of trauma. RESULTS/ANTICIPATED RESULTS: We demonstrated that neighborhood disadvantage is associated with decreased volume and alterations of resting state functional connectivity of structures implicated in affect processing, including the hippocampus, amygdala, and ventromedial prefrontal cortex. These results held even after controlling for relevant individual variables, including acute post-traumatic stress symptoms and years of education. Moreover, individuals from disadvantaged neighborhoods exhibited heightened activation of these same structures in response to aversive stimuli. Thus, brain regions critical for recognizing and processing negative stimuli are susceptible to the effects of area-level socioeconomic factors. DISCUSSION/SIGNIFICANCE OF FINDINGS: The results offer additional evidence that neurobiological mechanisms clarify how stress ‘gets under the skin’. Changes to key brain regions may explain why those living in disadvantaged neighborhoods are at a heightened risk of PTSD. Broadly, these findings should inform future policies and community-driven interventions aimed at reducing poverty.

PSD95-nNOS interaction alters the basolateral amygdala transcriptome following fear conditioning: implications for molecular mechanisms underlying PTSD

Jheel Patel, Melissa Haulcomb, Lianping Li, Guanglong Jiang, Erik Dustrude, Yunlong Liu, Yvonne Lai, Andrei Molosh and Anantha Shekhar
Indiana University School of Medicine

ABSTRACT IMPACT: This research takes a transcriptomic approach to parse genes and molecular pathways that underlie the fear memory circuitry and, in doing so, identifies therapeutic targets that can further be developed into treatments for fear disorders, such as post-traumatic stress disorder. OBJECTIVES/GOALS: Normal fear learning produces avoidance behavior that promotes survival, but excessive and persistent fear after trauma can lead to development of phobias and post-traumatic stress disorder (PTSD). Our goal is to understand the mechanism and identify novel genetic targets underlying fear responses. METHODS/STUDY POPULATION: Involvement of the basolateral amygdala (BLA) in fear acquisition is well established and requires activation of N-methyl-D-aspartic acid receptors (NMDARs). At a cellular level, NMDAR activation leads to production of nitric oxide (NO) by a process mediated by interaction between postsynaptic density protein 95 (PSD95) and neuronal nitric oxide synthase (nNOS). To elucidate mechanisms underlying the role of the PSD95-nNOS-NO pathway in conditioned fear, here we use rodent behavioral paradigms, pharmacological treatment with a small molecule PSD95-nNOS inhibitor, RNA-sequencing, and an AAV-mediated knockdown of the nNOS gene in the BLA. RESULTS/ANTICIPATED RESULTS: We show that treatment with ZL006 attenuates rodent cued-fear consolidation. Additionally, with RNA-sequencing, expression of 516 genes was restored with systemic ZL006 treatment. Network data and gene ontology enrichment analyses further revealed that CGMP effects, insulin-like growth factor binding, and cognition-related pathways were significantly altered. Finally, we show that a BLA-specific knockdown of nNOS attenuates cued fear consolidation, without adverse effects on other memory and motor behaviors. DISCUSSION/SIGNIFICANCE OF FINDINGS: Via a model of NMDAR-mediated fear consolidation, our results reveal novel pathways and genetic targets that underlie plasticity of fear memory circuitry. Importantly, these results will inform future therapeutic strategies for targeting fear related disorders like PTSD.

Temporal Evolution of Neural Activity in Human Brain Organoids

Kobina G. Mensah-Brown, James Lim, Dennis Jgamadze, Guo-li Ming, Hongjun Song, John A. Wolf and Han-Chiao I. Chen
University of Pennsylvania

ABSTRACT IMPACT: This study will provide the essential characterization of intrinsic neural activity in human brain organoids, both at the single cell and network levels, to harness for translational purposes. OBJECTIVES/GOALS: Brain organoids are 3D, stem cell-derived neural tissues that recapitulate neurodevelopment. However, to leverage their full translational potential, a deeper understanding of their intrinsic neural activity is essential. Here, we present our preliminary analysis of maturing neural activity in human forebrain organoids. METHODS/STUDY POPULATION: Forebrain organoids were generated from human iPSC lines derived from healthy volunteers. Linear microelectrode probes were employed to record spontaneous electrical activity from day 77, 100, and 130 organoids. Single unit recordings were collected during hour-long recordings, involving baseline recordings followed by glutamatergic blockade. Subsequently, tetrodotoxin was used to abolish action potential firing. Single units were identified via spike sorting, and the spatiotemporal evolution of baseline neural properties and network dynamics was characterized. RESULTS/ANTICIPATED RESULTS: Nine organoids were recorded successfully (n=3 per timepoint). A significant difference in number of units was seen across age groups (F(2,6) = 6.4178, p = 0.0323). Post hoc comparisons by the Tukey HSD test showed significantly more units in day 130 (51.67 ±14.15) than day 77 (16.33 ±14.98) organoids. Mean firing rates were significantly different in organoids based on age, with drug condition also trending toward significance (F(6,12) = 9.97; p = 0.0028 and p = 0.08 respectively). Post hoc comparisons showed a higher baseline firing rate in day 130 (0.99Hz ±0.30) organoids than their day 77 counterparts at baseline (0.31Hz ±0.066) and glutamate blockade (0.31Hz ±0.045). Preliminary network analysis showed no modularity or small-world features; however, these features are expected to emerge as organoids mature. DISCUSSION/SIGNIFICANCE OF FINDINGS: Initial analysis of brain organoid activity demonstrates changes in single unit properties as they mature. Additional work in this area, as well as further network analyses, will confer better sense of how to rationally utilize brain organoids for translational purposes.

Vaginal pH predicts cervical intraepithelial neoplasia-2 regression in women living with human immunodeficiency virus

Katherine Michel1, Christine Colie1, Robert D. Burk2, L. Stewart Massad3, Cuwei Wang3, Michaeline Hebrón3, Charbel Moussa3, Gypsyamber D’Souza4, Lisa Rahangdale3, Lisa Flowers5, Joel Milam3, Joel M. Palefsky6, Howard Minkoff5, Howard D. Strickler7 and Sebile G. Kassaye1
1Georgetown University, 2Albert Einstein College of Medicine, 3Washington University in St. Louis, 4Johns Hopkins University, 5University of North Carolina School of Medicine, 6Emory University, 7University of California Irvine, 8University of California San Francisco and 9Maimonides Medical Center

ABSTRACT IMPACT: The potential to use vaginal pH as a low cost, non-invasive diagnostic test at the point of CIN2 diagnosis to predict