Clinical Observation

Aberrant Functional Connectivity Patterns of Default Mode Network May Play a Key Role in the Interaction between Auditory Verbal Hallucinations and Insight

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Previous studies have reported that auditory verbal hallucinations (AVHs) may be caused by resting-state neuronal hyperactivity in the default mode network (DMN). Abnormally increased functional connectivity (FC) between the DMN and other cortical regions may cause disturbances in neuronal network architecture and interactions. Subsequently, disturbed neuronal network architecture and interactions may induce increased activation in auditory and speech perception areas in the absence of external auditory stimuli as well as reduced activation in the same areas in the presence of external auditory stimuli. These disturbances may be the neural basis of AVHs.[1] In addition, insight, which is another core characteristic of schizophrenia, has been associated with treatment compliance, relapses, long-term outcomes, and global functioning ability. Some studies have reported that insight is also related to disturbance of the DMN, especially self-monitoring: poor insight is associated with increased connectivity between the self-referential network and the left insula.[2] The self-referential network may be considered a component of the DMN.[2,3] Based on the aforementioned findings, we found that DMN alteration is associated both with AVHs and with insight. However, to the best of our knowledge, no one has yet studied FC patterns (FCPs) between the DMN and other brain regions related to schizophrenics’ experiences of AVHs with and without insight.

For this pilot study, we selected seven AVH-schizophrenic patients without insight, six AVH-schizophrenic patients with insight and 22 healthy controls (HCs) from our database for inclusion in FCP analysis. All subjects provided written informed consent prior for this study, and the protocol was approved by the Committee on Studies Involving Human Beings at Tianjin Anding Hospital. The mean antipsychotic dosage (chlorpromazine equivalents) was 374.0 ± 163.8 mg/d in AVH-schizophrenic patients without insight and 375.2 ± 190.5 mg/d in AVH-schizophrenic patients with insight (P = 0.98 for a contrast between the two patient groups). There were no significant differences in age, gender, or education level among the three groups.

Preprocessing was performed with Statistical Parametric Mapping software (SPM8, http://www.fil.ion.ucl.ac.uk/spm/software/spm8/), the Analysis of Functional NeuroImage (AFNI, http://afni.nimh.nih.gov/afni) package, and the...
When compared to HCs, A VH-schizophrenic patients without insight demonstrated increased FC in the PCC-frontal lobe-angular gyrus circuit; in addition, decreased FC was found in the PCC-frontal lobe-angular gyrus circuit. This finding provides converging support for our suggestion that DMN hyperactivity might play a key role in the interaction between AVHs and poor insight. In contrast, we found decreased FC in the PCC-frontal lobe-angular gyrus circuit. This finding provides converging support for our suggestion that DMN hyperactivity may play a key role in the interaction between AVHs and poor insight.\(^\text{[1-3]}\)

However, there are several limitations to the pilot study. First, the small sample size may affect the strength of our findings. These findings provide only initial evidence for further study. In future studies, we will consider this flaw and address this gap. Second, in this pilot study, we only enrolled chronic patients, and selection bias may reduce the strength of our findings. In further studies, we will conduct a well-designed long-term follow-up study enrolling a large sample to further explore mechanisms of AVHs, insight, and the interaction between AVHs and insight. We will acquire baseline MRI data from these drug-naïve first-episode patients, and MRI data will then be acquired once every 6 months for 2–3 years. Through these data, we can characterize the dynamic trajectory of patients’ symptoms and brain characteristics (such as the specific trajectory of neural markers of AVHs in schizophrenic patients and the specific trajectory of neural markers of insight in schizophrenic patients). Although such a study will be extremely time-consuming and laborious, it can precisely identify specific pathological targets and provide an objective index for precise treatment strategies, thereby elevating the early remission rate.

Although many flaws exist in this preliminary study and future studies are needed to clarify the results, our preliminary findings tend to support the hypothesis that aberrant FCPs in DMN might play a key role in the interaction between AVHs and insight. Although the findings of this pilot study are limited by the small sample size and other flaws, they may nevertheless provide useful clues for further study.

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Conflicts of interest
There are no conflicts of interest.
Figure 1: DMN functional connectivity patterns differences between AVH-schizophrenic patients without insight, AVH-schizophrenic patients with insight and healthy controls. (a) When compared with the AVH-schizophrenic patients with insight, patients without insight demonstrated increased FC in the PCC-frontal lobe-cingulate cortex circuit; in addition, decreased FC was observed in the PCC-right cerebrum circuit. (b) When compared with HCs, AVH-schizophrenic patients without insight did not display any differences in FC. (c) AVH-schizophrenic patients with insight demonstrated decreased FC relative to HCs in the PCC-frontal lobe-angular gyrus circuit. AVH: Auditory verbal hallucination; DMN: Default mode network. FC: Functional connectivity; PCC: Posterior cingulate cortex; HCs: Healthy controls.

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