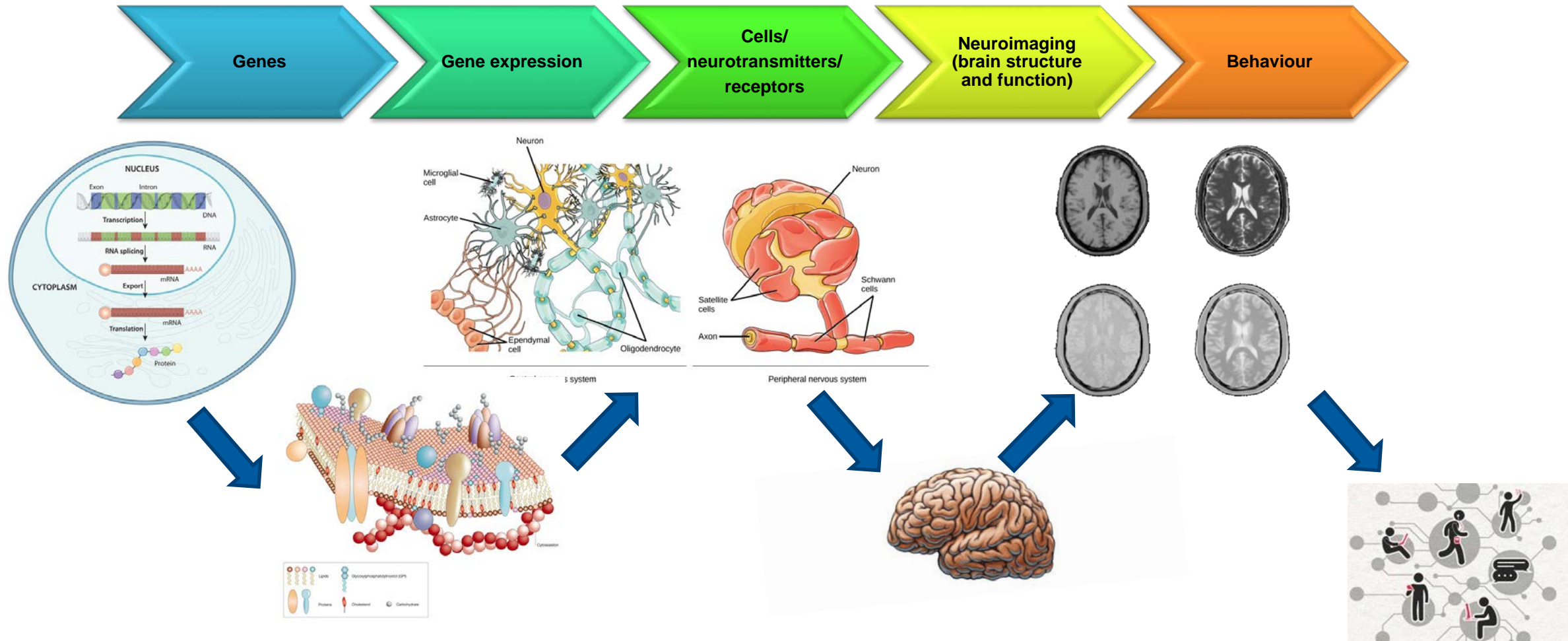


## Individualized assessment of resting state spatial activation patterns as a biomarker for Parkinson's disease

*Juergen Dukart*

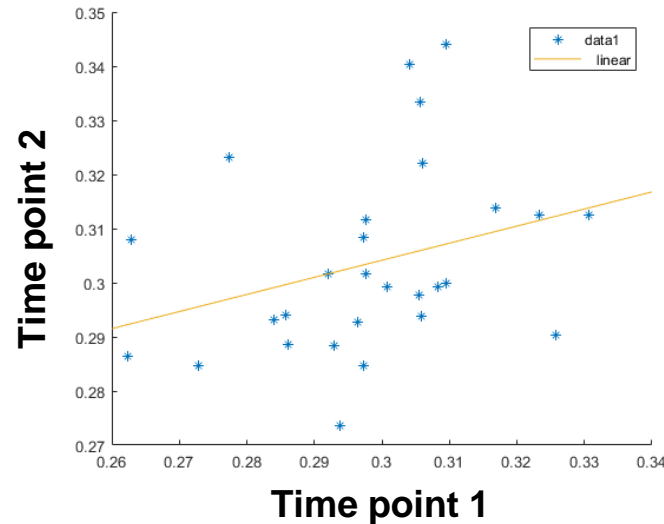
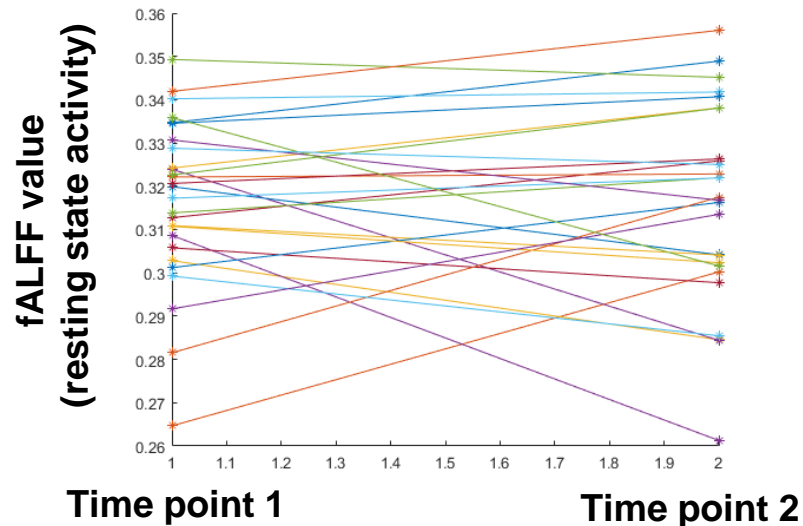
28.11.2019

# Ideally neuroimaging provides a link between biology and behaviour



# Generally rather low to fair reliability of region- and voxel-wise fMRI and rsfMRI analyses

Exemplary atlas region: ICC(reliability)=0.31

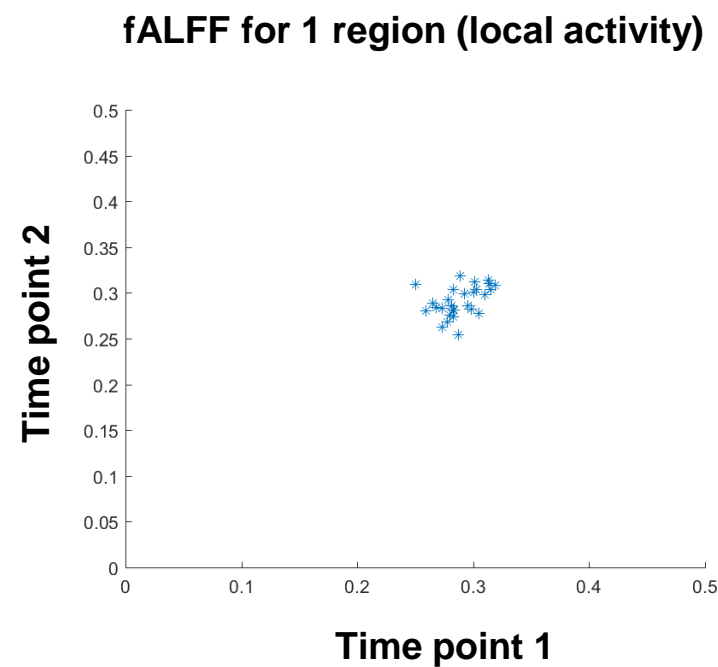


MID: Monetary Incentive Delay  
 ToM: Theory of Mind  
 FM: Emotional Face Matching  
 (f)ALFF: (fractional) Amplitude of low frequency fluctuations  
 ReHo: Regional Homogeneity  
 DC: Degree centrality  
