# Data Blitz Abstracts

## #1 The behavioral manifold of the Exploration-Exploitation dilemma and its implications for anhedonia and anxiety

Xinyuan Yan[1], Becket Ebitz[3], Collin Meyer[1], Cathy Chen[2], Dameon Harrell[1], Nicola Grissom[2], Suma Jacob[1], David Darrow[4] and Alexander B Herman[*1].

[1] Department of Psychiatry and Behavioral Sciences, University of Minnesota, Minneapolis, MN 55455, USA
[2] Department of Psychology, University of Minnesota, 75 E River Rd, Minneapolis, MN 55455, USA
[3] Department of Neuroscience, Universite de Montreal, 2900 Edouard Montpetit Blvd, Montreal, Quebec H3T 1J4, Canada
[4] Department of Neurosurgery, University of Minnesota, Minneapolis, MN 55455, USA

Making flexible decisions in a dynamic and uncertain world is critical for individuals to survive and thrive. One such decision is whether to exploit a known resource or explore for a potentially better one. The balance between exploration and exploitation is one important form of cognitive flexibility that may be affected by neuropsychiatric states including anhedonia and anxiety. We studied human exploration-exploitation behavior and its computational associations with anhedonia and anxiety in a large online sample (N = 1001). We administered an explore-exploit task, a restless 3-armed bandit, along with standard symptom inventories. By implementing t- distributed stochastic neighbor embedding (t-SNE) algorithm on model-free behavior, we found a low-dimensional manifold of behavior. On this manifold, we identified two distinct clusters of participants. Interestingly, these naturally produced clusters were comparable in anhedonia traits but showed a highly significant difference in anxiety traits. Notably, individuals in the high- anxiety cluster exhibited a higher degree of explorative behavior. Results from a novel foraging model showed that participants in the high-anxiety cluster had a larger learning rate for prediction errors, as well as a higher learning rate for learning environment richness, but less value difference sensitivity (all $p < 0.001$). Intriguingly, we found that environmental learning predicted anhedonia scores but not anxiety traits; value difference sensitivity predicted anxiety traits but not anhedonia scores in the high-anxiety cluster. Our findings may shed light on the computational decision processes underlying anhedonia and anxiety in a normative population and could have further implications for dissociating subtypes of clinical conditions.

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## #2 Shared and unique brain network features predict child and parental internalizing and externalizing problems

Yueyue Lydia Qu[1], Jianzhong Chen[2,3,4,5], Angela Tam[2,3,4,5], Leon Qi Rong Ooi[2,3,4,5,6], B. T. Thomas Yeo[2,3,4,5,6,7], Avram J. Holmes[1,8]

[1] Department of Psychology, Yale University, New Haven, CT, USA
[2] Department of Electrical and Computer Engineering, National University of Singapore, Singapore, Singapore
[3] Center for Sleep and Cognition, National University of Singapore, Singapore, Singapore
[4] Center for Translational MR Research, National University of Singapore, Singapore, Singapore
[5] N.1 Institute for Health & Institute for Digital Medicine (WisDM), National University of Singapore, Singapore, Singapore
[6] Integrative Sciences and Engineering Programme (ISEP), National University of Singapore, Singapore, Singapore
[7] Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, USA
[8] Department of Psychiatry, Yale University School of Medicine, New Haven, CT, USA

Converging evidence suggests that shared features within and between large-scale brain networks can predict individual differences within broad domains of cognition, personality and mental health. In this study, we examined if individual differences in whole-brain functional connectomes in children can predict both child self-reported and parental internalizing and externalizing behavior. In a large sample of 2,265 typically developing children from the Adolescent Brain Cognitive Development (ABCD) study, we leveraged multikernel ridge regression models to predict both self-reported and parental behavioral measures across four symptom categories: internalizing, externalizing, thought, and attention-deficit hyperactivity disorder (ADHD) problems from subject-specific functional connectivity matrices across four brain states. Our analysis revealed that predictive network features are distinct across the symptom categories but similar within each symptom category in children. Furthermore, predictor-feature weights associated with child internalizing and externalizing problems were more similar to the corresponding symptom categories in parents than other symptom categories. Overall, our findings reveal domain specific brain network features in children that are predictive of both child and parent self-reported internalizing and externalizing problems.

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**#3** **Persistent changes in the state representation underlying behavioral addiction**

Ayaka Kato[1], Kanji Shimomura[2,3,] Kenji Morita[2,4]

[1] RIKEN Center for Brain Science, 2-1 Hirosawa, Wako, Saitama, 351-0198, Japan.
[2] Physical and Health Education, Graduate School of Education, The University of Tokyo, Tokyo, Japan
[3] Department of Behavioral Medicine, National Institute of Mental Health, National Center of Neurology and Psychiatry, Kodaira, Japan
[4] International Research Center for Neurointelligence (WPI-IRCN), The University of Tokyo, Tokyo, Japan

Reinforcement learning models often describe behaviors of humans/animals assuming a certain internal representation of the current situation or "state". Because state representation serves as the bases of value computation and thereby of higher cognitive functions, its alternation could result in mental illness (Radulescu & Niv, 2019). We studied behavioral addiction from the perspective of state representation. Cessation of habitual gambling or gaming is extremely difficult, even with a strong will to quit. We employed a "successor representation (SR)" of states and proposed a dopamine-related mechanism that makes resistance to habitual reward acquisition particularly difficult. We hypothesized that after years of engaging in a certain reward-obtaining behavior without resisting temptation, a dimensionality-reduced SR based on the goal state can be formed, although not always, and can become rigid, i.e., not updated. In the model assuming such a rigid reduced SR, persistent large positive reward prediction error (RPE) is generated upon reaching the goal once the individual begins to resist the temptation. Such persistent RPE is somewhat similar to the hypothesized persistent fictitious RPE due to drug-induced dopamine (Redish, 2004). Also, introduction of punishment after reward is not effective in the model. These results suggest that formation of a rigid, coarse SR may be a common mechanism for addiction to both substance and non-substance rewards (Shimomura, Kato, et al., 2021). Finally, we would like to discuss our latest attempt to address the possibility that positive bias in RPE due to uncertainty in state transitions may relate to gambling addiction.

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## #4 Atypical Prediction Error Learning is Associated with Prodromal Symptoms in Individuals at Clinical High Risk for Psychosis: A Computational Single-Trial Analysis of the Mismatch Negativity

Colleen E. Charlton[a], Jennifer R. Lepock[b,c], Daniel J. Hauke[a,d,e], Romina Mizrahi[f,g], Michael Kiang[b,c,h,*], Andreea O. Diaconescu[a,c,h,i,*]

[a] Krembil Centre for Neuroinformatics, Centre for Addiction and Mental Health (CAMH), Toronto, Ontario, Canada
[b] Centre for Addiction and Mental Health (CAMH), Toronto, Ontario, Canada
[c] Institute of Medical Sciences, University of Toronto, Toronto, Ontario, Canada
[d] Department of Psychiatry (UPK), University of Basel, Basel, Switzerland
[e] Department of Mathematics and Computer Science, University of Basel, Basel, Switzerland
[f] Douglas Research Centre, Montreal, Quebec, Canada
[g] Department of Psychiatry, McGill University, Montreal, Quebec, Canada
[h] Department of Psychiatry, University of Toronto, Toronto, Ontario, Canada
[l] Department of Psychology, University of Toronto, Toronto, Ontario, Canada

∗Joint last author

In predictive coding theory, psychosis symptoms are hypothesized to originate from disturbances in hierarchical information processing, more specifically the misattribution of salience to irrelevant sensory stimuli driven by aberrant precision-weighting of prediction errors (PEs). Computational models have emerged as a powerful tool for understanding psychosis symptoms, including delusions. Whether such models are also able to explain one of the most reliable biomarkers for psychosis, namely the auditory mismatch negativity (MMN), remains unclear. In our work, the MMN was elicited in 31 help-seeking antipsychotic-naive clinically-high risk (CHR) for psychosis individuals and 23 healthy controls using an auditory oddball paradigm. A hierarchical Bayesian model of learning was applied to single-trial EEG data to understand the computational mechanisms underlying the auditory MMN and assess the temporal expression of subject-specific computational trajectories, namely precision-weighted PEs and uncertainty at different levels of the processing hierarchy. Prodromal positive symptom severity was assessed in CHR using the Scale of Positive Symptoms positive subscale. We find evidence for the role of two hierarchically- coupled PEs, low-level sensory PEs and high-level volatility PEs, in implicit, statistical learning and auditory perceptual inference underlying MMN generation. Furthermore, we find that prodromal positive symptom severity is associated with increased expression of sensory precision-weighted PEs and informational uncertainty about one's internal model of sensory inputs, which jointly increase learning from incoming PEs. Our findings highlight the value of computational models for understanding the progressive pathophysiological mechanisms of psychosis, and emphasize the role of aberrant PE learning in the emergence of prodromal positive symptoms.

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**#5** **Momentary happiness depends on state-value prediction errors during learning**

Chang-Hao Kao, Olivia D. Jorasch, Samuel D. McDougle, and Robb B. Rutledge

Department of Psychology, Yale University

The function of mood is unclear, but one proposal is that it represents the momentum of rewards in an environment, whether the environment is getting better or worse. In reinforcement learning tasks, momentary happiness is correlated with prediction errors depending on outcomes and the values of chosen options (Blain & Rutledge, 2020). In a reinforcement learning task with multiple states, we tested whether happiness is better explained by prediction errors depending on the value of chosen options or on the value of the current state. We tested participants (n=200) with a high value pair (reward probabilities of 80% and 50%) and a low value pair (reward probabilities of 50% and 20%). Pairs were randomly ordered, and feedback was revealed for chosen options. Participants periodically reported momentary happiness. Consistent with prediction errors depending on state values, happiness was higher after wins from the 50% option in the low value pair compared to the 50% option in the high value pair ($p<0.001$). Similarly, happiness was higher after losses from the 50% option in the low value pair compared to the 50% option in the high value pair ($p<0.001$). Using model comparison, a model including state values and state-value prediction errors outperformed a model including action values and action-value prediction errors. Additionally, lower baseline mood parameters after accounting for mood dynamics were associated with greater depressive symptoms ($rho=-0.27$, $p<0.001$), consistent with previous findings. These results suggest that in environments with multiple states like in the real world, happiness depends on state-value prediction errors.

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**#6** **Deep brain stimulation-induced improvement in cognitive control is mediated by theta oscillations: implications for psychiatric neuromodulation**

Anusha B. Allawala[1,2], Stephanie Vartany[3], Raissa Mathura[4], Harrison Ritz, Joshua Adkinson PhD[4], Ron Gadot[4], Amitai Shenhav, PhD, Wayne Goodman[5], MD, Nader Pouratian[6],MD, PhD, Kelly Bijanki[4], PhD, David A. Borton[1,7,8], PhD, Sameer A. Sheth[4], MD, PhD

[1] School of Engineering, Providence, RI, United States
[2] Carney Institute for Brain Science, Brown University, Providence, RI, United States
[3] Department of Neuroscience, Brown University, Providence, RI, United Statesman what
[4] Department of Neurosurgery, Baylor College of Medicine, Houston, TX, United States
[5] Menninger Department of Psychiatry and Behavioral Sciences, Baylor College of Medicine, Houston, TX, United States
[6] Department of Neurosurgery, University of Texas, Southwestern, Dallas TX, United States
[8] Department of Veterans Affairs, Providence VA Medical Center for Neurorestoration and Neurotechnology, Providence, RI, United States

Deficits in cognitive control, the ability to adjust response or attention in the face of competing or changing demands, are thought to be responsible for inflexible behaviors in neuropsychiatric diseases. Here we report findings from intracranial stereo-EEG recordings collected across prefrontal networks in 13 human subjects during a cognitive control task. We employed a forced two-choice control task that parametrically varied the strength in the target and the distractor interference of a visual stimulus, resulting in granular variation in response congruence. Reaction time(RT) and accuracy worsened with increasing levels of conflict across subjects(Cohen's daccuracy=0.7, Cohen's dRT= 0.2). Single-trial regression analyses revealed a parametric effect of task conflict with theta-band(4-7 Hz) power across the dorsolateral PFC(dlPFC), dorsal anterior cingulate cortex, orbitofrontal cortex(OFC) as well as the insula. Whereas 10 subjects underwent stereo-EEG implants for epilepsy monitoring, 3 were participating in a clinical trial of deep brain stimulation(DBS) for treatment-resistant depression(TRD) and were additionally implanted with DBS leads in the ventral striatum and the subcallosal cingulate. DBS improved behavioral performance, demonstrated by reduced RT(1080±10ms to 840±50ms), and improved accuracy(70±9.8% to 90±5%). While we observed an increase in theta power across the PFC and ACC in TRD participants following DBS, the effect of conflict in theta power was reversed(theta power decreased with increasing conflict in the dlPFC and OFC). Leveraging this behavioral paradigm with distributed intracranial recordings and causal manipulation broadens our understanding of neural substrates of controlled decision-making.

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**#7** **The causal role of dorsolateral prefrontal cortex in modulating the balance between Pavlovian and instrumental systems in the punishment domain**

Hyeonjin Kim[1*], Jihyun Hur[2], Mina Kwon[1], Soyeon Kim[1], Yoonseo Zoh[2], Woo-Young Ahn[1]

[1] Department of Psychology, Seoul National University, Seoul, Korea 08826
[2] Department of Psychology, Yale University, New Haven, CT 06511

The balance between Pavlovian and instrumental decision-making systems, known as Pavlovian-instrumental conflict, is critical for optimal decisions.To be specific, Pavlovian bias of approaching reward-predictive stimuli and avoiding punishment-predictive stimuli is often against the instrumental system. Although recent neuroimaging studies have suggested the prefrontal cortex such as the dorsolateral prefrontal cortex (dlPFC) is implicated in overcoming Pavlovian-instrumental conflict, its neural mechanisms remain rudimentary. Here, we investigated whether the dlPFC would have a causal relationship to modulating Pavlovian bias by using transcranial current direct stimulation (tDCS). In our double-blind study, participants received either anodal or sham stimulation over the right dlPFC for three successive days and performed a reinforcement learning task called the orthogonalized Go-Nogo task, which can assess the degree of Pavlovian bias. We hypothesized that the anodal group would show lower Pavlovian bias. We used computational modeling and hierarchical Bayesian analysis to estimate model parameters reflecting latent cognitive processes. Among several computational models, a model with separate Pavlovian bias parameters for reward and punishment domains showed the best fit. Both behavioral and computational modeling results indicated that the anodal group had significantly lower Pavlovian bias in the punishment domain than the sham group. In addition, the anodal group showed lower go bias and choice lapse rate parameter values than the sham group. Together, these findings suggest that anodal tDCS on the right dlPFC may lead to behavioral suppression of Pavlovian bias in the punishment domain, which sheds light on its causal neural mechanism.

