Atypical Development of Dorsal-posterior Insula Network in Clinical High-risk Patients of Schizophrenia in Shanghai

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INTRODUCTION

- The onset of psychotic symptoms occurs during young adulthood.
- CHR patients show language dysfunction (e.g., verbal communication and auditory hallucinations).
- Insula serves as a critical hub in speech and language (Price, 2010; Ardila et al., 2014; Oh et al., 2014)

Goals

- Is abnormal dorsal-posterior insula network a biomarker that emerges at the earliest stage of psychosis development or a pathological change after years of struggling and medication treatment?
- How does the alteration of the posterior insula network contribute to symptomatology development?

SEED SELECTION

Seed-to-voxel Analyses

Left pSTG Right pSTG

Rational for seed selection:

- pSTG is functionally connected with posterior insula, as well as premotor cortex, SMA, PreCG, and PCC (Cauda et al., Neuroimage, 2011)
- Arcuate fasciculus travels from pSTG and pass through posterior insula (Denni et al., 2014; Catani et al., 2005)


<table>
<thead>
<tr>
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<th>Clinical High Risk (CHR)</th>
<th>Healthy Controls (HC)</th>
<th>Statistical Significance</th>
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<tbody>
<tr>
<td># of participants</td>
<td>158</td>
<td>93</td>
<td>-</td>
</tr>
<tr>
<td>Gender (female/male)</td>
<td>78/80</td>
<td>43/50</td>
<td>χ²(1) = 0.12, p=0.72</td>
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<tr>
<td>Age (years)</td>
<td>18.81 ± 4.92</td>
<td>18.56 ± 4.26</td>
<td>t(249)=-0.41, p=0.68</td>
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<tr>
<td>Education (years)</td>
<td>10.51 ± 2.76</td>
<td>10.80 ± 2.28</td>
<td>t(249)=0.83, p=0.40</td>
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<tr>
<td>IQ</td>
<td>98.89 ± 12.83</td>
<td>104.0 ± 11.19</td>
<td>t(217)=3.01, p = 0.002</td>
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<tr>
<td>Hopkin’s Verbal Learning</td>
<td>46.98 ± 9.79</td>
<td>52.58 ± 6.45</td>
<td>t(210)=4.60, p &lt; 0.001</td>
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<tr>
<td>SIPS-positive</td>
<td>10.07 ± 3.60</td>
<td>-</td>
<td>-</td>
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<tr>
<td>SIPS-negative</td>
<td>11.65 ± 6.12</td>
<td>-</td>
<td>-</td>
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<tr>
<td>SIPS-disorganization</td>
<td>6.56 ± 3.20</td>
<td>-</td>
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<tr>
<td>SIPS-general</td>
<td>9.08 ± 3.22</td>
<td>-</td>
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<tr>
<td>SIPS-total</td>
<td>37.36 ± 10.82</td>
<td>-</td>
<td>-</td>
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<td>Medicine</td>
<td>29 CHR patients started taking psychotropic medication before the scan.</td>
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- SIPS: Structural Interview for Prodromal Syndromes of Schizophrenia
- Within CHR, age was not significantly correlated with SIPS measures.
- Within HC, age was not significantly correlated with IQ or verbal learning.

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IMAGING ACQUISITION AND ANALYSIS

- Acquisition
  Resting-state functional MRI: Siemens Trio 3T MRI scanner, 32-channel head coil; 37 interleaved oblique, 3.5 mm axial slices covering the entire brain. TR = 2500 ms, TE = 30 ms, FOV 224x224mm with 3.5 mm isotropic voxels, flip angle 90°. Participants were instructed “Keep your eyes open and think nothing in particular”.

- Analysis
  - Functional connectivity data were analyzed with CONN v17d and SPM12b. Sources of non-neurophysiological noise were identified through an anatomical component based approach (aCompCor).
  - Motion outlier criteria: composite movement (relative to the previous time point) > 1mm, global signal intensity > 3SD.
  - Motion outliers were regressed out in the first-level GLM.
  - Seed-to-voxel whole-brain analyses: Voxel-level p <0.001 (one-sided) and cluster-level FDR-corrected p < 0.05.

IMAGING RESULTS

- Significant Group x Age Interaction

- Within CHR: significant increase of connectivity with age

- Within HC: significant decrease of connectivity with age

- Better IQ and better verbal learning ability in HC are significantly associated with lower connectivity

CONCLUSION

- Abnormal developmental trajectory (increasing with age) of the dorsal-posterior insula network in CHR patients.
- Altered wiring of the auditory/speech network might underlie the mild cognitive impairment emerged earlier in CHR patients.