

Clinical Predictors of Response to *Pharmacological Interventions* in OBSESSIVE-COMPULSIVE DISORDER

CAN WE PREDICT WHO IS GOING TO BENEFIT FROM INTERVENTIONS?

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Clinical Predictors of Response to Pharmacological Interventions in OBSESSIVE-COMPULSIVE DISORDER

▶ OBJECTIVES

- Review the literature of predictors of response to SRI treatment in OCD
- Present the results of a post hoc analysis with data from our research group
- Discuss which conclusions can be drawn from the results reported so far

Clinical Predictors of Response to Pharmacological Interventions in OBSESSIVE-COMPULSIVE DISORDER

- ▶ Why do we need clinical predictors of response?
 - ▶ Insufficient response is common in OCD
(**60%** Pallanti et al., 2002; **70%** Belotto-Silva et al., 2012)
 - ▶ Non-responders suffer continued burden and might require additional treatment resources
(**Refractory OCD Burden** Ferrão et al., 2006; **Limitations of current treatment options** Declodt and Stein, 2010)
 - ▶ Predicting response may help treatment planning, tailoring and best allocation of resources for those most in need
(**Symptoms subtypes and CBTxSSRI** Starcevic & Brakoulias 2008; **Tic disorders and response to anti-psychotic augmentation** Bloch et al., 2006; **Psychotic spectrum and response to antipsychotic augmentation** McDougle et al., 1994)

Which factors are potential clinical predictors of response?

- ▶ **Baseline Functioning**

Social and Family Functioning, Marital Status

- ▶ **Personality**

Traits and comorbid Axis II diagnosis

- ▶ **Symptoms profile**

Age at onset, Duration, OCD symptoms dimensions, Sensory Phenomena and Insight

- ▶ **Family history**

OCD in 1st degree relatives

- ▶ **Accompanying disorders**

Mood disorders, anxiety disorders (social phobia), Impulse control disorders

- ▶ **History of treatment response**

Absence of previous failed treatment trials, initial improvement with treatment

Worse Outcome



- ▶ **Poor social and family functioning at treatment initiation** (Tukel et al., 2006)
- ▶ **Single Marital Status** (Shavitt et al. 2006)

Worse Outcome

- ▶ **Obsessive-compulsive Personality Disorder** (Cavedini et al., 2007)
Comorbid OCPD full diagnosis
- ▶ **Positive Schizotypal Symptoms** (Moritz et al., 2004 and Ravizza, 1995)
Schizotypal personality questionnaire
Comorbid Schizotypal personality disorder
- ▶ **Low Cloninger's self-directedness (TCI)** (Corchs et al., 2008)
Defined as the ability of an individual to control, regulate, and adapt behavior to fit the situation according to individually chosen goals and values
- ▶ **Lower motivation to change** (Pinto et al., 2007)
As measured by the University of Rhode Island Change Assessment (URICA)

Worse Outcome

- ▶ **Higher baseline severity** (Alarcon et al., 1993, Kim et al., 2011 and Eisen et al., 2010)
Based on the YBOCS score
- ▶ **Longer illness duration** (Ravizza et al., 1995 and Jakubovski et al., 2012)
- ▶ **Earlier age at onset** (Ackerman et al., 1994)
- ▶ **Less frequent sensory phenomena** (Shavitt et al., 2006)

