Brain Structure and the Prediction of Outcome in First-episode Schizophrenia and Affective Psychoses: a population-based study

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Prospective Relationship to Outcome from the First-episode of Psychoses

• Some suggested that enlarged lateral ventricles (DeLisi et al, 1992), internal capsule (Wobrock et al, 2009), and frontal (Prasad et al, 2005) and temporal (Milev et al, 2003; Bodnar et al, 2011) regions volume reduction are able to predict worse outcome after a follow-up of 1 to 5 years.

• On the other hand, many other studies yielded negative results (Goldman et al, 1996; DeLisi et al, 1997; DeLisi et al, 1998; Lieberman et al, 2001; van Haren et al, 2003; Robinson et al, 2004; Bachmann et al, 2007; Wobrock et al, 2009).
Cognition and Psychoses

• Cognitive impairment are already present at the first episode of schizophrenia (Galderisi et al, 2009; Kurtz et al, 2004; Ayres et al, 2007), are enduring in spite of improvement of other symptoms (Ventura et al, 2008; Ayres et al, in preparation; Wykes et al, 2011), and are more intensely associated with long-term social dysfunction than other symptoms (Green et al, 1996; Green et al, 2000; Ventura et al, 2009; Emsley et al, 2008).

• Subjects with affective psychoses also have enduring cognitive impairment, although less intensively than subjects with schizophrenia (Barret et al, 2009; Reichenberg et al, 2009; Zanelli et al, 2009).
Objectives and Hypothesis

- **Objectives**: to investigate the relation between brain abnormalities at the moment of the first-episode of psychosis and clinical measures taken after 1.5 years of follow-up; and to investigate whether any association are exclusive of subjects with schizophrenia or if they are also present among subjects with affective psychoses.

- **Hypothesis**: fronto-temporal brain abnormalities and lateral ventricle enlargement are able to predict significantly clinical variables at the follow-up, mainly among schizophrenia subjects.
Previous Data From This Sample

- Lateral ventricle enlargements in FES patients relative to controls: right lateral ventricles, bilateral temporal horns, and there was no differences between subjects with affective psychoses and controls (Rosa et al, 2010)
- GM reductions in FES patients relative to controls: bilateral prefrontal cortex, left superior temporal cortex, bilateral insula, right hippocampus/parahippocampal gyrus (Schaufelberger et al, 2007)
- GM increased in the right dorsal anterior cingulate cortex among BD patients relative to controls and Bilateral dorsolateral prefrontal cortex GM deficits among MDD relative to controls (Périco et al, 2009)
- Several GM density (mainly prefrontal and fronto-parietal areas) associated with cognitive performance at the moment of the First-episode of Psychosis (Minatogawa-Chang et al, 2009)
Methods

Sample

- Schizophrenia: N=55
- Affective Psychoses: N=41 (23 with BD and 18 with Psychotic Unipolar Depression) – confirmed by a SCID examination at the follow-up
- Population-based study

Neuro-imaging

- MRI 1,5T
- Lateral ventricle: manual measure (ROI method), with temporal horns measured separately. BET used to extract total brain volume to calculate the VBR (Ventricle-to-brain Ratio %) (Rosa et al, 2009)
- Gray-matter: Voxel-based Morphometry
Broad Outcome Evaluation at FUP

• **Psychotic Symptoms**: Positive and Negative Symptoms (PANSS; Kay et al, 1987).

• **Cognitive Dysfunction**: Forward and Backward Digit Spans (Wechsler Memory Scale – Third Edition; Wechsler, 1995) and Verbal Fluency (Controlled Oral Word Association Test: COWAT; Benton and Hamsher, 1978).

