(Occ), and MRS was performed with the point-resolved spectroscopy sequence (PRESS). Voxel data were analyzed for MEGA-PRESS spectroscopy with Gaussian curve fitting to the GABA peaks and LCModel software to determine peak concentrations of GABA+ (including signal from macromolecules) and creatinine (Cr), yielding GABA+/Cr ratios for analysis. All subjects completed the 9-item Psychological Stress Index (PSI-9), a validated measure of stress sensitivity and NA in psychosis.
Results: We have completed a preliminary analysis of 28 subjects (FEP: n = 11, 21.8 ± 2.7 years; HC: n = 11, 20.5 ± 3.2 years; APS: n = 6, 20.2 ± 3.9 years). Of the patient subjects, 6 APS subjects and 1 FEP subject were off medications. Analysis with ANCOVA, with group as a factor and PSI-9 scores as a covariate, yielding a significant inverse relationship of PSI-9 scores with mPFC GABA concentration (F[1,24] = 6.61, P = .02), but no effect of group (F[2,24] = 1.74, P = .20). There were no effects of group or relationships with PSI-9 scores in the Occ voxel (Ps > 0.2). We compared all subjects based on whether they were taking antipsychotic medications and found no differences for either voxel (Ps > 0.5). There were no other significant relationships between GABA concentrations and clinical symptoms, cognitive variables (MCCB) or functional level.
Conclusion: The data provide support for a relationship between GABA levels and NA, measured by the PSI-9 such that lower GABA concentrations in the mPFC are associated with higher levels of NA. The small sample size and preliminary nature of the data warrant caution. Nevertheless, given that potentiation of GABA activity with benzodiazepines reduces NA, the findings are of potential clinical relevance in understanding the role of GABA systems in affect regulation in psychosis.

51. OCCIPITAL ALPHA POWER DURING RESTING-STATE EEG IN CLINICAL RISK FOR PSYCHOSIS AND SCHIZOPHRENIA

Petra Rupert*, Anna Watters, Daniel Wolf, Monica Calkins, Ruben Gur, Raquel Gur, and Bruce Turetsky
University of Pennsylvania

Background: Identification of valid schizophrenia risk biomarkers, prior to the onset of psychosis, is critical for early treatment intervention and for understanding the progression from prodromal symptoms into full psychosis. Occipital alpha power is known to be impaired in schizophrenia patients, during both the resting state and during cognitive task activation. However, the status of this measure during the pre-clinical risk period is unknown. We investigated occipital lobe alpha power during resting state EEG as a potential biomarker of clinical risk and schizophrenia, and explored correlations with cognitive functioning and clinical symptoms.
Methods: Participants included 23 patients with schizophrenia (SZ), 31 clinical high-risk individuals (CR), and 30 healthy controls (HC). Participants underwent a structured clinical interview to assess symptoms using the Structured Interview for Prodromal Syndromes (SIPS) and completed a computerized battery to assess major domains of neurocognitive functioning. Resting state EEG was recorded for 2 minutes each in eyes-closed and eyes-open conditions. Data were segmented into 2-second artifact-free epochs and Fast Fourier Transformed into the frequency domain. Mean occipital alpha power (8–12 Hz) was then computed from O1, Oz and O2 electrodes.
Results: Both CR (P = .03) and SZ (P = .02) exhibited reduced alpha power in the eyes-closed condition compared to HC. SZ and CR were not significantly different from each other. There were no differences across groups in the eyes-open condition. Clinical symptoms and cognitive functioning were not significantly correlated with mean eyes-closed alpha power in the SZ or HC groups. However, in the CR group, lower alpha power was associated with poorer overall cognitive performance (r = .37, P = .04) and poorer complex reasoning (r = .51, P = .004). It was also paradoxically associated with fewer disorganized symptoms (r = .55, P = .002).
Conclusion: This study extends previous findings of decreased eyes-closed occipital alpha power in SZ to CR. Our results suggest that neural abnormalities detectable by EEG are present prior to the onset of threshold psychotic symptoms and associated with early cognitive impairment. The augmentation of occipital alpha power with eye closing has been linked to the modulation of neuronal input from the pulvinar nucleus to the visual cortex. Our findings therefore implicate a specific thalamocortical disconnection associated with psychosis risk. The routine use of EEG in the clinical assessment of the psychosis prodrome may provide a physiological marker linking neural pathology to higher order functioning. The predictive utility of this measure for transition to overt psychosis remains to be determined.

52. ABNORMAL ANTERIOR INSULA ACTIVITY DURING FEAR GENERALIZATION IN SCHIZOPHRENIA

Lauri Tuominen*[,1], Stephanie DeCross[1], Shahin Nasr[1], Emily Boeke[1], Rick Wolthusen[1], Roger Tootell[1], Oliver Freudenreich[1], Ann Shinn[2], and Daphne Holt[1]
[1]Massachusetts General Hospital; [2]McLean Hospital

Background: Generalization from previous experiences allows us to evaluate the affective value of novel events. A breakdown of this fundamental ability may lead to incorrect attributions of affective value that could give rise to psychotic symptoms. To examine this hypothesis, we tested whether the generalization of conditioned fear responses is abnormal in schizophrenia, using functional magnetic resonance imaging (fMRI).
Methods: 37 schizophrenia and 32 healthy subjects, matched for age, and sex, underwent an fMRI scan while participating in a Pavlovian fear conditioning and generalization paradigm. During the conditioning phase, one face was used as a conditioned stimulus and paired with an electrical shock (the CS+), whereas a different face was used as a neutral stimulus that was never paired with a shock (the CS−). In the generalization phase, five stimuli that were different morphs between the CS+ to the CS- were selected based on each individual's ability to discriminate the two faces. Afterwards, subjects were asked to rate the likelihood each stimulus was followed by a shock (explicit ratings). In the fMRI analyses, we identified the regions of the brain that showed significant CS+ vs. CS− responses during the conditioning phase in both groups. Those regions were then tested for generalization responses using an anatomical regions-of-interest approach and a mixed design ANOVA.
Results: There were no between-group differences in CS+ vs. CS− responses of the brain during the conditioning phase. In both groups, CS+ > CS− activation was observed in the anterior insula and dorsal anterior cingulate cortex, whereas the reversed pattern (CS− > CS+) was observed in the ventromedial prefrontal cortex and angular gyri. During the generalization phase, patients with schizophrenia exhibited impaired generalization, both behaviorally (explicit ratings) and in the brain, most prominently in the right anterior insula, due to a lack of differentiation between the morphs and the CS−. This abnormality correlated with positive symptom severity.
Conclusion: Schizophrenia patients are able to successfully acquire conditioned fear responses, but show impaired generalization of those fear memories. This impairment in fear generalization is associated with abnormal functioning of the anterior insula. These findings suggest that psychosis may arise in part from a deficit in the immediate retrieval of associative memory traces—a basic process that can be quantified as impaired fear generalization.

53. HIGHLY PSYCHOSIS-PRONE ADOLESCENTS SHOW INCREASED CAPTURE BY DISTRACTOR STIMULI AND MORE EFFORT TO INHIBIT EMOTIONAL STIMULI THAN TYPICALLY DEVELOPING CONTROLS

Abbie Popa*, Courtney Durdle, Hannah Morgan, Heather Shapiro, Tara Niendam, Cameron Carter, Steven Luck, and Tony Simon
University of California, Davis