 EC: Eigenvector centrality  
 CBF: Cerebral Blood Flow

Domain	Measure	Region-wise ICC Visit 1 to visit 2 median [ $P_5$ – $P_{95}$ ]
tb-fMRI	MID	0.70 [–0.00–0.88]
	N-back	0.38 [–0.09–0.68]
	ToM	0.42 [–0.09–0.69]
	FM	0.38 [–0.15–0.71]
rs-fMRI	Encoding	0.30 [–0.19–0.58]
	Recall	0.23 [–0.84–0.77]
	Recognition	0.48 [0.03–0.72]
	Go/no-go	–0.16 [–0.74–0.36]
	ALFF	0.72 [0.27–0.86]
	fALFF	0.57 [0.17–0.75]
ASL	ReHo	0.58 [0.21–0.78]
	DC	0.44 [–0.04–0.71]
	EC	0.36 [–0.15–0.67]
	Hurst	0.45 [0.18–0.64]
ASL	CBF	0.83 [0.42–0.91]

ICC criteria (Cicchetti, Domenic V. 1994):  
 Less than 0.40—poor.  
 Between 0.40 and 0.59—fair.  
 Between 0.60 and 0.74—good.  
 Between 0.75 and 1.00—excellent.  
 ICC – Intra-class correlation coefficient

