

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 $\alpha 7$ nicotinic acetylcholine receptor ($\alpha 7$ -nAChR) in the hippocampus of patients with schizophrenia has been suggested from study of postmortem tissue, and therapies that increase signaling through the $\alpha 7$ -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 $\alpha 7$ -nAChR in individuals with recent onset psychosis compared to healthy controls. Building on the recent development of $\alpha 7$ -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 $\alpha 7$ -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 ($P_s \leq 0.001$), 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 ($P_s \leq 0.002$). Controlling for BMI or race did not change the lower VT in individuals with NP compared to AP ($P_s = 0.01$), 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 $\alpha 7$ -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 patients 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 Voppel) and the transformation of research into clinically useful tools (Terje Holmlund).

First, Alban Voppel 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 usage 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 Holmlund 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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Background: Verbal communication disturbances are a key diagnostic feature of schizophrenia. These disturbances present in different aspects, which can be assessed by looking at form and meaning. However, research on this topic is often confounded by the effects of antipsychotic medication. It therefore remains unclear which aspects of language production are influenced by antipsychotics, and which disturbances can be viewed as true psychotic symptoms. Automated language analysis has recently shown to be a useful tool to characterize verbal communication disturbances in schizophrenia.

Methods: The spoken language of 42 healthy controls and 48 patients with a schizophrenia spectrum disorder was recorded using a semi-structured interview designed to elicit spontaneous speech in a natural setting. The audio was analyzed for measures of speed and quantity. For a subset of participants, the transcribed interview was analyzed using a novel Natural Language Processing (NLP) word2vec model to quantify incoherence. For patients, dopamine receptor affinity of their antipsychotic drug was estimated. Symptom severity was assessed by means of the Positive and Negative Syndrome Scale (PANSS).

Results: Overall, schizophrenia spectrum patients spoke slower and produced fewer words than the healthy controls. Language measures revealed medium to strong correlations with PANSS negative and general scores. Usage of antipsychotics with strong D2 receptor affinity was found to have the strongest effect on speech. Word2vec trained models were able to differentiate between patients and controls.

Conclusions: Automated assessments of aspects of verbal communication show promise in elucidating and quantifying various symptoms. Our results indicate that usage of antipsychotic medication has a marked effect on verbal communication in addition to disturbances that are better interpreted as part of the illness. These medication-effects should be taken into account when analyzing language disturbances in schizophrenia. Word2vec proved to be a useful tool to differentiate between subjects and controls, reflecting disturbances in both meaning and structure in verbal communication. This research illustrates the possibilities in automated assessment of language which can serve as measures of symptom severity, medication effects and open the door to diagnosis and prognosis.

24.2 NATURAL LANGUAGE PROCESSING STUDIES OF PSYCHOSIS AND ITS RISK STATES

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Background: Subtle disturbance in language production is evident in schizophrenia across illness stages. Recently, we have shown that reductions in semantic coherence and syntactic complexity are evident in schizophrenia prior to initial psychosis onset, and cross-validated a machine learning linguistic classifier/predictor of later psychosis onset in two independent clinical high risk (CHR) cohorts. In the current study, we turn our attention to the use of idiosyncratic speech and metaphor in spoken language in both schizophrenia patients and clinical high-risk youths, which can be considered to be a feature of semantic incoherence at the single word level (Kuperberg et al., 2010). Canonical examples from Andreasen (1986) include “time vessel” for “watch” and “hand shoe” for “glove”. Manual analyses have suggested increased use of idiosyncratic/bizarre metaphors among schizophrenia patients, as compared with controls (Billow et al., 1997). Herein, we used automated natural language processing to assess idiosyncratic speech in schizophrenia and its risk states.

Methods: Transcripts of open-ended interviews (Ben-David et al., 2014) were obtained from 18 patients with schizophrenia, 15 healthy controls, and 34 youths at clinical high risk (CHR) for psychosis, of whom five were known to develop psychosis within 2.5 years, previously assessed for

semantic coherence and syntactic complexity (Bedi et al., 2015). Metaphors were tagged as tokens in running text, using a metaphor detection algorithm (Do Dinh and Gurevych) that was trained on the VU Amsterdam Metaphor Corpus (Steen et al., 2010), using supervised sequential learning on a multilayer perceptron (1 hidden layer) with a sliding window (100 epochs). Each token was rated on sentiment and bizarreness of words was measured (measuring likelihood of next word in a 2-gram model).

Results: Schizophrenia patients had a significantly higher proportion of metaphor tokens in speech, as compared with healthy comparison subjects (6.3% vs. 5.2%, $t = 3.76$, $p < .001$); there were no sex differences in use of metaphor. We used leave-one-out cross-validation (LOO-CV) of metaphor, sentiment and bizarreness features, along with sex and age, to generate a support vector classifier with 84% accuracy ($p < .005$) in discriminating the speech of schizophrenia patients from healthy controls. We similarly used these same features to generate a convex hull classifier that had 97% accuracy in predicting psychosis in the CHR group. Finally, we applied the schizophrenia metaphor/sentiment/bizarreness classifier to the CHR cohort, tagging 29 of 34 CHR patients (including all CHR converters), suggesting that the idiosyncratic use of speech seen in schizophrenia might be characteristic of spectrum disorders, independent of psychosis outcome.

Conclusions: 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. In this first use of automated methods to detect idiosyncratic speech and metaphors in schizophrenia and its risk states, we find increased usage in schizophrenia, as compared with healthy individuals, a pattern that extends to the clinical risk state that is sensitive but not specific to psychosis outcome, suggesting it might be used as a screen to identify individuals with attenuated psychosis syndrome.

24.3 EARLY MARKERS OF THOUGHT DISORGANIZATION IN SPEECH STRUCTURE

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Background: Early psychiatric descriptions of psychosis identified the importance of assessing thought organization to differentiate syndromes that present a cognitive risk. In chronic psychotic patients, word graph analysis shows potential as complementary psychiatric assessment of aspects of speech structure in free speech.

Methods: This analysis relies mostly on connectedness (based on graph theory such as number of edges, largest connected component - LCC and largest strongly connected component - LSC), a structural feature of speech that is anti-correlated with negative symptoms.

Results: On recent onset psychosis, at the first clinical contact, graphs connectedness and similarities to random graphs combined into a single (Disorganization Index) were predictive of schizophrenia diagnosis six months in advance with more than 90% accuracy. In typical development the same connectedness attributes tracks cognitive development (such as IQ and theory of mind abilities) and reading acquisition. Here we report that a graph-theoretical computational analysis of verbal reports from subjects ages 2–62 reveals asymptotic changes over time that depend more on education than age. In typical subjects, repeated edges and lexical diversity stabilize after elementary school, whereas graph size and connectedness only steady after high school. Repeated edges decrease towards random levels, while lexical diversity, connectedness and graph size increase away from near-randomness towards a plateau in educated adults. Subjects with psychosis do not show similar dynamics, presenting at adulthood a children-like speech structure. Typical subjects increase the range of word recurrence over school years, but the same feature in subjects with psychosis resists education.

Conclusions: Despite exposure to education, subjects with psychosis retain a linguistic structure akin to that of children’s speech, failing to mature in