



PhD Rotation

Biomarker Development Group, INM7

Abhay Koushik

The Project

Modulation of PET filtered simultaneous EEG and rsfMRI connectivity by Ketamine & Midazolam

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- **Participants:** 30 male

Mean age: 27.3 ± 6.2 years (physically & psychologically healthy)

Mean BMI: 24 ± 3.5 (screened for recreational drug use)

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Modulation of PET filtered simultaneous EEG and rsfMRI connectivity by Ketamine & Midazolam

- **Participants: 30 male** ∴ GABA level (1) & EEG metrics (2) change across menstrual cycle
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3-way crossover design: Ketamine, Midazolam, & Placebo

0.25 mg/kg bolus dose

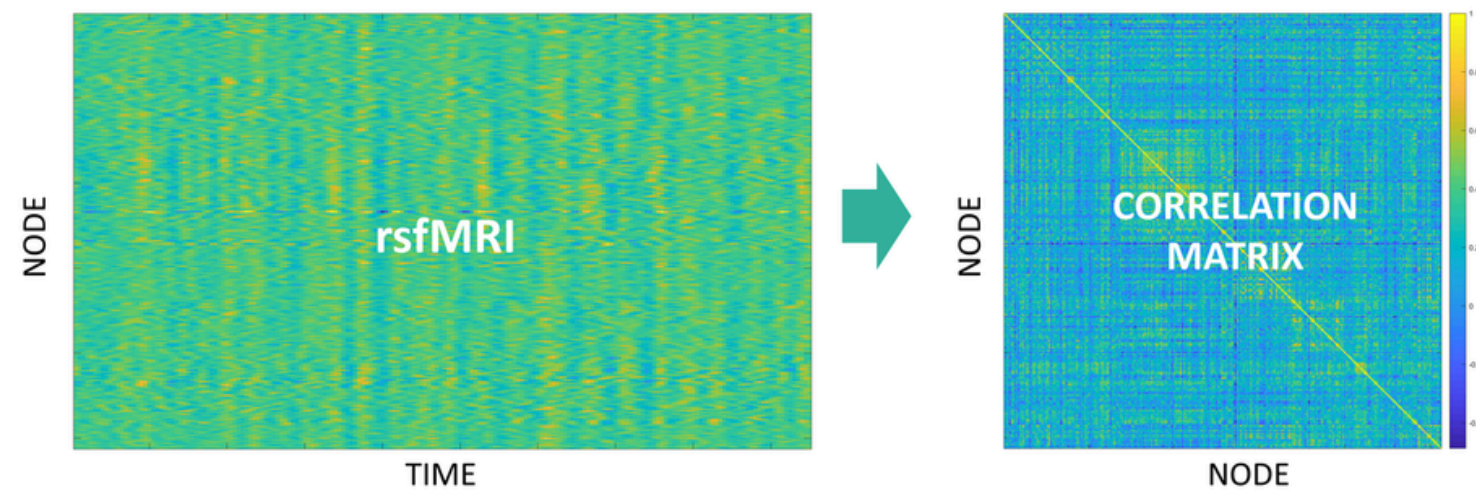
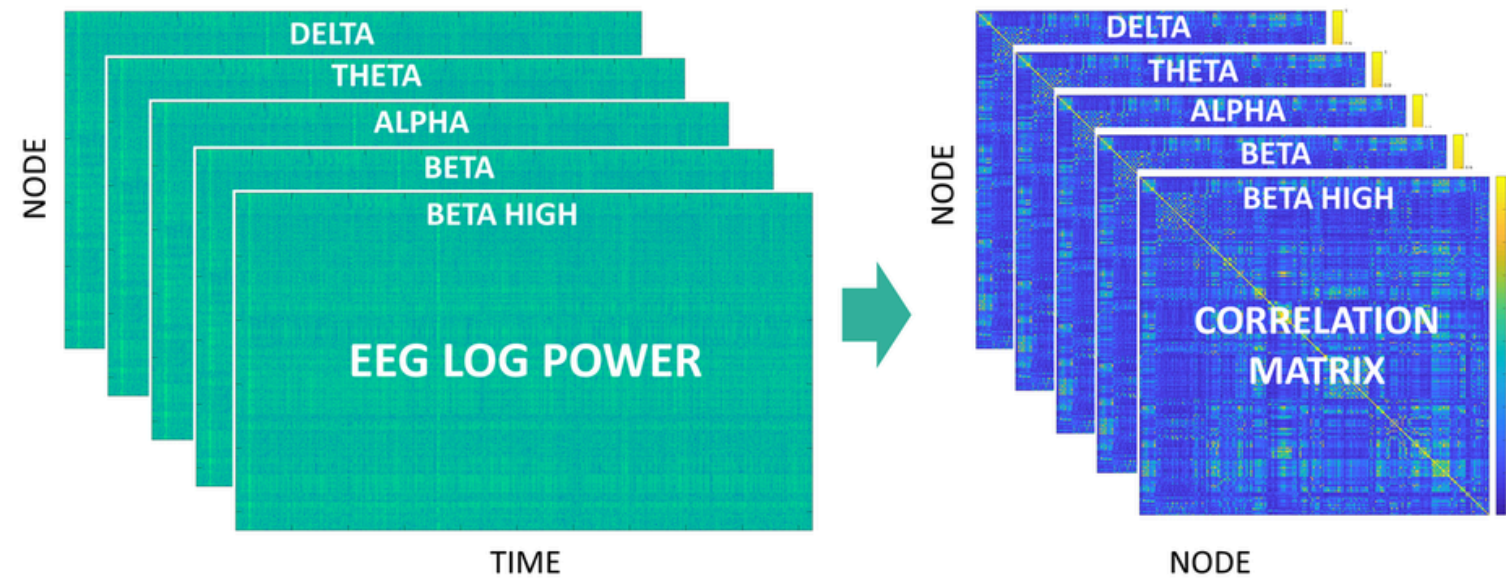
Then 0.25 mg/kg/hr infusion