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## #8 Individual differences in latent-cause inference map onto transdiagnostic dimensions of mental health

Dan-Mircea Mirea[1], Yeon Soon Shin[2], Sarah DuBrow[3], Yael Niv[1,4]

[1] Department of Psychology, Princeton University
[2] Department of Psychology, Yale University
[3] Department of Psychology, University of Oregon
[4] Princeton Neuroscience Institute, Princeton University

Research suggests that humans build internal models of the world in which similar experiences are assumed to be generated by the same latent cause. Optimal latent-cause inference supports appropriate generalization from old to new experiences. In contrast, suboptimal inference could result in overgeneralization in anxiety disorders or incoherent world models in schizophrenia. Here, we asked whether individual differences in latent-cause inference are associated with psychiatric symptoms.

Online participants (N = 565) assigned abstract visual stimuli ("microbes") with differing length and number of "spikes" to clusters. We used hierarchical fitting to compare five Bayesian-inference models of task behavior, and quantified latent-cause inference using the 4 parameters of the winning model: the tendency to form a new cluster (α), the probability of persisting in the current cluster (η), and the variability of clusters in terms of spike number (σ1) and length (σ2). Participants also answered psychiatric symptom questions as part of a larger sample (N = 1234), from which we derived transdiagnostic factors and factor scores for each participant.

We found two distinct patterns of associations between transdiagnostic factors and model parameters. The 'Schizotypy-mania-disinhibition' factor was associated with lower η (persistence parameter) and higher σ1 and σ2 (cluster-variability parameters), which might underlie symptoms of cognitive disorganization. In contrast, 'Obsessive-compulsivity' was associated with higher α (new-cluster parameter), which could be linked to heightened uncertainty about change (volatility) that encourages checking behaviors. Overall, the results suggest that aberrant latent-cause inference might contribute to a wide range of clinical conditions, from schizophrenia to OCD.

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# Poster Abstracts

## #1 Non-invasive and reversible neuromodulation of amygdala, anterior cingulate cortex and orbitofrontal cortex in the primate brain at rest and during credit assignment

Davide Folloni[1(presently at), 2], Elsa Fouragnan[2,3], Marco K. Wittmann[2] , Lea Roumazeilles[2] , Lev Tankelevitch[2] , Lennart Verhagen[2,4], David Attali[5,6,7], Charlotte Constans[5] , Jean-Francois Aubry[5] , Jerome Sallet[2,8], Matthew F.S. Rushworth[2]

[1(presently at)]Department of Neuroscience and Friedman Brain Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA.
[2] Wellcome Centre for Integrative Neuroimaging (WIN), Department of Experimental Psychology, Tinsley Building, Mansfield Road, Oxford OX1 3TA, University of Oxford, Oxford, UK.
[3] School of Psychology, University of Plymouth, Plymouth, UK.
[4] Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, Nijmegen, 6525 HR, Netherlands.
[5] Physics for Medicine Paris, ESPCI Paris, INSERM, CNRS, PSL Research University, Paris, France.
[6] GHU PARIS Psychiatrie and Neurosciences, site Sainte-Anne, Service Hospitalo-Universitaire, Pôle Hospitalo-Universitaire, Paris 15, F-75014 Paris, France.
[7] Université de Paris, F-75005 Paris, France.
[8] Université Lyon 1, Inserm, Stem Cell and Brain Research Institute U1208, 18 Avenue Doyen Lepine, 69500 Bron, France

Credit assignment is the association of specific instances of reward to the specific events, such as choices, that caused them. Without credit assignment, choice values reflect only an approximate estimate of how good the environment was when the choice was made.

First, we showed that focused Transcranial Ultrasound Stimulation (TUS) allows to non- invasively and transiently disrupt neural activity in a specific brain area with high spatial focality and neuromodulatory effects that may last up to 2 hours even in subcortical and deep cortical areas (Folloni et al., 2019; Fouragnan, Chau, Folloni et al., 2019; Bongioanni, Folloni et al., 2020). Next, by combining TUS and functional magnetic resonance imaging in macaques, we showed credit-assignment-related activity in prefrontal area 47/12o and global reward state-related activity in adjacent anterior insula. When credit assignment-related activity in area 47/12o was disrupted with TUS, macaques were worse at updating their decisions about which choice would be the best one to take as a function of whether or not reward had been delivered. In addition, choice value representations in other interconnected brain circuits, which normally guide decision making, were impaired. By contrast, global reward state-related activity in anterior insula, although adjacent to TUS-targeted area 47/12o, remained intact. Moreover, decision making was still guided by a general sense of global reward state (Folloni et al., 2021).

In addition to revealing multiple processes determining choice value, the results suggest TUS may be an ideal tool for simultaneous perturbation and recording from neural circuits in the primate brain.

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**#2**

# Our social worlds: navigating social spaces

Schafer M[1] , Kamilar-Britt P[1] , Sahani V[1] , Hurd Y[1] , Bachi K[1] , Schiller D[1]

[1] Mount Sinai School of Medicine

Navigating our social worlds depends on social mapping: the organization of multidimensional abstract social information. Here, we use a naturalistic social game to ask if during interactions 1) the hippocampus tracks other people like places in abstract social space akin to how it maps physical environments 2) if navigation-like behavior relates to real-world social networks.

In the game, participants interact with fictional characters to accomplish social goals (e.g., find a job). Unbeknownst to participants, their decisions with each character are modeled as trajectories through a social "power" by "affiliation" space – the so-called "social navigation" of relationships. To study neural representations of the character places, we analyzed hippocampal patterns in two independent samples (n=18, n=31) with functional magnetic resonance imaging (fMRI). To link navigation-like game behavior to real-world social behavior we also analyzed two online samples (n=697, n=290).

Both of our fMRI samples showed place-like representations in hippocampal patterns, in multiple complementary analyses. The effects were hippocampus specific and not explained by other measures of task behavior, task-based social information or structure, temporal drift or demographic variables. Thus, the hippocampus tracks people like social places during evolving social relationships – similar to how it tracks physical places during spatial navigation. Further, in our behavioral samples, 2D "social distancing" robustly and positively correlated both with more real-world social avoidance and smaller social networks - suggesting these game representations and behaviors are relevant to real-world social functioning. Current work is investigating how these spatial navigation-like representations relate to social dysfunction in psychiatric disorders.

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## #3 Modeling Multipronged Connectivity Profiles in the Striatum and their Misconfiguration in Addiction

Cole Korponay, Ph.D.[1] , Elliot A Stein, Ph.D.[2] , Thomas J Ross, Ph.D.[2]

[1] Basic Neuroscience Division, McLean Hospital, Belmont, MA
[2] Neuroimaging Research Branch, Intramural Research Program, National Institute on Drug Abuse, Baltimore, MD

Dysregulation of frontal cortical inputs to the striatum is foundational in the neural basis of psychiatric illnesses like substance use disorder (SUD). Individual striatal nodes receive appreciable input from numerous cortical nodes, and data increasingly indicate that combinational properties of these multivariate input profiles shape striatal function more so than the properties of any individual input. Here, we introduce an approach for modeling and detecting "misconfigurations" in the multipronged striatal connectivity profiles with frontal cortex using resting-state fMRI data. We apply this "connectivity profile analysis" (CPA) approach to a sample of 46 nicotine-dependent smokers and 33 non-smokers to examine the potential role of connectivity profile misconfigurations in SUD. We find that both dorsal striatum (DS) and ventral striatum (VS) connectivity profiles with frontal cortex are misconfigured in smokers – but in doubly distinct fashions. DS misconfigurations are characterized by rank order misarrangement, wherein the orders of strongest and weakest connections in connectivity profiles are significantly shuffled. Meanwhile, VS misconfigurations are characterized by abnormal aggregate connectivity profile strengths. Moreover, DS misconfigurations are stable across sated and acute abstinent states (indicative of "trait" circuit adaptations) whereas VS misconfigurations emerge only during acute abstinence (indicative of "state" circuit adaptations). Finally, we show that the magnitude of these connectivity profile misconfigurations is linked to nicotine dependence and withdrawal severity. Overall, we demonstrate the potential of neuroanatomy- informed neuroimaging approaches that more aptly model the neurobiological composition of corticostriatal circuits to yield deeper insights into the neural basis of psychiatric illnesses like SUD.

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**#4** **Surprising sounds increase risk taking and decrease choice perseveration**

Gloria W Feng & Robb B Rutledge

Yale University Department of Psychology

Surprising sensory events are common in daily life but often behaviorally irrelevant. Here, we tested whether incidental surprises influence decision making. Participants (n=1200) made choices between risky and safe options in which each option presentation was preceded by task-irrelevant six-tone auditory sequences. In two experiments (each n=200), “common” sequences heard before 75% of trials consisted of identical tones and “rare” sequences heard before 25% of trials ended with a novel deviant tone. Rare sequences simultaneously increased risk taking and increased switching away from the option chosen on the previous trial. Our computational model captured both changes with value-independent risk-taking and choice perseveration parameters, respectively. When sequence probabilities were reversed such that rare sequences consisted of the six identical tones, participants still increased option switching after hearing these sequences but did not increase risk taking. In two control experiments, both effects were eliminated when sequences were presented in a predictable manner. The choice switching effect may arise not from tone novelty but from recognizing surprising sequences. Thus, we find evidence for two dissociable influences of sensory surprise on decision making. Aberrant sensory processing is implicated in psychiatric disorders including schizophrenia and psychosis. Our findings offer a new way to evaluate patients and treatments by examining the relationships between sensory prediction errors and behavior. Altogether, we find that surprising sounds systematically alter human behavior, identifying a previously unrecognized source of behavioral variability in everyday decision making.

**#5**

# Latent-cause inference: a new way to look at schizophrenia-spectrum disorders

Sofiya Yusina[1] , Dan-Mircea Mirea[2], Yeon Soon Shin[3] , Sarah DuBrow[4] , Yael Niv[1]

[1] Princeton Neuroscience Institute, Princeton University, Princeton, NJ 08540
[2] Department of Psychology, Princeton University, Princeton, NJ 08540
[3] Department of Psychology, Yale University, New Haven, CT 06511
[4] Department of Psychology, University of Oregon, Eugene, OR 9740

Latent-cause inference is a process through which humans determine the hidden (latent) causes of events. Aberrant latent-cause inference could lead to suboptimal interpretation of causality, characteristic of psychopathologies like schizotypy or schizophrenia-spectrum disorders. In this study, we analyzed data from N=565 subjects. Subjects responded to a subset of questions from the Personality Inventory for DSM-5 that assessed schizotypal traits and completed the "Microbes Task" – a clustering task developed to quantify latent-cause inference in humans. Four individual-level parameters were derived by fitting a Bayesian model of latent-cause inference to the Microbes Task data. We hypothesized that higher schizotypy scores would be positively associated with a higher tendency to create new clusters and a higher propensity to create wider clusters, indicative of a fractured and incoherent interpretation of the causal relationships between events. This hypothesis was borne out when schizotypy scores were treated as a categorical variable. However, when schizotypy scores were analyzed as a continuous variable, only the propensity to create wider clusters was found to correlate significantly with schizotypy scores. Regression analysis was performed on subscale scores, yielding significant correlations between at least one latent-cause inference parameter and the subscales "Suspiciousness," "Perceptual dysregulation," and "Unusual beliefs & experiences." These are the three subscales that assess "positive" schizotypal traits, which correspond to the positive symptoms of schizophrenia. These findings suggest that schizotypy and other conditions with a proneness to psychosis may involve carving the world into fractured latent causes, offering a new theoretical understanding of cognitive deficits in schizophrenia-spectrum disorders.

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**#6** **Individual Differences in Latent-Cause Inference are Associated with Clinical Symptoms of Obsessive Compulsive Disorder**

Amy M. Rapp[1],Dan-Mircea Mirea[2],Yeon Soon Shin[3], Sarah DuBrow[4], Yael Niv[2,5], & H. Blair Simpson[1]

[1] Department of Psychiatry, Columbia University
[2] Department of Psychology, Princeton University
[3] Department of Psychology, Yale University
[4] Department of Psychology, University of Oregon
[5] Princeton Neuroscience Institute, Princeton University

Compulsivity is a hallmark characteristic of OCD, the prototypical compulsive disorder, where a behavior persists despite no longer being rewarded or adaptive. Unfortunately, first-line treatments only help ~50% of OCD patients and considerable functional impairment is associated with the disorder. Ambiguity about the neurocognitive mechanisms underlying compulsivity limits identification of novel treatment targets and treatment personalization. Theory-driven computational modeling could provide this much needed improved precision.

Patients with OCD who were unmedicated (n=36) or taking a stable SSRI dose (n=18) and healthy controls (n=34) were shown images of "stars" and asked to categorize them as belonging to specific galaxies (clusters) based on the number and length of their "rays." A computational latent- cause inference model that clusters stimuli into an unbounded number of clusters was fit to behavioral data to quantify how individuals infer cluster membership. Four parameters were estimated: (1) concentration parameter a (tendency to form new clusters), (2) temporal decay parameter l (rate at which previous stars are forgotten), and (3) two cluster-size parameters (variability of stars in a cluster, in terms of number s1 2and length s2 2 of rays). Individual parameter estimates were related to self-reported scores on the Obsessive Compulsive Inventory-Revised. Compulsive ordering was transdiagnostically associated with a in the full sample (r=0.22, p=0.04), driven by unmedicated OCD patients (r=0.44, p=0.01). Compulsive ordering was also associated with s1 2 in the unmedicated OCD subgroup (r=0.45, p=0.006). These findings highlight alterations in new cause formation and stimulus feature discrimination as potential mechanisms of compulsive behavior in unmedicated patients with OCD.

