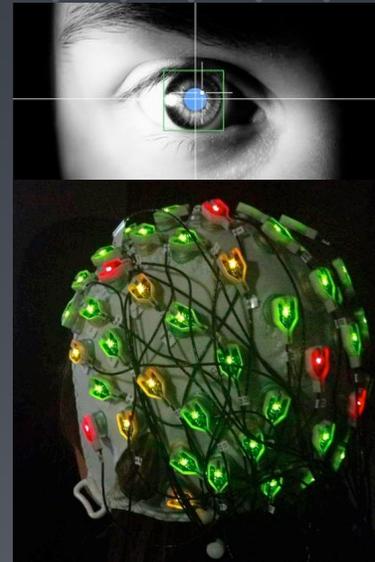




CANLAB

Clinical Affective Neuroscience Laboratory

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A warm welcome from Gregory P. Strauss, Ph.D.

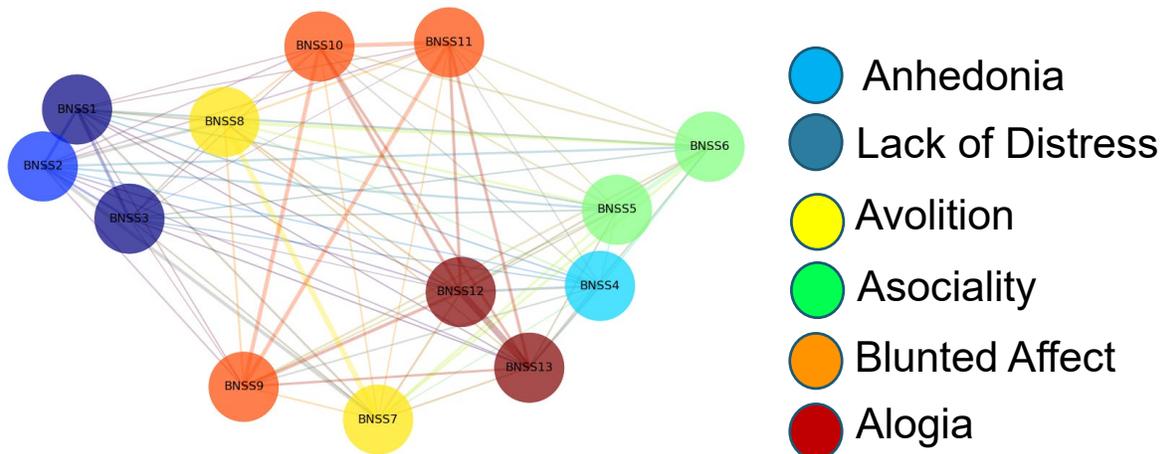
The overarching goal of the Clinical Affective Neuroscience Laboratory at the University of Georgia is to conduct research on the mechanisms underlying symptoms of schizophrenia and factors that predict conversion to psychosis in at-risk youth. We aim to use the knowledge gained from these studies to develop novel interventions and risk prediction methods for psychiatric conditions. We wish to thank the individuals who participated in our studies and the healthcare providers who made referrals. Your contributions have enabled us to make new contributions to the understanding of psychiatric conditions like schizophrenia and bipolar disorder. In 2018, our lab published 35 scientific papers, submitted an additional 15 papers that are under review, presented >20 talks and posters at scientific conferences, and acquired over \$3.5 million in new grants to fund our research. Below, we provide a summary of key findings and current directions in our research.

