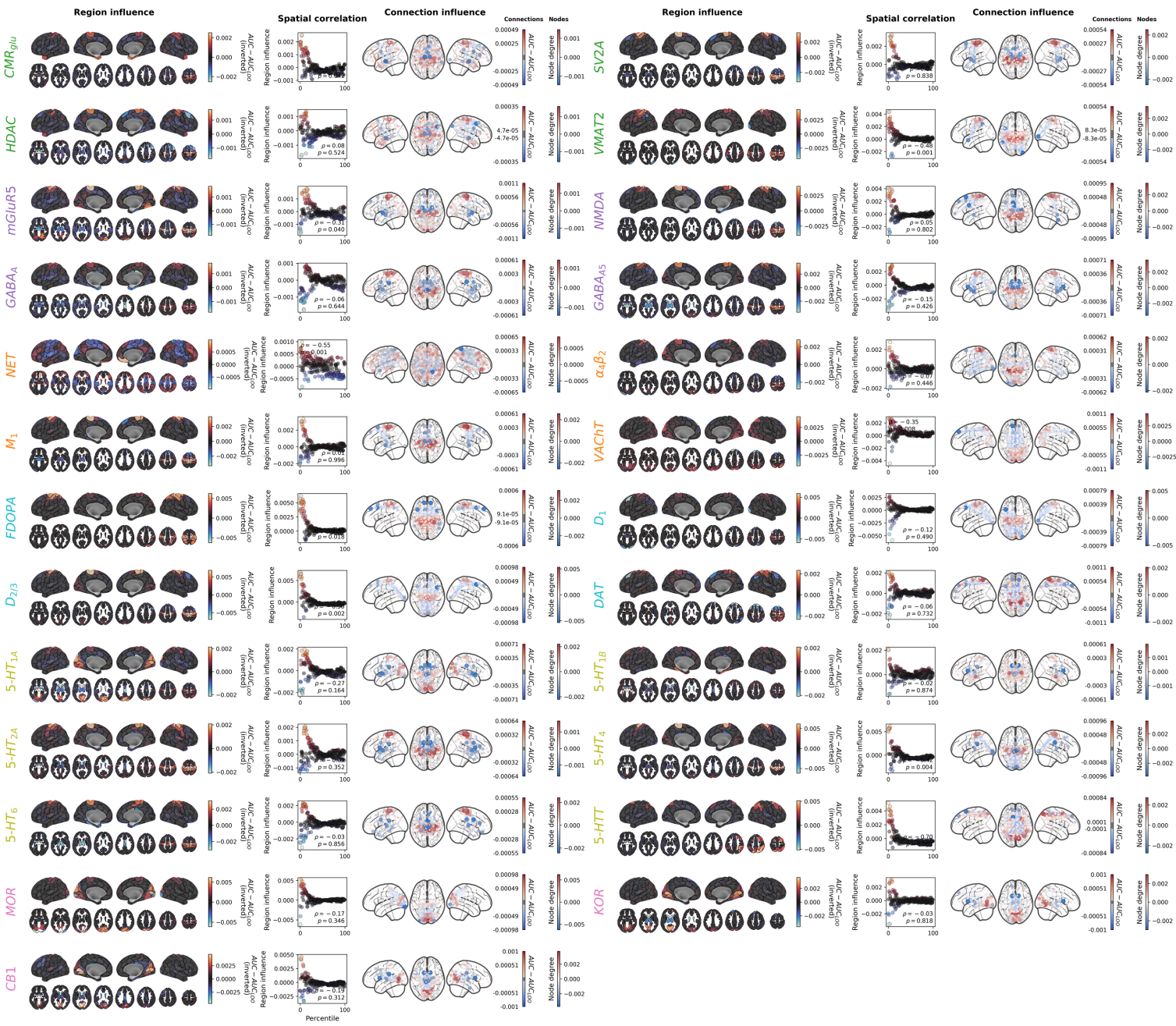


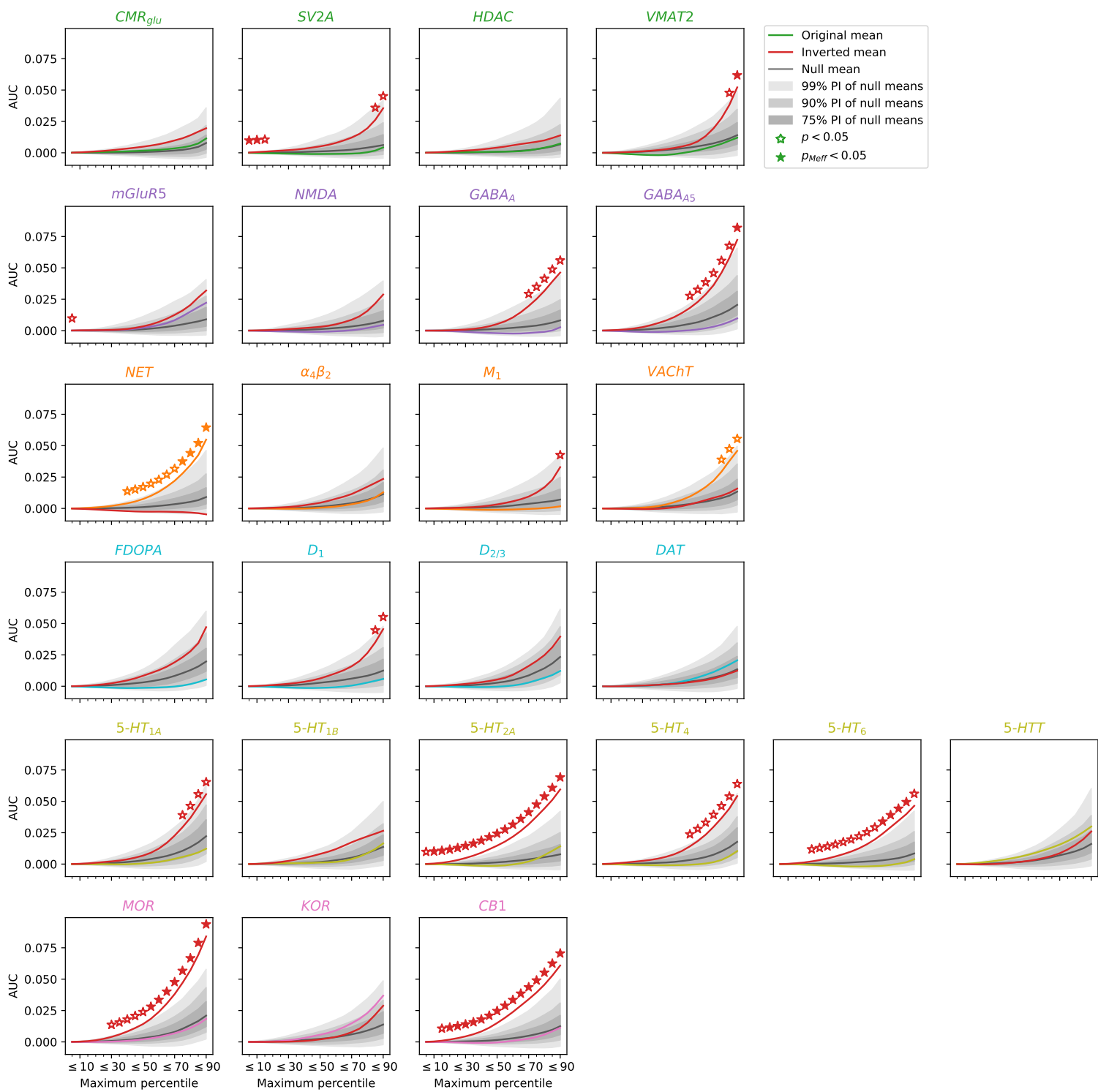
Fig. S12b: AUC–



**Fig. S12:** Leave-one-out analysis to identify influential regions and connections

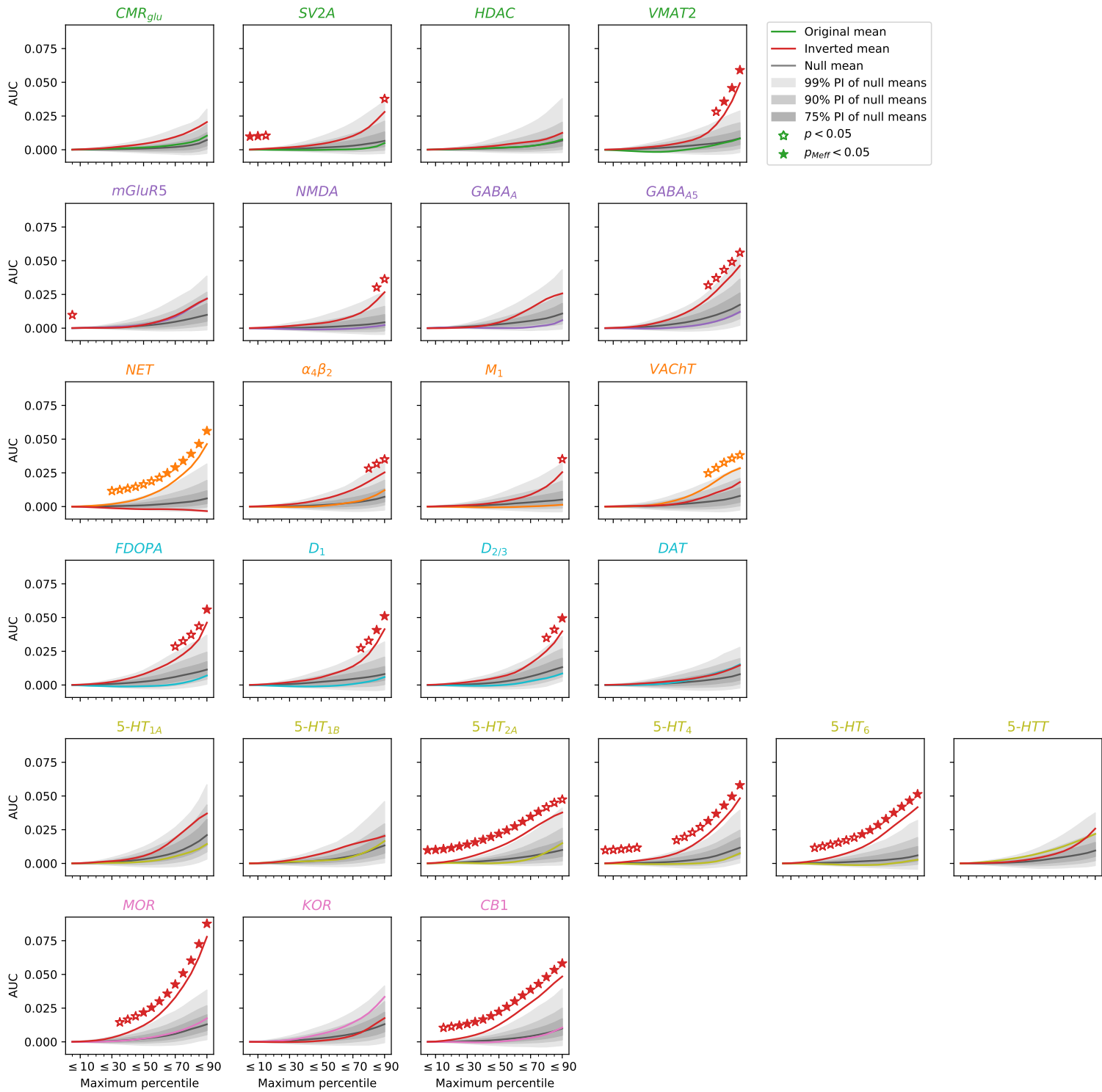
Regional (left, leave-one-region-out) and connection (right, leave-one-connection-out) influence on AUC for all 25 nuclear imaging reference maps (Schaefer200 + subcortex parcellation). **a** AUC+ maps; **b** AUC– maps. Color indicates direction and magnitude of influence. Displayed as in **Fig. 4a**. Abbreviations: AUC: area under the curve; see **Fig. 2** for reference map abbreviations.