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**#7**

# Linguistic markers of momentary mood dynamics during risky decision-making

Jihyun K. Hur, Jutta Joormann, Robb B. Rutledge

Department of Psychology, Yale University

Individuals with depressive symptoms have been characterized by negative emotional vocabularies in their daily language. They also report lower momentary mood during decision- making tasks. It is unknown whether linguistic features relate to affective experience during decision-making tasks. In this study (n=196), we assessed depressive symptoms using the Patient Health Questionnaire (PHQ-9) after asking participants to write text responses to nine short-answer neutrally framed questions based on the PHQ-9 (e.g., Think about your life overall. Is there anything you are particularly satisfied or dissatisfied with?). Participants also completed an established risky decision task with repeated happiness ratings as a measure of momentary mood. Replicating previous research, depressive symptoms were correlated with baseline mood parameters for the task estimated using a computational model of momentary mood dynamics ($p<0.0001$). Participants with higher depressive symptoms also used fewer positive affect words (e.g., good, love) and more negative affect words (e.g., bad, wrong). We found that baseline mood parameters were positively correlated with positive affect words ($p<0.0001$) and negatively correlated with negative affect words ($p<0.0001$). After controlling for overall depressive symptoms, we found that positive affect words were still correlated with baseline mood parameters ($p=0.01$), but negative affect words were not ($p=0.81$). Thus, we find that affective experience during a risky decision task relates not only to depressive symptoms assessed with a standard questionnaire, but also to the use of affective language. Our findings suggest that text data can provide insights into both mood disorders and mood dynamics.

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**#8** **Distinct Approaches to the Explore-Exploit Dilemma in Euthymic Bipolar Disorder**

Ironside, M.L.[1], Baribault, B.[1], Collins, A.G.[1], Clark, L.[2] , Michalak, E.[3] , Poh, C.[3] & Johnson, S.L.[1]

[1] Department of Psychology, University of California, Berkeley;
[2] Department of Psychology, University of British Columbia;
[3] Department of Psychiatry, University of British Columbia.

Past research suggests a reward hypersensitivity profile of bipolar disorder, including increased exploratory behavior in reward-rich environments, even during euthymia. Little research exists on the decision process during goal-pursuit within this group, which may offer greater specificity on where processes go awry as symptoms worsen. To this end, we used the Observe or Bet task to index explore-exploit decision making tendencies in a probabilistic, volatile reward learning environment in participants with bipolar disorder (n = 45) and psychiatric controls (n = 36). In this context, exploring was characterized as seeking information about underlying reward contingencies, and exploiting was characterized by 'betting' on one of two options to maximize reward. On average, both groups made equally profitable choices when exploiting and explored at similar frequencies, but the bipolar disorder group earned significantly fewer points during the task. We used a hierarchical Bayesian computational modeling approach to investigate this discrepancy. The best-fitting model incorporated a modified reinforcement learning algorithm including counterfactual learning. Posterior distributions of group-level parameter estimates revealed that participants with bipolar disorder were more likely to make choices inconsistent with learned values of options, and to assign greater initial values to exploring. There were no group differences in any other parameter estimates, including learning rates. These results suggest that differences in outcomes during goal-pursuit among people with bipolar disorder may be driven by differences in balancing the explore-exploit dilemma.

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## #9 Clinical utility of combining linguistic features with cognition to identify patients with schizophrenia and individuals at-risk for psychosis

Shalaila S. Haas[1], Agrima Srivastava[1], Linda A. Antonucci[2], Zarina R. Bilgrami[3], Shaynna N. Herrera[1], Marija Krcmar[4], Angela Lu[1], Alessia Mcgowan[1], Cansu Sarac[1,5], Riaz B. Shaik[1], William S. Stone[6], René S. Kahn[1], Romina Mizrahi[7], Barnaby Nelson[4,8], Guillermo Cecci[9], and Cheryl M. Corcoran[1,10]

[1] Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, NY, USA
[2] Laboratory X, Institute X, Department X, Organization X, City X, State XX (only USA, Canada and Australia), Country
[3] Department of Psychology, Emory University, Atlanta, GA, USA
[4] Orygen, Parkville, Victoria, Australia
[5] Department of Psychology, Long Island University Brooklyn, New York, NY, USA
[6] Department of Psychiatry, Harvard Medical School at Beth Israel Deaconess Medical Center, Boston, MA, USA
[7] McGill University, Montreal, QC, Canada
[8] Centre for Youth Mental Health, University of Melbourne, Parkville, Victoria, Australia
[9] IBM T.J. Watson Research Center, Yorktown Heights, NY, USA
[10] James J. Peters VA Medical Center Bronx, NY, USA

Neurocognitive pattern classification has been used to identify patients with schizophrenia (SCZ) and individuals at clinical high risk (CHR) for psychosis with high accuracy. However, few studies have assessed the contribution of linguistic features to identify patients at various stages of psychosis. We investigated the differential diagnostic value of combining linguistic features with cognition to discriminate patients with SCZ and CHR from healthy controls (HC). Automated NLP analysis was applied to speech samples obtained from 105 HC, 42 patients with SCZ, and 122 CHR. A multiclass machine learning analysis pipeline was used to classify SCZ and CHR from HC combining linguistic and cognitive features using a linear Support Vector Machine algorithm. The models distinguishing HC from SCZ and CHR were contrasted with respect to their performance and feature reliability, and applied to the held out patient group to examine their generalizability. The cross-validated classification accuracies were 75.7% (HC vs SCZ), 68.2% (HC vs CHR), and 65.5% (CHR vs SCZ). Linguistic features drove the HC-SCZ classification, while a combination of linguistic and cognitive features drove the HC-CHR model. Applying the HC-SCZ classifier to CHR resulted in 47.5% being classified as SCZ, whereas the HC-CHR model classified 78.6% SCZ patients as CHR. Decision scores of CHR significantly differed from both correctly classified SCZ and HC. These findings suggest combining linguistic features with cognition contributes to the individualized discrimination of patients at various stages of psychosis from healthy individuals, but do not generalize well to the different stages, suggesting different underlying disturbances.

**#10** **Alterations in Perceptual Learning Drive Speech Hallucinations in Medication-Free Patients with Schizophrenia**

Justin Buck[1] & Guillermo Horga[1]

[1] Columbia University and the New York State Psychiatric Institute

Recent behavioral and computational evidence suggests that auditory hallucinations arise from alterations in perceptual learning. However, most of these studies used simple auditory stimuli (e.g. tones) and were performed in medicated patients. The effects of antipsychotic medication on perceptual learning and the usual speech content of auditory hallucinations in schizophrenia suggest the need to evaluate perceptual learning involving speech in medication-free patients. 41 healthy controls and 54 medication-free patients with schizophrenia performed a novel speech discrimination task. Participants were presented with speech, non-speech, and blank stimuli at varying probabilities in a blocked structure and were asked to report when they heard speech. Symptom severity was measured clinically using the PANSS scale. Speech false alarms during the task specifically correlated with hallucination severity but not delusion severity, negative symptoms, or general psychopathology (partial Spearman ρ=0.43; p=0.0022). In a mixed-effects logistic regression, false alarms related to speech history and this effect depended on hallucination severity (p=0.028). To clarify this finding, we built a computational learning model that updates speech expectations on a trial-by- trial basis. Fitting this model to the data we found that individual learning rates correlated with both speech false alarms (Spearman ρ=0.77; p=4.04x10-11 ) and clinical hallucination severity (Spearman ρ=0.371; p=0.0080). Medication-free patients with schizophrenia show alterations in learning of speech probabilities that scale with task-based false alarms and clinical hallucinations outside the laboratory, suggesting generalizability and robustness of perceptual-learning models of hallucinations.

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**#11** **Latent-cause inference under varying beliefs about randomness captures individual differences in fear extinction**

Ines Aitsahalia[1] , Sashank Pisupati[1] , Sebastian N. Quinard[2] , Isabel M. Berwian[1] , Yael Niv[1,3]

[1] Princeton Neuroscience Institute, Princeton University
[2] Department of Computer Science, Princeton University
[3] Department of Psychology, Princeton University

Despite the prevalence of fear-based disorders, the computational mechanisms underlying individual differences in fear persistence and generalization remain unknown. We argue that under- and over-segmentation of latent causes can explain different forms of fear extinction failure, ranging from overgeneralization of fear and slow learning, to rapid new associative learning without updating old beliefs. These failures have been respectively linked to PTSD 1 , trait anxiety 2 , and spontaneous recovery of fear 3 . Using model simulations, we show that these different learning regimes can be achieved through a single parameter: the prior belief about the stochasticity of observations generated from a latent cause, which is related to the cognitive distortion of black-and-white thinking. A "deterministic" prior leads to surprising observations being interpreted as resulting from new latent causes. This gives the impression of rapid learning but fails to generalize across acquisition and extinction of fear associations. As such, extinction does not modify the original fear association, leading to spontaneous recovery of fear. On the other hand, a "stochastic" prior leads to slower learning, attributing disparate observations to a single cause and thus overgeneralizing between safe and dangerous stimuli, but also results in less spontaneous recovery after extinction. We tested this model in an online fear-conditioning task. Preliminary behavioral results show that individual differences obey the coupling predicted by our model between learning rates, generalization and spontaneous recovery. In ongoing work, we are investigating whether past experiences of controllability influence this prior, shaping future learning.

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**#12**

## Perceptual insight in health and psychosis

Andra Mihali[1], Florian Ragalmuto[1,2], Alissa Fogelson[1], Najate Ojeil[1], Marianne Broeker[1,3], Guillermo Horga[1]

[1] Department of Psychiatry, Columbia University, and New York State Psychiatric Institute, New York, USA
[2] Vrije Universiteit Amsterdam, Amsterdam, Netherlands
[3] University of Oxford, Oxford, UK Abstract Insight is an important yet understudied aspect of psychosis.

Insight refers to awareness of illness but also to the ability to question the truthfulness of percepts and beliefs. These processes are distinct but likely interrelated. Here, we formalized the latter process as perceptual insight and measured it as the extent to which subjective experiences match objective reality. To introduce a dissociation between subjective experiences and objective stimuli, we employed a motion after-effect illusion (MAE) which causes perceptual distortions. We developed and validated a psychophysics task (Mihali, Broeker and Horga, 2021) which asked participants to report both what they "See" under the MAE and separately, crucially, what they "Believe" about the true underlying stimulus. Healthy individuals (N = 44) could compensate in a meaningful way for perceptual distortions during "Believe" blocks. To dissect the computational processes of insight, we applied Bayesian models of perception to a subset of participants (N = 22). The winning model based on a formal model comparison included a perceptual-insight parameter which reflected the incorporation of knowledge about their distortions into their beliefs. This perceptual-insight model outperformed a number of alternative models, including one reflecting a simple response-bias strategy. Thus, we found that healthy individuals demonstrate perceptual insight. We also present preliminary data from an ongoing study in unmedicated patients with psychosis suggesting perceptual-insight impairments ascertained with this approach (N = 4). We hope that this emerging research will help clarify the mechanisms underlying impairments in insight in clinical populations and develop objective tools to quantify them.

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**#13** **Charting the computational foundations of aberrant decision-making in adolescents**

Catherine Insel, Natalie Biderman, Zarrar Shehzad, Daphna Shohamy

Zuckerman Institute, Columbia University

Adolescence is a period of heightened risk for psychopathology, and 25% of adolescents develop mood and anxiety disorders. Adolescents are also notorious for making maladaptive decisions. One hallmark of aberrant decision-making in psychiatric disorders is the failure to generalize positive experiences to guide adaptive behavior in new situations. If adolescents struggle to generalize learning from prior rewarding experiences, they may be less likely to approach positive experiences in their daily lives. To identify how reward generalization develops during adolescence, we developed a novel value-based decision-making task. 102 participants aged 10-25 made decisions between different objects, and they encountered 33 distinct categories of objects. Over time, they could learn that some categories were worth more money than others (e.g., balloons earned ~80¢ but masks earned ~20¢). We tested whether individuals generalized category value to guide adaptive decision-making when they were presented with novel choices. We found that younger adolescents did not use category value to guide decision-making. However, successful generalization emerged with age, and older adolescents were more likely to make adaptive decisions that maximized reward. Older adolescents also used category value to modulate explore/exploit decision strategies, but younger adolescents did not. Although younger adolescents did not make adaptive decisions, they still learned the category-value structure, and they reported explicit knowledge of the category values following the task. Together, these findings reveal that younger adolescents experience a knowledge-behavior gap that interferes with adaptive value-based decision- making. Future work will identify how aberrant decision-making processes relate to risk for psychopathology in youth.

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**#14** **Prioritized encoding of unexpected rewards enhances memory by suppressing noise during recall**

Salman E. Qasim, Kaustubh Kulkarni, Xiaosi Gu

How does our decision-making influence what, and how, we remember? Prior work has demonstrated that reward- prediction error (RPE), a critical signal for reinforcement learning, also enhances memory. Identifying how, specifically, RPEs enhance memory is crucial to understanding the linkage between decision-making processes and memory. Here, we tested the idea that encoding information about surprising rewards enhances memory by providing a source of information about past events that is more robust to noise during recall processes than perceptual features of the stimulus alone. We designed an experiment in which participants performed a gambling task in which they bet on specific images of faces, and were required to learn the value associated with different faces in order to maximize their reward. Then, the same face stimuli were presented in a recognition memory task along with novel face images, and participants had to indicate which images they had seen before. We computed the trial-by-trial RPE in the gambling task using reinforcement-learning models, and tested how these RPEs modulated subsequent recognition memory. We replicated prior findings demonstrating that the presence of positive RPEs (pRPE) enhances subsequent memory for the stimuli associated with them, compared to those associated with negative RPEs or no RPE. In line with this finding, when examining individual participants' memory performance we found that participants who relied more heavily on pRPEs than the perceptual features of the stimulus exhibited better memory than those who relied more heavily on perceptual features. However, this improved memory performance was primarily driven by significant improvement at rejecting novel lures. These results suggest that positive reward-prediction errors enhance memory by providing a recognition signal that is more robust to noise (and thus false recognition) than the intrinsic perceptual features of a stimulus alone.

