# Table of Contents

Ben-Zeev, Dror, Combining mHealth Technology an Pharmacotherapy to Improve Mental Health Outcomes and Reduce Human Rights Abuses in West Africa .................................................. 3

Bhat, Amritha, Mobile Mental Health in Community-Based Organizations in Rural India: A Pilot Randomized Controlled Trial ......................................................................................... 4

Bohjanen, Paul, Capacity-Building for Meningitis Research and Care in Rural, Northern Uganda ........ 4

Campbell, Megan, and Gebiso, Eengido Girma, Fostering Scientific Inclusion in Global Psychiatric Genetics: Lessons Learned and Paths Forward................................................................. 5

Crea, Thomas, Long Term Stress and Impairment in Children and Youth Following the 2014-2016 Outbreak of Ebola Virus Disease in West Africa ........................................................................... 6

Dulla, Chris Using Single Cell Biological Approaches to Understand CNS TB ................................ 7

Evangeline, Betcy, Comparison of Gene Expression in Monocytes Exposed to Taenia Solium Antigens and Mycobacterial Antigens of Healthy Subjects Living in an Endemic Region ..................... 7

Gallo, Carla, Isolation and Identification of CXCR4 and CXCR7 Agonists from Traditional Phytopharmaceuticals as Potential Novel Drugs for Mental Disorders ...................................................... 8

Hastings, Paul, Neural Mechanisms of Protective Effects of Early Nutrition on the Development of Social-Emotional Difficulties Among Children in Ghana .................................................. 8

Holmes, Martha, Neuroimaging and Gut Microbiome Markers of Development in HIV-Exposed Uninfected Infants ........................................................................................................ 8

Islam, Zhahirul, Gut Microbiome and their Regulation in Immune Responses in Guillain-Barre Syndrome: A Prospective Controlled Study ............................................................................. 9

John, Chandy, Malarial Impact on Neurobehavioral Development (MIND) ....................................... 10

Karsz, Alison, AHSA II: An Ethnographic Study Embedded in Randomized Controlled Trial ............ 10

Korte, Kristina, Validity and Reliability of the MINI and SCID in Sub-Saharan Africa ....................... 11

Laughton, Barbara, Extension of a Longitudinal Cognitive and Brain Imaging Study of Early-Treated Perinatally HIV Infected Children Through Adolescence ....................................................... 11

Lin, Pei-Yi (Ivy), Improving Infant Hydrocephalus Outcomes in Uganda: Predicting Developmental Outcomes and Identifying Patients at Risk for Early Treatment Failure after ETV/CPC ............. 12

Link, Abigail, Meningitis Causes and Outcomes in Rural Northern Uganda ..................................... 12

Mbirbah, Elizabeth, Factors that Influence Human Milk Oligosaccharides (HMOs) .......................... 13

McHenry, Megan, Advancing the science of neurocognitive physiology in adolescents living with HIV ........................................................................................................................................ 14

Meya, David B., Improving Diagnostics and Neurocognitive Outcomes in HIV/AIDS-related Meningitis .......................................................................................................................... 14
Moorthy, Ranjith, Correlation Between Monocyte Gene Expression and Inflammation on Brain Imaging in Patients with Solitary Cerebral Cysticercus Granuloma ..........................................................15

Mwanza, Jean-Claude, NeuroEbola: Baseline Demographic, Immunological, and Clinical Characteristics of Study Participants ..........................................................15

Pardo-Villamizar, Carlos, Neuroinfections Emerging in the Americas Study (NEAS): A Research Network to Establish the Role of Emerging Infections in the Incidence of Acute Neurological Problems in Colombia ........................................................................................................16

Paul, Robert, Mental Health Phenotypes of Well-Controlled HIV in Uganda .................................................................................................................................17

Post, Kristi, Neuropsychiatric Genetics of African Populations: Building the Research and the Researchers Together ..................................................................................18

Rai, Sauharda, Promoting gender equity in global mental health research capacity building in Low- and Middle-Income Countries: Efforts and learnings from Nepal ..............................................18

Rohloff, Peter, A Hybrid Implementation-Effectiveness Trial of the International Guide for Monitoring Child Development in India and Guatemala ..................................................................19

Vassileva, Jasmin, Addiction Neuroscience Research in Bulgaria: 20 Years of Global Brain Research ..19
Bazira, Joel, Genomic Research and Assay Development in the Fungal Pathogen Cryptococcus Neoformans

Cryptococcal meningitis, caused by the fungal pathogen Cryptococcus neoformans, is common in individuals with HIV/AIDS and estimated to kill 112,000 individuals annually. Despite improvements in standard of care, mortality remains high, causing 19% of HIV-related deaths. Both the host immune response and pathogen-specific factors influence patient outcome. To identify pathogen-specific factors that impact human disease, we previously performed a pathogen GWAS that identified 145 variants in 40 C. neoformans genes. To expand upon these human studies, we used a mouse inbred model of cryptococcal meningitis to decrease host variability and normalize the fungal burden. These mouse studies revealed the clinical isolates exhibit a spectrum of virulence ranging from attenuated to hyper-virulent. Four hyper-virulent isolates were identified and are of particular interest for several reasons. First, while the isolates are hyper-virulent in the mouse model, all came from patients who survived the cryptococcal meningitis infection. Second, the mouse immune response to most of the hyper-virulent isolates is characterized by excessive IFNγ production. IFNγ is considered protective against C. neoformans infection, yet excessive IFNγ production is observed during immune-reconstitution inflammatory syndrome (IRIS). We hypothesize that IFNγ production by the hyper-virulent isolates is beneficial in the context of HIV-related immune dysfunction, but may enhance risk of IRIS. While exciting, our current collection of four hyper-virulent isolates is insufficient. Moving forward we would like to 1) Perform a large GWAS with 500 clinical isolates and use a bioinformatics approach to predict hyper-virulent isolates; 2) Test the hypothesis that immune response to hyper-virulent isolates differs between healthy individuals when compared to HIV-infected individuals; and 3) Continue to define the underlying C. neoformans genetic polymorphisms that discern patient outcomes and develop diagnostic tools to differentiate isolates and inform patient care.