0.03 mg/kg bolus dose

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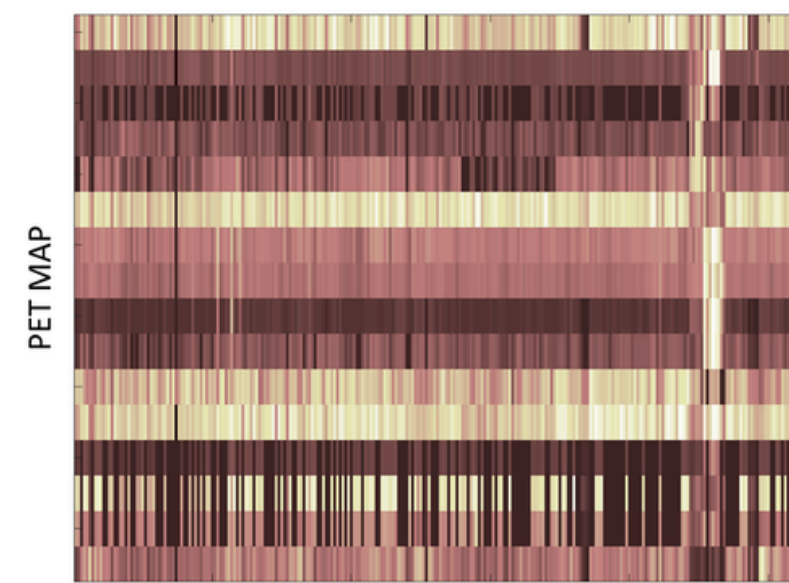
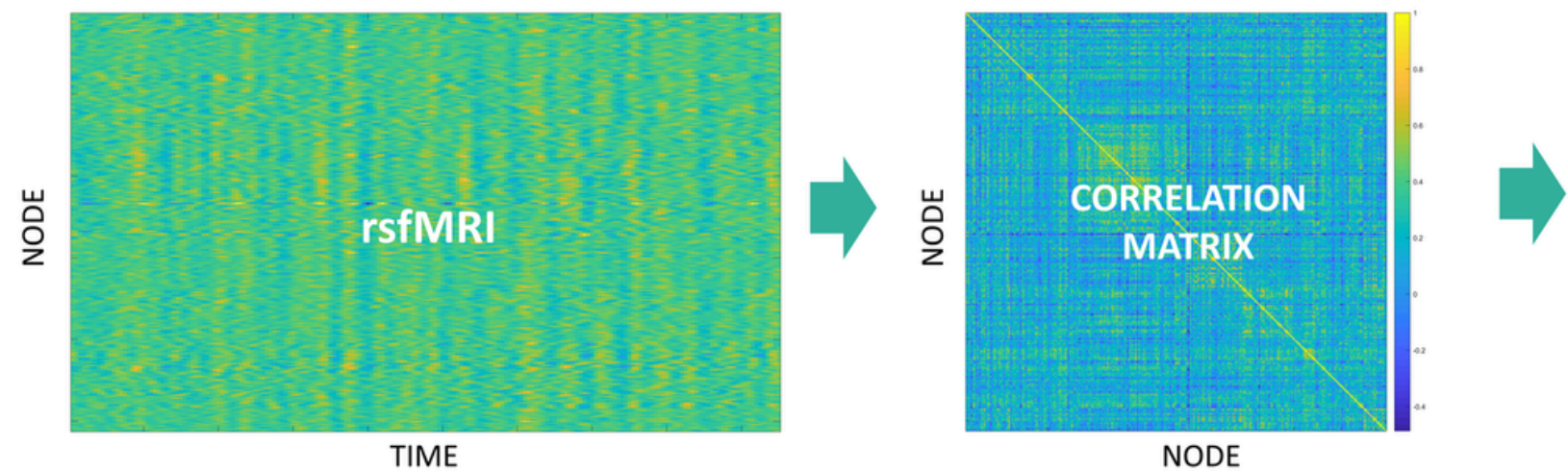
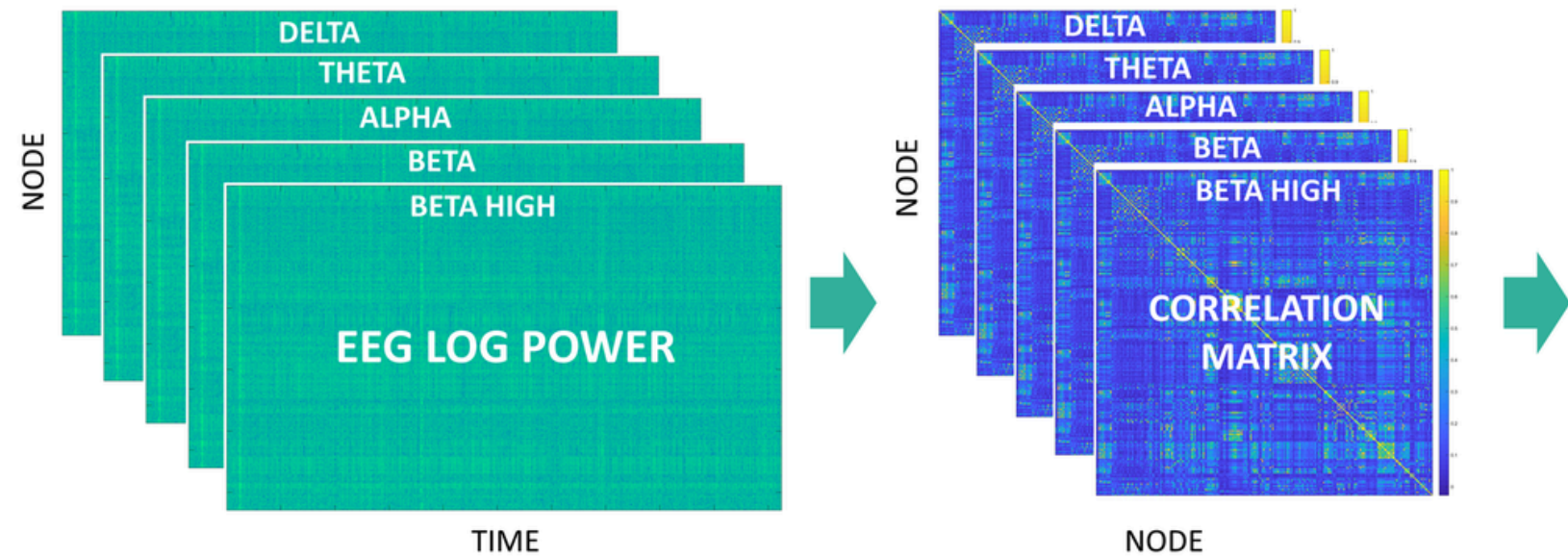
The Project Pipeline

FOR EACH SUBJECT SEPARATELY BEFORE AND AFTER KETAMINE

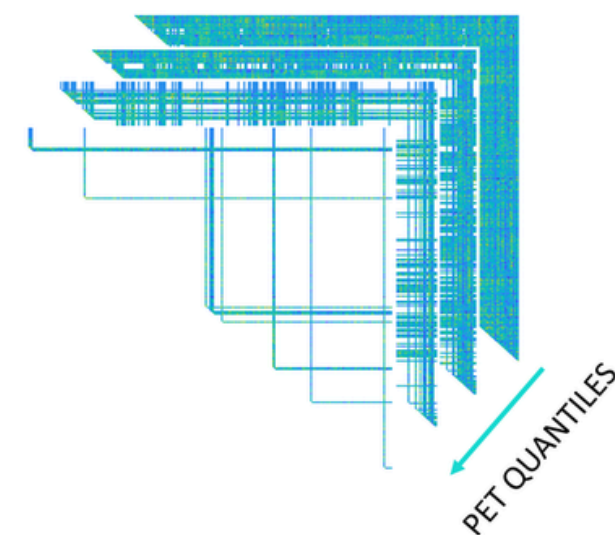
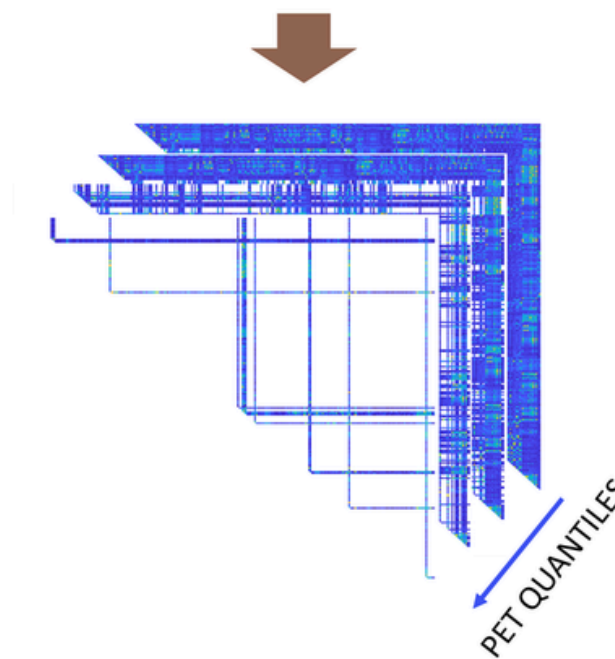