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**#15** **High-value decisions are fast and accurate, inconsistent with diminishing value sensitivity**

Blair R. K. Shevlin[1], Stephanie M. Smith[1,2], Jan Hausfeld[3,4,5] and Ian Krajbich[1,6]

[1] Department of Psychology, The Ohio State University;
[2] Anderson School of Management, UCLA;
[3] Thurgau Institute of Economics, University of Konstanz;
[4] Institute of Psychology, University of Bern;
[5] Faculty of Economics and Business, University of Amsterdam;
[6] Department of Economics, The Ohio State University

It is a widely held belief that people's choices are less sensitive to changes in value as value increases. For example, the subjective difference between $11 and $12 is believed to be smaller than between $1 and $2. This idea is consistent with applications of the Weber-Fechner Law and divisive normalization to value-based choice, and with psychological interpretations of diminishing marginal utility. According to random utility theory in economics, smaller subjective differences predict less accurate choices. Meanwhile, in the context of sequential sampling models in psychology, smaller subjective differences also predict longer response times. Using these models, we predict that decisions between high-value options to be slower and less accurate. In contrast, some have argued on normative grounds that choices between high-value options should be made with less caution, leading to faster and less accurate choices. Here, we model the dynamics of the choice process across three different choice domains, accounting for both discriminability and response caution. Contrary to our predictions, we mostly observe faster and more accurate decisions (i.e., higher drift rates) for high-value options. We also observe that when participants are alerted about incoming high- value decisions, they exert more caution and not less. We rule out several explanations for these results, using tasks with both subjective and objective values. These results cast doubt on the notion that increasing value reduces discriminability.

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**#16**

## Mood and vigor change across the lifespan

Huw Jarvis[1,2], Akshay Nair[1], Robb B. Rutledge[1]

[1] Department of Psychology, Yale University;
[2] School of Psychological Sciences, Monash University.

Reward influences both how we feel and how fast we act. These effects are thought to be underpinned by motivational processes in the brain, such as those governing the vigor with which we pursue rewards and the pleasure we derive from them. Previous work suggests motivation may change with age, but precisely which motivational processes are affected remains unclear. We investigated this question in a smartphone-based sample from the general population (ages 18-77, n=6690). Participants completed a task in which they tapped the screen to acquire rewards ('fish') as we systematically varied reward availability. Participants periodically reported their momentary happiness during the task using a slider, and separately completed questionnaires assessing symptoms of depression and apathy. Higher reward rates were associated with both greater vigor (i.e., shorter action latencies) and increased happiness, with more recent rewards having the most impact on happiness. Older people reported greater happiness on average, despite lower scores in the task. Consistent with our previous results in paid lab and online participants, we found an age-related effect of apathy on vigor. In younger but not older participants, greater apathy was associated with increased vigor sensitivity when moving between rich and poor reward environments ($p=0.002$). Together, these results shed light on the distinct motivational changes associated with aging, and highlight the utility of smartphone-based data collection for investigating mood and motivation in health and disease.

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## #17 Impaired Arbitration Between Decision-Making Strategies In Alcohol Users: A Computational Modeling Study

Srinivasan Ramakrishnan[1,2], Jeffrey Chen[2,3], Gopi K. Neppala[2], Riaz B. Shaik[2] , Wouter Kool[4] , Iliyan Ivanov[2] , Muhammad A. Parvaz [2,5]

[1] Department of Health Informatics, School of Health Professions, Rutgers University, New Jersey
[2] Department of Psychiatry Icahn School of Medicine at Mount Sinai, New York
[3] University of Pittsburgh School of Medicine, Pittsburgh, PA
[4] Department of Psychological & Brain Sciences, Washington University in St. Louis
[5]Department of Neuroscience, Icahn School of Medicine at Mount Sinai, New York

Studies of reinforcement learning propose that decision-making is guided by a tradeoff between computationally cheap model-free control (habit) and costly model-based (goal-directed) control. Indeed, humans depend on model-based control when higher rewards are atstake. Addicted individuals purportedly rely more on model-free control; however, it remains to be studied how they arbitrate between model-free and model-based control under higher stakes of reward.

Fifty-one individuals performed a modified 2-step learning task where model-based control is reward advantageous. Participants were grouped based on alcohol use [users (several times a month n=27) and non-users (rare n=24)]. Maximum a posteriori fitting of a dual-system reinforcement-learning model was used to assess the degree of model-based control (weighting parameter 0 to 1) for the low- and high-stakes trials separately. Analyses were performed using 2 (Stakes: high, low) x 2 (Groups: users, non-users) ANOVAs.

A significant Stakes by main effect ($F=5.53$, $p=.023$) and a Stakes x Group interaction ($F=5.00$, $p=.030$) were observed for the weighting parameter, driven by a significantly increased model-based control for high compared to low reward stakes in non-users ($t=2.99$, $p=.006$), and not in users ($p=.925$).

The results show that, unlike non-users, alcohol users did not engage greater goal- oriented control when the stakes were higher, and instead used a less cognitively taxing habitual approach, just as they did in the low stakes condition. Such impaired arbitration of model-based control may underpin maladaptive decision-making in alcohol users. Work is in progress to further characterize this behavior by behavioral parameters.

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**#18** **Neurocomputational mechanisms of belief updating during uncertainty**

Madeline O'Brien, Vincenzo G. Fiore, Matthew Heflin, and Xiaosi Gu

[1] Nash Family Department of Neuroscience, Icahn School of Medicine at Mount Sinai, New York, NY.
[2] Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, NY

The ability to adaptively make decisions in changing environments is a nonnegotiable survival skill. A crucial component of adaptive decision-making is updating one's beliefs to reflect new experiences: unexpected action-outcome pairings increase uncertainty and force the agent to balance their prior knowledge with incoming evidence to keep track of environmental contingencies. However, real-life actions are not always paired with immediate, unambiguous outcomes. Furthermore, nicotine use is associated with increased dopaminergic activation of brain regions involved in action selection. The current study investigates the potential role of these two environmental variables on belief updating while making decisions under uncertainty. Ongoing data collection uses two multi-option decision-making games played by nicotine users (n=26) and matched controls (n=18) to estimate belief updating rates using a traditional Bayesian updating rule, as compared against additional models featuring non-Bayes updating strategies. Demographic variables and self-report mental health scores are additionally collected from all participants. Paired t-tests demonstrate the use of Bayesian belief updating (with separate parameters estimated for evaluation of conflicting vs confirming evidence) in both smokers and controls regardless of outcome accessibility. An n-way ANOVA reveals that nicotine use does not affect belief updating speed ($p=0.6098$), but that outcome availability has a significant effect ($p=0.0056$). However, nicotine users report significantly higher planning impulsivity ($p=0.02$), trait pessimism ($p=0.01$), depression ($p=0.04$), and anxiety ($p=0.03$), as well as lower life satisfaction ($p=0.02$) and subjective happiness ($p=0.04$) than their control counterparts. General linear models reveal that these factors do not influence belief updating speed with feedback; however, higher trait pessimism ($p=0.055$) and lower subjective happiness ($p=0.067$) are trending towards significant contribution to slowing down belief updating without feedback. Once completed, ongoing whole-brain model-based imaging analyses will elucidate the neural signatures of these latent belief updating parameters.

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## #19 Does increased amygdala-perceptual functional connectivity underlie perceptual threat biases in girls with social anxiety?

Dana E. Glenn, Kalina J. Michalska

Department of Psychology, University of California, Riverside

Socially anxious youth are more likely than nonanxious youth to exhibit biases in processing facial emotions, which can undermine social interactions and exacerbate anxiety symptoms. Alterations in amygdala functional connectivity both with prefrontal regions and more basic perceptual regions have also been observed in socially anxious adults (Brühl et al., 2014). However, few developmental studies have examined whether amygdala-perceptual connectivity modulates perceptual representations of facial affect and none focus on youth of color, who are at elevated risk for anxiety. In a sample of preadolescent Latina girls ranging in social anxiety, we test whether altered amygdala-perceptual connectivity influences multivariate representations of fearful facial affect in face processing areas (fusiform face area, V1, inferotemporal cortex), as well as a control visual region (V4). Girls (N=48, M=10.1 years + 1.8) completed an emotion viewing task and labeled the gender of happy and fearful faces, morphed with neutral expressions at varying intensities. Generalized psychophysiological interaction analyses will examine task-dependent amygdala connectivity for each emotion type and intensity with parent- and child-reported social anxiety as second-level predictors. Multivoxel representations of each stimulus type will be extracted from all ROIs. We hypothesize that (1) social anxiety will be associated with increased amygdala-perceptual functional connectivity for fearful but not happy faces, and (2) increased amygdala-perceptual functional connectivity will predict more similar multivoxel representations between the morphed stimuli and fearful facial affect in face-processing but not control ROIs. Understanding the neural correlates of anxiety in Latina girls may inform generalizable
diagnosis and treatment.

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## #20 Early life adversity slows reinforcement learning and disrupts optimal decision making in adult mice

Meghan Gallo[1,3,4], Arif Hamid[2], Alana Jaskir[1], Tracy Pan[1,4], Dayshalis Ofray[3,4], Michael Frank[1], Christopher Moore[1], Kevin Bath[3,4]

[1] Brown University, Providence, RI;
[2] University of Minnesota, Minneapolis, Minnesota;
[3] Columbia University, New York;
[4] New York Psychiatric Institute, New York, NY

Early life adversity (ELA) confers risk for reward-related psychopathologies which may reflect the impact of adversity on mechanisms of reward learning and decision making. Specifically, a stressful, highly variable early environment may undermine expectations about richness and stability. In turn, animals may adopt strategies to optimize reward pursuit according to diminished expectations. To test this hypothesis, we use a mouse model of ELA to manipulate the reliability and quality of early life care and test adult outcomes on reward learning and decision making with a two-arm bandit task. Exposure to ELA leads to poorer choice discrimination, slows learning, decreases the impact of richness on choice, and slows reaction times as a function of reward. We formalize group differences in bandit task performance with different assumptions in an actor- critic reinforcement learning model. Our modeling shows that group differences can be accounted for with changes in learning rates, choice stochasticity, and a parameter indexing sensitivity to environmental richness. Each of these parameters is independently linked with aspects of striatal dopamine signaling, supporting the hypothesis that ELA alters the midbrain dopamine system. Ongoing modeling work is aimed at resolving the respective contributions of these parameters by leveraging behavior, striatal dopamine receptor expression, and the dynamics of dopamine signaling (via dLight fiber photometry) in the nucleus accumbens core.

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**#21** **Self-Esteem depends on beliefs about the rate of change of social approval**

Alexis An Yee Low[1*#], William John Telesfor Hopper[2#], Ilinca Angelescu[3], Liam Mason[3,4], Geert-Jan Will[5] and Michael Moutoussis[1,3 *]

[1] Wellcome Centre for Human Neuroimaging
[2] Paris Brain Institute, Paris, France
[3] Max Planck UCL Centre for Computational Psychiatry and Ageing Research, University College London, London UK
[4] Research Department of Clinical, Educational and Health Psychology, University College London, London, United Kingdom
[5] Institute of Psychology, Leiden University, Leiden, the Netherlands
[6] Leiden Institute for Brain and Cognition, Leiden, the Netherlands

A major challenge in understanding the neurobiological basis of psychiatric disorders is to rigorously quantify subjective metrics that lie at the core of mental illness, such as low self- esteem. Self-esteem can be conceptualized as a 'gauge of social approval' that increases in response to approval and decreases in response to disapproval. Computational modelling approaches have shown that learning signals that represent the difference between received and expected social approval drive changes in self-esteem. However, it is unclear whether self-esteem based on social approval should be understood as a value updated through associative learning, or as a belief about the self, updated by new evidence depending on how strongly it is held. Our results show that belief-based models explain self-esteem dynamics in response to social evaluation better than associative learning models. Importantly, our findings suggest that in the short term, self-esteem signals the direction and rate of change of one's beliefs about approval within a group, rather than one's social position.

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## #22 Transdiagnostic connectome-based predictive modeling of cognition in a developmental sample

Brendan D. Adkinson[1,2], Javid Dadashkarimi[3], Qinghao Liang[4], Dustin Scheinost[5]

[1]Yale School of Medicine
[2]Yale University Interdepartmental Neuroscience Program
[3]Yale University Department of Computer Science
[4]Yale University Department of Biomedical Engineering,
[5]Yale School of Medicine Department of Radiology and Biomedical Imaging

Prediction of inter-individual behavioral phenotypes remains a challenge. Stable prediction performance across a wide spectrum of clinical presentations offers enhanced practical utility. This study used connectome-based predictive modeling (CPM) for transdiagnostic prediction of cognition across multiple cognitive domains. Resting-state (n=691) and N-back task (n=738) fMRI data from the Philadelphia Neurodevelopmental Cohort (PNC) were used to construct 268x268 connectomes for young individuals aged 8-21 years. Participants were distributed throughout typical and atypical psychopathology as assessed by the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS). Models were trained with 10-fold cross-validation and evaluated with Pearson's r. We predicted measures from the Complex Cognition (Verbal Reasoning, Matrix Reasoning, and Line Orientation) and Executive (Conditional Exclusion, Continuous Performance, and Letter N-Back) scales of the Computerized Neurocognitive Test Battery (CNB). CPM successfully predicted measures of cognitive performance transdiagnostically ($r's > 0.16$, $p's < 0.05$). Models trained with task fMRI data outperformed those trained with resting-state fMRI data on average by 21%. On average, measures from the Complex Cognition scale were predicted nearly twice as accurately as measures from the Executive scale. These models were generated and validated in a large, behaviorally diverse cohort. Future directions include cross-validation in an external dataset.

**#23** **A Computational Model of Hopelessness and Active- Escape Bias in Suicidality**

Povilas Karvelis[1] & Andreea Diaconescu[1,2,3,4]

[1] Krembil Centre for Neuroinformatics, Centre for Addiction and Mental Health (CAMH), Toronto, Ontario, Canada
[2] University of Toronto, Department of Psychiatry, Toronto, Ontario, Canada
[3] Institute of Medical Sciences, University of Toronto, Toronto, Ontario, Canada
[4] Department of Psychology, University of Toronto, Toronto, Ontario, Canada

Currently, psychiatric practice lacks reliable predictive tools and a sufficiently detailed mechanistic understanding of suicidal thoughts and behaviors (STB) to provide timely and personalized interventions. Developing computational models of STB that are informed by behavioral, cognitive and neurobiological findings could help better understand STB vulnerabilities and guide personalized interventions. To that end, we present a computational model based on the active inference framework. With this model, we show that several STB risk markers – hopelessness, Pavlovian bias and active-escape bias – are interrelated via the drive to maximize one's model evidence. We propose four ways in which these effects can arise: (1) increased learning from aversive outcomes, (2) reduced belief decay in response to unexpected outcomes, (3) increased stress sensitivity and (4) reduced sense of stressor controllability. These proposals stem from considering the neurocircuits implicated in STB: how the locus coeruleus – norepinephrine (LC-NE) system together with the amygdala (Amy), the dorsal prefrontal cortex (dPFC) and the anterior cingulate cortex (ACC) mediate learning in response to acute stress and volatility as well as how the dorsal raphe nucleus – serotonin (DRN-5-HT) system together with the ventromedial prefrontal cortex (vmPFC) mediate stress reactivity based on perceived stressor controllability. We validate the model by simulating performance in an Avoid/ Escape Go/No-Go task replicating recent behavioral findings. This serves as a proof of concept and provides a computational hypothesis space that can be tested empirically and might speak to planful versus impulsive STB subtypes.

