Abstract

Background: Previous studies examining coherence and connectivity deviations in schizophrenia patients relied on standard coherence measures between recording sites. A coherence-imaging methodology where coherence is assessed within imaged brain structures was developed recently by our group. Magnetoecephalography (MEG) based coherence-imaging is yet to be applied to studying the coherence deviations in schizophrenia patients during the resting state.

Methods: Twelve patients diagnosed with schizophrenia and twelve healthy control subjects were studied. A ten minute resting state MEG brain scan was performed with eyes open. MEG coherence analysis was carried out to determine the cortical areas that interacted strongly within each frequency bin of 2Hz from 1-50Hz. A discriminant analysis on the schizophrenia versus control coherence imaged data aimed at extracting a global pattern of network difference between groups.

Results: Statistically significant increased coherences were detected in schizophrenia patients compared to controls in the left inferior frontal gyrus (BA47), left superior temporal gyrus (BA22), left superior frontal gyrus (BA8) as well as the left lateral orbitofrontal gyrus (BA47). These areas are involved in language, memory, executive and higher cognitive functioning.

Conclusion: We conclude that resting state coherences of schizophrenia patients deviate from normal subjects in several behaviorally salient regions. Analysis with MEG coherence-imaging can provide clues to the abnormal resting state which we propose is important to understand abnormalities detected with different methods of activation.

Methods

• Twelve chronic schizophrenia outpatients meeting DSM-IV criteria for both schizophrenia and its subtype.
• Twelve healthy control subjects (4 males and 8 females). Age range was 19-42 years old (mean 27.9 ± 5.5 years).

Discriminant Analysis

Discriminant analysis was used to quantify global differences in brain network function between groups. As a test for significance of these global differences, a non-parametric statistical approach showed that the whole brain coherence for each group was calculated using two versions of the total difference between group averages. The first version maintained the signed difference for all cortical sites. For the second measure of difference, the absolute value of individual cortical coherence differences were summed over the whole brain. Statistical P-values are based on groups of 12 subjects with 6 randomly chosen from each group. Thus, the 1000 group differences incorporates the random variability of the 24 subjects, but eliminate differences due to identification as schizophrenia or normal. P-values for the actual difference between schizophrenia and control subjects were calculated by how this difference ranked relative to the ranks of the 5000 random group difference amplitudes. So, the limit on p-value resolution was 1/5000.

Coherence Imaging

Transients and oscillations of brain electric activity are found in MEG, EEG and fMRI recordings of spontaneous brain activity. These transient waveforms and oscillations can be quantified by applying time-frequency decomposition techniques such as the discrete Fourier transform (DFT). After transformation to e.g. frequency representations, the strength of network interactions can be estimated by calculation of coherence, which is a measure of synchrony between signals from different brain regions at each frequency bin.

Coherence Imaging: Calculation

1. Calculate time sequence of brain activity (divide data into 7.5 sec windows)
2. Calculate FFT sequence (15 second windows) temporal sequences of sources are converted to temporal source FFT spectra
3. Calculate cross-spectral matrix between sources (ICA components) for each frequency
4. Calculate coherence between all network structures
5. For each active cortical site the average coherence with all other sources is calculated for each frequency.

Conclusions

Our preliminary MEG findings suggest possible biomarkers/indicators of an abnormal resting-state in schizophrenia patients. 

• As no task performance or cooperativeness is required (other than staying still during recording) this procedure may be useful in uncooperative or significantly cognitively impaired patients.

• Furthermore, resting-state indicators recorded by MEG can be used to quantitatively assess brain activation levels pre- and post-treatments in patients with schizophrenia.

• Though there is more left-sided mean coherence of regions in the frontal lobe in patients with schizophrenia, it remains to be seen where other areas of the brain may be assessed during the absence of certain active symptoms of the disease: auditory hallucinations, visual hallucinations, etc.

• Few drawbacks limit the generalizability of the results. First, it is the small sample size. Definitive correlations with clinical symptom-clusters could not be provided. Secondly, patients were medicated with various antipsychotic agents (majority on atypical antipsychotics). The effects of medications on the MEG signal are currently not well-known. Thirdly, there was an unmatched distribution of gender in our samples of schizophrenia patients and healthy controls. Furthermore, as in coherence imaging results, the localization of imaged brain activity is strongly dependent on the frequency bands with greatest power, investigation of coherent activity at narrow preselected bands is warranted.