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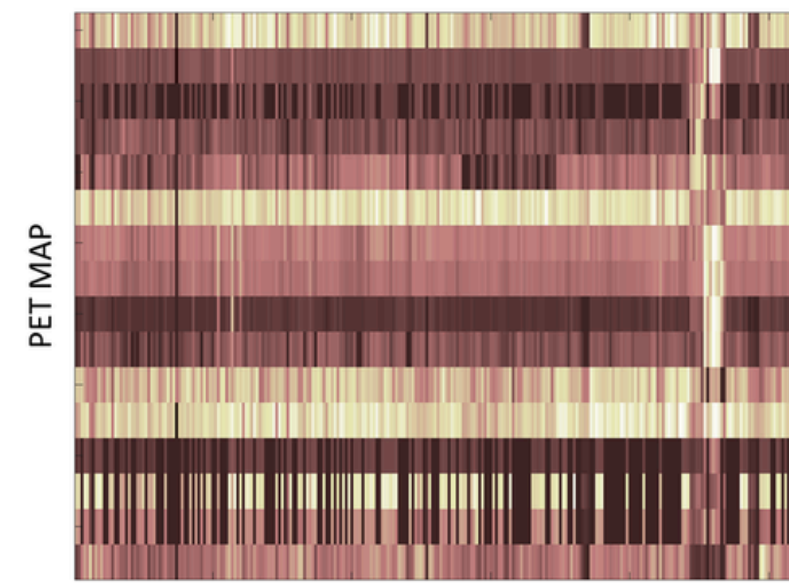
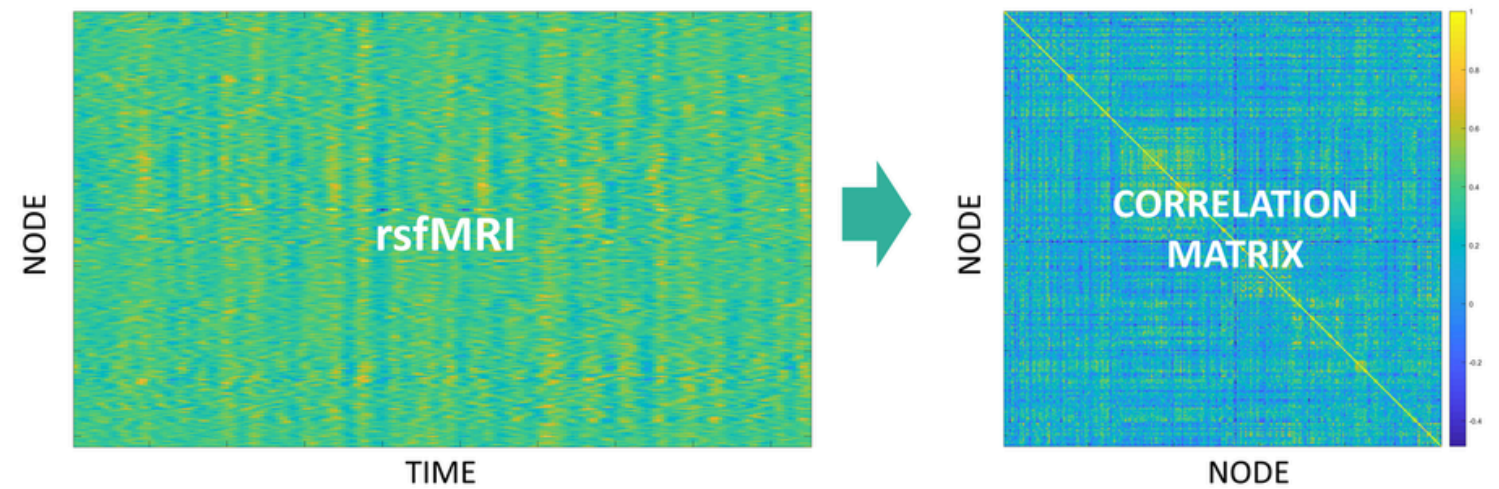
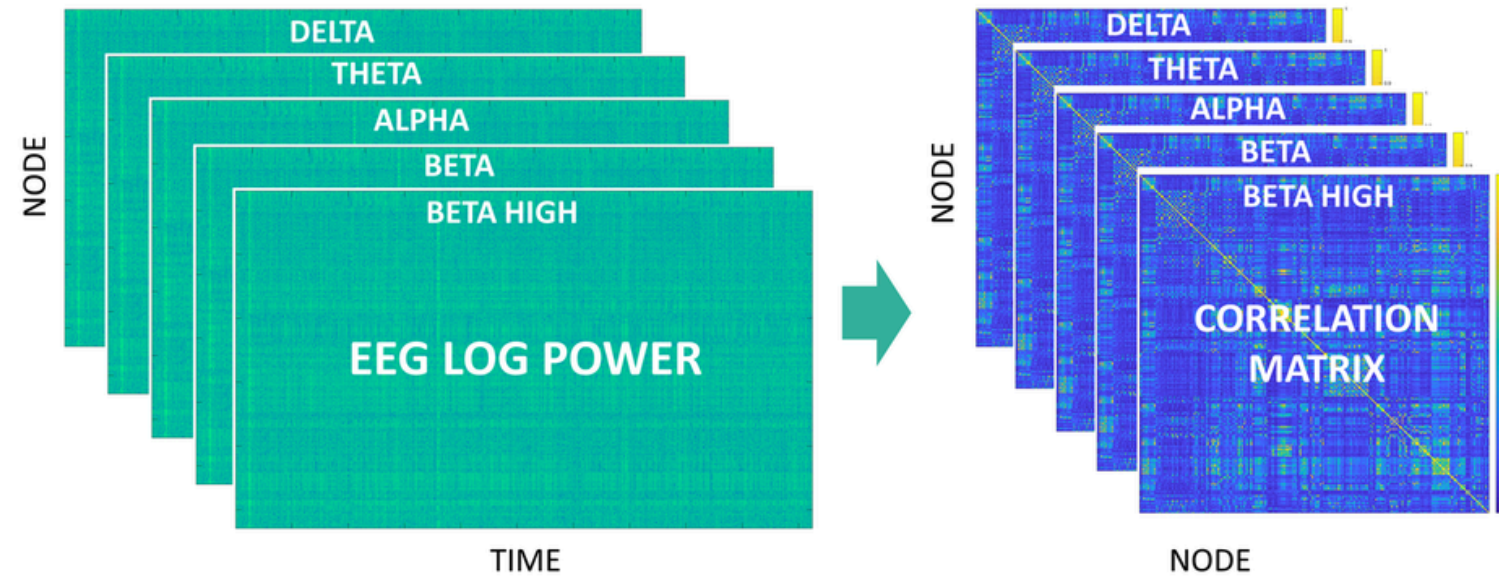


QUANTILE FILTERS (FROM 5th TO 95th)

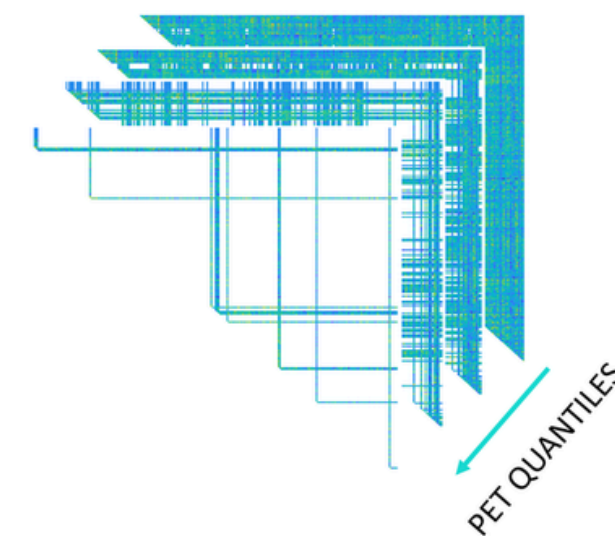
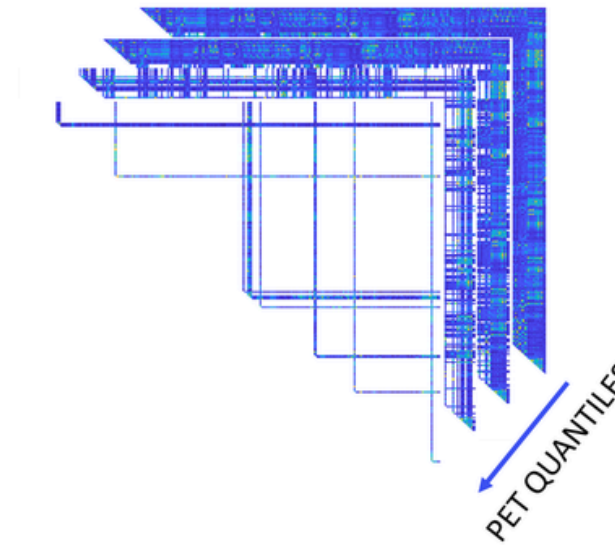