**Fig. S13a: Schaefer200**





**Fig. S13b: Schaefer200+Subcortical**

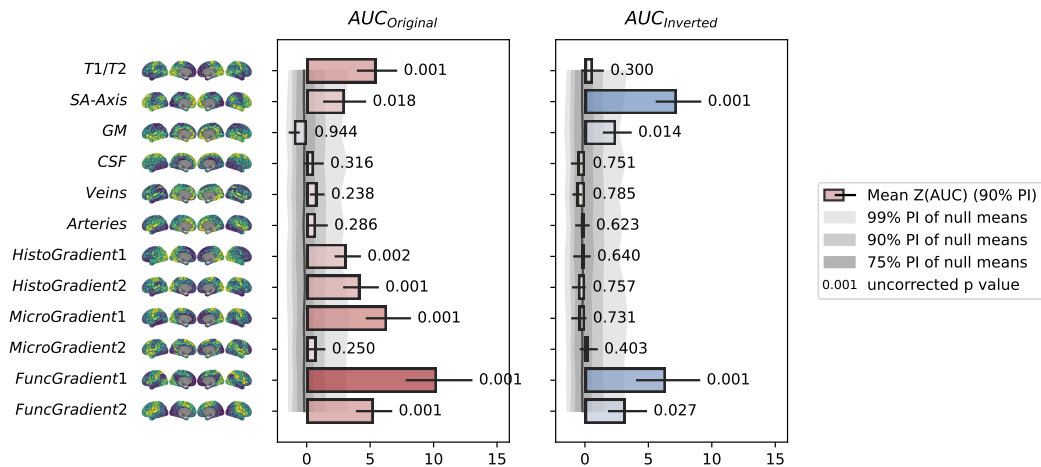


**Fig. S13:** NEOFC curves with AUC estimation restricted to lowered percentiles

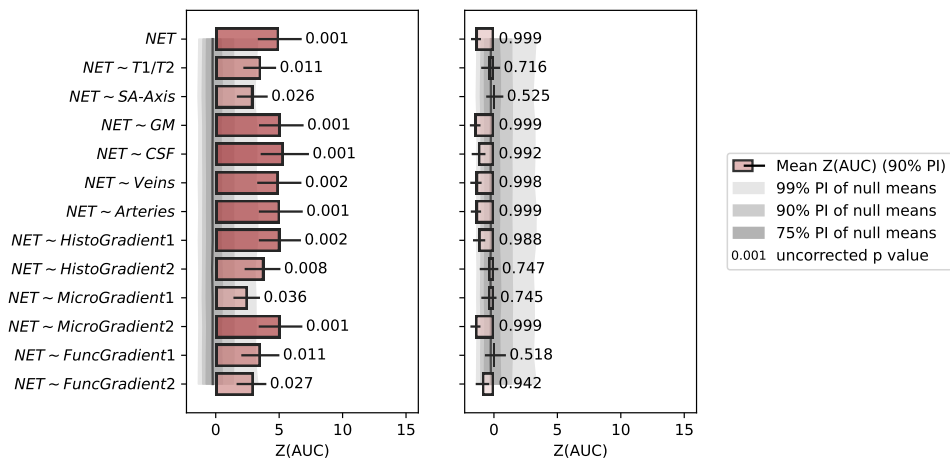
Sensitivity analysis assessing whether AUC effects are driven by the highest-density atlas regions. The maximum percentile threshold included in AUC calculation was systematically varied from 5 to 90, and significance reported as a function of this threshold for all 25 nuclear imaging reference maps. **a** Schaefer200 parcellation; **b** Schaefer200 + subcortex parcellation. Abbreviations: AUC: area under the curve; pMeff: p-value corrected for effective number of comparisons; see **Fig. 2** for reference map abbreviations.

