Background

- Abnormal white matter (WM) diffusivity measures have been associated with OCD [1], involving.
- Dysfunction of fronto-striatal circuitries is associated with obsessive-compulsive disorder (OCD) [2] [3].

Purpose

To investigate:
- whether WM alterations characterize OCD;
- the relationship between DTI measures of WM integrity and the exposure to current illness severity and drug status.

Participants

- Participants:
  - OCD: DSM-IV diagnostic criteria determined by the Structured Clinical Interview for DSM-IV (SCID).
  - Illness severity was rated on Yale-Brown Obsessive-Compulsive Scale (Y-BOCS).
  - HC: no DSM-IV axis I disorders (SCID-IV-NP).
  - ACE were rated on Risky Family Questionnaire (RF).
- All subjects did not have any current medical problems neither any past or history of neurological diseases.

Our sample

<table>
<thead>
<tr>
<th>40 OCD patients</th>
<th>41 Healthy Controls</th>
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<tbody>
<tr>
<td>33.88±10.73 yrs.</td>
<td>33.76±13.19 yrs.</td>
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<tr>
<td>18 drug-naïve</td>
<td>22 drug-treated</td>
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<tr>
<td>15M, 7F</td>
<td>11M, 7F</td>
</tr>
<tr>
<td>32,19 YBOCS</td>
<td>30.67 YBOCS</td>
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<tr>
<td>RF: 29.74</td>
<td>RF: 25.84</td>
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</table>

Results

1. Effect of diagnosis: illness severity influences WM diffusivity

- HC > OCD patients:
  - Diagnosis reduced, while treatment increased, FA in the right hemisphere (inferior fronto-occipital fasciculus (IFOF), cingulum, posterior thalamic radiation, optic radiation, inferior (ILF) and superior longitudinal fasciculus (SLF)) and bilaterally (anterior thalamic radiation (ATR), anterior corona radiata, genu and body of corpus callosum and forceps minor).
  - Opposite occurred for MD (bilateral IFOF, ATR, right ILF, left uncinate) and RD (left SLF and ATR).
- No alterations were observed for PD values.

What’s new:

- OCD sample without codiagnoses
- Comparison among drug-naïve, drug-treated and healthy controls
- Correlations with clinical variables
- TBSS analysis with 35 gradients at 3T

2. Effect of treatment: affects radial (but not axial) diffusivity

- Drug-treated patients showed reduced FA and increased MD and RD values when compared to healthy subjects.
- Drug-naïve patients did not significantly differ from controls in any of our analyses.

Conclusions

The observed changes of WM microstructure, that especially involve fronto-striatal circuitries of drug-treated OCD patients, may be due to the mechanisms of action of the taken antidepressant therapies. SSRIs (antidepressants) influence lipid metabolism, as cholesterol (Chl), which is mostly present in glial cells and is fundamental for myelination [4]. Thus SSRIs mechanism of action may affect WM connectivity. Furthermore, the localization of these changes confirm the hypothesis of the orbitofrontal dysfunction associated with the disorder.

Methods

- Technical features:
  - 3T MRI Philips scanner, 35 gradient directions, b-value: 900s/mm², EPI sequence, FOV: 231.43 x 126.5 x 240mm, slice thickness: 2.3mm.
- Data processing:
  - Simple least squares fit of the DTI model, fractional anisotropy (FA), mean diffusivity (MD), parallel diffusivity (PD), and radial diffusivity (RD) were calculated.
- Tract-Based Spatial Statistics (TBSS) analysis was performed with FSL.
  - Voxel-wise cross-subjects statistical analyses were conducted on the skeletonized FA, MD, PD and RD data, where FA > 0.2.
- Permutation-based non-parametric inference (5000 permutations) within the framework of the general linear model to investigate groups differences, accounting for age and gender effects.
- Threshold-free cluster enhancement (TFCE) estimated the clusters size for the multiple comparisons FWE (p<0.05) correction, without a priori binary clustering-forming definition.

In a nutshell

- Our experiment:
  - TBSS
  - Diagnosis effects
  - OCD severity
  - Treatment

- Results:
  - Widespread anomalies of WM (in particular in frontostriatal and parietal areas) in drug-treated OCD patients
  - Treatment affects FA and RD

References


No potential conflict of interest