**Funding/Acknowledgements**
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**#24**

## Imprecise Probabilistic Inference from Sequential Data

Arthur Prat-Carrabin and Michael Woodford

Columbia University

How people form expectations about possible future outcomes is a fundamental question in psychology. We investigate human departures from optimal Bayesian inference, through an inference task in which subjects are asked to estimate the probability of a binary event occurring, on the basis of successive realizations of the event. We find under-reaction of estimates to the presented evidence ("conservatism") after a few observations, and at the same time over-reaction to the evidence after a longer sequence of observations. In addition, the autocorrelation in estimates suggests that the response noise largely results from the imprecision of the subjects' mental representation of the decision situation, rather than arising upon response selection. We test and reject several models proposed in the literature (e.g., that people correctly update, but from an incorrect prior), and we find that subjects' estimates do not conform to key properties of the estimates of any Bayesian observer, even one with an imprecise memory. Overall, subjects' responses are consistent with a "noisy counting" model of probability estimation, in which they maintain an imprecise count of the net excess of one outcome over the other, but keep little track of the total amount of evidence accumulated. This model reproduces the behavioral patterns found in data, including the under-reaction to short series of observations and the over-reaction to longer series, and the autocorrelation in responses. The noisy-counting model allows subjects to give relatively reasonable responses to the task while economizing greatly on their attention to the presented evidence.

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## #25 How does mood influence computations of cost and reward in effort-based decision making?

Jamie C. Chiu, Isabel M. Berwian, Yael Niv

Effort-based decision making is the process of choosing how much effort one is willing to exert to obtain a reward. Effort-based decision making is often studied in clinical populations in an attempt to uncover potential underlying mechanisms of symptoms, such as anhedonia in depression and negative symptoms in schizophrenia.

However, there exists a knowledge gap on how mood influences effort-based decision making. Given that clinical populations tend to report worse mood than controls, it is important to distinguish how much of the impairments observed in patients' effort-based decision making is explained by the psychiatric disorder, versus what might be attributed to the individual's general mood state.

Here, we present the results of a study where participants' moods were manipulated during an effort-based decision making task. Using a combination of valued-based and drift-diffusion models, we assess the influence of mood on the calculations of: the perceived anticipatory cost of effort; the actual effort expenditure and ability to execute; the valuation of the expected reward; and the experience of the reward.

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## #26 Translating ecological momentary assessment data into clinical practice: A case-series analysis of dynamic factors associated with cannabis use

Marilyn L. Piccirillo[1], Matthew C. Enkema[2], Katherine T. Foster[1,3]

[1] University of Washington, Department of Psychology
[2] University of Washington, Department of Psychiatry and Behavioral Sciences
[3] University of Washington, Department of Global Health

Computational analysis of ecological momentary assessment (EMA) data can reveal clinically- relevant fluctuations in mood, cognitions, and behavior. However, it is challenging to draw actionable, clinical inferences from these analyses. We present a process for analyzing EMA data and generating recommendations that can be implemented into clinical practice. Participants (N = 30) reported motivation to reduce hazardous cannabis use. EMA assessed cannabis use, craving, affect, and coping four times a day for at least 16 days. We present EMA data from three individuals using a descriptive, case-series design. The first individual used cannabis with others (n = 10, 100.0%), when cravings were high (r = .71; OR = 0, p < .05), and when using fewer approach-related coping strategies (r = -.40; OR = .036, p < .05), suggesting they may benefit from peer-focused and approach-related coping interventions. The second individual used cannabis when experiencing higher cravings (r = .57; OR = .0002, p < .05), although, there were several instances that were not associated with use (n = 5; 38.5%). Functional analysis could identify social and situational factors that predict instances of non-use. The third individual used cannabis when alone (n = 9; 75.0%), during periods of lower (or even zero) cravings (n = 4, 33.3%), and when experiencing low positive affect (r = -.11; OR = .096, p < .05). They may benefit from introducing non-substance-related replacement behaviors into their daily routine. We discuss the process of translating EMA data into actionable, clinical recommendations, supportive of data-driven interventions.

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**#27** **The Cellular Underpinnings of the Macroscale Functional Organization of Cortex**

Xihan Zhang[1], Kevin M. Anderson[1], Hao-ming Dong[1,2], Emani Prashant[3,4], Avram J. Holmes[1,5]

[1] Department of Psychology, Yale University, New Haven, CT 06511
[2] State Key Laboratory of Cognitive Neuroscience and Learning, International Data Group/McGovern Institute for Brain Research, Beijing Normal University, Beijing 100875, China
[3] Program in Computational Biology and Bioinformatics, Yale University, New Haven, CT, USA
[4] Department of Molecular Biophysics and Biochemistry, Yale University, New Haven, CT, USA
[5] Department of Psychiatry, Yale University, New Haven, CT 06511

Human cognitive processes are organized along the macroscale functional organization axes on cortex sheet. One extends from unimodal perception regions to transmodal association regions serving higher- order cognitive and social functions, and another differentiates modality of primary sensory regions into visual cortex and somatomotor-auditory cortex.

The spatial distribution of these large-scale functional gradients is disrupted in patients with major depression, can predict post-treatment symptom improvement, and is gene ontologically enriched for synapse-related and neurotransmitter/receptor terms, which supports the abnormal excitatory/inhibitory neural activities as potential mechanisms of mental disorders from molecular perspective. Understanding the cellular basis of macroscale functional organization gradients is thus crucial for investigating neurobiological mechanisms and developing biotargets for treatment in mental disorder.

In this study we systematically investigate the subclasses of neuronal and nonneuronal cells found in postmortem human cortex and identified one excitatory neuron preferentially distributed along the transmodal pole in the transmodal-unimodal gradient, and an interneuron preferentially distributed along the other end of this gradient. Distribution of another subtype of excitatory neuron peaks at the occipital end of divergent-unimodal gradient then extends towards the somatomotor-auditory end. Our findings validated the mental illness-related interneuron, pvalbumin's contribution to large-scale functional activities, and suggested two understudied subclasses of excitatory neuron worth more research efforts in animal models.

## #28 Long term study of motivational and cognitive effects of low-intensity focused ultrasound neuromodulation in the dorsal striatum of nonhuman primates

F. Munoz [a, b], A. Meaney [b], D. Liu [a, b], A.N. Pouliopoulos[c] , E.E. Konofagou [d, e], V.P. Ferrera [a, b, f]

[a] Dept. of Neuroscience, Columbia University, United States
[b] Zuckerman Mind Brain Behavior Institute, Columbia University, United States
[c] Department of Surgical & Interventional Engineering, King's College London, UK
d Dept. of Biomedical Engineering, Columbia University, United States
[e] Dept. of Radiology, Columbia University, United States f Dept. of Psychiatry, Columbia University, United States

Noninvasive brain stimulation using transcranial focused ultrasound (FUS) has many potential applications as a research and clinical tool, including incorporation into neural prosthetics for cognitive rehabilitation. It is important to test whether repeated long-term application of FUS to deep brain targets improves or degrades behavioral and cognitive function. We investigated the effects of FUS in the dorsal striatum of nonhuman primates (NHP) performing a visual-motor decision-making task for small or large rewards. Over the course of 2 years, we performed 129 and 147 FUS applications, respectively, in two NHP. FUS (0.5 MHz @ 0.2 - 0.8 MPa) was applied to the putamen and caudate in both hemispheres to evaluate the effects on movement accuracy, motivation, decision accuracy, and response time. Sonicating the caudate or the putamen unilaterally resulted in modest but statistically significant improvements in motivation and decision accuracy, but at the cost of slower reaction times. The effects were dose (i.e., FUS pressure) and reward dependent. Interestingly, sonication resulted in significant changes in resting state functional connectivity by increasing the mean correlation between caudate and dorsomedial prefrontal (9m and 10mr), superior temporal (RT, RTM and RTp), and insular cortex (Iai and Id). The results indicate that applying FUS to the dorsal striatum can positively impact the motivational and cognitive aspects of decision making. The capability of FUS to improve motivation and cognition in NHPs points to its therapeutic potential in treating a wide variety of human neural diseases, and warrants further development as a novel technique for non-invasive deep brain stimulation.

## #29 A Deflationary, Active Inference Account of Emotion Episodes: Integrating Psychological Constructionist and Dimensional Appraisal Theories

Alessandra N. C. Yu[1,2], Ryan Smith[3], Edda Bilek[4,5], Sarah N. Garfinkel[2], & Karl J. Friston[4]

[1] Nash Family Department of Neuroscience, Icahn School of Medicine at Mount Sinai, New York, NY 10029, United States
[2] Institute of Cognitive Neuroscience, UCL, Alexandra House, 17-19 Queen Square, London WC1N 3AZ, United Kingdom
[3] Laureate Institute for Brain Research, Tulsa, OK, United States
[4] Wellcome Centre for Human Neuroimaging, Institute of Neurology, University College London, 12 Queen Square, London WC1N 3AR, United Kingdom
[5] Department of Psychiatry and Psychotherapy, Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Square J5, Mannheim 68159, Germany

The scientific study of emotion is embedded in a representationalist framework, relying on abstract intentional constructs that may be deflated to neurocomputational mechanisms characterizing probabilistic relationships between subject and object (Egan, 2018). Two prominent accounts of emotion episodes—the theory of constructed emotion (Barrett, 2017) and component process model (Scherer, 2001)—contradict each other on the semantic surface, but can be integrated in mechanistic terms. We present a deflationary account of emotion episodes from first principles by building central mechanisms from both accounts into a partially observable Markov decision process model under the neurocomputational process theory of active inference (Friston et al., 2017). Here, emotion episodes are hidden states of an internal generative model in the Bayesian brain, inferred as best explanations in the processing of increasingly complex multimodal sensory information, including appraisals, interoception, and action tendencies. Across three stages of development and simulations, we demonstrate that the model successfully learns granular emotion concepts from synthetic childhood into adulthood, engages in motivation- dependent explore-exploit behavior, and acquires alexithymia when overly motivated to be confident in its emotional awareness. In validating this integrative model's capacity to formalize emotional phenomena of interest, we provide proof of principle that the two accounts of emotion can be merged in functional terms under active inference. This unifying endeavor offers promising directions for the empirical study of emotion and encourages a theoretically-driven approach to characterizing affective disorder in computational psychiatry, as well as highlighting conceptual implications for cross-disciplinary pluralism between philosophy of emotion and affective neuroscience.

## #30 Modeling risk and reward expectation and surprise in human neuronal populations during impulsive choice.

R.L. Cowan[1], T.S. Davis[1], B. Kundu[1], J.D. Rolston[1], & E.H. Smith[1]

[1] Department of Neurosurgery, University of Utah, Salt Lake City, UT 84132, USA

Impulsive choice is a facet of impulsivity that may lead to one choosing smaller, immediate rewards over larger, delayed rewards. Here we examined impulsive choice behavior and broadband high frequency (70-150Hz) local field potentials (HFA) in humans undergoing intracranial seizure monitoring. We fit reinforcement learning models to behavior during the Balloon Analog Risk Task and measured whether the optimal learning rate (□) for each participant (1) related to impulsivity scores and (2) depended on reward or risk outcomes. For each intracranial contact, we modeled HFA as a linear combination of (1) risk and reward value expectation (VE), (2) risk and reward prediction error (PE). We report a higher percentage of significant electrode contacts for less impulsive subjects compared to more impulsive subjects for reward VE (7.35%, 2.58%; $X^2(1) = 0.03$, $p < 0.01$), reward VE and PE (1.75%, 0.74%; $X^2(1) = 5.87$, $p = 0.02$), risk VE (13.69%, 8.54%; $X^2(1) = 18.90$, $p < 0.01$), risk VE and PE (1.28%, 0.29%; $X^2(1) = 8.60$, $p < 0.01$), and both risk and reward VE and PE (2.36%, 1.18%; $X^2(1) = 5.63$, $p = 0.02$). No significant differences in the proportion of reward and risk PE contacts were observed between more impulsive and less impulsive subjects ($p$'s $> 0.05$). VE was preferentially encoded in left hemisphere medial prefrontal in less impulsive subjects and lateral prefrontal contacts in more impulsive subjects. Impulsivity correlates to HFA encoding of VE consequently modulating decision-making and providing insight to the neural underpinnings of impulsivity and addiction disorders.

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## #31 Altered brain dynamics in bipolar disorder and schizophrenia during rest and task switching

Jean Ye[1], Huili Sun[2], Siyuan Ga [2], Dustin Scheinost[1,2,3]

[1] Interdepartmental Neuroscience Program
[2] Department of Biomedical Engineering
[3] Department of Radiology and Biomedical Imaging, Yale University, New Haven CT

Nonlinear manifold learning can be used to create a low-dimensional space shared by multiple tasks from which representative brain states can be found. Putatively, neuropsychiatric disorders (e.g., bipolar disorder (BD) and schizophrenia) are characterized by altered brain dynamics. Here, we examined how brain dynamics in this space vary in BD and schizophrenia during rest and task switching. Timeseries fMRI data from the Human Connectome Project (N=390; 6 tasks) were embedded into a low-dimensional space using 2-step Diffusion Maps. Four states were identified with K-means clustering and characterized as high-cognition, low-cognition, cue, and fixation. The centroid of each cluster was identified as the representative timeframe. Rest and task switching timeseries data were next extracted from controls, individuals with BD or schizophrenia in the UCLA Consortium for Neuropsychiatric Phenomics dataset. The four representative timeframes were then regressed from each volume using nonnegative least squares. State contributions (each state's coefficients summed across volumes divided by the sum of all coefficients) and state contribution variability (the standard deviation of each state's coefficients) were computed for each individual and compared between groups using Hotelling T-tests with FDR correction. While BD (N=35;15 females) showed significantly different state contribution variability (p=0.0375) compared to control (N=104;49 females) during rest, both BD (N=44;19 females) and SCZ (N=44;9 females) showed significantly different state contributions (p=0.0375;p=0.0375) compared to control (N=116;54 females) in task switching. These findings suggest altered brain dynamics in BD and schizophrenia and indicate that different brain measures might be sensitive to aberrant brain dynamics in different conditions.