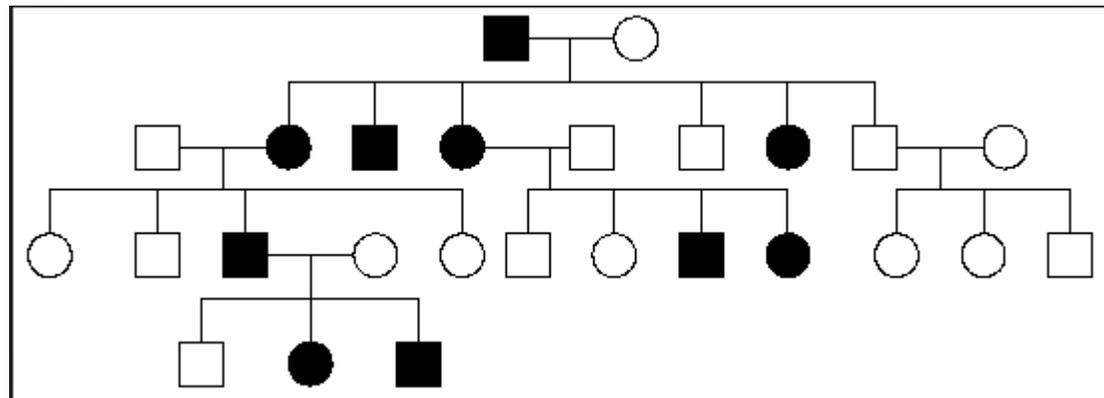


Worse Outcome

- ▶ **Hoarding** (Mataix-Cols et al., 1999, Black et al., 1998 and Stein et al., 2008)
 - Out of a five factor solution for the YBOCS SC
 - Out of the Maudsley Obsessive-Compulsive Inventory
 - Out of a five factor solution for the YBOCS SC (Hoarding/symmetry symptom dimension)
- ▶ **Lack of major symptoms of the sexual/religious/harm-related/checking dimensions** (Landeros-Wiesenberger et al., 2010)
 - Out of a four factor solution

Worse Outcome

- ▶ **Lower insight** (Catapano et al., 2010, Ravi Kishore et al., 2004 and Erzegovesi et al., 2001)
As measured by The Brown Assessment of Beliefs Scale (BABS)
- ▶ **Lower frequency of positive family history for OCD in first degree relatives** (Erzegovesi et al., 2001)



Worse Outcome

- ▶ **Generalized Social Phobia** (Carrasco et al., 1992 and Belotto-Silva et al., 2012)
- ▶ **Major Depression** (Belotto-Silva et al., 2012, Shetti et al., 2005, Jakubovski et al., 2012 and Marks et al., 2011)
- ▶ **Impulse Control Disorders** (Fontenelle et al., 2005)
Defined as the impulse control disorders not elsewhere classified of the DSM-IV plus alcohol and drug dependence, paraphilias and bulimia nervosa/binge eating disorder
- ▶ **Number of psychiatric comorbidities** (Belotto-Silva et al., 2012)

Better Outcome and Treatment-Related Factors

- ▶ **Absence of previous failed treatment trials** (Denys et al., 2003 and Ackerman et al., 1998)
- ▶ **Previous history of symptom remission with treatment** (Ackerman et al., 1998)
- ▶ **Higher intensity of initial side effects** (Ackerman et al., 1996 and 1998)
- ▶ **Early improvement with treatment** (Ackerman et al., 1996)

Early Improvement as a Predictor of Outcome: *METHODS*

Post hoc analysis (Belotto-Silva et al., 2012 and Diniz et al., 2011)

145 DSM-IV-defined OCD patients

12-week SRI trial (mainly fluoxetine)

Broad Inclusion Criteria

YBOCS

Early Improvement as a Predictor of Outcome: *STATISTICAL ANALYSIS*

- ▶ Sensitivity/Specificity for different cut-offs
- ▶ Stepwise logistic regression model controlled for:
 - ▶ sex
 - ▶ current age
 - ▶ marital status
 - ▶ educational level
 - ▶ age at OCD symptoms onset
 - ▶ socioeconomic status
 - ▶ baseline Y-BOCS score
 - ▶ DY-BOCS scores (symptoms subtypes)
 - ▶ BDI and BAI scores (depression and anxiety severity)
 - ▶ the presence of Axis I comorbid disorders

In the logistic regression model, the only variable that remained associated with treatment response was early improvement (OR=1.05, $p < 0.0001$).