NEWSLETTER

2018

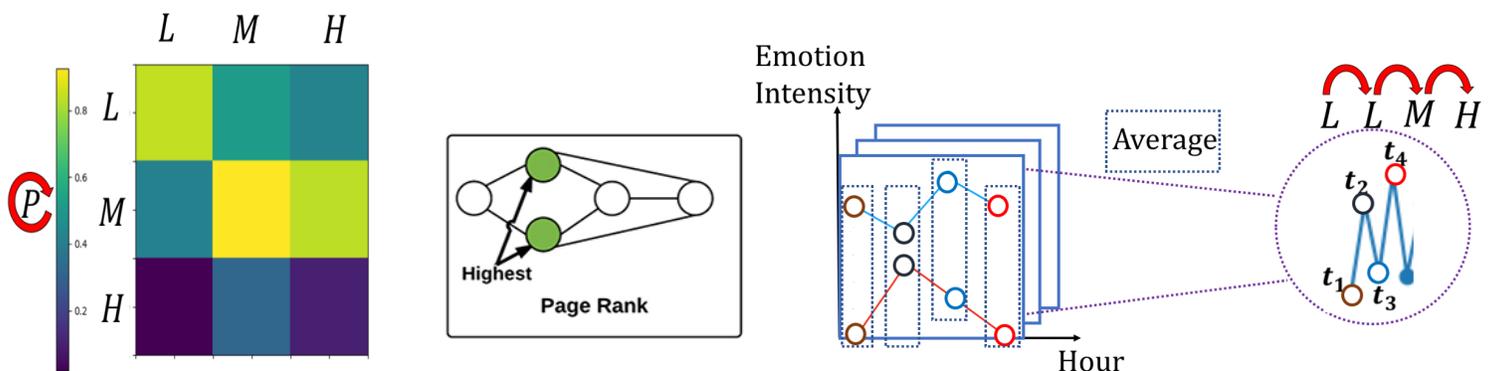
Challenging assumptions about the structure of negative symptoms

Negative symptoms reflect reductions in emotion, communication, and behavior. They are common to schizophrenia and other psychiatric conditions. Recently, the field has contended that negative symptoms are best viewed as 2 dimensions reflecting diminished expression and diminished experience. However, across a series of 5 papers, our lab has challenged that notion using Confirmatory Factor Analysis and Network Analysis, consistently finding that negative symptoms reflect 5 domains: anhedonia, avolition, asociality, alogia, blunted affect. These findings suggest the search for pathophysiological mechanisms and targeted treatments should focus on these 5 domains and that a revision to DSM-5 diagnostic criteria may be warranted. Collaborators: Farnaz Esfahlani, Hiroki Sayama, Anthony Ahmed, Brian Kirkpatrick, Daniel Allen, Eric Granholm, Jim Gold



Modeling anhedonia: a stochastic dynamical systems approach

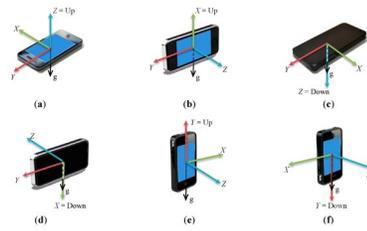
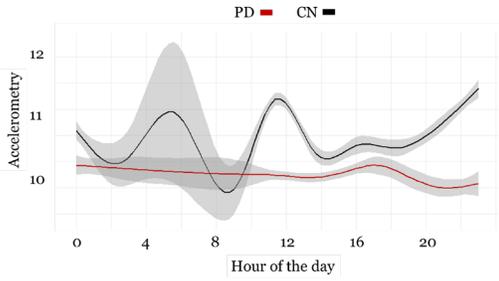
Anhedonia has traditionally been considered a diminished capacity to experience positive emotion in schizophrenia. However, laboratory studies challenge that notion, indicating that hedonic response is intact in schizophrenia. Our lab has been examining whether anhedonia reflects a reduction in the frequency of pleasurable activities that results from disruptions in the temporal dynamics of emotion. We have mathematically modeled ecological momentary assessment data of real-world emotion reports using Markov chain analysis, network analysis, and machine learning and found that reductions in the frequency of pleasurable activity are associated with disruptions in the persistence of positive emotion. Collaborators: Farnaz Esfahlani, Hiroki Sayama.