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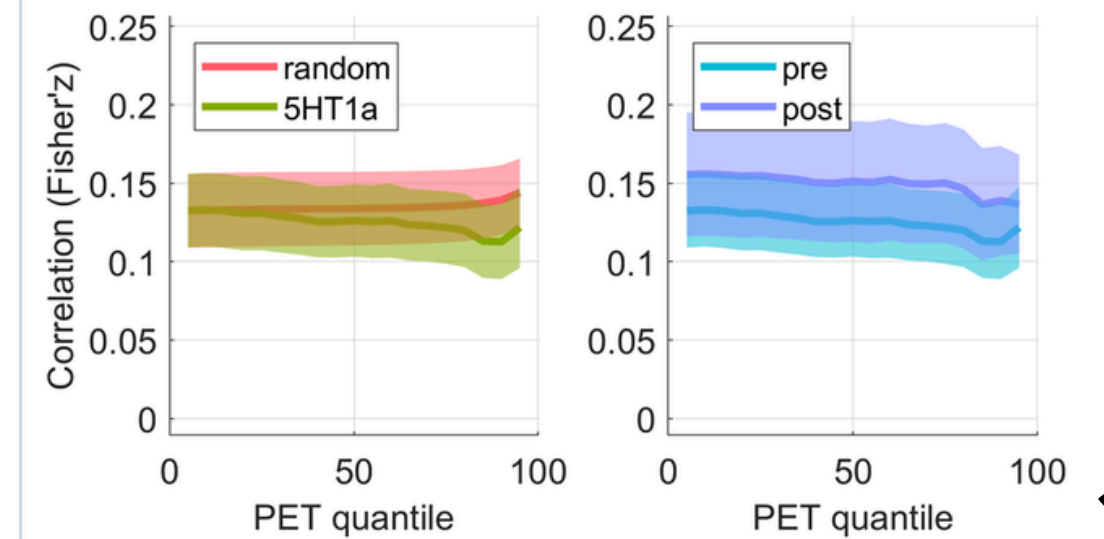
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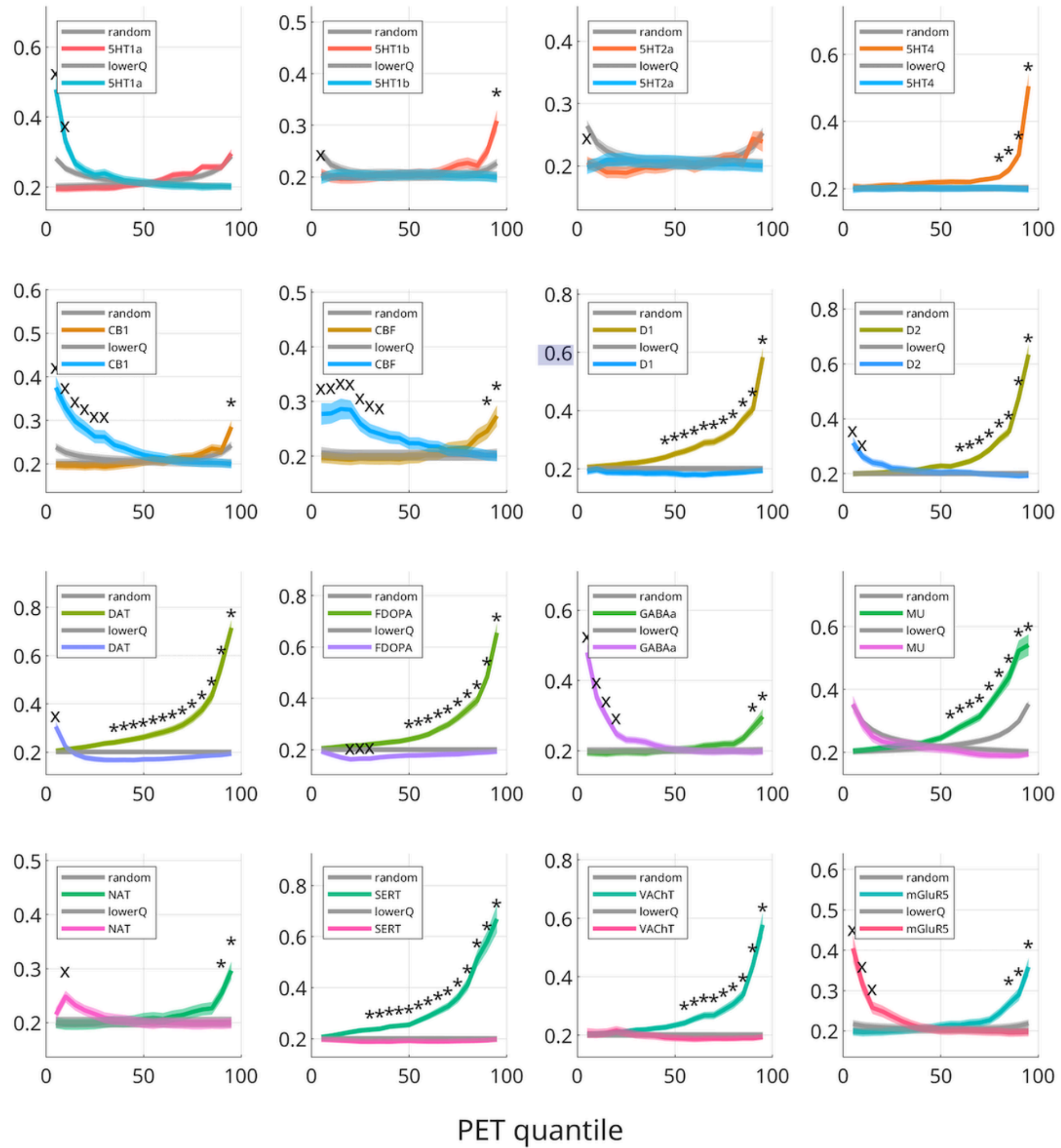
AVERAGE CONNECTIVITY PER SUBJECT PER PET MAP (AND EEG BAND)