# Within region reliability is rather moderate for most functional MRI measures

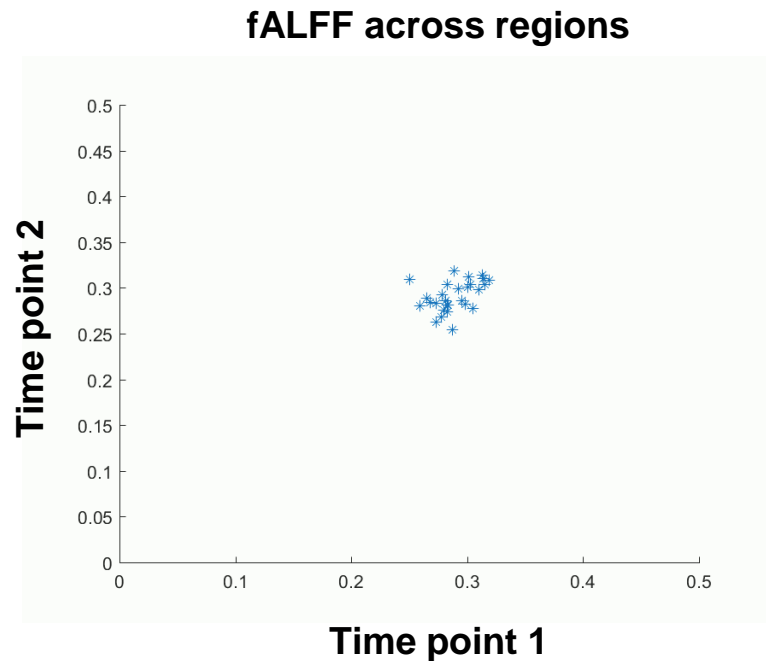


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		Visit 1 to visit 2 median [ $P_5$ – $P_{95}$ ]
Between ICC		
tb-fMRI	MID	0.70 [–0.00–0.88]
	N-back	0.38 [–0.09–0.68]
	ToM	0.42 [–0.09–0.69]
	FM	0.38 [–0.15–0.71]
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# Spatial reliability across regions is consistently higher than the reliability within each region for task-based fMRI and rsfMRI



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 ReHo: Regional Homogeneity  
 DC: Degree centrality  
 EC: Eigenvector centrality  
 CBF: Cerebral Blood Flow

		Visit 1 to visit 2 median [ $P_5$ – $P_{95}$ ] <b>Between ICC</b>	Visit 1 to visit 2 median [ $P_5$ – $P_{95}$ ] <b>Within ICC</b>
tb-fMRI	MID	0.70 [–0.00–0.88]	0.79 [–0.32–0.93]
	N-back	0.38 [–0.09–0.68]	0.81 [0.61–0.94]
	ToM	0.42 [–0.09–0.69]	0.58 [–0.10–0.83]
	FM	0.38 [–0.15–0.71]	0.80 [0.63–0.93]
	Encoding	0.30 [–0.19–0.58]	0.73 [0.47–0.94]
	Recall	0.23 [–0.84–0.77]	0.72 [0.25–0.89]
	Recognition	0.48 [0.03–0.72]	0.72 [0.48–0.86]
rs-fMRI	Go/no-go	–0.16 [–0.74–0.36]	0.24 [–1.11–0.66]
	ALFF	0.72 [0.27–0.86]	0.96 [0.73–0.98]
	fALFF	0.57 [0.17–0.75]	0.98 [0.95–0.99]
	ReHo	0.58 [0.21–0.78]	0.96 [0.86–0.98]
	DC	0.44 [–0.04–0.71]	0.89 [0.62–0.95]
	EC	0.36 [–0.15–0.67]	0.65 [0.19–0.92]
	Hurst	0.45 [0.18–0.64]	0.92 [0.77–0.96]
ASL	CBF	0.83 [0.42–0.91]	0.96 [0.91–0.98]

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Less than 0.40—poor.