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**#32** **Sex-Differences in Paraventricular Thalamic Nucleus Functional Connectivity Network Development in Children and Adolescents**

Bianca Leonard[1-3], Sarah M. Kark[2], Evelyn Gordi[2], Steven L. Small[8], Curt Sandman[4], Elysia Davis[5], Laura Glynn[6], Tallie Z. Baram[1,7], Michael A. Yassa[1-3,7]

[1] Center for the Neurobiology of Learning and Memory, University of California, Irvine, Irvine, CA, USA
[2] Department of Neurobiology and Behavior, University of California, Irvine, Irvine, CA, USA
[3] School of Medicine, University of California, Irvine, Irvine, CA, USA
[4] Department of Psychiatry and Human Behavior, University of California, Irvine, Irvine, CA, USA
[5] Department of Psychology, University of Denver, Denver, CO, USA
[6] Department of Psychology, Chapman University, Orange, CA, USA
[7] Department of Anatomy & Neurobiology, University of California — Irvine, Irvine, CA, USA
[8] School of Behavior and Brain Sciences, University of Texas at Dallas, Dallas, TX, USA

The paraventricular thalamic nucleus (PVT) is thought to integrate salient experiences, arbitration of motivational conflict, retrieve long-term emotional memories, and regulate behavior. In rodents, the PVT has been found to encode early-life experiences, granting it the potential to influence consequential motivated behaviors later in life and modulate susceptibility to neuropsychiatric disorders. However, little is known about the development of PVT circuitry in humans. Our group recently demarcated the functional network of the PVT in adults using resting state functional magnetic resonance imaging (rsfMRI). The developmental trajectory of the PVT network in children and adolescents remains unknown. We investigated functional connectivity (FC) of the PVT circuitry in 178 children (age range: 9-17 years) using 3T rsfMRI. We entered a PVT mask as a seed region and mapped the PVT FC while controlling for nearby thalamic subnuclei. Preliminary results suggest children and adolescents have broadly similar PVT networks engaged as adults. Males and females have very different PVT FC seed-to-voxel maps between the ages 8-17. Females receive greater input from frontal regions, particularly medial prefrontal cortex to PVT where males receive greater limbic input (nucleus accumbens, hippocampus, amygdala). In females, frontal and temporal lobe PVT connectivity increases with age, where males have smaller increases to temporal and parietal regions. Increases in frontal connectivity in females with age is consistent with an earlier puberty initiation and frontal lobe development. Next steps include applying this analysis pipeline to the Human Connectome Project Developmental data (n = 652, ages 5-21).

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## #33 Intolerance of Uncertainty May Be More Strongly Associated with Mental Health Outcomes than Financial Adversity in US College Students During COVID-19

Larkin S. McReynolds PhD MPH, Micheline Bresnahan PhD, Christina W. Hoven, DrPH, MPH, Keely Cheslack-Postava PhD, Megan Ryan BA, Yael Cycowicz PhD, Diana Rodriguez Moreno PhD, George Musa PhD, Lawrence Amsel MD MPH

College students have been uniquely affected by COVID-19, and the ordinary uncertainty of this transitional period in their life course was undoubtedly amplified by the uncertainties related to the pandemic. Individual differences in the capacity to tolerate uncertainty have been show to impact decision- making and especially the ability to decide on future plans. The attendant worry may partly explain the reported associations of intolerance of uncertainty (IU) with anxiety, depression, and OCD. On the other hand, a facility to tolerate uncertainty has been understood to be a component of the capacity to cope with adversity, and may impact how individuals cope with all the uncertainties intrinsic to COVID-19. In addition, in the U.S. during the first wave of the pandemic, there was widespread financial distress. Sudden changes in college students' financial situation are likely key factors driving the increase in their depression and anxiety during the pandemic. Previous research documented the connections between economic hardship and the onset and continuation of MH problems. Therefore, as part of our comprehensive online study of the impact of COVID-19 on college student MH, we wanted to examine the impact of an adversity (financial hardship) and the impact of a capacity to cope (tolerance of uncertainty) on these MH outcomes. We examined the students' reported levels of depression and anxiety as a function of their financial stress and their capacity to tolerate uncertainty.

1,636 undergraduate students attending a U.S. college or university completed our online survey between September 2020 and March 2021. Students reported on their current levels of depression (via the Patient Health Questionnaire, PHQ-9), anxiety (via Generalize Anxiety Disorder Scale. GAD-7), intolerance of uncertainty (via the Intolerance of Uncertainty Scale, IUS-12), and COVID-related financial adversity. Multivariate logistic regression analyses examined independent associations between COVID-related financial adversity and intolerance of uncertainty with moderate/severe depression and anxiety, controlling for sociodemographic and institutional characteristics.

Students who reported COVID-related financial adversity were approximately 2-times more likely to report high levels of depression (AOR=2.00 ($p<.001$), and anxiety (AOR=1.92, $p<.001$), than those with no financial adversity. Students reporting IUS-12 scores above the mean were even more likely to report depression (AOR=2.54, $p<.001$) and anxiety (AOR=3.03, $p<.001$). These results retained significance in models that included both financial adversity and intolerance of uncertainty, with no significant interaction.

These results confirmed that both COVID-related financial adversity and students' intolerance of uncertainty are strongly associated with outcomes of depression/anxiety. This supports the idea that an individual's inability to cope, exemplified here by IUS-12, is associated with MH outcomes, and may be even more important to consider than the adversity itself, where clinical attention usually focuses. Moreover, we found this effect to be independent of the impact of the adversity on MH. This emphasizes the importance of our public health efforts focusing on interventions that strengthen an individual's ability to cope, including their ability to tolerate uncertainty. In the college context, administrators should consider both the financial concerns of students, as well as work on developing workshops, classes and interventions that strengthen their students' coping capacity. While interventions to increase tolerance for uncertainty and other emotional capacities, such as the SEYLE program, do exists, they have been underutilized. Our findings call for this to change.

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**#34**

## How Negative Schizotypy Influences Decision-Making in the Beads Task

Serena DeStefani

Rutgers University

Recently, there has been a growing interest in how probabilistic accounts of psychosis can be used to build a computational theory of schizophrenia capable of explaining abnormal behavior. However, these accounts have focused almost exclusively on positive symptoms of psychosis, such as delusions and hallucinations, not considering negative symptoms such as indifference and withdrawal. We aim to extend the previous paradigm by considering the subclinical tendency to negative symptoms (negative schizotypy) that we may find in the general population. To do so, we use the beads task, in which participants are asked to guess the identity of a jar from which colored beads are being extracted. This task has been widely used in the literature, showing that a tendency to positive symptoms (delusions) correlates positively with hastiness in decision-making. As of today, nobody has studied whether a tendency to negative symptoms in the general population correlates with conservatism in decision-making. A pilot study conducted on 30 participants contradicts the classic findings, showing that the correlation between delusional thinking (as measured by the PDI and SPQ scales) and hastiness in decision making (as measured by the number of draws needed to come to a decision) goes in the opposite direction as assumed ($r(28)=.48$, $p<.01$). In addition, the study shows how decomposing the PDI and SPQ in positive and negative subscales improves the model's prediction accuracy, highlighting the need for a more nuanced explanation of abnormal behavior.

**#35** **Developing an understanding of the functional connectomics of affective and psychotic illness**

Connor Lawhead*, Jocelyn A. Ricard*, Sidhant Chopra, Bryce Gillis, Lia Chen, Julia Moses, Crystal Blankenbaker, Joanna Tao, Katie Fairbank-Haynes, Poornima Kumar, Arielle Rubenstein, Ilan Harpaz-Rotem, B.T.T. Thomas Yeo, Justin T. Baker, Avram J. Holmes

*C.L. and J.A.R. contributed equally to this work.

Psychiatric illnesses are heterogeneous in nature, making it difficult to establish which brain- behavior relationships are consistently or uniquely disrupted within a given clinical population. Individual differences in behavior are reflected in variability across the collective set of functional brain connections (functional connectome). Accordingly, the transdiagnostic symptom profiles observed in psychiatric patients may map onto detectable patterns of network function. Here, we present initial efforts to build a large, open repository of neuroimaging data to characterize the network features that link individual variation in functional connectomes with symptom profiles across affective and psychotic illnesses. Through an ongoing multisite collaboration spanning Yale University and McLean Hospital, we are actively recruiting a cross-diagnostic sample of >270 individuals. While participant recruitment is ongoing, we present a summary of collected demographic, in vivo imaging, and behavioral phenotypes that encompasses measures of clinical symptoms, cognition, personality, and socioemotional functioning. An initial overview shows that controls and patients are relatively demographically diverse and there is a wide range in clinical expression of symptoms. The dataset from this study will be openly shared, allowing for precise mapping of clinical presentations to markers of brain function to create disease connectomic “fingerprints” that are commonly disrupted across distinct forms of pathology and appear to scale as a function of illness severity. Through this approach, we hope to yield insights into the neural and behavioral bases of affective and psychotic illnesses, providing a crucial step towards the establishment of a new framework for psychiatric classification.

## #36 Vaccination Acceptance Among US College Students is Associated with Both Explicit and, Game Theory Based, Implicit Measures of Altruism

Lawrence Amsel MD, MPH, Micheline Bresnahan PhD, Christina W. Hoven DrPH, MPH, Keely Cheslack- Postava PhD, Megan Ryan BA, Yael Cycowicz PhD, Diana Rodriguez Moreno PhD, George Musa PhD, Larkin S. McReynolds PhD, MPH

At the outset of the COVID-19 pandemic vaccine science had advanced to the point where the development of a highly effective vaccination and its FDA approval took under one year. We were on the threshold of a public health success that did not happen, because vaccination uptake hinges on individual behavior. The weak link in the chain. Even prior to COVID-19, vaccination refusal was identified by the World Health Organization one of the most significant threats to public health. The vaccine intentions/acceptance literature is extensive, and has focused on psychological antecedents (confidence, constraints, complacency, calculation, collective responsibility), with variations for different diseases and groups. A key demographic group in the current pandemic is young adults, who are not particularly threatened by COVID-19, and yet can spread the disease to more vulnerable populations. The drivers of acceptance in this group, therefore, likely align with prosocial values and attitudes of collective responsibility. Therefore, as part of our comprehensive online study of the impact of COVID-19 on college student MH, we wanted to examine the impact of altruism measured in two ways – explicitly through self-report of values, based on the well-studied Moral Foundations Questionnaire (MFQ), and implicitly, based on behavior elicited in a game theory task known as the ultimatum game (UG).

1,636 undergraduate students attending a U.S. college or university completed our comprehensive online survey between September 2020 and March 2021. Among the items in that survey, students reported on their values in the MFQ, responded to monetary division offers in the UG, and reported their vaccination status and/or intentions. Multivariate logistic regression analyses examined independent associations of altruism /social fairness elicited via the Fairness module of the Moral Foundations Questionnaire (explicit) and the Ultimatum Game (implicit) with COVID-19 vaccine attitudes, controlling for demographic and educational factors.

84% of students reported they had already been vaccinated, or would do so when it was made available. Another 16% did not intend to be vaccinated. Analyses indicated that both measures of altruism/social fairness were associated with willingness to be vaccinated. The AOR for accepting the vaccine based on the MFQ- Fairness subscale was 1.32 (p=.004), and the AOR for accepting the vaccine based on altruistic decisions in the UG (accepted less than equal vs accepting only equal or greater offers) was 2.79 (p=.043).

While many studies have explored vaccine hesitancy based on manifest reasons given by individuals, these tend to have limited capacity to offer insights into the underlying attitudes and stances that are actually driving these decisions. We had hypothesized that vaccine decisions were driven as much, if not more, by an individual's characteristic concern for others- their altruism or fairness (or lack thereof) than by the "reasons" given. These results confirmed our hypothesis on two levels: a self-report that Fairness is a highly prioritized value, based on Jonathan Haidt's well studied MFQ; and behaviors on the ultimatum game in which one's altruism is revealed by a willingness to take a smaller piece of the pie in order to ensure that both parties get some reward, a behavior that reveals altruism without asking about it. Note also that there is no reference to vaccination stances in either of these altruism measures. It is also notable that, as found in other implicit measures, this implicit measure of altruism is more strongly associated with target behavior- getting vaccinated- than is the explicit self-report. This suggests that, for college students, ad campaigns aimed at increasing knowledge about vaccines may not be as effective, in increasing vaccine acceptance, as multi-modal interventions that model and promote prosocial behaviors and encourage social cohesion and mutual support.

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**#37** **A 3D Online Game for Visual Discrimination and Emotional Context**

Gozde Kadioglu[a], Dimitris Pinotsis[a,b]

[a] Centre for Mathematical Neuroscience and Psychology and Department of Psychology, City —University of London, EC1V 0HB, UK
[b]The Picower Institute for Learning & Memory and Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA

Previous research shows that colours and textures influence our decisions by evoking emotions that affect our behaviour. However, the experiments used to test this were not as realistic nor representative of the interactive experience we have with our environment. The aim of the current study was to investigate the effects of different emotional contexts on visual discrimination and decision making, while using more interactive experiments. Specifically, how do perceptual-cognitive skills affect decision making, and how do we integrate pre- existing knowledge with new information from our environment? Moreover, how does this affect motor behaviours when executing appropriate actions? The current study examined the effects of warm and cool colours, and simple and complex textures, on perceptual decision making. A virtual game was developed for the current study, consisting of a visual discrimination task and a video to induce certain emotions in participants. Participants chose between objects with warm vs. cool colour, and simple vs complex texture. Response time and performance were recorded. Results showed that participants' reaction times were shorter, and performance was better for simple textures in high arousal high valence environments. In exciting and non-exciting environments, they performed better.