GROUP COMPARISONS TO RANDOMIZED PET MAPS

PAIR-WISE PRE AND POST KETAMINE COMPARISONS

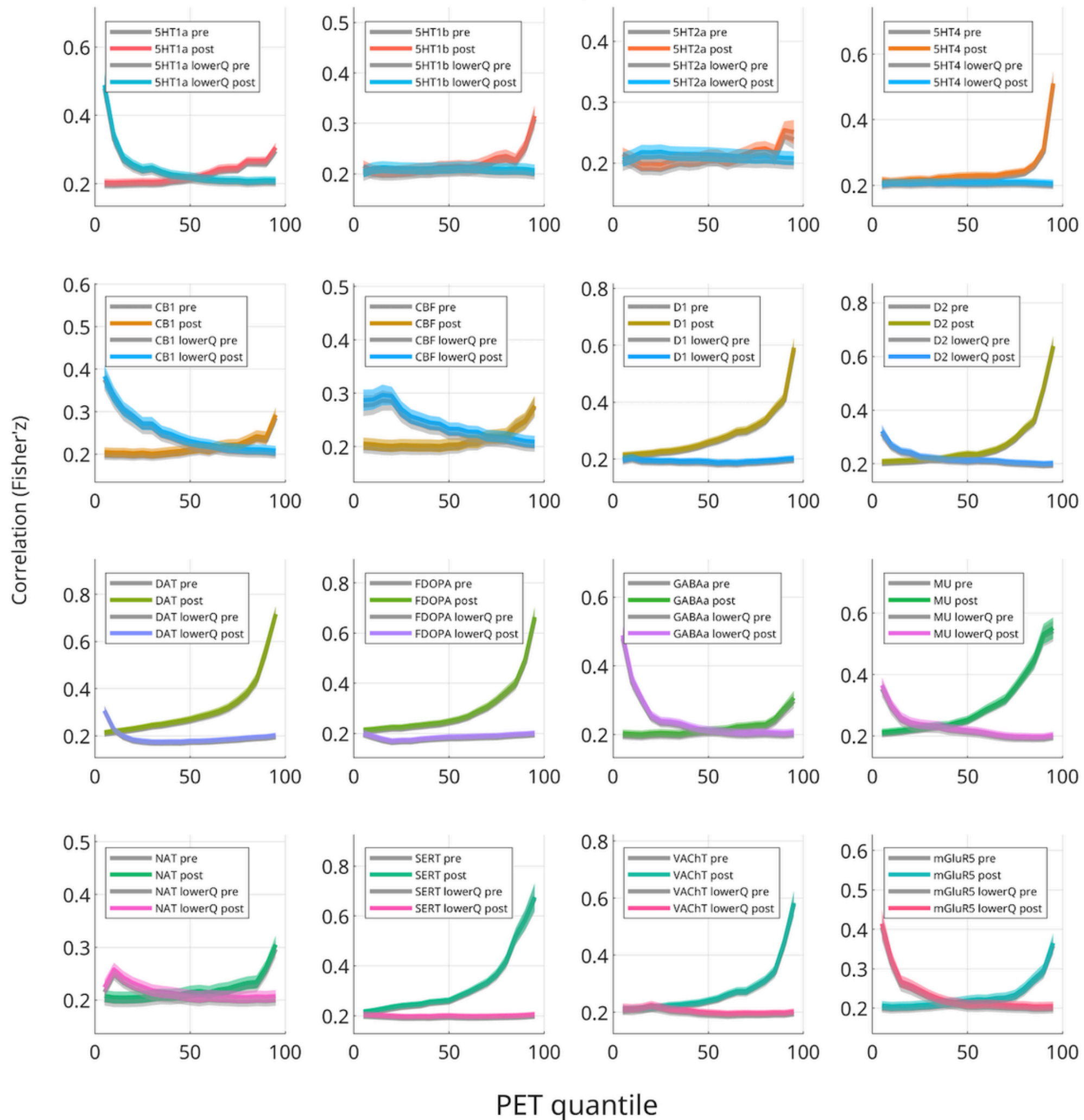


EEG PLA Alpha bothQ



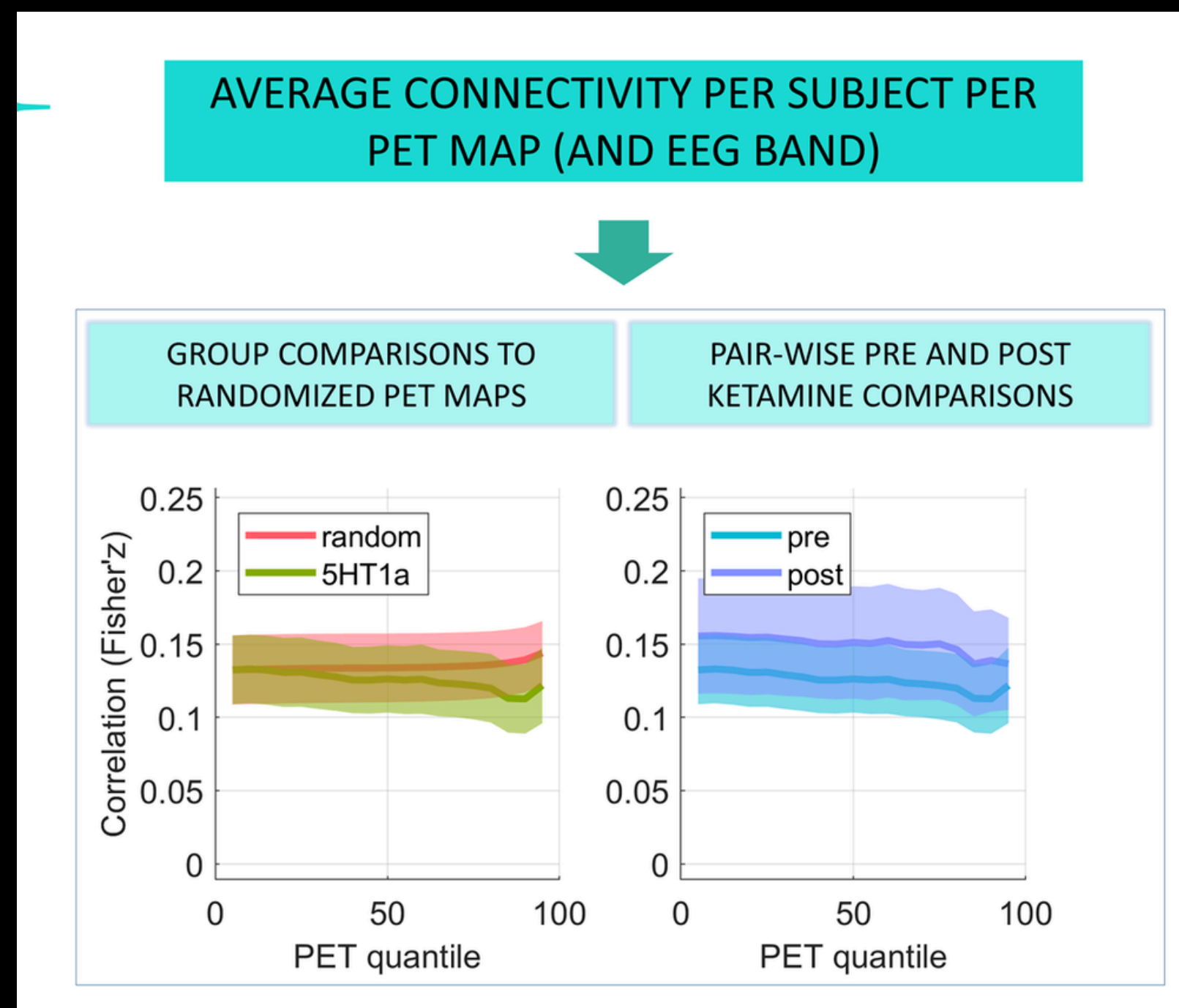
**Pre-Random Placebo PET Filtered
Alpha EEG Band Connectivity**

EEG PLA: Alpha bothQ



**Pre-Post Placebo PET Filtered
Alpha EEG Band Connectivity**

Further Comparison of Pre-Post Administration



STATISTICAL ANALYSIS

Linear Mixed Model

Corr ~ 1 +

Group + Modality +

NT_map + Quantile_compare +

Group x Quantile_compare +

(1 | Subject)

