BOLD variability and normative modelling feature construction for prediction in mental health

FOR 5187 PREACT

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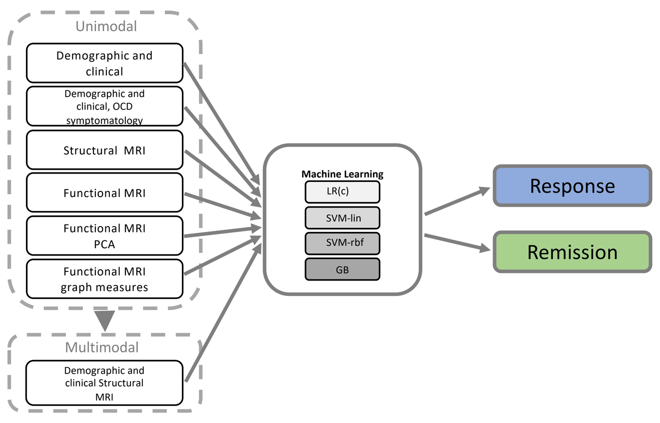
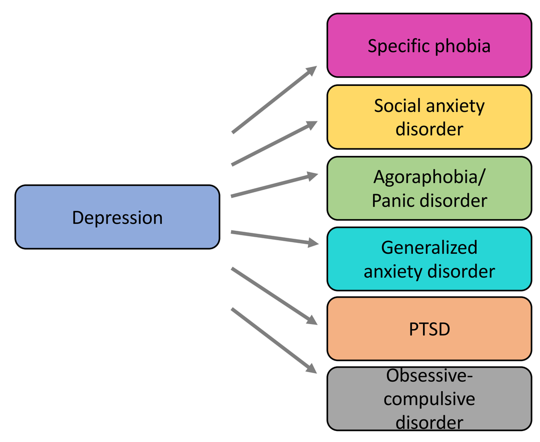
PREACT subproject 9

Generalizing predictive patterns of treatment (non-) response: from **specific phobia** and **obsessive-compulsive disorder** to the **anxiety spectrum**

Generalization | Transdiagnostic



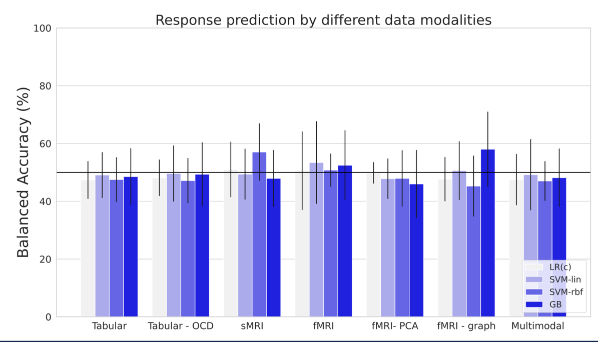
Cross-diagnostic generalization within PREACT



Nested CV
- 7 outer folds, 5 inner folds
- 10 repeats with different seeds for training/test splits

Motivation

EPOC dataset



- CBT treatment response prediction in OCD is at chance level
- MRI and fMRI features for treatment prediction neccesitate further development

Normative modelling

- Schizophrenia and MDD prediction based on structural MRI normative modelling features outperforms classification with raw MRI features (Rutherford et al., 2023; Shao et al., 2024)
- Normative modelling of resting-state functional connectivity differentiates subgroups of MDD patients (Sun et al., 2023)

BOLD variability

- Task-based BOLD variability outperforms self-reports and mean BOLD fMRI for treatment outcome prediction (Mansson et al., 2022)
- Resting-state fronto-limbic BOLD variability correlates with emotion regulation across psychiatric disorders (Kebets et al., 2021)
- Resting-state BOLD variability displays transdiagnostic patters across schizophrenia, MDD and bipolar disorder (Wei et al., 2023)

ML prediction of treatment response and OCD diagnosis with normative modelling and BOLD variability features