• **Social Functioning**: DAS Scale (Psychiatric Disability Assessment Schedule; WHO, 1988; Menezes et al, 1993) – sample dichotomized in: “Good” and “Poor” Outcome.
Statistics

- VBRs: Regression Analysis on SPSS

- Regional GM: SPM, with SVC (frontal and temporal lobes, insulas and hippocampi-parahippocampi)

- Predictors: Brain Measures (VBRs and Regional GM)

- Clinical variables at follow-up; Also: clinical measures at the time of the MRI, exposure to antipsychotics (total, typical, atypical)

- Covariates: age, interval between MRI and follow-up, gender, respective clinical measure at the time of the MRI
First-Episode Psychosis*

- **Right Precuneus** correlated positively with Positive Symptoms (not shown)
- **Right Fusiform Gyrus** correlated negatively with Verbal Fluency
- **Middle Frontal Gyri** correlated negatively with Negative Symptoms
- **Right Middle Temporal Gyrus** correlated positively with Forward Digit Span (not shown), and **Right Parahippocampal Gyrus** correlated negatively with Backward Digit Span

*: all clusters with corrected $p < 0.05$
Schizophrenia*

- Left Inferior Frontal Gyrus and Pre-cuneus correlated positively with Positive Symptoms (not shown)
- Left Middle Frontal Gyrus and Insula correlated negatively with Negative symptoms
- Right Middle Frontal Gyrus, Right Parahippocampal Gyrus and Right Inferior Temporal Gyrus, were negatively associated with Backward Digit Span

*: all clusters with corrected $p < 0.05$
Affective Psychoses*

- Left Insula correlated positively with Verbal Fluency (not shown)
- Right Superior Frontal Gyrus correlated positively with Forward Digit Span
- Left Insula and Superior Temporal Gyrus were negatively associated with Backward Digit Span

*: all clusters with corrected $p < 0.05$
Schizophrenia vs Affective Psychoses*

- Greater correlation between clusters in Left Inferior Frontal Gyrus (not shown), Left Insula and Right Sub-gyral Temporal Lobe and Verbal Fluency among subjects with Affective Psychoses in comparison to subjects with Schizophrenia

- Also: Left Sublobar Insula and Backward Digit Span

*: all clusters with corrected p < 0.05
## Ventricle-to-brain Ratios

### Stepwise Linear Regression Analysis of Outcome

<table>
<thead>
<tr>
<th>Outcome Variable</th>
<th>First-episode Psychosis Group</th>
<th>Schizophrenia Subgroup</th>
<th>Affective Psychosis Subgroup</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Brain Region</td>
<td>t</td>
<td>p</td>
</tr>
<tr>
<td>Forward Digit Span</td>
<td>Right Temporal Horn</td>
<td>-2.921</td>
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<tr>
<td>Backward Digit Span</td>
<td>Right Temporal Horn</td>
<td>-2.797</td>
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</table>
### DAS Scale

<table>
<thead>
<tr>
<th>Group</th>
<th>Direction</th>
<th>Brain Region</th>
<th>df</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-episode Psychosis</td>
<td>“Poor” (N=41)</td>
<td>VBR – Left Lateral Ventricle</td>
<td>65.787</td>
<td>7.515</td>
<td>0.008</td>
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<tr>
<td></td>
<td>“Good” (N=33)</td>
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</tbody>
</table>

- **Schizophrenia Subgroup**: “Poor” Outcome subjects exhibited GM reduction in Right Middle Frontal Gyrus

*^*: all clusters with corrected $p < 0.05$
Discussion

- Our results indicate that fronto-temporal regions (including the temporal horns of the lateral ventricles) are the regions whose volumes are most significantly predictive of outcome, mainly in regard to cognitive deficits.

- The present findings are in agreement with previous studies that have shown correlations between brain volume deficits at the FEP and poorer outcome (DeLisi et al, 2002; Prasad et al, 2005; Milev et al, 2003, Bodnar et al, 2011).

- Although subjects with affective psychoses have less brain abnormalities than the subjects with schizophrenia at their first-episode, some of those abnormalities seem to be more able to predict outcome in affective psychoses individuals.

- Investigations of longer-term follow-up are necessary.
Conclusions

• Well-validated methodology

• Statistics included many variables as confounders

• Analysis of other possible predictors: medication intake and outcome variables at the baseline

• Yielded positive results, mainly regarding cognitive tasks: the prediction of outcome among subjects with psychoses is feasible
Thank you!

- Authors report no conflict of interest