Ben-Zeev, Dror, Combining mHealth Technology an Pharmacotherapy to Improve Mental Health Outcomes and Reduce Human Rights Abuses in West Africa

In West Africa, healers greatly outnumber trained mental health professionals. People with serious mental illness (SMI) are often seen by healers in “prayer camps” where they may also experience human rights abuses. We developed M&M, an 8-week long dual-pronged intervention involving a) a smartphone-delivered toolkit designed to expose healers to brief psychosocial interventions and to encourage them to preserve human rights (M-Healer app), and b) a visiting nurse who provides medications to their patients (Mobile Nurse). We conducted a single-arm field trial of M&M with people with SMI and healers in a prayer camp in Ghana. Healers were provided with smartphones with M-Healer installed and were trained by practice facilitators to use the digital toolkit. In parallel, a study nurse visited their prayer camp to administer medications to their patients. Clinical assessors administered study measures to participants at pre-treatment (baseline), mid-treatment (4 weeks) and post-treatment (8 weeks). Seventeen participants were enrolled in the study and most (n=15, 88.3%) were retained. Participants had an average age of 44.3 (SD: 13.9) and 59% (n=10) were male. Four healers were trained to use M-Healer. On average, they self-initiated app use 31.9 (SD: 28.9) times per week. Healers watched an average of 19.1 videos (SD: 21.2), responded to 1.5 prompts (SD: 2.4), and
used the app for 5.3 days (SD: 2.7) weekly. Pre/post analyses found a statistically significant and clinically meaningful reduction in psychiatric symptom severity, psychological distress, shame, and stigma. We recorded a significant reduction in days chained (1.6 to 0.5) and a promising trend for reduction in days of forced fasting (2.6 to 0.0, p = 0.059). We did not identify significant pre/post changes in patient-reported working alliance with healers (Working Alliance Inventory), depressive symptom severity (Patient Health Questionnaire-9), quality of life (Lehman Quality of Life Interview for the Mentally Ill), beliefs about medication (Beliefs about Medications Questionnaire – General Harm sub-scale) or other human rights abuses. No major side effects, health and safety violations, or serious adverse events occurred over the course of the trial. The M&M intervention proved to be feasible, acceptable, safe, and clinically promising. Preliminary findings suggest the M-Healer toolkit may have shifted healer behaviors at the prayer camp so that they commit fewer human rights abuses.

Bhat, Amritha, Mobile Mental Health in Community-Based Organizations in Rural India: A Pilot Randomized Controlled Trial

Undiagnosed and untreated depression is a significant cause of morbidity and mortality in low-middle-income countries (LMIC) such as India. The rates of diagnosis and treatment of depression among women in rural India are disproportionately low. Stepped care approaches support appropriate treatment of symptoms while reducing the burden on healthcare systems, and mobile technology can reduce the mental health treatment gap given its reach and easy access. However, in rural south India, illiteracy and the practice of sharing mobile phones as a family resource present hurdles to the adoption of mobile mental health (mHealth) based interventions. We tested the feasibility of a community based multiple user mHealth application to screen depression, track symptom severity and support the delivery of stepped care treatment. We first adopted a user centered participatory approach to design and develop a multiple-user, voice-response, mobile application (“MITHRA”), to be used in community based organizations (self help groups SHGs) for screening, tracking and supporting stepped care treatment for depression, including select modules of the Healthy Activity Program, a brief psychological intervention based on behavioral activation. The application includes audio, video and enhanced touchscreen capabilities. We next used a randomized-control design, to examine the feasibility and utility of “MITHRA” deployed at SHGs (n=3) vs enhanced usual care (n=3). We recruited and randomized 85 women to intervention and control. Our retention rate was 92% at 3 months and 6 months. We supported mentored participation of Psychiatry and Community Medicine residents from India in the research project and supported professional development of the research team through didactics and hands on training in qualitative methods.

Bohjanen, Paul, Capacity-Building for Meningitis Research and Care in Rural, Northern Uganda

Most people in sub-Saharan Africa live in rural areas where health infrastructure and resources are lacking. We sought to improve care of cryptococcal meningitis (CM) at Lira Regional Referral Hospital (LRRH) in rural, northern Uganda, an area with high prevalence of HIV and limited health infrastructure. In 2017, we initiated a CM diagnosis and treatment program (CM-DTP) at LRRH that introduced rapid
cryptococcal antigen (CrAg) testing for the diagnosis of CM and provided standard of care CM treatment and monitoring. During the period from 2017 to 2019, the CM-DTP led to improved diagnosis and treatment of CM as well as improved overall survival among patients with meningitis. During this period, we found that approximately 90% of patients with CM were already on antiretroviral therapy (ART) to treat HIV infection, suggesting that most patients with CM were failing ART. Although approximately one-third of patients with meningitis had CM, the etiology of meningitis in most patients was unknown due to a lack of diagnostic capabilities. A major goal of this R21 grant is to build capacity for meningitis diagnosis, care, and research at LRRH. In September of 2021, we began a pilot project to evaluate the etiologies of all meningitis at LRRH, and through this Fogarty R21 grant, we increased capacity for meningitis research at LRRH in a partnership involving University of Rochester (R21 prime institution), Lira University (R21 subaward), and the Infectious Diseases Institute (IDI) at Makerere University (R21 subaward). When we began our pilot project, diagnostic capacity at LRRH was limited. In partnership with our collaborators at IDI, we established protocols in the LRRH Microbiology Laboratory to perform gram stain, culture, and sensitivities on CSF. We also implemented point of care detection of bacterial antigens in CSF (Pastorex), detection of cryptococcal antigen (Immy), PCR testing for common etiologies of meningitis (BioFire) and TB meningitis (Gene X-pert). The project has also trained Ugandan clinical research staff related to research methods and data management. In addition, our research team is training health care providers at LRRH, Lira University and throughout the region in standard of care protocols for treatment of meningitis. Grants management staff at University of Rochester have also helped Lira University develop new grants management policies to support NIH grants.