Digital phenotyping: Novel mobile assessments of negative symptoms

Negative symptom assessment has historically relied on psychiatric rating interviews. Although these have resulted in invaluable information about the nature of negative symptoms and measurement tools for clinical trials, they have inherent limitations. We have been exploring whether “digital phenotyping” via mobile technologies such as smart phones and bands can account for some of these limitations and provide more ecologically valid measures of negative symptoms. Our results suggest that novel mobile technologies, such as geolocation, accelerometry, and automated measures of facial and vocal affect are reliable and valid. Using these measures, we have gained insight into the contexts in which negative symptoms emerge and environmental factors that influence them.

Collaborators: Alex Cohen, Brian Kirkpatrick



Correlation of EMA measures and geolocation

	Δ d	Δ mh	Home %	Goal-directed	Social activity	Anhedonia	Avolition	Asociality	
Δ d	1	0.42	-0.33	0.08	0.05	-0.03	-0.05	0.06	Δ d
Δ mh	0.58	1	-0.88	0.37	0.22	-0.04	-0.03	0.22	Δ mh
Home %	-0.46	-0.82	1	-0.42	-0.19	0.12	0.09	-0.16	Home %
Goal-directed	0.18	0.29	-0.38	1	0.28	-0.22	-0.13	0.17	Goal-directed
Social activity	0.17	0.25	-0.26	0.25	1	0.17	0.14	0.69	Social activity
Anhedonia	0.01	-0.02	-0.02	0.01	0.01	1	0.87	0.53	Anhedonia
Avolition	0.01	0.01	-0.04	0.02	0.02	0.81	1	0.45	Avolition
Asociality	0.09	0.09	-0.14	0.16	0.34	0.55	0.5	1	Asociality

Correlation magnitude: -1.0 -0.5 0.0 0.5 1.0

Note: p < .05 for all colored cells

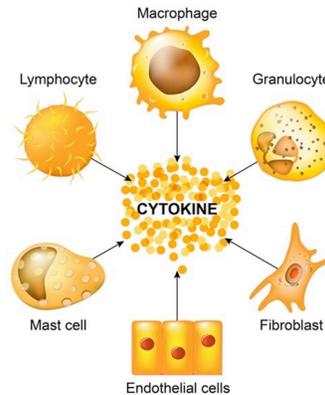
Computationally phenotyping negative symptoms

We are currently examining whether there are subtypes of individuals with schizophrenia who can be computationally phenotyped using neurocomputational models of reinforcement learning, effort-cost computation, and the expected value of control. We are also examining whether these computational phenotypes exist in bipolar disorder and predict negative symptom severity transdiagnostically. Collaborators: Amitai Shenhav, Anne Collins, Michael Treadway

$$P(a1, t) = \exp(w(s, a1, t)/\beta) / (\exp(w(s, a1, t)/\beta) + \exp(w(s, a2, t)/\beta))$$

Blood-based biomarkers of negative symptoms

In a recent study, we found that negative symptoms are associated with cytokines, a blood-based biomarker of inflammation. We are examining whether inflammatory processes play a key role in the link between certain aspects of reward processing and negative symptoms in people diagnosed with schizophrenia and youth at-risk for developing a psychotic disorder. Collaborators: Brian Miller, Katie Erlich.



