O3. Oral Session: fMRI

O3.1. NEUROTYPING UNTREATED FIRST EPISODE SCHIZOPHRENIA ON THE BASIS OF SLOW-WAVE RESTING-STATE DYNAMICS

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Background: Coherence in the phase of oscillatory neuronal activity indicates functional interaction among brain regions at rest. Infra-slow fluctuations in BOLD signal (band 5 - 0.01 to 0.027 Hz - and band 4 - 0.027 to 0.073 Hz) has been observed using resting state fMRI when employing frequency-domain analysis, and has been previously shown to be altered in schizophrenia. In the current study, we examined the strength and the dynamic variance of phase coherence in these 2 bands (using a sliding window approach) among 6 large-scale brain networks (default-mode, fronto-parietal, salience, sensorimotor, visual, cerebellar) in 129 drug-naïve patients with schizophrenia and 197 healthy controls. Our motivation was to exploit the large-scale resting-state slow-wave oscillatory dynamics to parse the heterogeneity of schizophrenia.

Methods: Four 6*6 matrices depicting patient vs. control differences in dynamic variance and mean of phase coherence (vPC and mPC respectively) in the slow 4 and slow 5 bands were constructed from resting state fMRI time series obtained from 6 networks based on 160 nodes of Dosenbach's atlas. Deviations in mean/variance of phase coherence among the 6 networks were identified after FDR correction for each matrix ($p < 0.05$). A latent profile analysis (LPA) was undertaken on the basis of the identified deviant features in the patient group. LPA is a Finite Mixture Modelling approach to identify naturally occurring sub-groups of patients on the basis of multivariable data. The identified subgroups were compared in terms of the severity of clinical symptoms across van der Gaag's 5 factors of PANSS scale.

Results: Patients with schizophrenia showed increased vPC between salience-sensorimotor and visual-cerebellar networks in band 5; decreased vPC between DMN-sensorimotor and DMN-cerebellar networks in band 4. Patients also had a decrease in mPC between DMN-visual and DMN-cerebellar networks in band 5. We were able to identify 3 subgroups of patients using LPA. SZ1 (n=28) and SZ2 (n=45) had higher overall burden of symptoms compared to SZ3 (n=56). SZ2 had the highest burden of negative syndrome score and showed most deviance from healthy controls (5 out of 7 features significantly different from the healthy cohort). SZ1 had the highest burden of positive syndrome scores and had 4 out of 7 features deviant from HC. In contrast, SZ3 had least deviation from HC (3 out of 7 features) and also had less symptom burden across all symptom dimensions.

Discussion: Various abnormalities have been reported in the interactions among the large-scale networks in schizophrenia, with lack of consistency ascribed to syndromic heterogeneity. We illustrate how deviations in time-varying nature of slow-wave oscillations in resting state fMRI can be exploited to meaningfully reduce heterogeneity of this illness. The 3 subgroups thus identified not only show differential symptom burden but also exhibit hierarchical deviation from a normative group of healthy controls (SZ2>SZ1>SZ3>HC). To our knowledge this is the first attempt to stratify 'neurotypes' among drug-naïve patients with schizophrenia on the basis of large-scale network dynamics. Given the widespread availability of resting-fMRI data, we anticipate independent replication of our results in the near future.

O3.2. BRAIN HYPERACTIVATION DURING MEMORY RETRIEVAL PRECEDES AND PREDICTS CONVERSION TO PSYCHOSIS IN INDIVIDUALS AT CLINICAL HIGH RISK

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Background: Memory deficits are a hallmark of psychotic disorders such as schizophrenia. However, whether neural dysfunction underlying these deficits is present prior to onset of illness and potentially predicts conversion to psychosis are unclear. This study aimed to investigate: 1) baseline brain functional alterations during memory processing in subjects at clinical high risk (CHR); 2) whether alterations are more severe in converters compared with non-converters and are thus predictive of psychosis; and 3) associations of these alterations with task performance, baseline symptoms and memory ability.

Methods: A sample of 155 individuals at CHR (including 18 subjects who later converted to psychosis (age 17.22 ± 3.44 years, 10 male) and 137 subjects who did not convert (age 19.01 ± 4.19 years, 81 male)) and 108 healthy controls (age 20.30 ± 4.85 years, 58 male) were drawn from the second phase of the North American Prodrome Longitudinal Study (NAPLS-2) consortium. All participants underwent functional magnetic resonance imaging (fMRI) with a paired-associate memory paradigm, which consisted of one run for encoding and another run for retrieval. During encoding, participants were presented a series of semantically unrelated word pairs and were asked to remember the presented word pair. During retrieval, a pair of words was presented on the screen on each trial and subjects were asked to indicate whether the given word pair had been presented during the encoding session. Active baseline conditions were included in the task for both encoding and retrieval runs.

Data processing was performed for each run, following the standard procedures using the Statistical Parametric Mapping software (SPM12). At individual level, preprocessed images were entered into a general linear model (GLM), generating individual contrast maps (task vs baseline). These contrast maps were further used for a group-level GLM analysis, modeling group, sex, age and site as regressors. Significance was determined using family-wise error (FWE) correction across all voxels in the brain.

The observed activation alterations were further tested for potential associations with task performance, clinical symptoms and/or general memory ability. Task performance was measured using the percentage of correct responses and the mean reaction time during retrieval. Clinical symptoms were evaluated by the summed scores of each domain (positive, negative, disorganization, general) in the Scale of Prodromal Symptoms (SOPS). Memory ability was quantified by the Brief Visuospatial Memory Test- Revised (BVMT-R) and the Hopkins Verbal Learning Test- Revised (HVLT-R) total recall scores.

Results: No significant group differences in activation were found during encoding. However, during retrieval, a significant group effect was observed in five brain regions: left dorsolateral prefrontal cortex (T = 4.75, PFWE = 0.034), left ventrolateral prefrontal cortex (T = 4.99, PFWE = 0.013), left inferior parietal lobule (T = 4.73, PFWE = 0.035), left superior temporal gyrus (T = 5.71, PFWE = 0.001), and right middle temporal gyrus (T = 4.89, PFWE = 0.019). This effect was indicative of greater activation in converters than non-converters and controls and was particularly manifest in unmedicated subjects (P < 0.001). Baseline hyperactivation was correlated with retrieval reaction time during scan in converters (R = 0.61, P = 0.009), and with baseline positive, negative and disorganization symptoms (R > 0.18, P < 0.003) and memory scores (R < -0.15, P < 0.01) in the whole sample.

Discussion: These findings suggest that hyperactivation during memory retrieval may mark processes associated with conversion to psychosis; such measures have potential as biomarkers for psychosis prediction.

Abstracts for the Sixth Biennial SIRS Conference