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Linear Mixed Model

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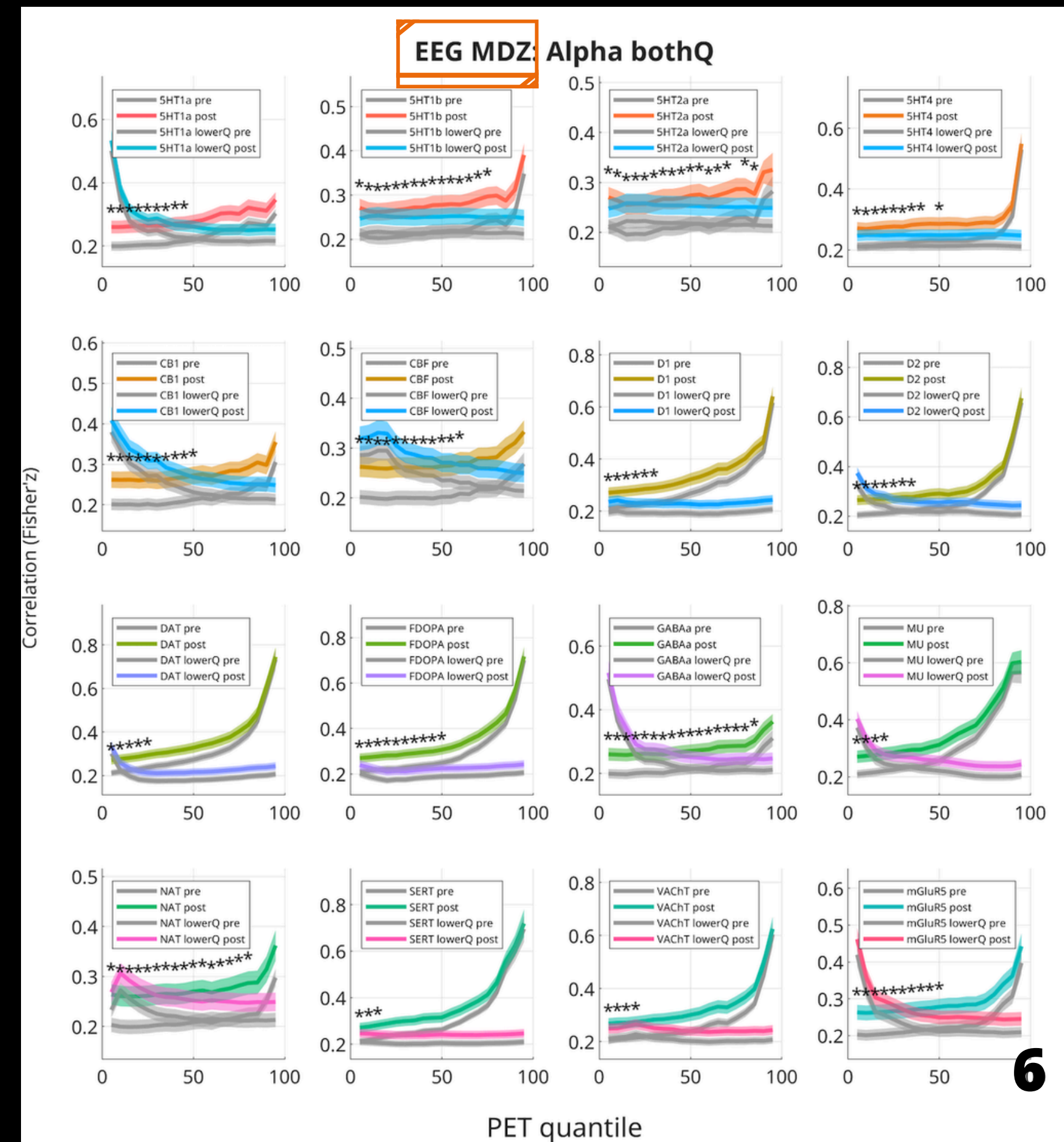
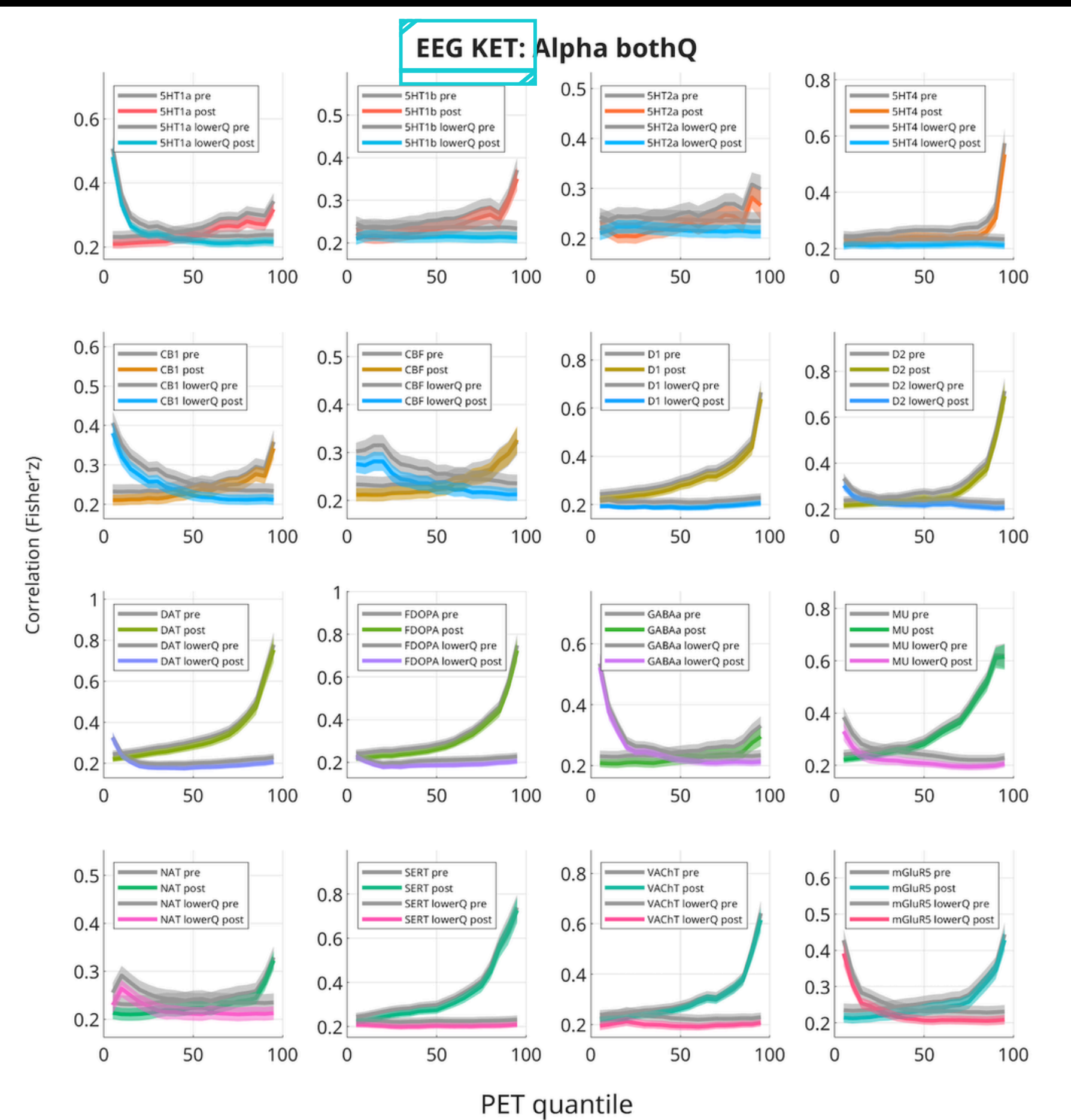
Model Results

Fixed Effect Omnibus tests

	F	Num df	Den df	p
Group	3456.7	2	117007	<.001
Modality	10939.9	4	116989	<.001
NT_map	2026.7	15	116989	<.001
Quantile_compare	55339.7	1	116989	<.001
Group * Quantile_compare	76.2	2	116989	<.001