**Fig. S14**

Raw covariates



NET Residuals

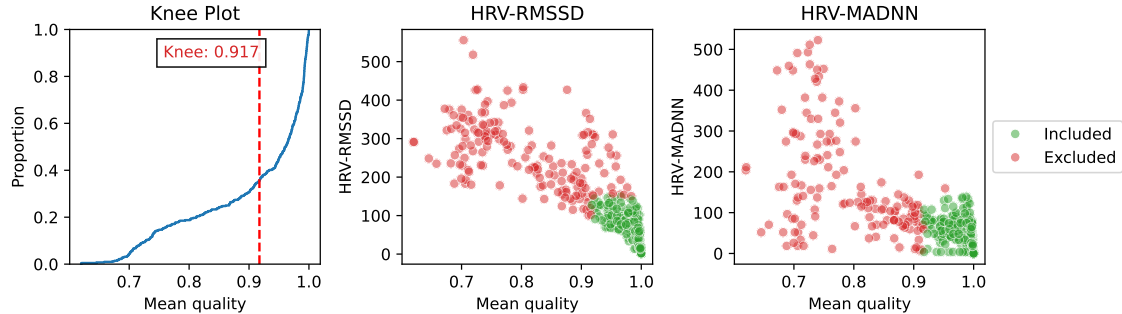


## **Fig. S14:** Effects of covariate regression on NET AUC results

Sensitivity analysis testing whether the NET AUC+ effect is driven by spatially confounding factors. Each spatial covariate map was individually regressed from the NET atlas and NEOFC AUC+ estimation was rerun on the residuals (Schaefer200 parcellation). Covariate maps included T1/T2 ratio, sensory-association axis, BigBrain gradient maps, gray matter and cerebrospinal fluid probability maps, and probability maps of cerebral veins and arteries. AUC+ results after regression are shown in comparison to the unregressed baseline. Displayed as in **Fig. 2c**. Abbreviations: AUC: area under the curve; PI: percentile interval; NET: norepinephrine/noradrenaline transporter; SA: sensory-association; GM: gray matter; CSF: cerebrospinal fluid.

