Schizophrenia faces many challenges due to complexity at multiple levels, from genetic, physiological to symptoms levels. The explosion in genetics information, the development of multimodal functional and structural imaging techniques and of ecological momentary assessment, generate large data sets. Computational approaches were proposed to allow the translation of knowledge and understanding between numerous levels of analysis, from subcellular to sociological (Redish and Gordon, 2016). This symposium aims to discuss various computational approaches towards the understanding of psychopathological, neurocognitive as well as predicting functional outcomes of schizophrenia.

Dr. Powers will discuss novel findings on specific psychotic symptom dimensions using computational modeling of sensory processing: hallucinations of simple tones produced by audiovisual Pavlovian conditioning occur more frequently in individuals who experience daily hallucinations, engage a network of brain regions previously identified as being important for clinical hallucinations, and occur because of the over-weighting of priors during perceptual inference. Critically, higher-level learning parameters identified using this approach differentiate those with psychosis from those without, regardless of hallucination status. These approaches have relevance to risk stratification in individuals at clinical high risk of developing psychosis and may be useful in identifying differential contributions of neurotransmitter systems to specific computational abnormalities in psychosis.

Cognitive deficits are core symptoms of psychotic disorders like schizophrenia, responsible for significant functional impairment and disability. Yet quantifying cognition in schizophrenia remains a challenge in the busy clinical setting. Digital technologies like smartphones represent a novel proxy for relevant cognitive symptoms given the complex social, executive, working memory, psychomotor processing, and attentional domains often involved in using these devices. Dr. Torous will share novel results of smartphone based micro-cognitive measures (MCM) captured in patients with schizophrenia, with MCM defined as a multimodal stream of data variably composed of smartphone metadata, smartphone digital phenotyping data, and smartphone cognitive assessments.

Dr. Hess investigated clinical and metabolic features that allow to assess the risk of poor functional outcomes in early psychosis patients (EPP), using state of the art topological analysis. Three clusters of EPP with similar metabolic and/or clinical profiles were identified. The comparison of these clusters allowed to characterize patients’ subgroups that displayed distinct social and occupational functioning after 3 years of follow-up. These novel findings suggest that topological analysis of a combination of symptoms and blood metabolic profile might contribute to the prediction of functional outcome at early stages of psychosis.

Dr. Koutsouleris will present recent findings from the multi-site European PRONIA project (Personalised Prognostic Tools for Early Psychosis Management). The project’s first results highlight the potential of multimodal machine learning techniques to establish an individualized prediction of clinically relevant outcomes in adolescents and young adults in at-risk or early stages for psychosis or recent-onset depression. He will discuss the challenges of translating these tools to clinical real-world with a focus on how to optimally combine examinations under the premises of accuracy, economic viability, and patient safety.

29.1 COMPUTATIONAL MODELING OF PERCEPTION AND BEHAVIOR REVEALS HIDDEN INSIGHTS INTO MECHANISMS OF PSYCHOTIC SYMPTOMS

Albert Powers*,1, Christoph Mathys2, Philip Corlett3

1Yale University School of Medicine; 2SISSA; 3Yale University

Background: Because it happens so quickly and automatically, it may be intuitive to think of perception as a passive process in which our brains simply receive input about our surroundings via our sensory organs. However, it has long been clear that perception is, instead, an active process, characterized by the building of an internal model of our environment, blending incoming sensory evidence with prior beliefs about what is around us. Within this framework, hallucinations may be thought to arise from an increased influence of these prior beliefs during perception.

Methods: To test this idea, we adapted a classical sensory conditioning paradigm to the functional imaging setting: participants were exposed to repeated pairings of a salient visual stimulus with a faintly-presented auditory stimulus and subsequently reported the perception of the auditory stimulus even when it was not present, contingent on the presence of the visual—a conditioned hallucination. We recruited participants who differed orthogonally in whether they had hallucinations and/or psychosis, resulting in four groups: those with psychosis both with hallucinations (P+H+) and without (P+H-), otherwise healthy voice-hearers (P-H+), and healthy controls (P-H-).

Results: We found that conditioned hallucinations readily occur in all subjects but with markedly increased frequency in those who hallucinate (P+H+ and P-H+), regardless of psychosis status. Conditioned hallucinations activated stimulus-responsive auditory cortex in addition to a network of regions active during clinical hallucinations. Computational modeling demonstrated an increased reliance on heightened prior beliefs in those with hallucinations (encoded by anterior insula and superior temporal sulcus), regardless of psychosis status. By contrast, those with psychosis exhibited a decreased recognition of changing stimulus contingencies (encoded by cerebellum and hippocampus), regardless of hallucination status.