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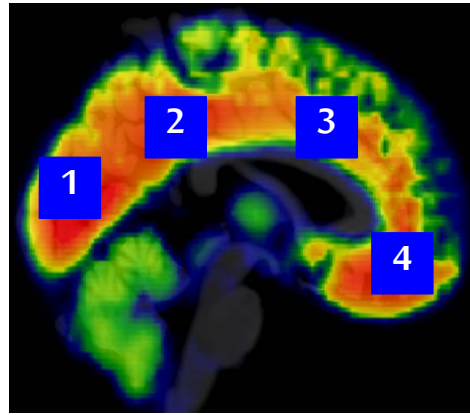
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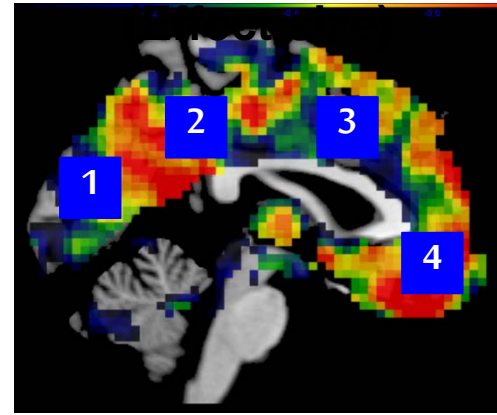
# Pharmacodynamic mapping of drug receptor profiles using Cerebral Blood Flow – Illustration of the concept

Correlating spatial profiles of receptor densities and drug/disease effects

Receptor density



Disease/ drug effect

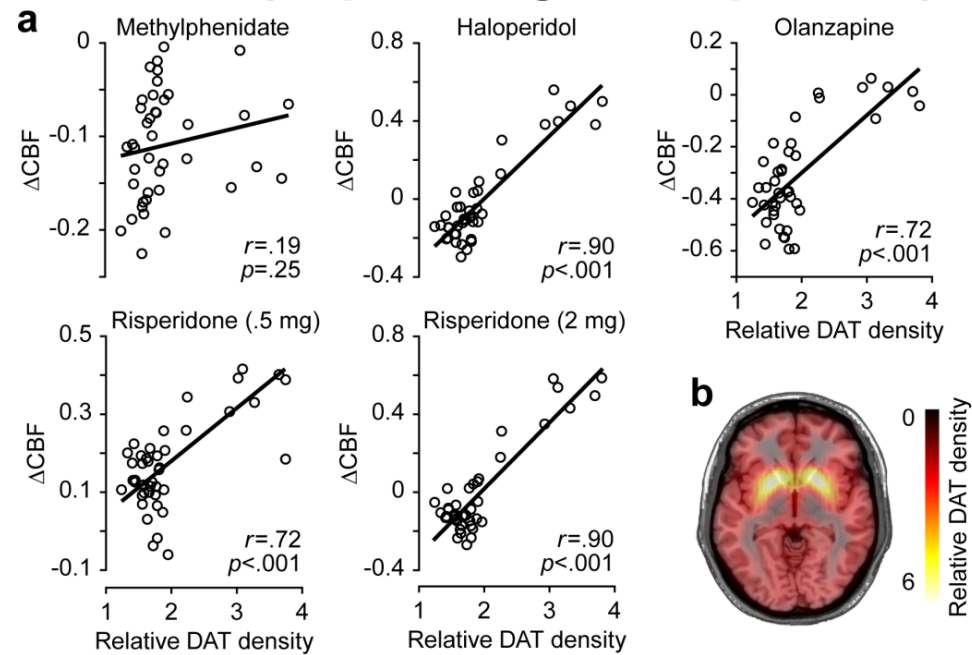


Correlations



# Spatial patterns of resting state regional activity are predictive of the underlying mechanism of action of respective compounds

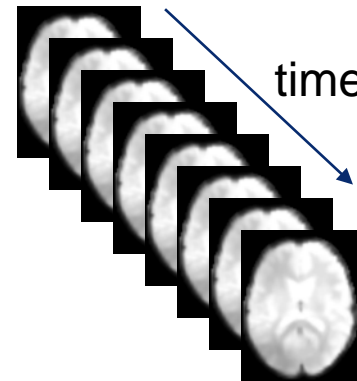
## Correlations with in vivo receptor density estimates (dopamine compounds)



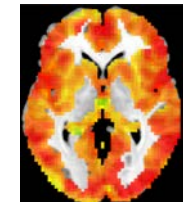
# Study design – applying the spatial correlation approach to Parkinson's patients resting state fMRI data

Group	PD patients	Healthy controls
N	30	30
Age (mean±SD [range])	64.6±7.7 [46-82]	63.5±7.9 [46-83]
sex (male/female)	13/17	15/15
UPDRS total off (mean±SD [range])	45.3±15.0 [11-95]	-
UPDRS total on (mean±SD [range])	23.9±10.6 [5-47]	-
UPDRS I off (mean±SD [range])	1.6±1.7 [0-7]	-
UPDRS I on (mean±SD [range])	1.5±1.7 [0-7]	-
UPDRS II off (mean±SD [range])	13.1±6.4 [3-31]	-
UPDRS II on (mean±SD [range])	7.7±4.8 [0-17]	-
UPDRS III off (mean±SD [range])	30.6±9.9 [8-64]	-
UPDRS III on (mean±SD [range])	14.7±7.5 [4-31]	-