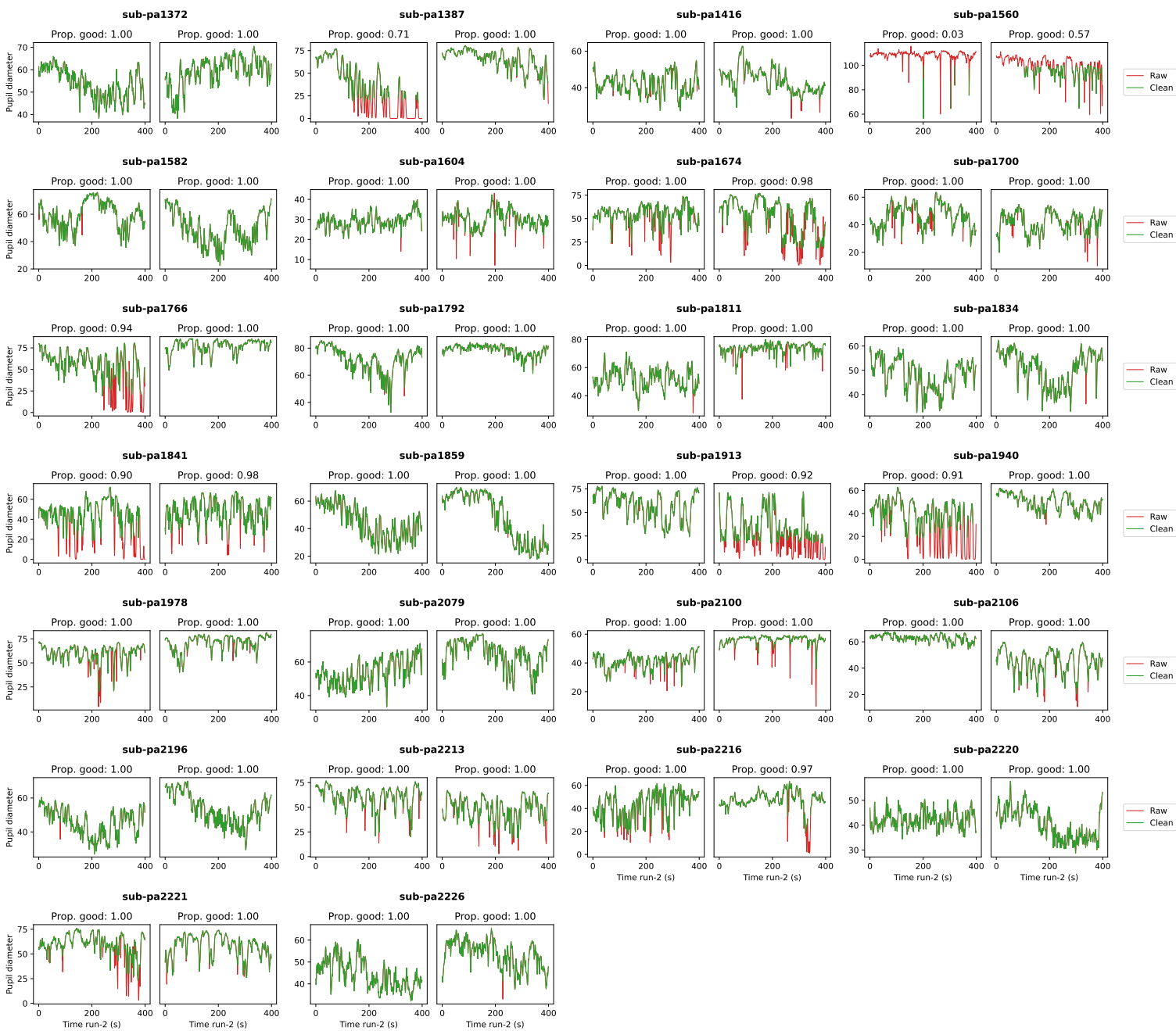


**Fig. S15**



## **Fig. S15:** Quality control of HCP-YA physiological data (heart-rate variability)

Quality control of HRV estimates derived from PPG recordings (HCP-YA dataset). Left: empirical cumulative distribution of mean PPG signal quality index; red dashed line indicates the data-driven knee-point threshold used for session exclusion. Center and right: RMSSD and MadNN as a function of mean PPG quality index; color indicates included (green) and excluded (red) sessions based on quality threshold and upper HRV bound (150 ms). Abbreviations: HRV: heart rate variability; PPG: photoplethysmography; RMSSD: root mean square of successive differences; MadNN: median absolute deviation of NN intervals.

