Clinical Predictors of Response to Pharmacological Interventions in Obsessive-Compulsive Disorder

Can we predict who is going to benefit from interventions?
Funding Agencies

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No conflicts of interest
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 Decloedt 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 & Brakoulis 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

*Literature Review: Predictors of Pharmacological Response in OCD*
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)
  - Shizotypal 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)

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Literature Review Predictors of Pharmacological Response in OCD
**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)

![Genetic diagram showing family history for OCD](image-url)
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)

**Literature Review Predictors of Pharmacological Response in OCD**
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

Unpublished Data.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

Unpublished Data.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

Unpublished Data.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

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

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