Feature construction

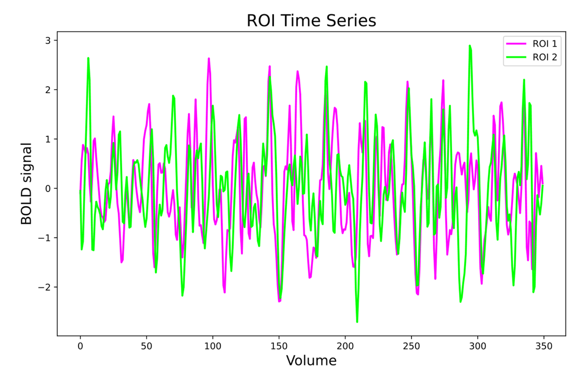
Normative modelling

- Pretrained normative models available for structural MRI and fMRI (Rutherford et al., 2023)
- Structural MRI models
  - 57.000 subjects across 82 sites
  - 187 features based on Destrieux atlas
  - Cortical thickness and subcortical volume
- Functional MRI models
  - 22.000 subjects across 40 sites
  - 136 features from Yeo 17 networks atlas
  - Resting-state functional connectivity across 17 network ROIs

Model fitting
- 50% of data used for adaptation of the pretrained models to our data site
- Remaining 50% of data used for normative modelling
- One normative model fit for each of the 187 / 136 ROIs (structural / functional)
- Normative model deviation scores used as input to ML pipeline

BOLD variability

- Resting-state functional MRI run with 350 volumes
- Head-motion, slice-timing and distortion corrected, smoothed 7mm FWHM kernel, detrended, low-pass and high-pass filtered
- Standard deviation (SD) over 350 volumes
- Schäfer atlas 200 ROI parcellation
- Yeo 17 networks atlas with each network treated as an ROI
- ROI SD values used as input to ML pipeline