## #38 Alcohol reverses the effects of KCNJ6 (GIRK2) noncoding variants on excitability of human glutamatergic neurons

Dina Popova[1], Isabel Gameiro-Ros[2], Mark M. Youssef[3], Petronio Zalamea[1], Ayeshia D. Morris[4], Iya Prytkova[2], Azadeh Jadali[3], Kelvin Y. Kwan[3], Chella Kamarajan[5], Jessica E. Salvatore[6], Howard J. Edenberg[7], Xiaoling Xuei[8], David B. Chorlian[5], Bernice Porjesz[5], Samuel Kuperman[9], Danielle M. Dick[10], Alison Goate[11], Jay A. Tischfield[1], Zhiping P. Pang[1,12], Paul A. Slesinger[2] and Ronald P. Hart[1,3,*]

[1] Human Genetics Institute, Rutgers University, Piscataway, NJ 08854
[2] Nash Family Department of Neuroscience, Icahn School of Medicine at Mount Sinai, New York, NY 10029
[3] Department of Cell Biology & Neuroscience, Rutgers University, Piscataway, NJ 08854
[4] Joint Program in Toxicology, Rutgers University, Piscataway, NJ 08854
[5] Dept. of Psychiatry & Behavioral Sciences, SUNY Downstate Health Sciences University, Brooklyn, NY 11203 6 Department of Psychiatry, Rutgers Robert Wood Johnson Medical School, Rutgers University, Piscataway, NJ 08854
[7] Department of Biochemistry and Molecular Biology, Indiana Univ School of Medicine, Indianapolis, IN 46202
[8] Department of Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, IN 46202
[9] Department of Psychiatry, University of Iowa Carver College of Medicine, Iowa City, IA 52242
[10] Rutgers Addiction Research Center, Robert Wood Johnson Medical School, Rutgers University, Piscataway, NJ 08854
[11] Department of Genetics & Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY 10029
[12] Child Health Institute, Robert Wood Johnson Medical School, Rutgers University, New Brunswick, NJ 08854

Synonymous and noncoding single nucleotide polymorphisms (SNPs) in the KCNJ6 gene, encoding G protein-gated inwardly rectifying potassium (GIRK2) channel subunit 2, have been linked with increased electroencephalographic frontal theta event-related oscillations (ERO) in subjects diagnosed with alcohol use disorder (AUD). To identify molecular and cellular mechanisms while retaining the appropriate genetic background, we generated induced excitatory glutamatergic neurons (iN) from iPSCs derived from four AUD-diagnosed subjects with KCNJ6 variants ('Affected: AF') and four control subjects without variants ('Unaffected: UN'). Neurons were analyzed for changes in gene expression, morphology and physiological properties at the level of single neuron as well as network. Single cell RNA sequencing suggests that KCNJ6
AF variant neurons have altered patterns of synaptic transmission and cell projection morphogenesis. Results confirm that AF neurons express lower levels of GIRK2, have greater neurite area, and elevated excitability. Interestingly, exposure to intoxicating concentrations of ethanol induces GIRK2 expression and reverses functional effects in AF neurons. Ectopic overexpression of GIRK2 alone mimics the effect of ethanol to normalize induced excitability. We conclude that KCNJ6 variants decrease GIRK2 expression and increase excitability and that this effect can be minimized or reduced with ethanol.

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## #39 Prediction of alcohol use initiation in pre-adolescents using the Generalized Kernel Machine approach on multi-view data from the ABCD Study

Faith Adams, Md Ashad Alam, PhD, Iliyan Ivanov, MD, Muhammad A Parvaz, PhD

Early alcohol use (i.e., sipping) predicts adolescent drinking behaviors. The context of alcohol acquisition (i.e., with or without parental supervision) may influence this transition from low-level use to problematic use. Studies have identified impulsivity (e.g., elevated sensation seeking), clinical (e.g., behavioral problems) and brain/behavior (e.g., reward-related activations) factors associated with overall alcohol use. However, current knowledge regarding the interplay of, or interactions between, these clinical and neurobehavioral factors associated with alcohol acquisition is limited and requires assessments with large and generalizable samples of adolescents.

In this study, we applied Generalized Kernel Machine (GKM), a multivariate data integration approach, to the Adolescent Brain Cognitive Development (ABCD) study, to examine triplets [one variable from impulsivity, clinical, and brain/behavior (reward-related activations from select regions-of-interest (ROI) during the MID task)], that best distinguish between unsupervised initiators (n=179) and supervised initiators (n=1174). Subsequently, we examined specific associations between variables in each triplet using logistic regressions.

Of all possible triplets, 445 triplets differentiated the groups at $p < .05$. One notable triplet interaction significantly differentiating groups included those with: lower lack of perseverance, higher depressive symptoms, and higher right ventral striatum (VS) activation [reward outcome contrast]. Across the significant triplets, the most frequently occurring variables were sensation seeking [impulsivity domain; 101 triplets], aggressive behavior [clinical domain; 34 triplets] and reward-related brain activations of the opercular part of the inferior frontal gyrus (17 triplets), cuneus (13 triplets), and putamen (12 triplets).

Application of GKM to multi-view data considerably reduced the variable space and isolated multidimensional features that significantly differentiated unsupervised and supervised initiators.

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## #40 Pathway-based polygenic risk scores to dissect the heterogeneity of psychiatric disorders

Judit García-González[1*], Shing Wan Choi[1*], Yunfeng Ruan[2], Hei Man Wu[1], Jessica Johnson1, Clive J Hoggart[1], Paul F. O'Reilly[1]

[1] Department of Genetics and Genomic Sciences, Icahn School of Medicine, Mount Sinai, New York City, NY 10029, USA
[2] The Broad Institute of MIT and Harvard, Cambridge, Massachusetts, USA * These authors contributed equally to this work

Polygenic risk scores (PRS) summarize the joint effect of common genetic risk variants and have become widely applied across biomedicine. PRS may act as important disease stratifiers because they provide individual-level estimates of genetic predisposition to disease. However, current PRS aggregate risk variants across the genome to a single number, ignoring how the burden of genetic risk varies across biological pathways. This is despite known functional sub-structure of risk – mapping onto distinct biological pathways – and the etiological heterogeneity of most psychiatric disorders. Thus, distilling genetic risk to a single number may result in a key loss of information about an individual's disease etiology profile, and, consequently, the most promising personalized interventions. Here we evaluate the performance of pathway-based PRSs, in which PRS are calculated across pathways for each individual, and we introduce a software, PRSet, for computing and analysing pathway PRSs. We find that pathway PRSs for Schizophrenia and Alzheimer's disease have similar power for evaluating pathway enrichment of GWAS signal as the leading methods, with the distinct advantage of providing estimates of pathway genetic liability at the individual-level. Exemplifying their utility, we demonstrate that pathway PRSs can stratify diseases into subtypes in the UK Biobank with substantially greater power than genome-wide PRSs. Compared to genome-wide PRSs, we expect pathway-based PRSs to offer greater insights into the heterogeneity of psychiatric disorders, and to develop higher resolution models of genetic risk that can be used for better understanding of the disease etiology, patient stratification and ultimately optimized treatment.

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## #41 Enhancing the Psychometric Properties of the Iowa Gambling Task Using Generative Modeling

Holly Sullivan-Toole, Ph.D.[1], Nathaniel Haines, Ph.D.[2], Kristina Dale, M.S.[1], & Thomas M. Olino, Ph.D.[1]

[1] Temple University, Department of Psychology and Neuroscience
[2] The Ohio State University, Department of Psychology

Poor psychometrics, particularly low test-retest reliability, pose a major challenge for using behavioral tasks in individual differences research. Here, we show that joint generative modeling of the Iowa Gambling Task (IGT) substantially improved test-retest reliability and enhanced the IGT's validity for use in characterizing internalizing pathology, compared to the traditional analytic approach. IGT data (n =50) was collected across two sessions, one month apart. Our joint generative model incorporated (1) the Outcome Representation Learning (ORL) computational model at the person-level and (2) a group-level model that explicitly modeled test-retest reliability, along with other group-level effects. Compared to the traditional 'summary score' (proportion good decks selected), the ORL model provides a theoretically rich set of performance metrics (Reward Learning Rate (A+), Punishment Learning Rate (A-), Win Frequency Sensitivity (βf), Perseveration Tendency (βp), Memory Decay (K)), capturing distinct psychological processes. While test-retest reliability for the traditional summary score was only moderate (r = .37, BCa 95% CI [.04, .63]), test-retest reliabilities for ORL performance metrics produced by the full generative were substantially improved, with test-retest correlations ranging between r = .64–.82 for the five ORL parameters. Further, while summary scores showed no substantial associations with internalizing symptoms, ORL parameters were significantly associated with internalizing symptoms. Specifically, Punishment Learning Rate was associated with higher self-reported depression and Perseveration Tendency was associated with lower self-reported anhedonia. Joint generative modeling offers promise for advancing individual differences research using the IGT, and behavioral tasks more generally, through enhancing task psychometrics.

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**#42** **Iterative simulation to understand modulation of brain activity in health and disease.**

Sergio Miguel Tomé [1,2], Juan Manuel Corchado[1]

[1] Departamento Informática y Automática, Universidad de Salamanca, Plaza de la Mer- ced s/n, 37008, Salamanca, Spain.
[2] Departamento of Cell Biology, Downstate Health Sciences University, Brooklyn, New York 11203, NY, USA

Dopamine has been related with schizophrenia, major depressive disorders, and bipolar affective disorder. The research for the last few years has shown that dopamine trans- mission does not happen only by synaptic transmission but in many instances by a kind of precise volume transmission. Thus, understanding the dynamics of dopamine transport through the human brain is important for our understanding of how those psy- chiatric disorders emerge. In addition, the concentration of a drug drives the effects ex- perienced by a patient. Therefore, understanding how the distribution of a drug happens within the brain becomes a key element on our way to understand the brain function in health and disease. Despite the importance of how endogenous and exogenous sub- stances diffuse through the brain, we have little knowledge about this. Simulation in silico is a way to understand the diffusion of endogenous and exogenous substances through the brain, but even the simulation of a few cubic centimetres is a huge technological challenge. The number of molecules that are needed for a realistic simulation is larger than the memory resources available in the current commercial computers. For example, simulating the diffusion of 1 mg. of benzodiazepine would need almost 29 million Tera- bytes of storage if the position of each molecule was required to be known for each step of the simulation. The Hippocampus Extracellular Space Simulator Project proposes a hybrid tiered architecture with two levels to carry out an iterative simulation of a relevant number of molecules over functionally relevant distances for basic and clinical research.

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## #43 Anxiety is Associated with Diminished Information-Seeking and Low Expectations of Uncertainty Reduction

Yaniv Abir[1], Camilla van Geen[2,3], Brena Bessa[1], Maya Leshkowitz[4], Ran Hassin[5], Caroline Marvin[1*], Daphna Shohamy[1,2,6*]

[1] Department of Psychology, Columbia University, New York, NY, United States.
[2] Zuckerman Mind Brain Behavior Institute, Columbia University, New York, NY, United States.
[3] Department of Psychology, University of Pennsylvania, Philadelphia, PA, United States.
[4] Department of Cognitive Sciences, The Hebrew University of Jerusalem, Jerusalem, Israel.
[5] Department of Psychology and The Federmann Center for the Study of Rationality, The Hebrew University of Jerusalem, Jerusalem, Israel.
[6] Kavli Institute for Brain Science, Columbia University, New York, NY, United States.

*These authors contributed equally to this work.

The study of anxiety from an information-processing perspective has successfully uncovered anxiety-related changes in responses to presented information. Yet, in everyday life information is rarely presented to us. Instead, we actively choose what information to seek. Here, we ask how information-seeking is altered along the spectrum of trait anxiety. Anxiety may motivate individuals to reduce uncertainty and gain assurance by seeking information, or it may be associated with diminished information-seeking, due to its demotivating effects.

In two experiments (total n=5557 general US population), participants decided whether to seek answers to a variety of factual questions. We also measured expectations of answer utility and expectations that the answer will reduce the uncertainty inherent in the question. Overall, individuals sought answers with high utility and high expectations of reducing uncertainty. Crucially, anxiety was associated with diminished information-seeking. Surprisingly, we found that individuals along the anxiety spectrum reported similar expectations of informational-utility. Instead, anxiety was associated with diminished expectations that a forthcoming answer would reduce the uncertainty inherent in the question. We contrasted anxiety with acute concerns about a current event (the onset of COVID-19), which were associated with correlated changes to information seeking and value expectations, but not with expectations of uncertainty reduction. Our results highlight the importance of studying information seeking in computational psychiatry: The value of information is fundamentally separable from the expectation of attaining the information, decomposing motivation into two dimensions that may be differentially implicated in healthy and disordered behavior.

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## #44 Characterizing test-retest reliability of resting state functional connectomes in depressed adolescents

Christopher C. Camp[1], Lillian Eisner[2], Stephanie Noble[3], Dustin Scheinost[3], Argyris Stringaris[4], and Dylan M. Nielson[2,5]

[1] Interdepartmental Neuroscience Program, Yale University;
[2] Section for Clinical and Computational Psychiatry, Emotion and Development Branch, National Institute of Mental Health, NIH;
[3] Department of Radiology and Biomedical Imaging, Yale University School of Medicine, Yale University;
[4] Division of Psychiatry and Division of Psychology and Language Sciences, University College London;
[5] Center for Multimodal Neuroimaging, National Institute of Mental Health, NIH

fMRI has been used to investigate biomarkers for major depressive disorder (MDD), but unreliable results can restrict clinical utility. Despite this, few studies have assessed reliability in depressed populations, and none have done so across adolescence, when onset risk increases substantially. We leveraged univariate and multivariate metrics to characterize the longitudinal reliability of an adolescent cohort.

42 adolescents with MDD and 27 healthy volunteers (HV) were scanned at baseline and after one year (median age = 15.63; 17 males). Test-retest reliability of resting state connectivity was measured through Intraclass Correlation Coefficient (ICC), the ratio of between-subject to within-subject variation, and two recently introduced multivariate metrics: fingerprinting (FI), the proportion of subjects most similar to themselves at a subsequent time point, and discriminability, the proportion of within-subject measurement distances smaller than between-subject distances.

Edge-level ICCs in MDDs were greater than in HVs ($\mu MDD = 0.40 > \mu HV = 0.25$; Wilcoxon rank-sum test: $p < .005$). ICCs in both groups were comparable to healthy adults. Connectomes were more discriminable than chance (DiscrMDD = .78, DiscrHV = .74; permutation tests $p < 0.01$) and more identifiable than chance (FIMDD = .55; FIHV = .67; Poisson(1) test: $p < .001$). Reliability metrics did not vary with clinical scores, medication, or pre-correction motion.

Overall, depressed adolescents were more reliable than HVs at the edge level. Nonetheless, both MDD and HV ICCs were poor, limiting the potential of connectome edges as univariate biomarkers. However, the high discriminability and fingerprinting results indicate that multivariate connectome measures may be suitable as biomarkers of depression.

