Conclusions: In human pregnancy, perinatal choline supplementation enhances the development of cerebral inhibition, rescues genetically vulnerable individuals, and improves behavioral outcomes.

23.4 PET-BASED PRECISION NEUROIMAGING OF THE ALPHA7 NICOTINIC ACETYLCHOLINE RECEPTOR IN PATIENTS WITH RECENT ONSET OF PSYCHOSIS

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Background: Low availability of the α7 nicotinic acetylcholine receptor (α7-nAChR) in the hippocampus of patients with schizophrenia has been suggested from study of postmortem tissue, and therapies that increase signaling through the α7-nAChR may ameliorate signs and symptoms of psychosis, including associated cognitive deficits. Here we used [18F] ASEM with positron emission tomography (PET) to test for hypothesized low in vivo availability of the hippocampal α7-nAChR in individuals with recent onset psychosis compared to healthy controls. Building on the recent development of α7-nAChR-targeted medications and in line with precision health initiatives that aim to customize therapeutic strategies to patient subgroups, we also tested whether individuals with non-affective psychosis (NP) have lower [18F] ASEM binding compared to individuals with affective psychotic disorder (AP).

Methods: This prospective study was approved by a Johns Hopkins Institutional Review Board. Each non-smoker participant provided written informed consent. Individuals with recent-onset (within five-years) psychosis were included if they had: 1) schizophrenia or schizoaffective disorder (grouped NP) or 2) bipolar I disorder (referred to as AP). Limited medication use (lithium or antipsychotic monotherapy) was allowed. Eleven patients and five new healthy controls completed [18F] ASEM PET, and we pooled their data with those of all ten healthy individuals <50-years-old from our published study of the α7-nAChR in healthy aging. [18F] ASEM kinetics were modeled using Logan graphical analysis with a metabolite-corrected arterial input function from 90 min dynamic data. Hippocampal total distribution volume (VT) values were derived from images after partial volume correction (PVC). Group differences in VT were tested using analysis of variance and using analyses of covariance to control for potential confounding effects of age, sex, race, or body mass index (BMI).

Results: Among individuals with recent-onset psychosis, five had NP [schizophrenia (N=3), schizoaffective disorder (N=2)] and six had AP. There were significant group differences [using three groups (Controls, AP, NP) or two groups (Controls, AP+NP)] on hippocampal VT (P ≤ 0.001), even after adjusting for age (each P ≥ 0.001). Individuals with recent onset psychosis (AP+NP) had lower VT (15.97 ± 2.50) than healthy controls (19.55 ± 2.49, P = 0.001), though VT in the AP group alone (17.57 ± 2.24) did not differ from healthy controls. VT was lower in individuals with NP (14.05 ± 0.89) compared to healthy controls (P < 0.001) or compared to those with AP (P = 0.04) and remained lower in those with NP compared to healthy controls after adjusting for each covariate separately (Ps ≤ 0.002). Controlling for BMI or race did not change the lower VT in individuals with NP compared to AP (Ps = 0.01), but significance was lost after adjusting for age. Among patients (AP+NP), higher VT was associated with better processing speed and verbal memory after adjusting for age. VT estimates from images without PVC did not change these results and produced parametric images that support group differences outside hippocampus.

Conclusions: These results suggest that low availability of the α7-nAChR may be linked to recent onset of psychosis, particularly recent onset of NP. Further study is needed to assess its clinical relationship to neuropsychiatric symptoms.

24. ANALYSIS OF LANGUAGE IN SCHIZOPHRENIA

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Language is an essential anamnestic source of information in psychiatry. More specifically, disorganized language is a core criterion for schizophrenia and analyzing this language may hold clues as to what it is that goes astray in the schizophrenic brain. However, language, in part due to its wide range of applications and nuances, is difficult to analyze and quantify. Through the advent of computational language processing, it has become possible to study a patient’s language functioning in an objective, quantifiable way. This creates the opportunity to use language as a marker for diagnosis, prognosis and perhaps treatment response of a patient with a schizophrenia spectrum disorder. Since language involves so many complex cognitive functions, a wide variety of aspects of verbal communication can be assessed by means of automated language analysis.

The speakers in this symposium will use a wide range of approaches to assess different aspects of language in schizophrenia subjects, covering early detection and diagnosis (Natalia Mota), classification based on specific language markers (Guillermo Cecchi), symptom assessment and side-effects of medication (Alban Voppe) and the transformation of research into clinically useful tools (Terje Holm Lund).

First, Alban Voppe will present research investigating language disturbances in schizophrenia-spectrum disorders, both innate and those stemming from medication side-effects. Making use of among other measures a novel word2vec semantic and linguistic approach, disturbances were found between schizophrenia-spectrum patients and healthy controls, as well as between patients depending on dopaminergic characteristics of antipsychotics. Quantified markers derived from spontaneous language can be used both in assessing symptoms as well as side-effects that present possible confounders.

Secondly, Dr. Guillermo Cecchi (IBM) will present research involving metaphor analysis in ultra-high-risk as well as schizophrenia-spectrum disorder. His research shows that automated linguistic analyses of schizophrenia and its risk states can be extended from semantic coherence metrics at the phrase or sentence level to the level of single words. Since this method is also sensitive in regards to ultra-high-risk participants, it might be used as a screen to identify individuals with attenuated psychosis syndrome.

Thirdly, Dr. Natalia Mota will present her research concerning early markers of thought disorganization found in speech structure. Using graph theoretical measures, disorganization was used to predict diagnosis; these measures were also used for assessing cognitive development. Subjects with psychosis were found to retain a linguistic structure more akin to that of children’s speech, failing to mature in complexity. Early identification of risk could make use of these measures of cognitive development of speech.

As fourth presenter, Dr. Terje Holm Lund will focus on challenges that need to be solved for successful implementation of language technologies in psychiatry, as well as some of the opportunities for translating the recent advances into clinically useful tools. Although new technological frameworks that leverage speech technology and natural language processing methods provide unprecedented opportunities for remotely monitoring behavior, the challenge of creating a useful analytic framework for clinical purposes remains.

Finally, the discussant, Dr. Cheryl Corcoran will review the presented data in the context of her experience and ongoing leadership in the field of language analysis in psychosis, leading audience discussion and outlining suggestions for future research in this promising and fast-developing field.

24.1 VERBAL COMMUNICATION DISORDERS IN SCHIZOPHRENIA SPECTRUM PATIENTS: SYMPTOM AND SIDE EFFECT

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SIRS 2019 Abstracts