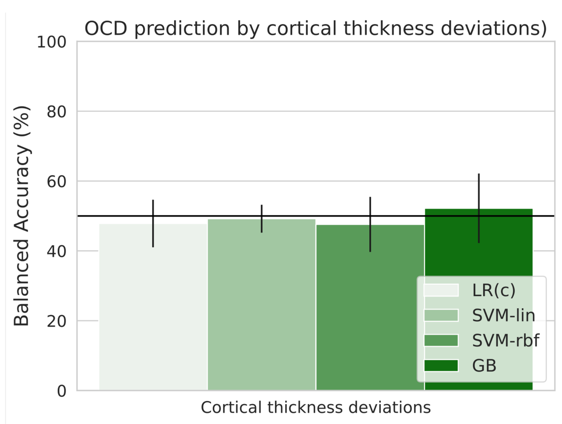


SD ROI 1
SD ROI 2

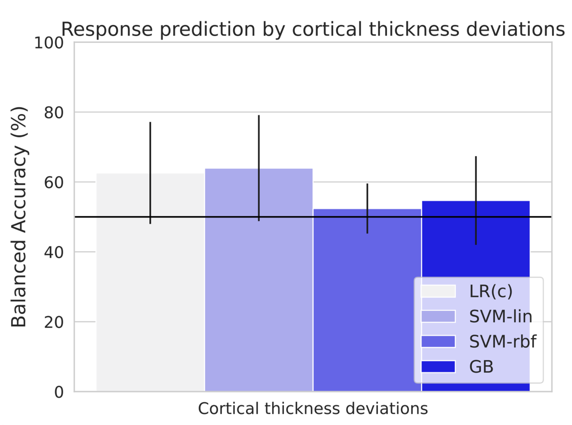
Results

Normative modelling structural MRI

OCD diagnosis

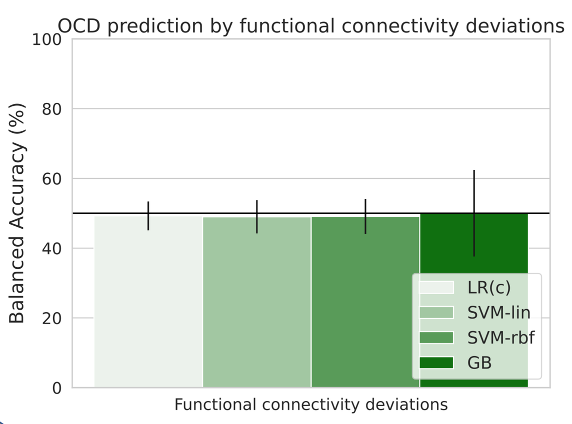


Treatment response

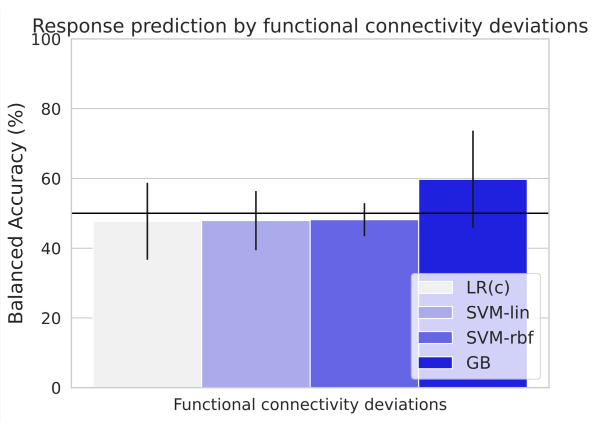


Normative modelling resting-state functional connectivity

OCD diagnosis



Treatment response



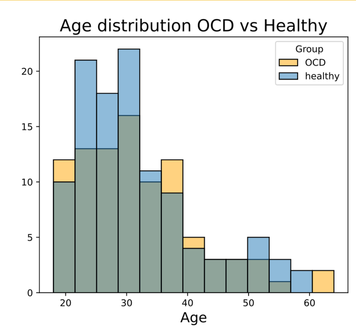
Correlation with symptom severity

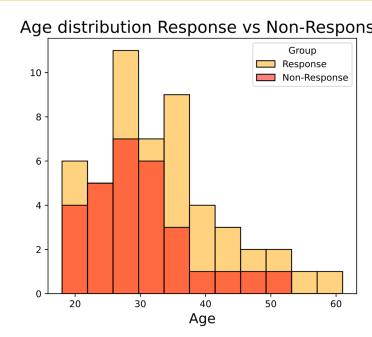
ROI	r	pval	pval_Bonf
LimbicA_LimbicB_Z_predict	0.24	0.02	0.66
LimbicA_ControlC_Z_predict	0.09	0.4	11.28
LimbicA_ControlA_Z_predict	0.1	0.37	10.28
LimbicA_ControlB_Z_predict	0.12	0.26	7.23
LimbicA_DefaultC_Z_predict	0.15	0.17	4.75
LimbicA_DefaultA_Z_predict	0.24	0.02	0.69
LimbicA_DefaultB_Z_predict	0.18	0.08	2.32
LimbicB_ControlC_Z_predict	0.05	0.63	17.51
LimbicB_ControlA_Z_predict	0.07	0.53	14.73
LimbicB_ControlB_Z_predict	-0.07	0.49	13.62
LimbicB_DefaultC_Z_predict	0.04	0.67	18.89
LimbicB_DefaultA_Z_predict	-0.09	0.39	10.92
LimbicB_DefaultB_Z_predict	-0.04	0.7	19.71
ControlA_ControlC_Z_predict	0.08	0.48	13.42
ControlB_ControlC_Z_predict	0.18	0.09	2.45
ControlC_DefaultC_Z_predict	-0.01	0.96	26.81
ControlC_DefaultA_Z_predict	0.06	0.56	15.66
ControlC_DefaultB_Z_predict	0.07	0.48	13.46
ControlA_ControlB_Z_predict	0.14	0.18	5.15
ControlA_DefaultC_Z_predict	0.04	0.71	19.78
ControlA_DefaultA_Z_predict	0.03	0.78	21.74
ControlA_DefaultB_Z_predict	0.12	0.27	7.64
ControlB_DefaultC_Z_predict	0.04	0.7	19.66
ControlB_DefaultA_Z_predict	-0.08	0.47	13.14
ControlB_DefaultB_Z_predict	0.02	0.88	24.75
DefaultA_DefaultC_Z_predict	0.16	0.13	3.53
DefaultB_DefaultC_Z_predict	0.16	0.13	3.77
DefaultA_DefaultB_Z_predict	0.07	0.52	14.63