Conclusions: These results may represent an objective means to distinguish people with hallucinations from those without, and, orthogonally, a need for treatment from those without. Preliminary data indicate these measures may also be useful in risk stratification in those at clinical high risk (CHR) of psychosis. Future work will focus on characterizing the predictive power of these measures in both diagnosis and treatment selection.

29.2 DIGITAL PHENOTYPING OF MICRO-COGNITIVE MEASURES (MCM) IN PATIENTS WITH SCHIZOPHRENIA

John Torous*,1, Hannah Wisniewski1, Matcheri Keshavan1, Gang Liu2, Ian Barnett1

1Harvard Medical School; 2Harvard TH Chan School of Public Health; 3University of Pennsylvania

Background: Cognitive deficits are core symptoms of psychotic disorders like schizophrenia, responsible for more functional impairment and disability than classical symptoms like auditory or visual hallucinations. Yet quickly quantifying cognition remains a challenge, and even brief assessments often requires at least 30 minutes. Because of the inability to easily assess cognition - cognitive side effects of medications are rarely tracked, referrals for cognitive remediation therapy are rarely made, and accommodations for patients’ specific cognitive deficits are rarely considered.

Methods: We define micro-cognitive measures (MCM) to be a multimodal stream of data that is variably composed of 1) smartphone metadata 2) smartphone digital phenotyping data, and 3) smartphone cognitive assessments. By smartphone metadata we refer to the ability to now automatically collect phone behaviors that are related to cognitive domains such as attention associated with phone checking behaviors, memory associated with recalling passwords, and specific patterns of speech associated with language.

In this observational 3-month study with 30 participants with a confirmed diagnosis of schizophrenia, the Brief Assessment of Cognition (BACS) was administered before and after 90 days of capturing micro-cognitive measures via a smartphone app. Participants downloaded the app onto their personal smartphone and were promoted to take assessments of memory...
and attention 5 days per week for all weeks of the study. There was no compensation for app use.

**Results:** While our study is currently collecting ongoing data, results will be finalized by early 2019. To date participants in the study are completing ~60% of prompted assessments with the rate of engagement declining over the 90-day study duration. There have been no adverse reported events. Qualitative feedback from participants about the app has been positive.

**Conclusions:** It is feasible to collect micro-cognitive measures via smartphones in patients with schizophrenia. Understanding both the validity and reliability of these new measures will require continued careful research.

### 29.3 TOPOLOGICAL ANALYSIS ENABLES PREDICTION OF FUNCTIONAL AND SOCIAL OUTCOMES IN EARLY PSYCHOSIS

Kathryn Hess*, 1 Margot Fournier*, Martina Scolamiero1, Mehdi Gholam-Rezaee2, Raoul Jenni2, Dean Jones1, Michel Cuenod3, Philippe Conus4, Kim Do1
1 EPFL; 2 Center for Psychiatric Neuroscience, Lausanne University Hospital; 3 EPFL/EPFLKTH; 4 University Hospital of Lausanne; 5 Center for Psychiatric Neuroscience, Lausanne University Hospital (CHUV); 6 Emory University

**Background:** Predicting functional outcome is a major challenge in service care of early psychosis patients (EPP). We investigated clinical and metabolic features that enable objective assessment of the risk of poor functional outcomes in early psychosis patients (EPP), using state-of-the-art topological data analysis (TDA). The guiding philosophy of TDA is that the shape of large data sets, encoded by a mathematical signature, should reveal important relations among the data points. Our primary TDA tool is Mapper, which provides unsupervised multivariate pattern analysis of high-dimensional data, producing a compressed visual representation of the data giving a strong indication of where to look for meaningful clustering. Application of Mapper has already led to a number of remarkable results, including the identification of a new subtype of breast cancer and of two phenotypically distinct types of fragile X syndrome.