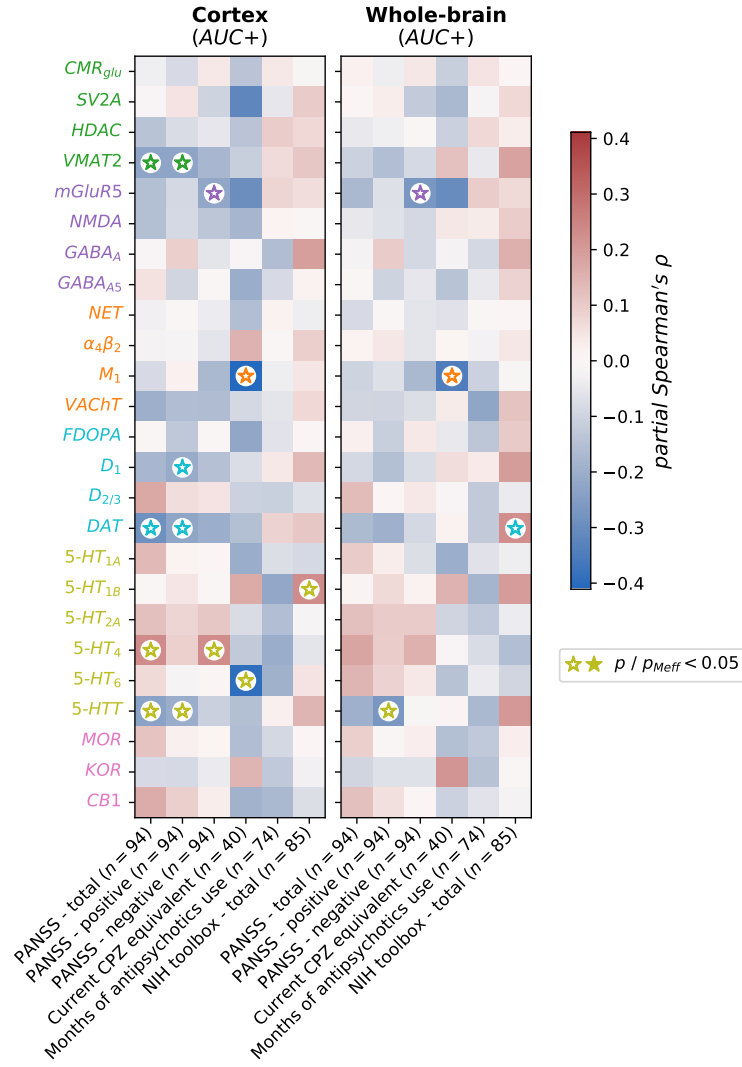
**Fig. S16**

## **Fig. S16:** Quality control of YRSP physiological data (pupil diameter over time)

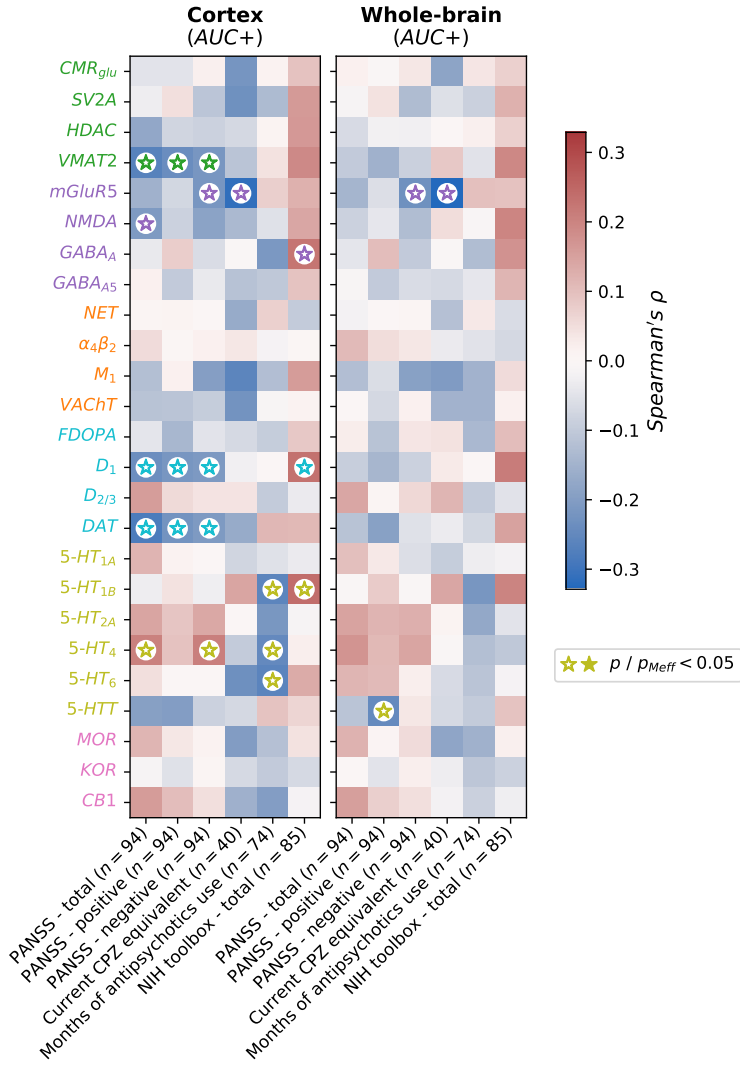
Raw (red) and cleaned (green) pupil diameter time series for both runs of each participant in the YRSP dataset. Panel titles indicate the proportion of valid data points after artifact removal. Sessions with fewer than 80% valid data points were excluded from analyses. Abbreviations: YRSP: Yale Resting-State Pupillometry dataset.

Fig. S17

Partial Spearman correlations



Spearman correlations



## **Fig. S17:** Associations of AUC scores with clinical variables

Associations of NEOFC AUC+ and AUC- scores (Schaefer200 and Schaefer200 + subcortex parcellations) with six clinical and cognitive outcomes in the psychosis group. Both Spearman and partial Spearman correlations were computed, adjusting for sex, age, mean FD, global connectivity, and current antipsychotic dose. Correlations with antipsychotic outcomes were calculated without the antipsychotic covariate. Abbreviations: AUC: area under the curve; PANSS: Positive and Negative Syndrome Scale; CPZ: chlorpromazine; FD: framewise displacement; Meff: effective number of tests.