Resting state BOLD



Fractional Amplitude of  
Low Frequency fluctuations  
(fALFF)

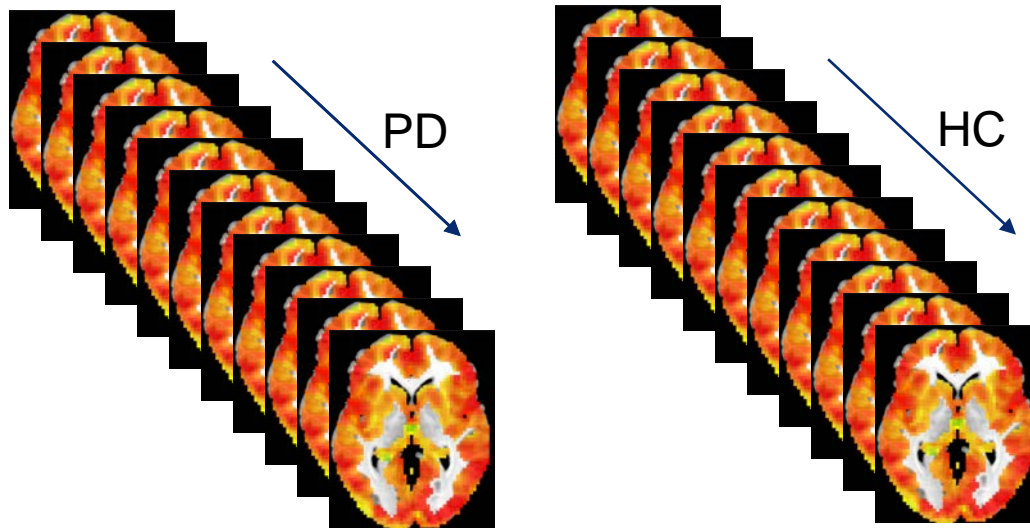


- PD patients scanned on and off levodopa