Campbell, Megan, and Gebiso, Eengido Girma, Fostering Scientific Inclusion in Global Psychiatric Genetics: Lessons Learned and Paths Forward

Genomic studies have yet to adequately represent the entirety of the global population. While there have been improvements over the last decade, primarily driven by increased data from Asian populations, less than 3% of data currently included in genetic studies are from African populations. Increasing data collection in previously underrepresented areas of the world through collaborative efforts is the best solution to this issue. However, to do this, we must overcome the legacy of abuse and distrust from potential partners driven by centuries of “safari research” and colonialism. Building trust and equitable global partnerships in scientific research takes time and a commitment to a shared goal that includes success of both the research and the researchers. Investing in the next generation of students and early-career researchers is an ideal way to reach that goal. Unfortunately relying on traditional models, such as lab exchanges and one-off short courses, has had limited success, often leading to brain drain. This talk will present lessons learned from the Global Initiative for Neuropsychiatric Genetics Education in Research (GINGER) program, a training program established in 2016 that runs in collaboration with multiple large psychiatric genomic collections in Africa. Current GINGER Research Fellows will present strategies and considerations GINGER made for establishing, maintaining, and sustaining equitable collaborations, and share lessons learned during their experience on what worked, what challenges arose and what they advise for others who aim to build integrated training and research programs.
Crea, Thomas, Long Term Stress and Impairment in Children and Youth Following the 2014-2016 Outbreak of Ebola Virus Disease in West Africa

The 2013-2016 Ebola virus disease (EVD) epidemic in West Africa resulted in more infections and deaths than all prior outbreaks in the 40-year history of this virus combined. Among the more than 28,000 people infected with EVD approximately 21% were children under the age of 16, and more than 16,000 children lost one or both parents. This study examines the physical and ecological effects of EVD on children’s long-term mental health and physical sequelae among EVD-infected (n=222), EVD–affected (n=208), and control (n=233) children ages 10-17 in Sierra Leone. Preliminary results suggest that caregiver functioning is an important predictor of children’s mental health. EVD-affected children may be at greater risk of behavioral difficulties and physical sequelae compared to either infected and control groups, highlighting the need for social interventions in the immediate aftermath of infectious disease outbreaks.

Davidson, Leslie, Challenges in Using the WHODAS 2, A Disability Measure Based on the International Classification of Functioning, Disability and Health, in Adolescents in South Africa

The Asenze Cohort Study was initiated in 2006 after pilot support from the Fogarty Brain Disorders Program in 2003 and then from NIDA and Fogarty. Researchers at the University of KwaZulu-Natal and Columbia created and followed a cohort of 1581 Zulu children, 4-6 years old, along with their primary caregivers, identified through a house-to-house survey in a peri-rural setting in KwaZulu-Natal, South Africa at the epicenter of the HIV/AIDS epidemic. We followed them up in four waves through mid-adolescence, retaining almost 1200. We are just now funded by NIMH to launch a fifth wave in 2024. The domains we investigate are wide ranging but always include cognitive assessment, behavioral and/or mental health measures. One example from our research addresses the impact on childhood cognitive performance of intrauterine exposure to HIV without HIV infection. Children infected with HIV in utero (LHIV) or immediately postpartum perform worse on cognitive testing compared to those without in utero HIV infection (HEU). However, there is controversy in the literature about the cognitive performance of children whose mothers were living with HIV infection during pregnancy but were not HIV infected at birth or perinatally (HEU) compared to children of uninfected mothers (HUU). The study covered five contiguous areas of the Valley of 1000 Hills, containing a Zulu population who has survived the challenges of Apartheid, poverty, poor education, few opportunities for employment and until 2003 the failure of their government to recognize HIV as a virus. We compared cognitive scores for LHIV children with those who were HEU and those who were HUU. Children with missing values for HIV infection or for cognitive testing were excluded from these analyses leaving a sample of 985 ranging from age 13-17. In waves 1 and 2 the children were on average 5 and 7 years old and were given a series of subtests from the KABC. In wave 3, at average age 16, we introduced a new test of cognitive function, the NeuroScreen (Robbins et al.). Using different measures of cognitive ability over time and different analytic approaches the results essentially demonstrated the same finding. The children living with HIV scored significantly lower compared with those who were exposed in utero but not infected and with
those with no HIV exposure. There was no evidence that children exposed in utero to, but not infected by, HIV performed any worse cognitively than born to mothers who were not HIV infected.

Dulla, Chris Using Single Cell Biological Approaches to Understand CNS TB

Tuberculosis (TB) can lead to severe neurological dysfunction when infection spreads to the CNS (CNS-TB) and is the cause of significant neurological complications around the world. Here we will use single cell and single nuclei RNA-sequencing of human brain and CSF samples from patients with CNS-TB, along with a spectrum of rodent models that represent different severities of CNS-TB, to determine how different cell types contribute to human CNS-TB. We will work to build single cell/single nuclei RNA-seq research capacity at the University of Cape Town by developing research infrastructure in South Africa and facilitating skills transfer through a structured training and skills development program.