Note. Satterthwaite method for degrees of freedom

Further Comparison of Pre-Post Administration



Ketamine

Midazolam

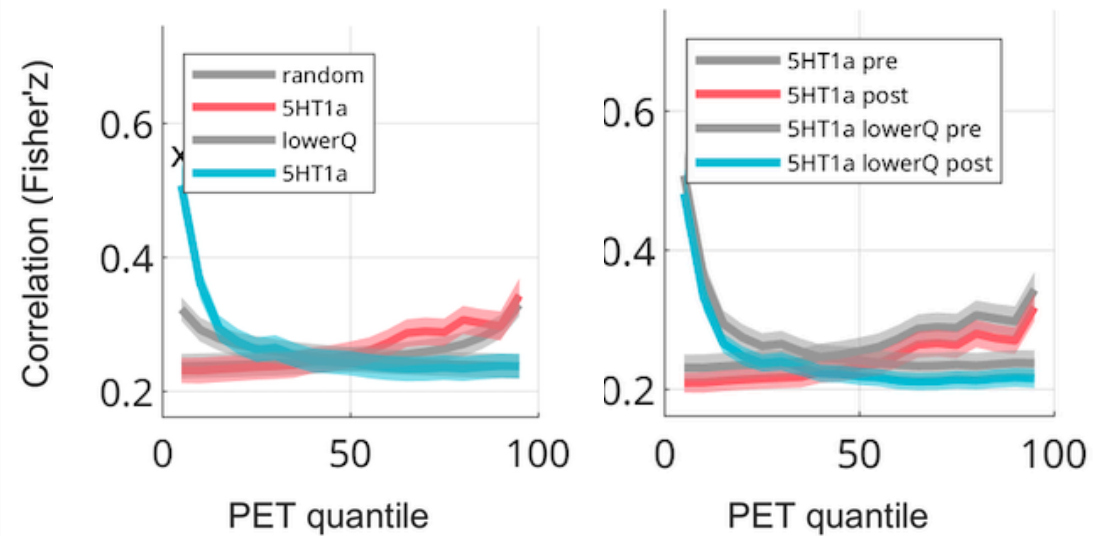
Placebo

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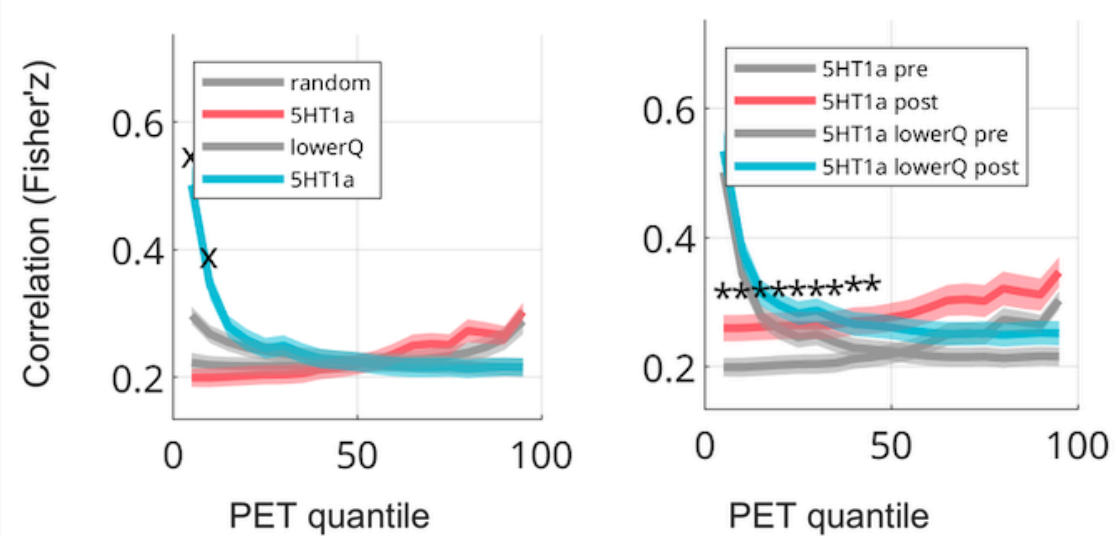


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GROUP COMPARISONS TO
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MIDAZOLAM

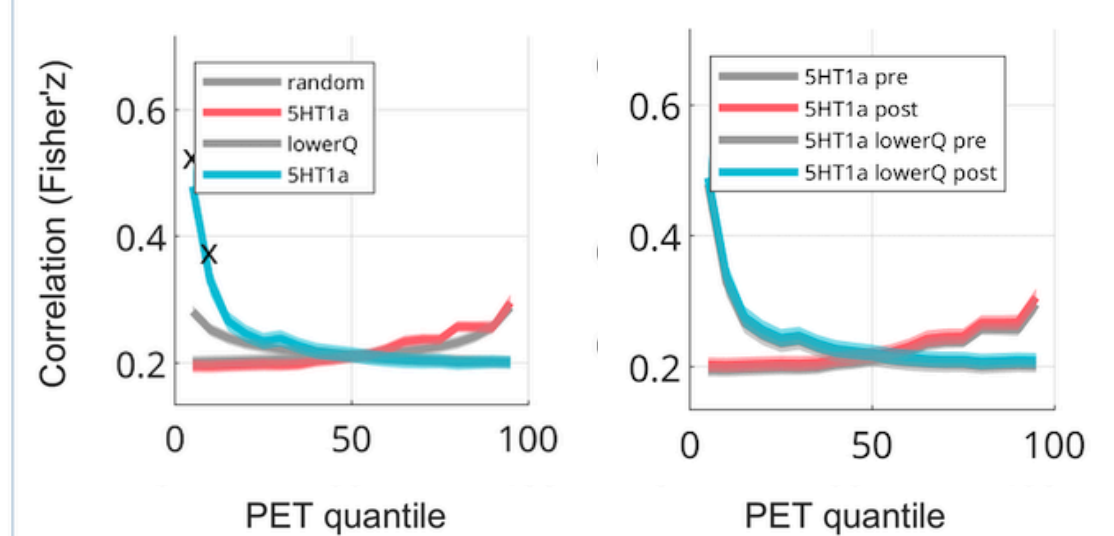


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Ketamine

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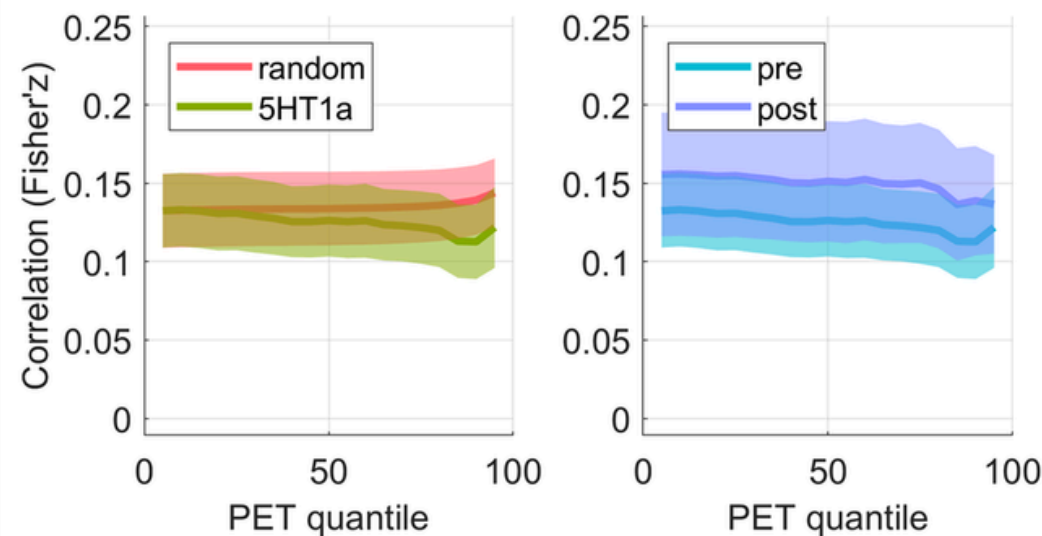
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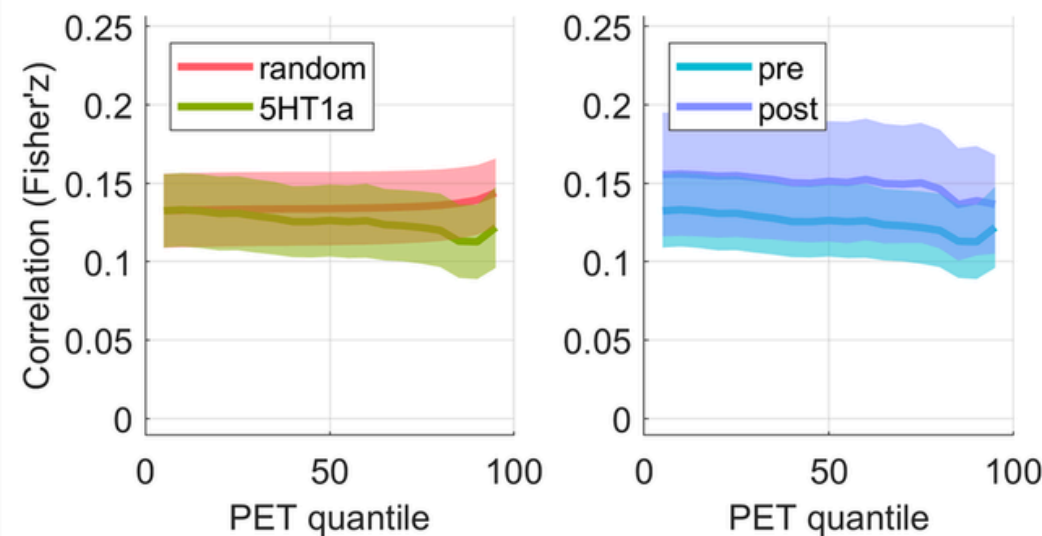