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**#45**

Luis Sordo Vieira[1,2], Carol A. Mathews[1]

[1] Department of Psychiatry, University of Florida, Gainesville Florida
[2] Department of Medicine, University of Florida, Gainesville Florida

Hoarding disorder (HD) is a DSM-5 psychiatric disorder associated with difficulty discarding seemingly useless objects, leading to accumulation of clutter in living and workspaces, and impairment in daily functioning. Several venues of research suggest that HD is associated with various psychiatric disorders, most strongly with OCD, MDD, ADHD. Furthermore, other disorders such as GAD and Panic Disorder commonly co-occur with HD. On the other hand, there are few published reports on the associations of HD with other neurological disorders.

To better understand the relationships between HD and other psychiatric/neurological conditions, we applied methods from network analyses, including community detection and bootstrapping methods for edge estimation and significance testing. Our main dataset is the Brain Health Registry (N=15,978), a large online registry with the goal of studying brain aging and disorders, to parse out which disorders are directly associated with HD (vs which association might be better explained through a secondary association with a more prevalent disorder).

Our analyses suggest that MDD, OCD, and ADHD form a strong triad of disorders associated with HD, and the association of HD with other anxiety disorders are weak or mediated through another disorder. A seeming relationship between MCI and HD could be better explained by a relationship between MCI and ADHD and OCD. Conclusions: We found that an increase in hoarding severity is associated with higher psychiatric burden. Moreover, ADHD, OCD, and MDD are the strongest correlates with HD.

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## #46 Computational characterization of social inference deficits associated with autism traits during observational learning

Qianying Wu1* , Caroline J. Charpentier1 * , Sarah Oh1 , Jamie D. Feusner2,3,4, Reza Tadayon- Nejad3 , Jeffrey Cockburn1 , Ralph Adolphs1 , John P. O'Doherty1

1Division of Humanities and Social Sciences, California Institute of Technology
2Department of Psychiatry, Division of Neurosciences and Clinical Translation, University of Toronto
3Semel Institute for Neuroscience and Human Behavior, University of California Los Angeles
4Centre for Addiction and Mental Health, Toronto

*These authors contributed equally.

One's ability to infer the goals and intentions of others is crucial for social interactions and, more generally, to function in society. This skill set varies broadly across individuals, and deficits are commonly associated with autism spectrum disorders (ASD). However, despite the importance of social inference, the underlying computational principles and the link between their disruption and individual variability remain poorly understood.

We characterized individual differences in social learning via a large-scale online study. Adult participants from the general population (N=901) completed an observational learning task that involves a tradeoff between two strategies: imitation (repeat the observee's most recent action) and emulation (infer the observee's goal). Self-report questionnaires were collected to assess symptom dimensions relevant to psychopathology, including the Social Responsiveness Scale (SRS) as an index of autism-like traits. Using computational modeling, we quantified individual tendencies to rely on imitation versus emulation learning.

We find that autism severity was associated with a deficit in social goal inference, including reduced task performance ($R = -0.231$, $p<0.001$) and lower emulation propensity as quantified by the model ($R=-0.152$, $P<0.001$). The latter association holds when controlling for other model parameters, (e.g., decision noise, heuristics) as well as other psychiatric symptom dimensions (e.g., depression, social anxiety, etc).

Our findings suggest that social inference deficits typically observed in autism may be related to a difficulty in inferring other people's goals and intentions when learning from observation. Further investigations in diagnosed ASD patients are warranted to confirm the clinical relevance of this finding.

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**#47** **Deconstructing Mapper to reveal the brain's dynamic organization**

Daniel Haşegan[1], Caleb Geniesse[1], Samir Chowdhury, Ph.D.[1], Manish Saggar, Ph.D.[1]

[1] Department of Psychiatry and Behavioral Sciences, Stanford University, Stanford, CA, USA

Although neuroimaging data is almost always high-dimensional, the underlying dynamical trajectory of neural activity is thought to be lower-dimensional. Revealing the shape (or topology) of such neuronal activity dynamics could potentially hold the key to anchoring psychiatric disorders into biological features. While Topological Data Analysis (TDA), specifically the Mapper algorithm, is a mathematically rigorous tool for dissecting the underlying shape of high-dimensional datasets, its use in the field of neuroimaging is still in its nascent stages. One potential reason for such low usage could be the steep learning curve associated with the steps/concepts related to the TDA-based Mapper approach. Here, we aim to deconstruct the Mapper algorithm to reveal its functioning and provide guidelines for parameter choices at each step. Using a synthetic and a real continuous multitask dataset, we reveal how parameters at each step affect insights generated using Mapper. Specifically, we examined the (a) choice of distance metrics, (b) need for dimensionality reduction, and (c) range of traditional Mapper parameters for both datasets. Importantly, deconstructing Mapper's steps using a synthetic dataset, with ground truth about data generation (i.e., loop trajectory), provided a unique opportunity to evaluate parameter choices that best capture the shape of the data. Further, similar deconstruction using a real multitask fMRI dataset, with ground truth about transitions in cognitive states (or tasks), enabled analyzing the parameters that best capture transitions in brain activity over time. Altogether, we hope that our work provides an introduction to Mapper steps and also prescribes essential guidelines for using Mapper on neuroimaging datasets.

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**#48**

## Altered sense of social control in adolescents with eating disorder

Qixiu Fu[1], Jessica Harper[2], Jayme Palka[2], Carrie McAdams[2], Xiaosi Gu[1]

[1] Icahn School of Medicine at Mount Sinai, New York, NY
[2] UT Southwestern Medical Center, Dallas, TX

Adolescence is a critical period for learning to navigate the social world and exploit its controllability. As such, a diminished sense of social control is detrimental to mental health, such as observed in eating disorders (ED). Here, we examined social controllability in adolescents with (n = 27; age = 15.17 ± 1.34) and without (n = 28; age = 15.45 ± 1.62) ED as they played an interpersonal exchange paradigm in which they could use their actions to influence the monetary offers from others. We applied computational modeling to estimate two key parameters: estimated control (i.e., how much influence one had on future offers) and initial norm (i.e., offer amount participants expected to receive prior to any interactions); participants also self-reported perceived control after the game. We found no group difference in estimated control (P = .66) or initial norm (P = .60), but a reduced sense of control in ED group (t (53) = - 2.18, p = .03). In healthy adolescents, perceived control was driven by model- estimated control (r = .62, p = .0004), but not initial norm (r = - .04, p = .85). Strikingly, adolescents with ED showed a completely reversed pattern in that their perceived control was primarily correlated with initial norm expectation (r = .47, p = .01) instead of model-estimated control (r = .05, p = .80). These findings suggest that a stable relationship between subjective awareness of controllability and one's actual behavioral influence protects against disordered eating, while altered social norm expectation contributes to a diminished sense of control in adolescents with ED.

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**#49** **The Role of Self-efficacy and Response-efficacy during Perceived Control**

Yun-Yen Yang and Mauricio R. Delgado; Psychology, Rutgers University, Newark, NJ

Perception of control refers to the belief that one's own behavior can lead to a desirable outcome. Participants often prefer situations where they are able to exert control (e.g., picking an airline seat) over not being in control (e.g., letting the computer assign them a seat) even at a cost – a process thought to be mediated by the ventromedial prefrontal cortex (vmPFC; Wang et al., 2019). Importantly, perceived control can be distinguished into two components: self-efficacy - the belief of an individual in successfully executing a behavior; response-efficacy - the belief that the behavior will lead to an expected outcome. Here, we investigate how self-efficacy and response-efficacy are evaluated to form perceived control and influence decisions. Participants made perceptual evaluations about whether they could hit a moving target on the screen (self- efficacy) presented with a card that highlighted the probability of the correct evaluation being worth a reward (response-efficacy). We scanned participants while they were presented with these two pieces of information simultaneously and asked them to rate their confidence in a) performing the behavior and b) the trial leading to a reward. Preliminary results suggest that participants were more sensitive to changes in self-efficacy than response efficacy information. That is, participants valued self-efficacy more than response efficacy information while making choices. Using fMRI, we observed activity in the vmPFC which positively correlated with self- efficacy, whereas activity in the striatum positively correlated with response efficacy. Further analysis will examine how self-efficacy and response-efficacy are integrated to influence decision making.

**#50**

## Impaired Computations of Social Control in Autism Spectrum Disorder

Sarah M. Banker[1,3,4], Soojung Na[1,4], Sarah Barkley[3], Jadyn Trayvick[3], Daniela Schiller[1,2,4], Xiaosi Gu[1,2,4], Jennifer Foss-Feig[2,3]

[1] Nash Family Department of Neuroscience, Icahn School of Medicine at Mount Sinai, New York, NY
[2] Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, NY
[3] Seaver Autism Center for Research and Treatment, Icahn School of Medicine at Mount Sinai, New York, NY
[4] Center for Computational Psychiatry, Icahn School of Medicine at Mount Sinai, New York, NY

Individuals with autism spectrum disorder (ASD) are thought to show alterations in social decision-making, but the nature of these alterations remains poorly understood. To investigate this, we utilized a proactive social decision-making task that mimics the types of interactions with which people with ASD struggle daily. Adults with ASD (n=37; age: mean 26.1, range 18.4- 41.5; sex: 62.2% male) completed a social controllability paradigm in which they accepted or rejected splits of $20 proposed by virtual partners. Unbeknownst to the participants, in one condition ('controllable') but not the other ('uncontrollable'), their decisions influenced future offers. At the end of the task, participants rated how much influence they believed they had in each condition. Computational modeling approaches extracted parameters of interest. T-tests compared group differences between ASD and a previously collected sample of typically- developing (TD) individuals (n=45). Unlike TD individuals, who have been shown to engage a mental model of forward thinking to estimate social controllability 2-steps ahead, ASD individuals did not appear to simulate outcomes beyond the current trial (t-test comparing BIC scores from 0-step model with 1-step model: $t=0.15$, $p=0.88$). After extracting parameters from the winning models, we found that, in the controllable condition, ASD participants received lower offers ($t=-2.73$, $p=0.008$), perceived having less control ($t=-3.08$, $p=0.003$), showed higher initial offer expectations ($t=3.70$, $p<0.001$), and showed slower norm adaptation speeds ($t=2.12$, $p=0.03$) than TD individuals. Together, these results suggest that individuals with ASD show disrupted detection of and adaptation to social norms, as well as disrupted perception and exertion of social control.

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**#51** **A Unified Account of Adaptive Learning in Different Statistical Environments**

Niloufar Razmi, Department of Neuroscience, Brown University Providence, Rhode Island 02912 USA
Matthew R Nassar, Department of Neuroscience, Brown University Providence, Rhode Island 02912 USA

Humans adjust their learning rate rationally according to local environmental statistics and calibrate their learning rate based on the broader statistical context. To capture the broad range of dynamic learning behavior that humans show in response to changes in local environmental statistics, we introduce a generalized framework of adaptive learning based on dynamic state representation. We will first present our biologically plausible neural network model which shifts its internal context upon receiving supervised signals that are mismatched to its output, thereby changing the "state" to which feedback is associated. By introducing the state transitions, we show how either increase learning or decrease learning depending on the duration over which the new state is maintained. We will then extend this model by tackling the larger question as to how structure governing state transitions can be inferred from data. To do so, we develop a Bayesian model in which changepoint, oddball and reversal contexts can be inferred using a sticky variant of the Chinese restaurant process. We show that this model can learn how to behave appropriately in different environments by learning the underlying structure i.e., how the states transitions. Finally, we describe ongoing attempts to incorporate structure learning into our neural network model, thereby allowing it to develop appropriate adaptive learning strategies de novo.

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**#52** **Testing whether poor credit attribution predicts conversion to chronic pain**

Sienna Bruinsma, Frederike Petzschner*, Matthew Nassar*

*These authors contributed equally

While almost a quarter of American adults suffer from chronic pain, little is known as to what factors facilitate the transition from acute to chronic pain. In the present study, we designed a task that assesses if and how people can learn the short- and long-term consequences of their actions and whether poor credit attribution can predict the development of chronic pain. Our task requires participants to evaluate the short- and long-term consequences that different activities have on perceived pain levels. We compare several models in their ability to perform short and long-term credit assignment. We find that standard model-free algorithms, such as temporal difference learning (TD) cannot capture credit assignment to actions with long-term consequences. Long-term credit assignment can be better captured by models that take the causal structure of the environment into account such as, Bayesian causal inference. Next, we plan to test this task in both individuals with chronic and acute pain to see whether failures in credit attribution are associated with chronic pain states and can predict the risk of developing chronic pain in acute pain patients. Furthermore, we plan to compare whether credit assignment in the task translates to real world behavior by measuring daily reports of activities and pain intensity over the course of four months in the same participants. Ultimately, we aim to develop a model of short and long-term credit assignment and assess its predictive validity for chronic pain.

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**#53** **Temporal representation adaptation as a computational link between early life unpredictability and anhedonia**

Nora C. Harhen, Aaron M. Bornstein University of California, Irvine

An unpredictable early life environment can have enduring effects on mental health. Despite widespread evidence for this relationship, its underlying mechanism remains unclear. Here, we focus on anhedonia and three associated phenotypes — impaired reward learning, diminished reward expectation, and negativity bias. We propose that these phenotypes emerge from the optimization of temporal representations to the environment. We formalize this proposal with a model of interval timing (Ludvig et al, 2008). Briefly, the model represents intervals with a population of "temporal receptive fields" (TRFs) whose shape determines representational precision. We simulated two groups of agents, ELU and control, learning to pair a cue with reward across two environments. Modeling development, TRFs could only adapt to the initial environment, which differed between groups. ELU agents received rewards at a variable interval while the control's was fixed. We measured prediction error magnitude at cue and outcome. Temporal variability produced broadly tuned TRFS in ELU agents, impairing learning ($t(198)=15.15$, $p<.0001$, $d=2.45$) and reducing reward anticipation ($t(198)=-15.45$, $p<.0001$, $d=4.12$). In the following environment, all agents received rewards at a fixed interval. Both groups asymmetrically responded to reward receipt versus omission however, in opposing directions ($t(198) =-7.18$, $p<.0001$, $d=1.17$). Reproducing the negativity bias found in anhedonia, ELU agents responded more strongly to reward omission. Given anhedonia is a transdiagnostic symptom, these results suggest a common mechanism for a number of psychiatric disorders, potentially explaining their high comorbidity rates.

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