Prediction of response to cognitive-behavioral therapy in obsessive-compulsive disorder: a multivariate analysis of resting state functional connectivity

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Background

- Cognitive-behavioral therapy (CBT) is effective for many for reducing symptoms of obsessive-compulsive disorder (OCD), although the response still varies significantly between individuals.
- Specialized CBT for OCD is limited in availability, expensive, stressful, and time-consuming.
- This underscores the importance of developing reliable predictors of response to treatment to help with clinical decision-making.
- Several studies have examined clinical and neurobiological features pretreatment that are correlated with response to treatment.²³ Only one has examined functional connectivity as a predictor,4 and none have applied multivariate approaches.
- We used a multivariate pattern recognition approach applied to resting state functional connectivity pre-CBT in order to make predictive inferences on the individual patient level, as to their degree of response to treatment.
- We applied the same approaches to pre-treatment symptomatology in order to further elucidate mechanisms of functional connectivity associated with obsessions and compulsions.

Success with CBT varies. The ability to use insights from a patient's neural activity patterns to predict their response could help adjust our approach or seek alternative treatment methods – saving patients time, money, and energy.

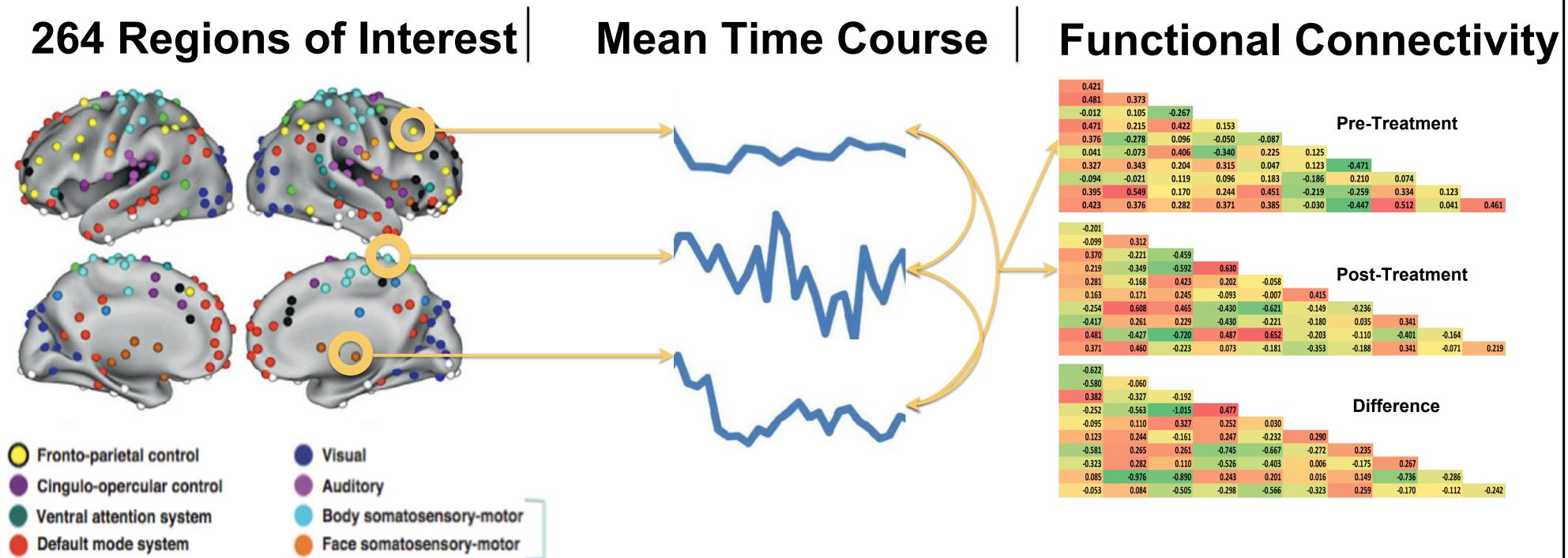
Methods