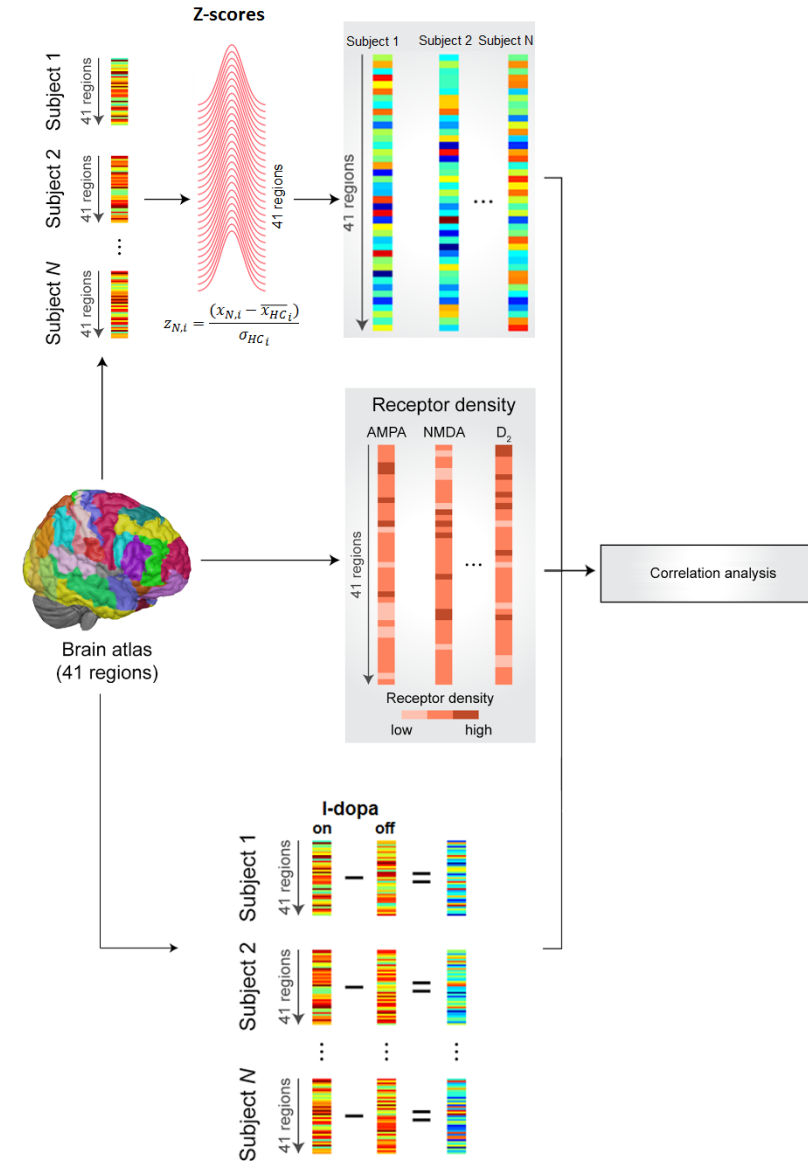
# Statistical analyses

1.



Voxel-wise group  
comparisons of fALFF maps

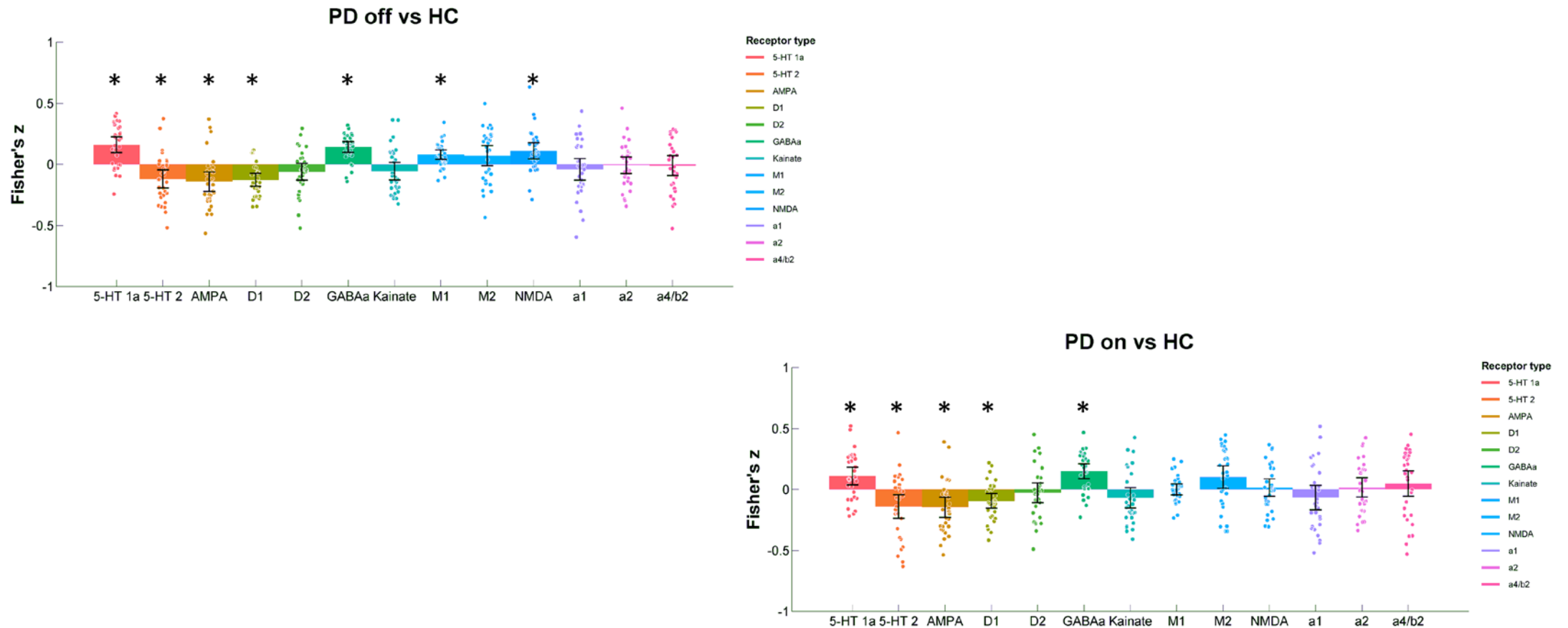
2.