Improvement at the 4th week

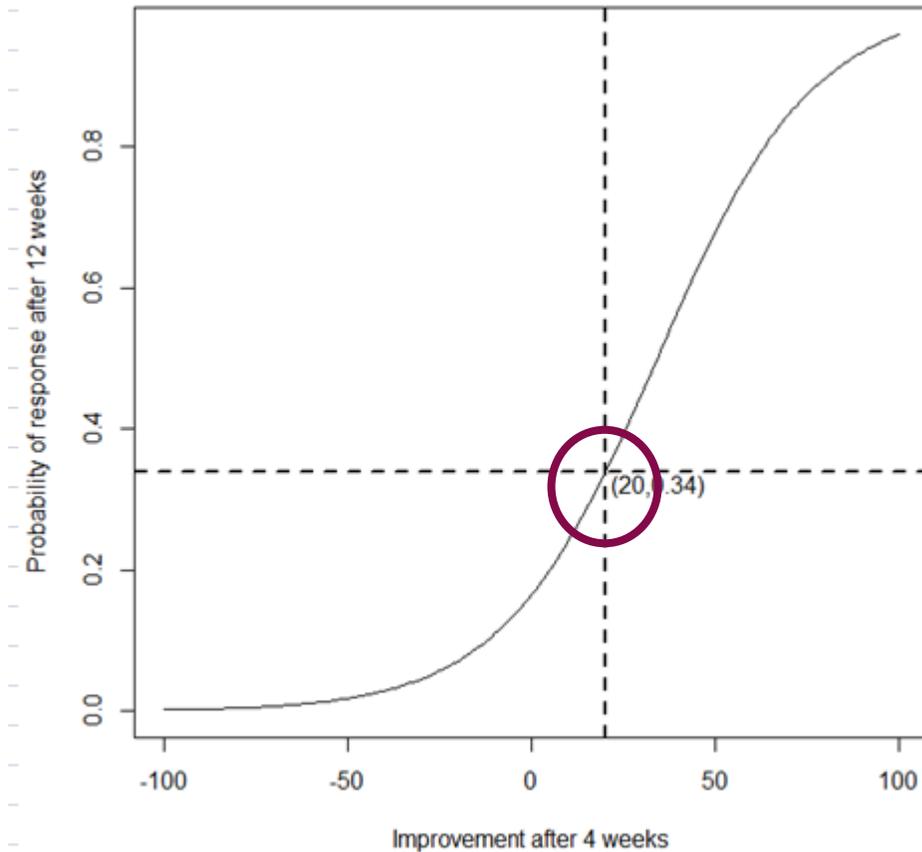
20% Cut-off

Non-improvers

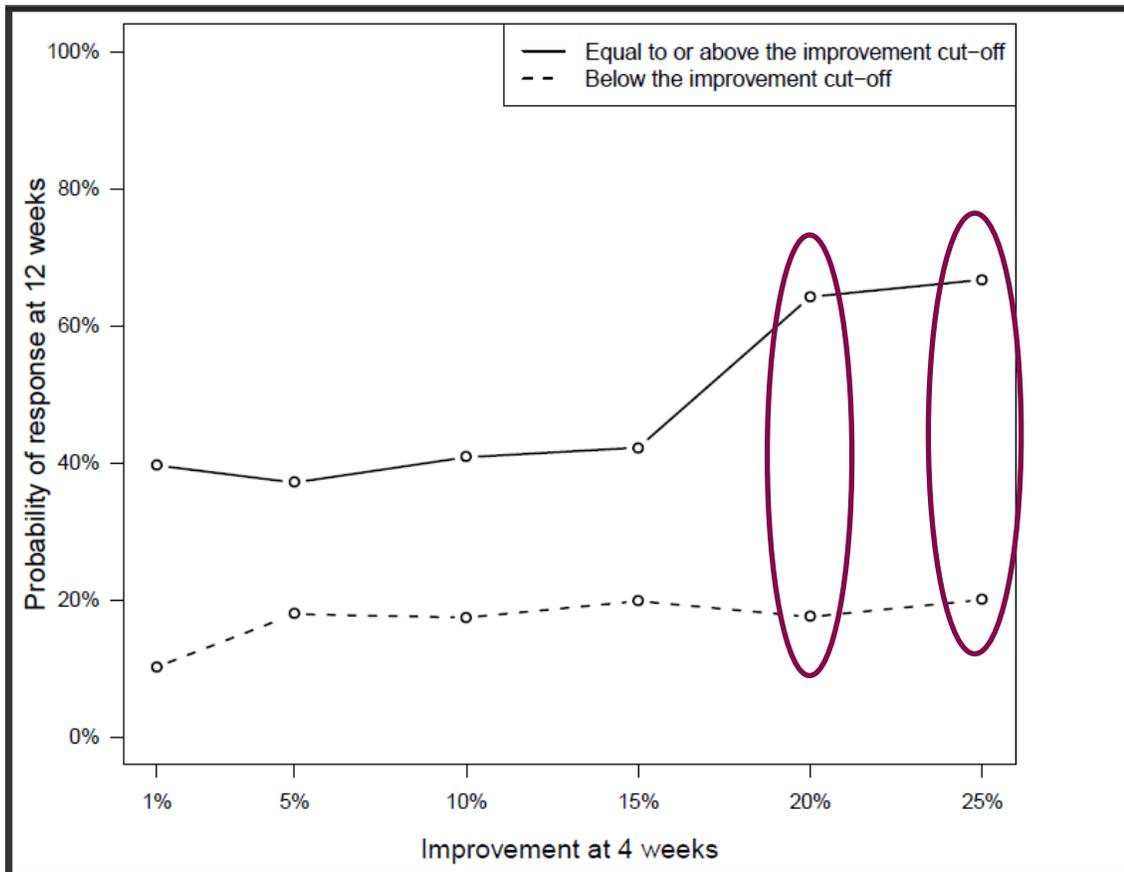
Below Cut-off= a percentage reduction of the initial YBOCS score smaller than 20%