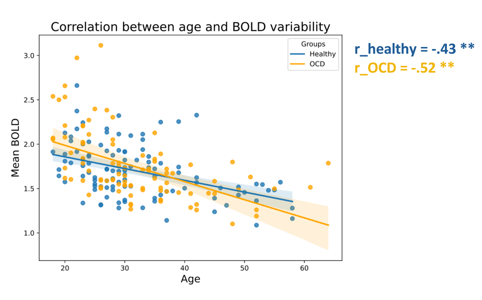
Limbic ROI connectivity deviations relate to symptom severity (not Bonferroni corrected) in OCD patients

BOLD variability

Age distribution and correlation with age







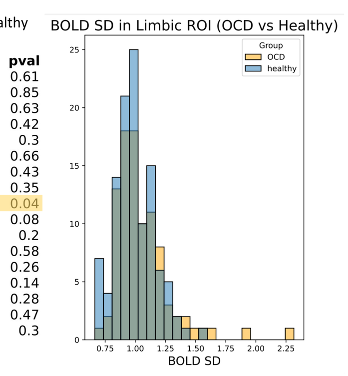
BOLD variability is negatively correlated with age in both healthy subjects and OCD patients

SD BOLD group differences - OCD patients & healthy controls -

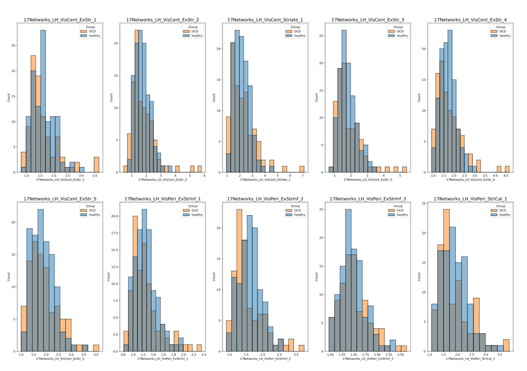
Yeo 17 networks ROIs

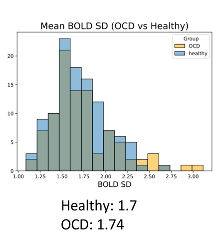
BOLD SD t-test for OCD vs Healthy

ROI	pval
Visual Central (Visual A)	0.61
Visual Peripheral (Visual B)	0.85
Somatomotor A	0.63
Somatomotor B	0.42
Dorsal Attention A	0.3
Dorsal Attention B	0.66
Salience / Ventral Attention A	0.43
Salience / Ventral Attention B	0.35
Limbic A	0.04
Limbic B	0.08
Control C	0.2
Control A	0.58
Control B	0.26
Temporal Parietal	0.14
Default C	0.28
Default A	0.47
Default B	0.3



Schäfer 200 ROIs

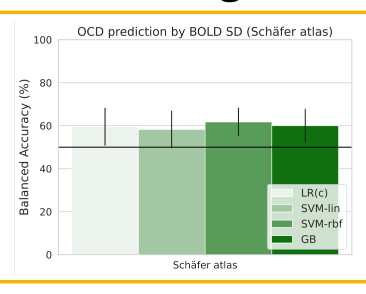




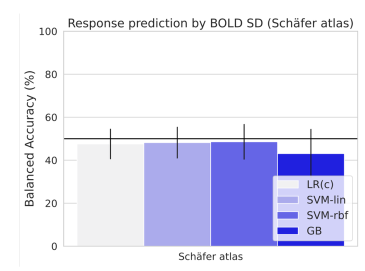
Limbic network as possible predictor in PREACT data analysis

BOLD variability ML prediction

OCD diagnosis



Treatment response



Discussion & future work

- Normative modelling and resting-state BOLD variability features were not predictive of OCD diagnosis or treatment response, but point to limbic ROIs as feature selection targets in the PREACT dataset
- Normative modelling features show more promise for treatment response prediction while resting-state BOLD variability have more potential for OCD diagnosis prediction
- Limbic network functional connectivity deviation scores correlate with OCD symptom severity on an uncorrected significance level and limbic network BOLD variability differs between OCD patients and healthy controls on an uncorrected significance level

Further research
- Do features that differentiate OCD and healthy cohorts differ from features that are predictive of treatment outcome?
- Can we build predictive features for treatment response from normative modelling on BOLD variability?

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