Results: After bolus injection of [18F]FNDP, high levels of brain radioactivity were observed in healthy participants, with peak gray matter activity within 10 minutes post injection and steady decline over the remaining scan. [18F]FNDP total distribution volume (VT) was well-estimated in several brain regions from 90-minute data using the 2-tissue compartment model with metabolite-corrected arterial input function, supporting early efforts to use [18F]FNDP PET in clinical research. Using [18F]ASEM PET, VT was lower in individuals with NP (14.1 ± 0.9) compared to healthy controls (19.6 ± 2.5, P < 0.001) or compared to those with AP (17.6 ± 2.2, P = 0.04). Among patients, higher [18F]ASEM VT was associated with better processing speed and verbal memory after adjusting for age. Finally, [11C]CMPPF PET in living baboon brain shows promising, high uptake and specific binding, as well as higher VT after systemic administration of lipopolysaccharide to activate microglia. Movement of this radiotracer into human neuroimaging studies is underway toward the ultimate goal of testing whether [11C]CMPPF PET supports the hypothesized subgroup of individuals with psychosis who have aberrantly high microglial response.

Conclusions: Use of PET-based imaging even in smaller-scale studies may facilitate clinically meaningful subtyping of individuals with aberrant neuroimmune response among those with psychosis. Future work should pursue evaluation of approaches such as a generative adversarial network to augment what can be discovered from relatively small PET samples, and assessment of clinical decision-making value from use of a growing number of radiotracers for PET-based molecular phenotyping of subpopulations of patients.

14.4 IMPROVING SPECIFICITY AND HARMONIZING MULTI-SITE DIFFUSION MRI DATA TO IDENTIFY LIFESPAN TRAJECTORIES IN PSYCHOSIS

Ofer Pasternak*,1, Suheyla Cetin Karayumak1, Maria Di Biase1, Martha Shenton1, Marek Kubicki1
1Harvard Medical School

Background: Diffusion MRI abnormalities are frequently reported in psychosis studies, leading to hypotheses regarding the involvement of white matter disruptions, as well as their lifespan trajectories. Nevertheless, little consensus exists regarding the location and extent of such disruptions. Poor reproducibility could result from lack of standardization in acquisition and analysis approaches, heterogeneity of subject populations with regard to demographics, clinical presentation, medication confounds, and/or, importantly, statistically underpowered samples to detect subtle abnormalities. In addition, common diffusion metrics reflect non-specific signals associated with numerous microstructural changes, which could also vary as a function of illness-related processes. Careful consideration of these design and methodological factors could improve reproducibility, and thereby improve our capacity to reliably infer conclusions regarding the progression of psychosis. Here, we applied novel strategies to overcome key limitations and use of specific imaging markers, improve our capacity to detect reliable and valid information regarding the pathophysiology of psychosis. Specifically, we identified co-occurring cellular and extracellular abnormalities, which fluctuate as a function of age and disease progression. Building on these findings, a Big Data approach provided superior statistical power, resulting in refined and robust estimation of lifespan trajectories associated with each imaging marker. Based on our experience, we can provide practical recommendations for designing and analyzing smaller studies targeting unique/homogenous populations, as well as multi-site studies, which attempt to bolster statistical power.

Plenary Session

15. SCHIZOPHRENIA AND GLUTEN: NEW TARGET AND PRECISION MEDICINE

Deanna Kelly
University of Maryland Baltimore, Maryland Psychiatric Research Center

Deconstructing the illness of schizophrenia is of particular interest as this heterogeneous disorder may be composed of etiologically distinct disorders with different mechanisms which could all serve as treatment targets for components of the disorder. One specific group with elevated peripheral and central inflammatory response is those with schizophrenia having elevations in antigliadin antibodies (AGA IgG). In addition to evidence of high peripheral and central inflammation, this subgroup may be distinct by having lower positive symptoms and high kynurenine levels. It remains unclear, however, how these elevations in AGA IgG and immune activation in this subgroup may contribute to the illness and schizophrenia psycho-pathology; however, it may be related to gut permeability or mimicry/cross reactivity to proteins present. This population may represent a subgroup which may have personalized, and targeted treatments developed. This talk will discuss the emerging association of inflammation and immune activity in schizophrenia, review the data that helps characterize the subgroup with AGA IgG and present ongoing work for treatment targets and mechanisms of action connecting gluten to schizophrenia. This work suggests that more personalized treatments targeting diet modulation or immune/inflammation may play future roles in schizophrenia treatment.

Concurrent Symposia

16. WHAT VISUAL PERCEPTUAL ANOMALIES CAN TELL US ABOUT SCHIZOPHRENIA: NEURAL MECHANISMS AND THEIR DIAGNOSTIC SPECIFICITY

Scott Sponheim
Minneapolis VA / University of Minnesota