**Methods:** Recruitment: 101 EPP with informed consent were recruited from the Lausanne “Treatment and early Intervention in Psychosis Program". They had reached the psychosis threshold on the CAARMS scale. Patients were assessed at entrance of the program by PANSS and MADRS, functioning by SOFAS and GAF scales. After 3 years of clinical follow-up, EPP were evaluated for symptoms levels, social and occupational functioning. Metabolomics: Plasma extracts at the program begin were analyzed by liquid-chromatography-mass spectrometry. Features data (m/z, retention time, integrated ion intensity) were extracted using xMSanalyser v1.3.5 with apLCMS v5.9.4. Mapper: Using the Mapper algorithm, we built a topological map representing the EP cohort through the lens of the PANSS scores at baseline. The mapper algorithm captures the shape of high dimensional data through a graph. Nodes represent patients or groups of patients. Edges between nodes represent shared patients.

**Results:** Three distinct clusters of patients could be identified: Group A, characterized by low levels of negative (N2) and depression symptoms (G6); group B, characterized by high levels of positive symptoms (P1, 6) having the worst outcome; and group C with high levels of negative (N2) and depression symptoms. Comparison of the groups after 3-years of clinical follow-up showed that group A displayed significantly better social and occupational functioning. The same grouping and predictions were confirmed in a second independent cohort of EPP. Inclusion of the metabolomics data revealed that group A had a distinct profile, which may serve as predictor of functional outcome in EPP.

**Conclusions:** These novel findings suggest that topological analysis of a combination of symptoms and blood metabolic profile might contribute to the prediction of functional outcome at early stages of psychosis.

### 29.4 IMPLEMENTING PRECISION PSYCHIATRY FOR THE EARLY RECOGNITION OF ADVERSE OUTCOMES IN PSYCHOSES: FINDINGS FROM THE PRONIA STUDY

Nikolaos Koutouleri1, Stefan Borgwardt2, Paolo Brambilla3, Rachel Upthegrove4, Eva Meisenzahl1, Raimo Salokangas2, Stephen Wood2, Marlene Rosen2, Theresa Haidl2, Rebekka Lenc1, Alessandro Bertolino3, Dom Dwyer*1
1 Ludwig-Maximilian-University; 2 University of Milan; 3 University of Birmingham; 4 University of Turku; 5 Oxygen, the National Centre of Excellence in Youth Mental Health; 6 University of Cologne; 7 University of Muenster; 8 University of Bari

**Background:** The clinical high-risk state for psychosis does not only confer an elevated risk for developing psychotic disorders but is associated with pluripotent risks for adverse clinical and functional outcomes. Establishing generalizable tools that provide quantitative risk estimates for these outcomes is a key step toward the implementing personalized preventive intervention that scale beyond the

**Methods:** The talk will present recent findings from the PRONIA study (Personalized Prognostic Tools for Early Psychosis Management) demonstrating the feasibility of predicting functional and clinical outcomes in adolescents and young adults in a clinical high-risk state for psychosis (CHR) or with recent-onset depression (ROD). The talk will highlight the use of machine learning and multivariate data mining concepts and link those applications to potential clinical utility of these models for an improvement of early recognition and prevention.

**Results:** I will present and discuss the performance and decision rules generated by the machine learning analysis of clinical, imaging-based, genetic and combined data for the individualized prediction of (1) social and role functioning outcomes, (2) transition to psychosis, and (3) remission vs. non-remission from symptomatic states in CHR and ROD patients.

**Conclusions:** The recent findings generated by the PRONIA consortium suggest that generalizable and clinical useful prediction pathways can be established to support the early recognition of adverse outcomes in CHR and ROD patients. External and prospective validation of these prognostic pathways is needed across healthcare systems to benchmark the clinical and health economic utility of these precision psychiatry methods.

### 30. ULTRA HIGH-FIELD 7-TESLA NEUROIMAGING: NEW INSIGHTS INTO MECHANISMS OF PSYCHOSIS

Lena Palaniyappan
University of Western Ontario

The ability to visualize alive human brain’s function, structure and chemical composition in ultra-high field 7-Tesla MRI has opened the doors for several neuroscientific advances in recent times. This symposium will focus on the data gathered from this high-resolution access to a patient’s brain tissue to question some of the existing views on the mechanisms linked to psychosis.

The symposium has the following objectives each discussed by the presenters:

(a) Dr. Frangou will demonstrate how the increased spatial resolution of 7T structural imaging enabled the development and validation of a new method for deriving lamina-specific measures of intracortical myelin. Using this measure, it is possible to identify brain regions of disrupted intracortical organization in schizophrenia that map to symptomatic severity and cognitive disruption.