7 a priori networks of interest

- Participants: 43 medicated and unmedicated adults with OCD.
- Treatment: intensive, daily individual exposure and response prevention (a type of CBT) for 4 weeks: 90 min/day.
- Resting state functional magnetic resonance image BOLD data before and treatment, and T1-weighted anatomical scans.
- OCD symptomatology measured using the Yale-Brown Obsessive Compulsive Scale (YBOCS).
- Image preprocessing: parcellation of the brain into 264 ROIs, each belonging to one of 14 functional networks previously derived from metaanalyses of functional studies.⁵
- Pearson-correlation matrix for each mean time course resulted in a 264 x 264 matrix containing the pairwise functional connectivity values (r-values) across all ROIs.
- Matrix cells corresponding to each functional network were identified to create feature sets.
- Leave-one-patient-out cross-validation to assess the predictive power of our feature sets in regards to our behavioral measures of interest: preand post-CBT YBOCS scores and the change in YBOCS scores from pre- to post-CBT.
 - Least absolute shrinkage and selection operator (LASSO) regression model trained on n-1 patients using their feature sets.
- Correlated the predicted values with the actual values in order to yield a multiple R^2 as a measure of our model's feature-dependent predictivity.

- Widely-used measure of severity of obsessions and compulsions in OCD
- Range: 0-40. 5 items index obsession severity; 5 items index compulsion severity

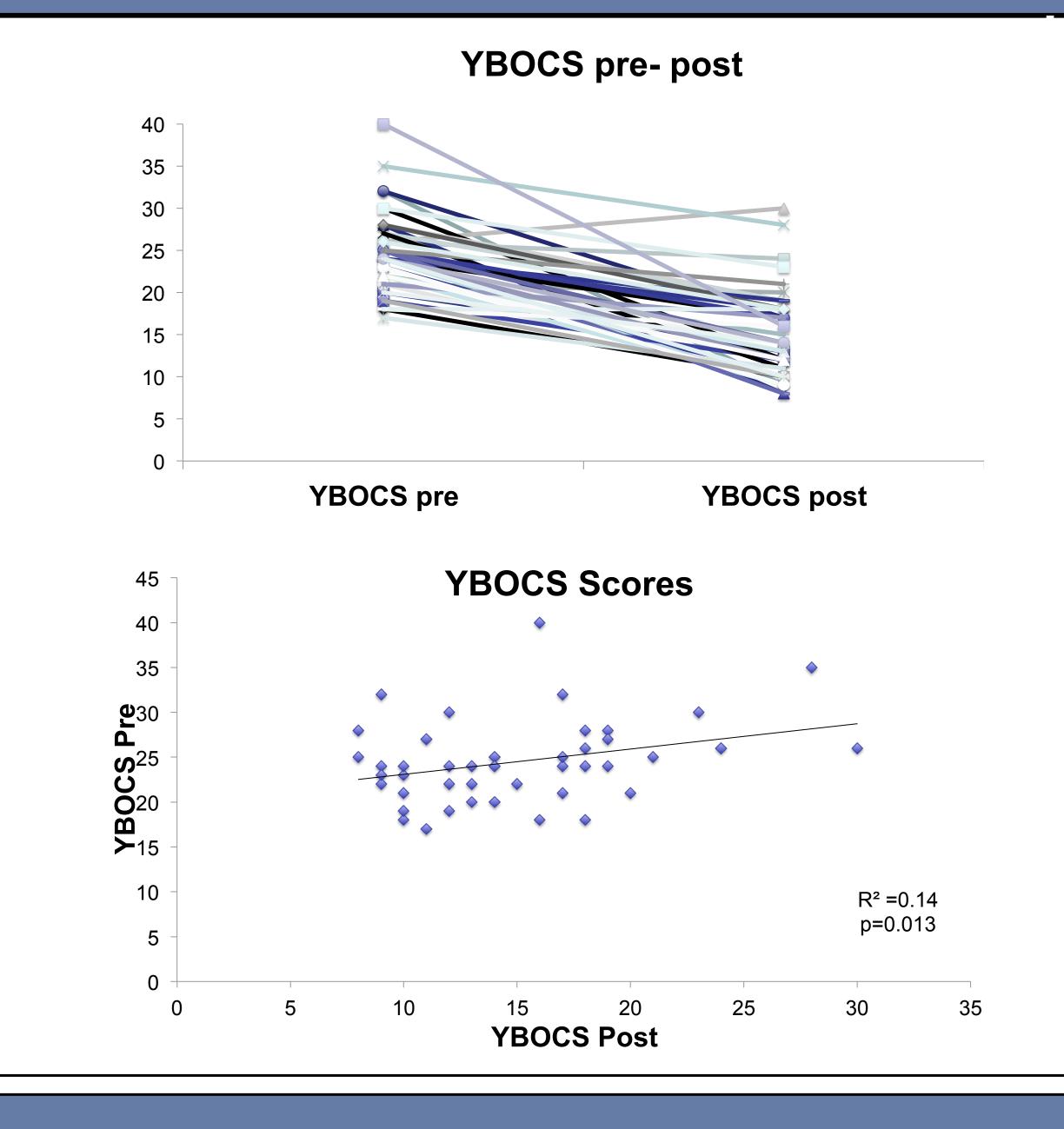
YBOCS (Yale-Brown Obsessive Compulsive Scale)