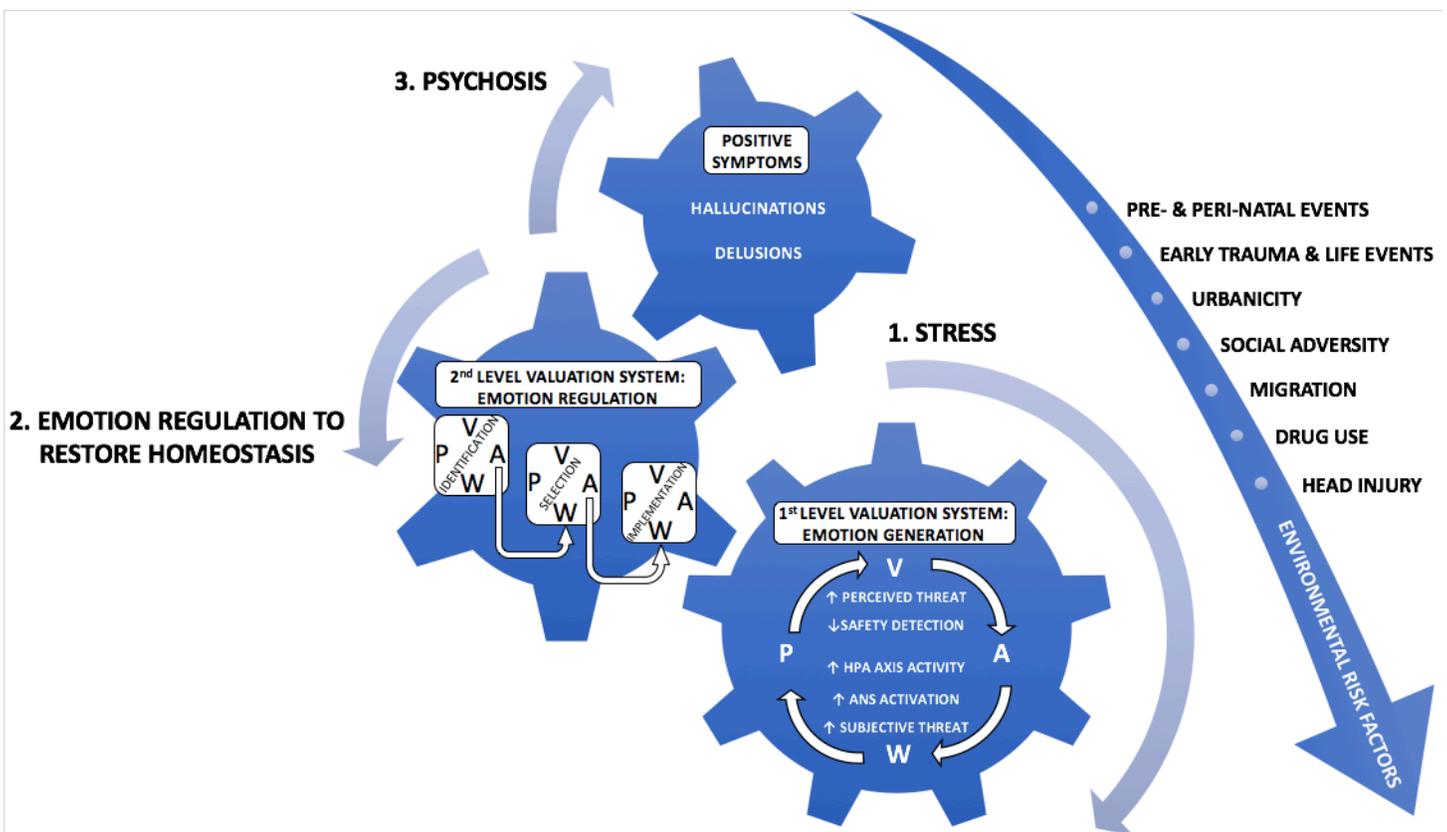
Enhancing psychosis risk prediction algorithms

Given that few individuals achieve recovery after the onset of a psychotic disorder, there is increasing interest in the early identification and prevention of psychosis. Psychotic disorders are typically preceded by a prodromal (i.e., pre-illness) phase characterized by functional decline and subtle attenuated symptoms that progressively worsen over the course of several months to years. This period is of interest both as a window for investigating processes involved in disease onset and as a potential point of intervention and prevention. State of the art clinical assessments are now available to identify a group of youth at “clinical high risk” (CHR) for developing a psychotic disorder based on attenuated positive symptom criteria. However, more than 75% of youth identified as CHR do not convert to full psychotic illness within two years and it remains unclear which pathophysiological processes are most predictive of psychosis risk. Our lab is currently exploring whether the assessment of negative symptoms via clinical rating scales, ecological momentary assessment, and social media can enhance psychosis risk prediction algorithms. We are also examining whether computational and digital phenotypes improve the prediction of developing a psychotic disorder. Collaborators: Vijay Mittal, Elaine Walker, Anne Collins