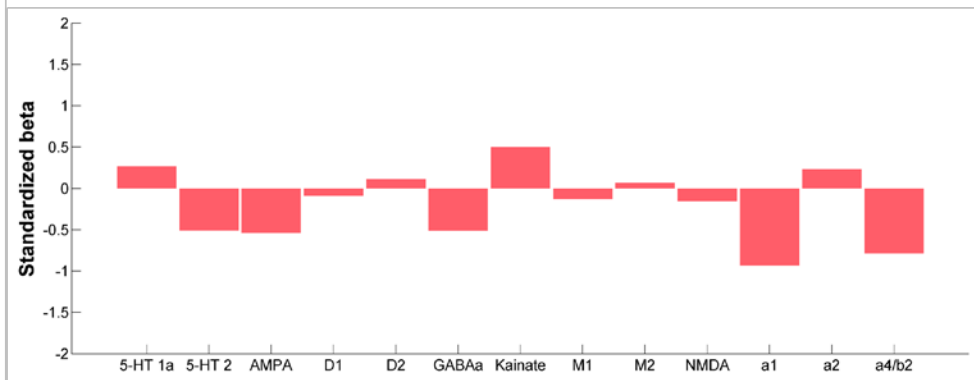
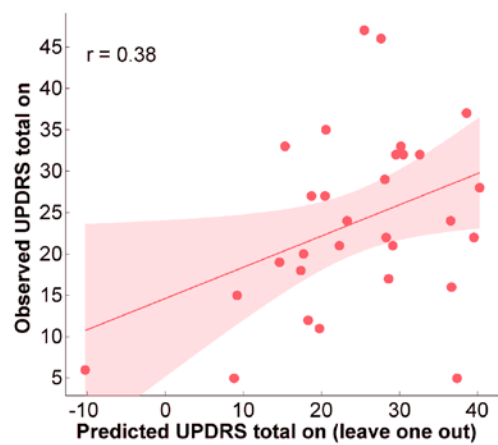
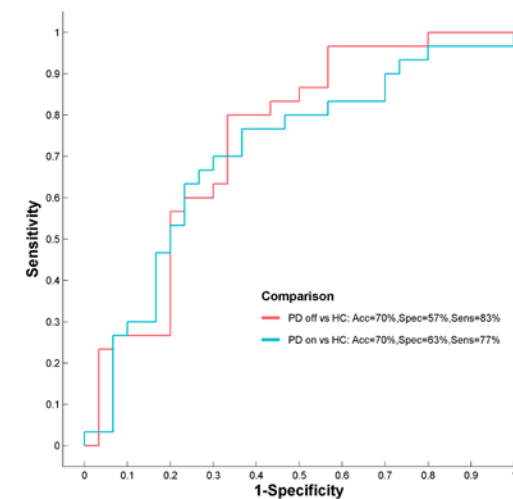
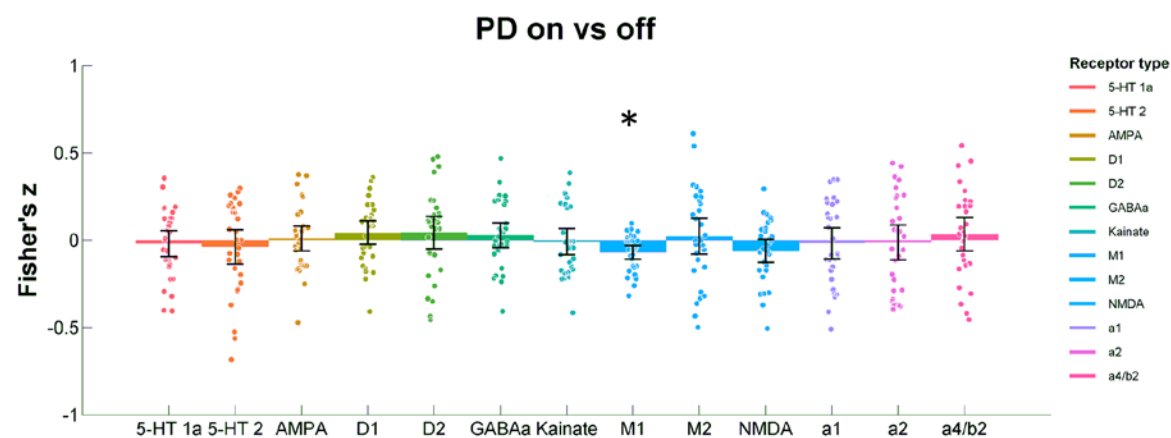
# Results – significant differences in spatial correlation but not in voxel-wise analyses