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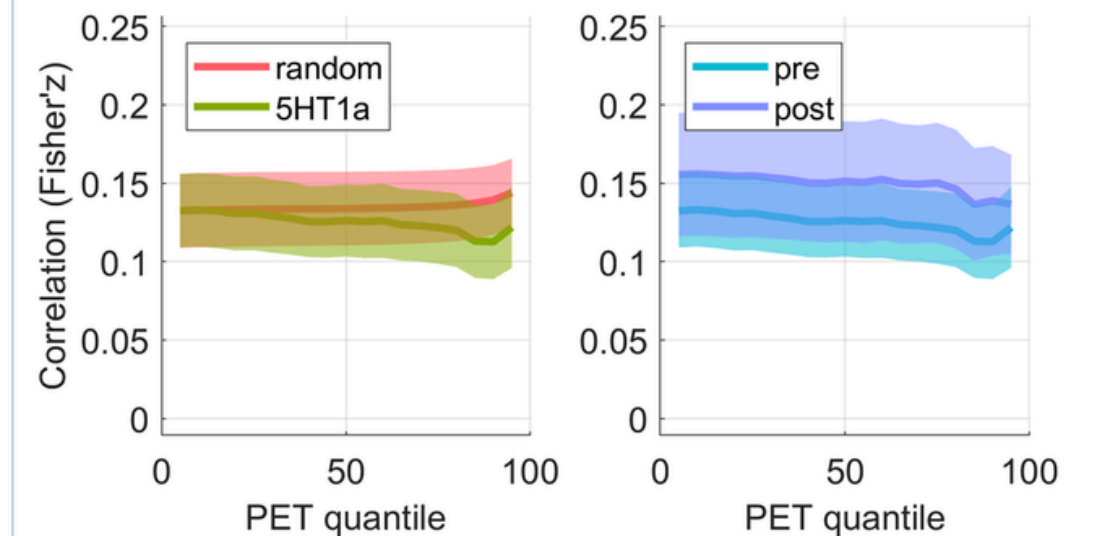


AVERAGE CONNECTIVITY PER SUBJECT PER
PET MAP (AND EEG BAND)



GROUP COMPARISONS TO
RANDOMIZED PET MAPS

PAIR-WISE PRE AND POST
~~KETAMINE~~ COMPARISONS
PLACEBO



Both EEG & rsfMRI Connectivity
More Analysis Underway...

RESULTS

Fixed Effects Parameter Estimates

Names	Effect	Estlmate	SE	95% Confidence Interval		df	t	p
				Lower	Upper			
(Intercept)	(Intercept)	0.25897	0.00535	0.24849	0.26945	26.0	48.44	<.001
Group1	MDZ - KET	0.03051	5.21e-4	0.02949	0.03153	117013.1	58.62	<.001
Group2	PLA - KET	-0.01133	5.21e-4	-0.01235	-0.01031	116989.0	-21.76	<.001
Modality1	Beta - Alpha	-0.05928	6.63e-4	-0.06058	-0.05798	116989.0	-89.38	<.001
Modality2	BetaHigh - Alpha	-0.09683	6.63e-4	-0.09813	-0.09553	116989.0	-146.00	<.001
Modality3	Delta - Alpha	-0.00540	6.63e-4	-0.00670	-0.00410	116989.0	-8.14	<.001
Modality4	Theta - Alpha	0.02313	6.63e-4	0.02183	0.02443	116989.0	34.88	<.001
NT_map1	5HT1b - 5HT1a	-0.00488	0.00119	-0.00720	-0.00255	116989.0	-4.11	<.001
NT_map2	5HT2a - 5HT1a	-0.01531	0.00119	-0.01764	-0.01299	116989.0	-12.90	<.001
NT_map3	5HT4 - 5HT1a	0.01117	0.00119	0.00884	0.01349	116989.0	9.41	<.001
NT_map4	CB1 - 5HT1a	-0.00958	0.00119	-0.01190	-0.00725	116989.0	-8.07	<.001
NT_map5	CBF - 5HT1a	-0.01164	0.00119	-0.01397	-0.00932	116989.0	-9.81	<.001
NT_map6	D1 - 5HT1a	0.05656	0.00119	0.05423	0.05888	116989.0	47.67	<.001
NT_map7	D2 - 5HT1a	0.04259	0.00119	0.04027	0.04492	116989.0	35.90	<.001
NT_map8	DAT - 5HT1a	0.08491	0.00119	0.08259	0.08724	116989.0	71.57	<.001
NT_map9	FDOPA - 5HT1a	0.06091	0.00119	0.05858	0.06323	116989.0	51.33	<.001
NT_map10	GABAA - 5HT1a	-0.00518	0.00119	-0.00750	-0.00285	116989.0	-4.36	<.001
NT_map11	MU - 5HT1a	0.06597	0.00119	0.06365	0.06830	116989.0	55.61	<.001
NT_map12	NAT - 5HT1a	-0.01131	0.00119	-0.01364	-0.00899	116989.0	-9.53	<.001
NT_map13	SERT - 5HT1a	0.09341	0.00119	0.09109	0.09574	116989.0	78.73	<.001
NT_map14	VACHT - 5HT1a	0.04352	0.00119	0.04119	0.04584	116989.0	36.68	<.001
NT_map15	mGluR5 - 5HT1a	0.00470	0.00119	0.00238	0.00703	116989.0	3.96	<.001
Quantile_compare	Quantile_compare	0.00180	7.66e-6	0.00179	0.00182	116989.0	235.24	<.001
Group1 * Quantile_compare	MDZ - KET * Quantile_compare	-2.15e-4	1.87e-5	-2.52e-4	-1.78e-4	116989.0	-11.53	<.001
Group2 * Quantile_compare	PLA - KET * Quantile_compare	-1.84e-4	1.90e-5	-2.21e-4	-1.47e-4	116989.0	-9.68	<.001

Random Components

Groups	Name	SD	Varlance	ICC
Subject	(Intercept)	0.0278	7.70e-4	0.130
Residual		0.0718	0.00515	

RESULTS

Post Hoc Comparisons - Modality

Comparison			Difference	SE	z	P _{bonferroni}
Modality		Modality				
Alpha	-	Beta	0.05928	6.63e-4	89.38	<.001
Alpha	-	BetaHigh	0.09683	6.63e-4	146.00	<.001
Alpha	-	Delta	0.00540	6.63e-4	8.14	<.001
Alpha	-	Theta	-0.02313	6.63e-4	-34.88	<.001
Beta	-	BetaHigh	0.03755	6.63e-4	56.61	<.001
Beta	-	Delta	-0.05388	6.63e-4	-81.24	<.001
Beta	-	Theta	-0.08241	6.63e-4	-124.26	<.001
BetaHigh	-	Delta	-0.09143	6.63e-4	-137.85	<.001
BetaHigh	-	Theta	-0.11996	6.63e-4	-180.87	<.001
Delta	-	Theta	-0.02853	6.63e-4	-43.02	<.001

More Analysis Underway...

EEG x fMRI Comparisons

Thank You!

Any QUESTIONS