Evangelie, Betcy, Comparison of Gene Expression in Monocytes Exposed to Taenia Solium Antigens and Mycobacterial Antigens of Healthy Subjects Living in an Endemic Region

Innate immune inflammation is an early host response against infecting organisms that functions to control the pathogen and activate adaptive immunity. Gene activation in innate immune cells (monocytes) differs significantly between patients with brain infection by Taenia solium (neurocysticercosis, NCC) and Mycobacterium tuberculosis (brain tuberculoma), both of which can cause epilepsy. We previously identified 14 genes upregulated in the monocytes of patients with NCC-associated epilepsy compared to epilepsy of unknown etiology and severe headaches. Expression of 3 of these genes is significantly greater in NCC patients compared to those with brain tuberculoma. To investigate whether these findings in patients with NCC and brain tuberculoma are observed in-vitro, gene expression and cytokine production in monocytes from healthy subjects living in a region endemic for cysticercosis and tuberculosis, following exposure to T solium and M tuberculosis antigens were studied. Expression of the 14 NCC-associated genes (TAX1BP1, RAP1A, TAGAP, CHN2, SLC8A1, MZB1, PECAM1, GBP1, GBP1P1, PLCG2, IL20RB, LRRFIP2, FEZ2 and TOR3A) and mRNA for IFN-β, IL-1β, TNF-α and IL-10 were determined by qPCR in CD14+ monocytes from 12 healthy donors cultured with 10μg T solium antigens (TsAg) or M tuberculosis antigens (PPD) for 4 to 24 hours. TsAg significantly upregulated TAX1BP1, RAP1A and CHN2 expression at 4 and 24 hours and expression of pro-inflammatory cytokines IFN-β at 4 and 24 hours, TNF-α and IL-1β at 24 hours, and anti-inflammatory cytokine IL-10 at 4 and 24 hours compared to non-stimulated cells. PPD significantly upregulated RAP1A at 4 hours and decreased expression of MZB1 at 4 hours and of TAX1BP1 and SLC8A1 at 4 and 24 hours compared to non-stimulated cells. IFN-β and IL-10 expression were significantly increased by PPD at 24 hours. Expressions of six NCC-associated monocyte genes CHN2, MZB1 and PECAM1 at 4 hours, RAP1A at 24 hours, TAX1BP1 and SLC8A1 at 4 and 24 hours and the cytokine IL-1β at 4 hours were significantly increased by stimulation with TsAg compared to PPD. The in-vitro results confirm gene expression patterns in monocytes from healthy subjects exposed to TsAg are similar to gene expression changes seen in-vivo in patients with NCC. NCC-associated monocyte genes up-regulated in NCC patients and down-regulated in brain tuberculoma patients follow similar expression trends in monocyte cultures exposed to T solium.
and M tuberculosis antigens suggesting their role in innate immune-triggered inflammation. Pathogen-specific innate immune responses offer the possibility of using immune gene activities to distinguish between infections.

Gallo, Carla, Isolation and Identification of CXCR4 and CXCR7 Agonists from Traditional Phytopharmaceuticals as Potential Novel Drugs for Mental Disorders
Not Available

In 2009, our team of researchers at the University of Ghana and University of California Davis began a randomized controlled trial of a lipid-based nutrient supplement (LNS) administered to pregnant women from ≤ 20 weeks gestation through 6 months postpartum, and to their infants from age 6 to 18 months, comparing outcomes to control groups who received maternal micronutrient capsules during pregnancy and postpartum (n = 1,320). There were 1,228 live births, and offspring were assessed at 6 months, 18 months (n = 1,039), and 5 years (n = 966). At 5 years, children who had received LNS had fewer caregiver-reported emotional and behavioral problems than children in the control groups, and receipt of LNS buffered against the association of living in more disadvantaged home contexts with having more problems (Ocansey et al., 2019). We hypothesized that the essential fatty acids, vitamins and minerals included in the LNS, including iron, linolenic acid and alpha-linolenic acid, fostered healthy early brain and nervous development, promoting child mental health and resilience. In 2019, we received funding from NICHD and the Fogarty Center to examine the effects of LNS on neurobiological maturation (brain gray and white matter; immune system; autonomic nervous system; adrenocortical and adrenogonadal (pubertal) hormones; anthropometrics), and mental health and well-being. At 10 years, we saw 979 families in field lab, home and school contexts, including assessments of parasympathetic and sympathetic nervous system functioning (n = 966), tonic hormones from hair samples (n = 790), inflammatory markers from blood spots (n = 930), computer-administered tasks, home observations, and self-, mother- and teacher-reports. At 10.5 years, 240 randomly selected children (120 from LNS, 120 from control groups) completed magnetic resonance imaging (MRI) with diffusion weighted imaging (DWI), on a 3T scanner. Currently, at 12 years, children are repeated the assessments completing at 10 years (n = 852 as of 9/18/23). Published and preliminary findings from pre-registered analyses will be presented in this talk.