Emotion regulation in schizophrenia and youth at-risk for psychosis

The stress-vulnerability model remains one of the leading theories on the origins of psychosis. However, heightened stress reactivity alone only modestly predicts conversion to psychosis among clinical high-risk youth and has not led to breakthroughs in prevention. To develop novel targets for early intervention, the field is in need of new approaches that evaluate additional pathophysiological processes that might give rise to psychotic disorders. Abnormalities in emotion regulation (ER) (i.e., the ability to decrease the intensity or frequency of negative emotion using strategies) have been shown to predict the emergence and maintenance of several psychiatric disorders. However, ER has yet to be extensively studied in relation to psychosis. Our lab is systematically examining emotion regulation abnormalities in adults with schizophrenia and youth at clinical high-risk for psychosis through the lens of Gross' extended process model. Individuals with psychotic disorders display specific abnormalities at each stage of the emotion regulation process in the extended process model: identification (a threshold for detecting the presence of an emotion and determining whether to regulate that is too low), selection (choosing an excessive number of strategies and those that are contextually inappropriate), implementation (reduced prefrontal inhibitory control over the amygdala that results in ineffective execution of specific strategies), and monitoring dynamics (switching too often, stopping too late). Abnormalities at each of these stages are predicted by specific moderators (e.g., emotional awareness, cognitive effort, visual attention). We are currently examining whether these abnormalities exist in youth at clinical high-risk for psychosis and whether they predict the development of a psychotic disorder above and beyond stress reactivity alone. Collaborators: Farnaz Esfahlani, Hiroki Sayama, Dean Sabatinelli, William Horan.



Implicit and explicit cognitive effort in schizophrenia

Due to the role that cognitive impairment plays in functional disability in psychotic disorders (PDs), it is critical that progress be made in understanding mechanisms leading to cognitive deficits, in order to develop effective treatments and reduce disability. Past studies suggest that PDs are characterized by a “generalized” neurocognitive deficit, which is thought to have a common underlying etiology that broadly impacts all domains of cognitive functioning. Although central nervous system and general systems abnormalities have been proposed to account for the generalized deficit, these theories have yet to lead to significant treatment advances. We are investigating a novel motivational account of the generalized neurocognitive deficit based on a new theoretical model of motivation-cognition interactions generated from recent breakthroughs in the field of cognitive neuroscience. We are evaluating the central hypothesis that there are two motivational pathways to the generalized neurocognitive deficit. The first pathway involves *implicit cognitive effort processes*. We propose that anterior cingulate cortex (ACC) dysfunction causes impairment in implicitly monitoring effort allocation, which leads to a failure to achieve an efficient balance between effort expenditure and conservation. Deficits in effort monitoring are costly when patients perform demanding tasks over an extended period of time, leading to rapid cognitive resource depletion that is represented physiologically as decreased functional connectivity in the fronto-parietal network and increased connectivity in the default mode network. With depleted cognitive resources, people with PDs become more prone to utilizing less effortful reactive control processes and fail to recruit more effortful proactive control processes needed to support a range of mental operations. The second pathway involves *explicit cognitive effort processes*. We propose that people with PDs have deficits in reward anticipation and value representation that result from reduced activation of the ventral striatum (VS) and ventromedial prefrontal cortex (vmPFC), which propagate forward and impair explicit effort cost decision-making abilities. In turn, experiencing effort expenditure as being subjectively costly leads patients to be less likely to recruit effortful proactive control and sustain dorsolateral prefrontal cortex (DLPFC) activation throughout tasks where reward incentives are offered for optimal performance. Failure to value available incentives in turn leads to global cognitive impairment across a range of domains because proactive control mechanisms are not recruited to support performance. Our preliminary EEG, pupillometry, and eye tracking data provide support for these two pathways and their association with the generalized neurocognitive deficit; in future studies we will test the hypothesized neuroanatomy using fMRI. Collaborators: Larry Sweet, Jennifer McDowell, Brett Clementz, Andrew Westbrook.