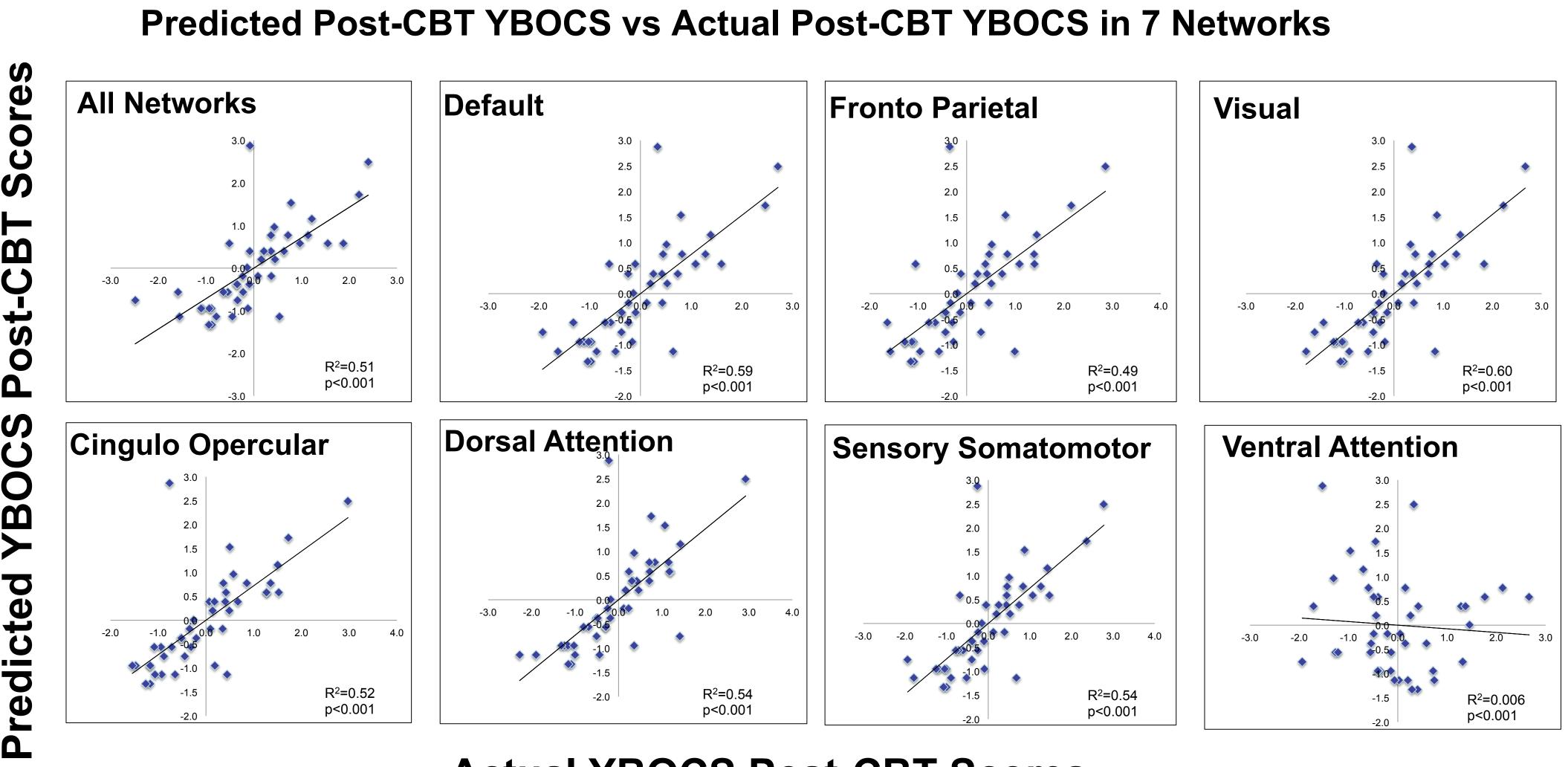


Results

Characteristics	OCD (N=43)		
	value	SD	P Value
Female/male	21/22		
Age	33	10.7	
Education, years	15.6	2.4	
WASI IQ	108.2	9.1	
GAS	57.6	8.5	
Number on serotonin-reuptake inhibitor	14		
Number with psychiatric comorbidities:	31		
Number without psychiatric comorbidities:	12		
YBOCS total pre-CBT	24.5	4.7	
YBOCS total post-CBT	15.0	5.2	<0.0011
YBOCS Obsessions (1-5) pre-CBT	11.9	2.7	
YBOCS Obsessions (1-5) post-CBT	7.9	3.1	<0.0011
YBOCS Compulsions (6-10) pre-CBT	12.6	2.2	
YBOCS Compulsions (6-10) post-CBT	7.0	2.7	<0.0011
HAMA pre-CBT	12.4	5.4	
HAMA post-CBT	8.4	5.1	<0.0011
MADRS pre-CBT	15.3	9.5	
MADRS post-CBT	10.8	8.9	<0.0011
GAS pre-CBT	57.6	8.5	
GAS post-CBT	69.6	13.3	<0.0011

¹Paired t-test, comparing pre- versus post-CBT





Actual YBOCS Post-CBT Scores

- OCD symptoms improved with CBT; YBOCS decreased on average by 39%.
- YBOCS post-treatment scores are strongly predicted by pre-treatment connectivity in multiple networks combined with pre-treatment YBOCS scores.
- Pre-treatment connectivity is more predictive of YBOCS post-treatment scores than is pre-treatment YBOCS alone.
- Post treatment connectivity shows strong relationship with residual symptom severity (data not shown).

Conclusions

- This represents the first study in OCD to use multivariate pattern recognition approaches to determine neurobiological markers predictive of response to treatment.
- The combination of strength of functional connectivity in multiple networks and pre-treatment OCD symptom severity are highly predictive of symptom severity after intensive CBT.
- Pre-treatment OCD symptom severity by itself is only moderately predictive of symptom severity after treatment, and adding pre-treatment OCD symptoms as a feature only marginally improved the predictive ability beyond network connectivity alone. Thus, brain connectivity may be a more useful prognostic biomarker for response to treatment than patients' subjective reports of symptoms.
- Results have clinical implications for identifying individual OCD patients who will maximally benefit from treatment with intensive CBT, and have implications for further understanding the pathophysiology of OCD.

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