Holmes, Martha, Neuroimaging and Gut Microbiome Markers of Development in HIV-Exposed Uninfected Infants
Viral infections, such as cytomegalovirus (CMV) and HIV, contribute to hearing loss in infants and children. However, the pathways and mechanisms involved are not well understood. In infants, CMV infection and in utero HIV exposure have been linked to abnormalities in brain, immune and gut microbiome outcomes. In a recent publication, we hypothesized several pathways that underlie an
auditory-gut-brain axis, which may be helpful in better understanding how viral exposure and infections lead to hearing loss. We present results from a birth cohort in Cape Town, South Africa that included infants uninfected but exposed to HIV (iHEU). Within the framework of the auditory-gut-brain axis, we used mediation analysis and logistic regression to study the relationships between the gut bacterial microbiome, brain imaging and auditory/language outcomes in infants with HIV exposure and congenital CMV infection. We report altered white matter integrity between the left medial geniculate nucleus and cerebral cortex, which along with the Acinetobactor genus, strongly predicts HIV exposure status. We identified Finegoldia magna and Sphingomonas koreensis as bacterial mediators of the effects of HIV exposure and congenital CMV on auditory tracts. Taken together, our findings suggest specific bacteria within the auditory-gut-brain axis are involved in central auditory disruptions in iHEU infants with and without congenital CMV infection.

Islam, Zhahirul, Gut Microbiome and their Regulation in Immune Responses in Guillain-Barre Syndrome: A Prospective Controlled Study

Guillain–Barré syndrome (GBS), a life-threatening post-infectious disease, induced by an aberrant autoimmune response targeting the peripheral nervous system, characterized by rapidly progressive bilateral weakness. Campylobacter jejuni, the most common preceding infection occurs in GBS, however, 1 in 1000 C. jejuni infected enteritis develop the autoimmune sequelae. The determinants of GBS progression and clinical outcome has yet unclear. Host gut microbiota plays a vital role in regulation of cellular immune response in autoimmune diseases pathogenesis including GBS. Gut microbiota exacerbates the subsets of pathogenic T-helper (Th) cells via regulating the activation and expansion of regulatory T-cells (Tregs) and regulatory B cells (Bregs). Therefore, we conducted a case-controlled study with GBS patients and healthy controls (HCs) to (i) identify and compare microbial taxa in the host gut between case and control using 16S rRNA sequencing and find the association with GBS development and its severity; and (ii) determine the Tregs, Bregs and Th-cells (Th1, Th2 and Th17 cells) using flow cytometry and find the host gut microbiota regulation in breaching immune tolerance during GBS development. We found that the gut microbial community were distinct in GBS compared to HCs (p=0.001) and significantly differ in severe GBS patients compared with mild cases (p=0.011). Bacilli, Enterococcaceae, Streptococcaceae and Bacteroidaceae were differentially abundant in GBS (LDA>3.0) whereas Bacteriodota and class Negativicutes were with high LDA (>4.0) in HCs. Phylum Actinobacteriota and class Negativicutes under Firmicutes phylum were differentially abundant at 6 months follow-up (LDA>3.0) compared to acute-GBS. The CD4+CD25+FoxP3+ Tregs and CD19+CD38+CD24+IL10+ Bregs were significantly reduced at acute-GBS compared with HCs and associated with clinical recovery. In contrary, CD4+IFNγ+ (Th1) and CD4+IL17+ (Th17) cells were increased significantly during acute phase, while CD4+IL4+ (Th2) decreased compared with HCs. In GBS, high abundance of Verrucomicrobiota phylum was significantly correlated with low CD4+FoxP3+ and CD4+CD25+FoxP3+ Tregs expression, while elevated abundance of Actinobacteria class was correlated with low CD4+CD25+ Tregs expression. Proteobacteria was correlated with IgM+ B-cells upregulation, while Acidaminococcaceae and Eubacteriaceae families were significantly downregulated IgM+ B-cells and CD19+IL10+ Breg expression. Veillonellaceae family upregulates switched-IgA+IL10+ B-cells and CD19+IL10+ Bregs expressions and Leuconostocaceae, Erysipelactoclostridiaceae, and Erysipelotrichaceae families favored CD38+CD24+IL10+ Breg expressions. Thus, host gut microbiota can
regulate immune response of regulatory T- and B-cells that lead to breach immune tolerance by modifying Th-cells expression during GBS development. These findings are further verifying with shotgun sequencing to identify the species level involvement in immune regulation in GBS.

John, Chandy, Malarial Impact on Neurobehavioral Development (MIND)
Cerebral malaria (CM) and severe malarial anemia (SMA) are estimated to affect >500,000 children and 1-5 million children, respectively, in sub-Saharan Africa annually. Our research studies in Ugandan children have demonstrated that CM and SMA are associated with significant neurobehavioral impairment (NBI). Our data suggest that: 1) the pathogenesis of CM and SMA-related NBI differs; 2) CM and SMA lead to greater NBI than other forms of severe malaria; 3) NBI persists for at least 2 years; and 4) several host immune response factors are associated with NBI in children ≥5 years of age but not in children <5 years of age. Retrospective studies suggest NBI is present up to 9 years after CM, but there are no prospective studies on the duration of NBI after CM beyond 2 years, or on chronic cognitive or mental health sequelae of other forms of severe malaria such as SMA. We prospectively enrolled >1,700 children in 3 studies that assessed NB sequelae of severe malaria. These studies provide a unique cohort in which to assess the effects of the 5 major forms of severe malaria on long-term cognition and mental health. Our study has 3 aims: 1) to establish the duration and age-specific manifestations of neurobehavioral sequelae of severe malaria from childhood to early adulthood; 2) to determine the functional and economic costs of neurobehavioral sequelae of severe malaria, and 3) to identify the metabolic, immunologic and parasitic factors predictive of long-term neurobehavioral and functional impairment after severe malaria. We recently completed enrollment of 1,020 children 4-20 years after their severe malaria episode. We predict that severe malaria-related NBI will persist into adolescence and young adulthood, leading to substantial societal and economic costs, and that a number of risk factors for impairment will be detectable only as the child gets older and can be tested for higher level skills. Identification of risk factors present at a young age will allow for early intervention. We expect the study to constitute a major advance in the understanding of the neurobehavioral, functional and socioeconomic costs of severe malaria, and form the basis for interventions to prevent or decrease neurobehavioral impairment in the millions of children who suffer from severe malaria.