Improvers

Above Cut-off= a percentage reduction of the initial YBOCS score equal to or above 20%



Early Improvement as a Predictor of Outcome: *RESULTS*



This graph represents the probability of being classified as a responder (at least 35% reduction from initial Y-BOCS score) at 12 weeks given different cut-offs of Y-BOCS score percent reduction at 4 weeks. The continuous line connects those who improved at least as well as that specific cut-off, whereas the interrupted line connects those who improved less than the specific cut-off. The distance between the lines is greater above the 20% cut-off and only a slight difference at this distance is observed between the 20% and 25% cut-offs.

Unpublished Data. Early improvement as a predictor of outcome. Costa and Diniz et al.

Early Improvement as a Predictor of Outcome: *RESULTS*

Sensitivity, specificity, accuracy rate, positive predictive value (PPV), negative predictive value (NPV) and probability of response for different cut-off points for early improvement (% reduction of baseline Y-BOCS score).

Cut-off point	Sensitivity (%)	Specificity (%)	Accuracy rate (%)	PPV (%)	NPV (%)	Probability of response (%)			
						Below cut-off point (no improvement at 4-weeks)	n (%)	Above or equal to cut-off point (improved at 4-weeks)	n (%)
1%	43.1	88.4	56.6	89.8	39.6	10.2	49 (33.8)	39.6	96 (66.2)
5%	45.1	76.7	54.5	82.1	37.1	17.9	55 (37.9)	37.1	90 (62.1)
10%	55.9	72.1	60.7	82.6	40.8	17.4	69 (47.6)	40.8	76 (52.4)
15%	63.7	62.8	63.4	80.2	42.2	19.8	85 (58.6)	42.2	60 (41.4)
20%	78.4	60.5	73.1	82.5	54.2	17.5	97 (66.9)	64.2	48 (33.1)
25%	90.2	46.5	77.2	80.0	66.7	20.0	113 (77.9)	66.7	32 (22.1)

Unpublished Data. Early improvement as a predictor of outcome. Costa and Diniz et al.

Predictors of Outcome: *CONCLUSIONS*

▶ 1. Familial Type OCD and Prognosis

- Given results regarding early age at onset, comorbid tic disorders, sensory phenomena, positive family history in 1st degree relatives, symmetry and ordering symptoms
- It is not necessarily related to worse prognosis! (It might be indeed the opposite)

Predictors of Outcome: *CONCLUSIONS*

▶ 2. Treatment-related factors

- When analyzed in combinations with other clinical variables, treatment related factors show a higher predictive power than remaining variables
 - **Absence of previous failed treatment trials** (Denys et al., 2003)
 - **Early improvement 1st and 4th week** (Ackerman et al., 2006); **4th week** (Costa and Diniz et al., unpublished results)