1. No significant differences between PD and HC in voxel-wise group comparisons

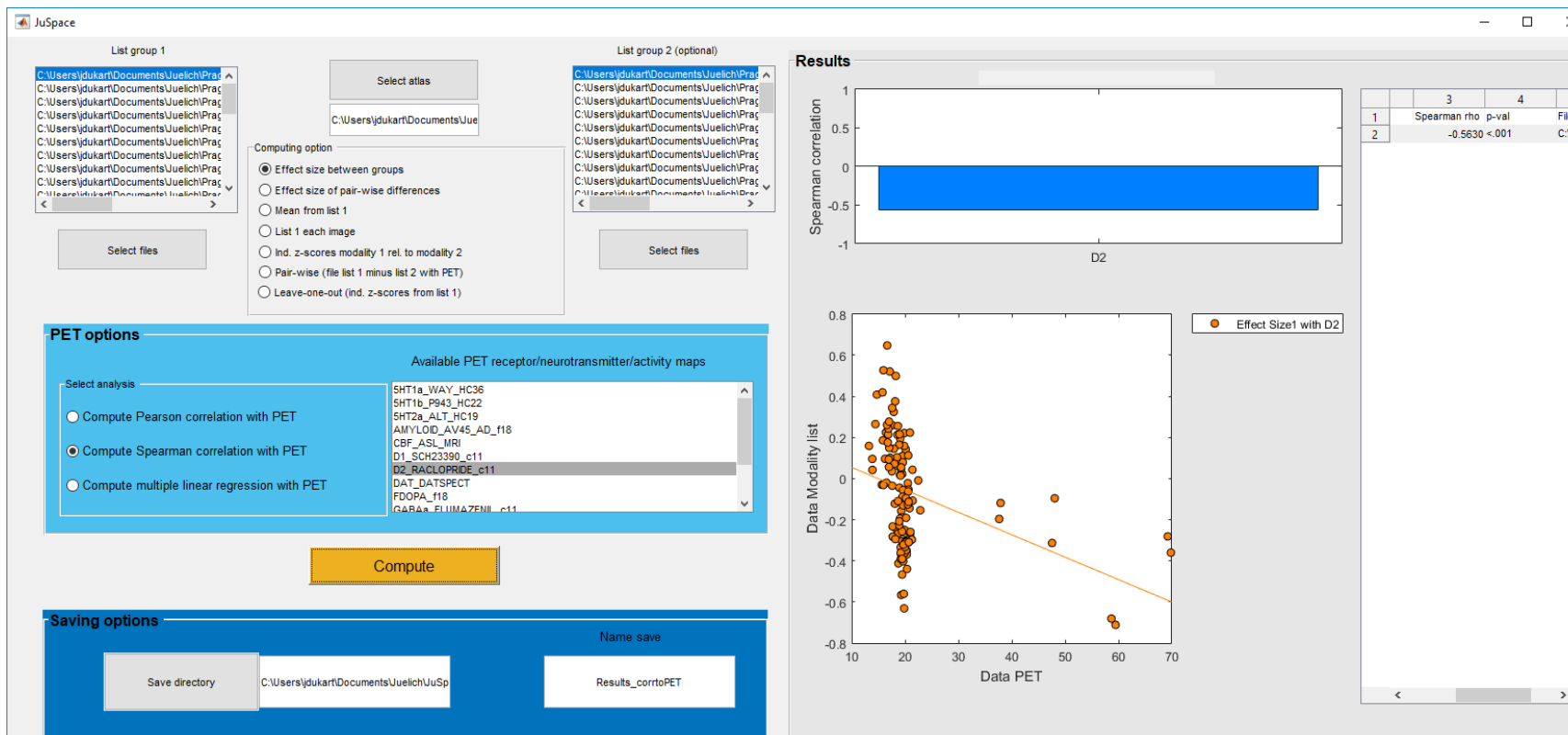
2.



# Results



# JuSpace: A tool for spatial correlation analyses of functional and structural neuroimaging data with positron emission tomography derived receptor maps



Available maps	Description
5HT1a	Serotonin system
5HT1b	Serotonin system
5HT2a	Serotonin system
AMYLOID	Alzheimer's pathology
CBF	Resting state activity in healthy
D1	Dopamine system
D2	Dopamine system
DAT	Dopamine system
FDOPA	Dopamine system
GABAA	GABA system
NAT	Noradrenaline
SERT	Serotonin system
TAU	Alzheimer's pathology

# Key features

- ❖ **Allows for cross-modal correlation (Pearson/Spearman/multiple linear regression) of PET and (rs-f)MRI data**
- ❖ **Supports within and between subject designs**
- ❖ **Group- and individual subject level data**

# Conclusions

- PD patients show distinct spatial patterns of resting state alterations that match the distribution of several neurotransmitter systems (including dopamine and serotonin)
- The JuSpace tool provides the possibility to link individual subject and group level data to underlying receptor maps
- The proposed spatial correlation approach provides results that are better interpretable in terms of underlying biology
- Substantially increases the reliability of rs/fMRI analyses as compared to “classical” voxel- or region-based approaches





**THANK YOU FOR YOUR ATTENTION!**