Karsz, Alison, AHSA II: An Ethnographic Study Embedded in Randomized Controlled Trial
A leading cause of global disability, depression is widespread among women in low- and middle-income countries (LMIC). Poverty is a major cause of depression, while depression worsens poverty. Funded by NIMH’s Global Brain Initiative, ASHA I is a groundbreaking trial that seeks to address the poverty-depression syndemic via an integrated intervention model with both psychotherapeutic and economic components. ASHA I is a two-arm clinical trial carried out in villages in the Rangpur district of northern Bangladesh—a flood prone region with high rates of rural poverty. Treatment groups of 12-15 women, led by village health workers, are cluster-randomized into the experimental or control arm of the trial. In the experimental, integrated intervention arm, participants will receive a significant cash and skill transfer, plus a brief WHO manualized psychotherapy. In the control arm, participants receive
The ASHA II project will embed an ethnographic research study inside the ASHA RCT. Led by an interdisciplinary team of psychologists, anthropologists, and maternal health specialists in the US and Bangladesh, ASHA II will investigate the complex relationships between intervention processes and social contexts at the individual, household, neighborhood, and village levels. Although ethnographic inquiry—the holistic study of local sociocultural contexts—is well suited to the generation of new knowledge, ethnographic studies are rarely integrated into mental health treatment trials. The research team will use a rapid ethnography (RE) approach to conduct qualitative interviews, focus groups, and structured observations. A comparative analysis will examine differences across study arms (integrated treatment vs control), participant engagement (retention/vs attrition) and clinical outcomes (treatment response vs none). This will allow us to generate hypotheses about key moderating and mediating variables affecting outcomes. A capacity building program will train three young graduates in anthropology from a local university in Rangpur, providing didactic training as well as a practicum in field research. Fellows will receive training in data collection, clinical trial design, research ethics and data analysis, and are expected to seek research positions following their traineeship.

Korte, Kristina, Validity and Reliability of the MINI and SCID in Sub-Saharan Africa

Diagnostic tools, such as the Mini International Neuropsychiatric Interview (MINI) and the Structured Clinical Interview for the DSM-5 (SCID), aim to increase the validity and reliability of diagnostic assessment. However, these tools were created in high-income countries (HICs) with limited investigation regarding the use of these tools in low and middle-income countries (LMICs). Thus, there is a need to examine the psychometric properties of these measures in LMICs. The aim of the present investigation was to examine the validity and reliability of the MINI and SCID in three countries in Sub-Saharan Africa (i.e., Ethiopia, Kenya, and Uganda). The validity of the MINI and SCID was examined in a study of 954 participants (n = 667 cases; n = 287 controls) with and without a psychotic disorder, defined as having any psychotic or bipolar disorder for the purpose of the Neuropsychiatric Genetics of African Populations (NeuroGAP) study. Test-retest reliability of the MINI was examined in a subset of 303 participants (n = 164 cases; n = 139 controls) from the overall sample. Results revealed that 84.0% (n = 561) of cases and 1.7% (n = 5) of controls were diagnosed with any psychotic spectrum disorder in the MINI compared to 92.2% (n = 615) of cases and 2.7% (n = 7) of controls when using the SCID. Further, both the MINI and SCID provided excellent diagnostic accuracy for the NeuroGAP psychotic disorders with area under the curve (AUC) values of .91 (SE = .02) for the MINI and .94 (SE = 02) for the SCID when using chart diagnoses as the reference diagnoses. Positive predictive values (PPV) were high for both the MINI and the SCID, with the PPVs being slightly higher for the SCID than the MINI. The MINI demonstrated adequate test-retest reliability. Country level analyses for Ethiopia, Kenya, and Uganda followed a similar pattern as results for the overall sample. Limitations and future directions will be discussed.

Laughton, Barbara, Extension of a Longitudinal Cognitive and Brain Imaging Study of Early-Treated Perinatally HIV Infected Children Through Adolescence

Not Available
Lin, Pei-Yi (Ivy), Improving Infant Hydrocephalus Outcomes in Uganda: Predicting Developmental Outcomes and Identifying Patients at Risk for Early Treatment Failure after ETV/CPC

Neonatal hydrocephalus is a major global health issue, especially in low- and middle-income countries (LMICs) where post-infectious hydrocephalus is endemic yet access to neurosurgical care is limited. CURE Children’s Hospital of Uganda (CCHU) developed endoscopic third ventriculostomy/choroid plexus cauterization (ETV/CPC) as the only implant-free treatment for hydrocephalus. A rigorous randomized control trial found ETV/CPC is as effective as the traditional treatment of implanting a ventriculoperitoneal shunt (VPS), but with ETV/CPC failures occurring within six months of treatment instead of posing lifelong risks like shunts (Kulkarni et al., 2017). Thus, if ETV/CPC is successful for six months, the patient is likely cured for life. However, about a third of treatments fail and reducing this rate has been challenging because the mechanism action of ETV/CPC is not understood. Unlike a shunt that simply drains cerebral spinal fluid (CSF), ETV/CPC alters CSF dynamics in a complex way. Because CSF dynamics strongly affects cerebral physiology, we proposed a new approach of using brain physiology measurements as early mechanistic indicators of treatment response, long-term brain growth, and neurodevelopmental outcomes. Our group at Boston Children’s Hospital (BCH) pioneered development of advanced quantitative frequency-domain near-infrared spectroscopy and diffuse correlation spectroscopy (FDNIRS-DCS) as a noninvasive bedside monitor of cerebral blood flow (CBF) and oxygen metabolism (CMRO2) in neurocritical care. In this study, we partnered with CCHU to use FDNIRS-DCS to prospectively measure CBF and CMRO2 in a large cohort of infant hydrocephalus patients and create the first large-scale dataset of the longitudinal evolution of cerebral structure, physiology, and long-term neurodevelopmental outcomes during hydrocephalus progression and treatment. Up to date, we successfully recruited 300 patients (110F/190M; average age: 71.9±55.8 days) within 20 months, fully meeting our proposed recruitment targets. Participants undergo a series of prospective assessments in a physiology laboratory we built onsite specifically for this study (Vadset et al., 2022), including cerebral physiology (FDNIRS-DCS & Doppler HUS), brain structure (2D, 3D HUS & CT), anthropometric measurements, and neurodevelopmental assessments (BSID-3 and Vineland-3). We perform assessments during inpatient care and at scheduled follow-ups at 6, 12, and 24 months. The follow-ups are still ongoing, we have completed 269, 149, and 41 at the 6-, 12-, and 24-month follow-ups, respectively with an excellent follow-up rate of 98%. From this data we aim to develop early, objective predictors of response to treatment and identify modifiable factors to improve outcomes.

Link, Abigail, Meningitis Causes and Outcomes in Rural Northern Uganda

Meningitis is a major public health concern, causing high mortality and morbidity worldwide. In rural Uganda, diagnostic tests to determine causes of meningitis are often lacking or suboptimal. Culture and gram stain of CSF are not available in most health centers, and even where available, diagnostic accuracy is poor due to prior use of antibiotics. Utilizing modern molecular diagnostics (antigen detection and PCR-based assays) avail rapid turn-around times (1-2 hours) and are unaffected by antibiotic exposure; however, the accessibility to these modern diagnostics is limited in Uganda. To better characterize the causes of meningitis in rural, northern Uganda, we utilized rapid molecular
diagnostics in conjunction with traditional diagnostic methods, such as gram stain and culture to identify the common causes of meningitis, and we tracked in-hospital outcomes. From September 2021 to July 2023, we enrolled 284 patients who presented with signs and symptoms of meningitis at Lira Regional Referral Hospital (LRRH) in rural, northern Uganda and assessed in-hospital mortality. CSF samples from these patients were tested using gram stain and culture, India ink, rapid antigen detection by cryptococcal antigen lateral flow assay (Immy) and Pastorex antigen agglutination, and PCR by BioFire and TB Gene Xpert. A confirmed etiology of bacterial meningitis (BM) was found in 44 patients, cryptococcal meningitis (CM) in 39, tuberculosis meningitis (TBM) in 10, and viral meningitis (VM) in 10. Among patients with a confirmed meningitis etiology, 24% were infected with more than one pathogen.

Compared to standard methods (gram stain, India ink, culture), rapid molecular testing was far superior for determining the etiology of meningitis in these patients. In-hospital mortality rates were 70% for TBM, 31.8% for BM, 28.2% for CM, and 10% for VM. Patients with the highest risk for death were those with TBM with or without infection with a co-pathogen. Our results show that traditional tests such as culture resulted in low diagnostic yield compared to rapid molecular testing, questioning the reliability of this test, especially in the setting of high antibiotic utilization prior to hospital admission. The high rate of multiple pathogens identified in the CSF of patients with meningitis in this study emphasizes the need for further investigation into the true prevalence of co-infections and the risk factors associated with co-infection acquisition and mortality. A concerted diagnostic effort is needed to comprehensively diagnose all meningitis pathogens in each patient to guide proper treatment and saves lives.

Mbirbah, Elizabeth, Factors that Influence Human Milk Oligosaccharides (HMOs)

Cytomegalovirus (CMV) is a common viral infection that can be passed from mother to infant via breastfeeding. Infants with CMV infection are at risk of development delays as well as hearing and vision loss. Human milk contains nutrients such as proteins, amino acids, lipids, carbohydrates, vitamins and minerals as well as non-nutritive bioactive components such as immune factors, hormones, microorganisms and complex carbohydrates known as human milk oligosaccharides (HMOs). HMOs form the third most abundant solid component of human milk and influence infant health and development. Few studies have explored the effects of viral infections on HMOs, with none studying CMV infection. Mother-infant pairs were recruited in Cape Town, South Africa and human milk samples were collected from 2 to 5 weeks postpartum. Milk samples were tested for CMV using the fast track diagnostic (FTD) assay. High performance liquid chromatography was used to quantify 19 abundant HMOs. Statistical analysis was performed to identify CMV status group differences. We report results for 27 mother-infant pairs (13 mothers living with CMV). We found higher concentrations of disialyl-lacto-N-hexaose (DSLNH) in mothers with CMV (P=0.017) and a higher proportion of DSLNH per total HMO concentration in mothers with CMV (P=0.080). Our data suggest maternal CMV infection may influence DSLNH concentration and relative abundance. DSLNH is an acidic HMO that bears sialic acid (N-acetylneuraminic acid) that has been linked to variations in the infant gut microbiome. Future work will examine possible associations with gut microbiome and cognitive factors in infants to better understand this finding.
McHenry, Megan, Advancing the science of neurocognitive physiology in adolescents living with HIV

Adolescents living with HIV (ALHIV) have been shown to experience neurocognitive impairment compared to their uninfected peers, but the underlying neurophysiology considered to be the fundamental building blocks of complex cognitive processing have not been rigorously studied within this population. There is a critical need for a comprehensive study of neurophysiology and cognitive function in ALHIV, especially in sub-Saharan Africa, which comes with unique health and socio-demographic risk factors that compound the adverse effects of HIV infection. The specific objectives of this project were to: (1) determine the potential neurophysiological impact of perinatally acquired HIV in adolescents and its relationship to cognitive deficits using a comprehensive battery of event-related potentials (ERP) tasks and cognitive measures; and (2) support capacity building for EEG/ERP research in Kenya, and interdisciplinary neurophysiological research more broadly across sub-Saharan Africa. The central hypothesis was that ALHIV will show altered neurophysiology and impaired cognition compared to their unexposed peers. The rationale for this study was that ERP studies are uniquely suited determine which sensory and information processing stages are impaired and contribute to cognitive abnormalities in ALHIV. In Aim 1, we determined potential impact of HIV infection on neurophysiology and neurocognition in adolescents. We characterized ERP responses and their relationship to cognitive function in ALHIV (14-17 years old) compared to uninfected adolescents (n=50 per group) to develop a model to determine childhood factors predictive of poor neurophysiological and cognitive outcomes. Both cognitive and sensory ERP paradigms were performed. Associative motor learning and motor coordination were also measured because they are sensitive assays of the integrity of brain motor systems. A culturally adapted version of the NIH Toolbox Fluid Cognition tests was administered to assess neurocognition. In Aim 2, we built capacity for interdisciplinary neurophysiological research in sub-Saharan Africa by supporting intensive training for faculty development and tiered mentoring in neurophysiological methodological techniques. We supported the faculty and students within the Moi University Masters of Medical Psychology program in performing neuropsychological work, for both clinical and research purposes. This was done through training workshops, virtual seminars, and on-site supervision, which has culminated into two annual, national symposia to foster neurophysiological research collaboration across Kenya. Because of the support from this grant, we completed the first comprehensive neurophysiological study of ALHIV in sub-Saharan Africa, and Moi University is now among the most robust Kenyan academic centres with capacity for research in neurophysiology.

Meya, David B., Improving Diagnostics and Neurocognitive Outcomes in HIV/AIDS-related Meningitis

Central nervous system (CNS) infections are common across all ages in Sub-Saharan Africa in people with or without HIV-infection. In persons with HIV, cryptococcal meningitis has historically been the second most common AIDS-defining illness in Africa and the most common cause of adult meningitis in Sub-Saharan Africa overall. The next most common cause of meningitis is likely TB meningitis, although CSF diagnostics are challenging. With the widespread availability of antiretroviral therapy (ART), long term survival in persons living with AIDS and CNS infections should be possible, but delayed or
inaccurate diagnoses and limited therapeutic options contribute to poor outcomes. Furthermore, with the ‘test and treat’ strategy of immediate ART initiation, more people are presenting with CNS infections unmasked after starting ART, yet their outcomes are unclear. We propose to continue a prospective cohort study of 1200 new HIV-infected persons presenting with suspected CNS infection in Kampala and Mbarara, Uganda. We will use point-of-care and molecular diagnostics to rapidly determine the etiologies of CNS infections, with a specific focus on optimizing and validating new diagnostic tests, such as a semi-quantitative cryptococcal antigen (CrAg-SQ) lateral flow assay and the Xpert MTB/RIF Ultra for TB meningitis. Second, we propose to compare the real world outcomes of implementing the Ambition trial regimen to the Ambition trial for cryptococcal meningitis. Finally, we continue to measure neurocognitive performance to investigate the effect of recent ART initiation on neurologic outcomes.

Moorthy, Ranjith, Correlation Between Monocyte Gene Expression and Inflammation on Brain Imaging in Patients with Solitary Cerebral Cysticercus Granuloma

Solitary cysticercus granuloma (SCG) is the most common form of neurocysticercosis (NCC) in Indian patients. Degeneration of the larva of Taenia solium leads to the release of parasite antigens, inflammation, brain edema, and seizures. In many cases, SCG spontaneously resolves within a year of diagnosis. However, whether the resolution of the granuloma and the associated reduction in inflammation impact immune responses in peripheral blood remains unstudied. Previously, we identified 14 genes in peripheral blood monocytes that were upregulated in NCC patients, including those with SCG. Our aim was to investigate whether changes in inflammation associated with SCG observed during follow-up of patients with brain imaging were also reflected in changes in expression of these NCC-associated genes in monocytes. CD14+ monocytes were isolated from 20 patients with SCG at initial diagnosis and at follow-up at least 6 months later. Gene expression was measured using qPCR at each visit and normalized to B2M. At a median follow-up of 14 months, 11 patients showed resolution of SCG, four patients had persistent SCG, and five patients exhibited calcification of the granuloma. Initial imaging revealed edema in 17 patients, which had resolved completely in 15 patients and had significantly reduced in the other two at follow-up. The expression levels of monocyte genes, specifically LRRFIP2, TAXIBP1, and MZB1, were significantly lower at follow-up, irrespective of the status of the SCG on follow-up imaging (resolved, persistent or calcified). Our findings show that expression levels of monocyte genes involved with inflammatory processes decrease in patients with SCG concomitant with follow-up imaging that reveals a reduction in inflammation as revealed by complete or near-complete resolution of edema, as well as resolution or reduction in the enhancement of the granuloma.

Mwanza, Jean-Claude, NeuroEbola: Baseline Demographic, Immunological, and Clinical Characteristics of Study Participants

The 2018-2020 Ebola virus (EBOV) outbreak in Congo was the largest outbreak for Congo, and the 2nd largest after the one in West Africa. There were 3461 confirmed cases, of whom 2299 died and 1162 survived. When the outbreak started in Congo, we have learned from the West African outbreak that some survivors have eye and/or brain disease. Because these two organs share anatomo-physiological
similarities, are immunologically privileged, and EBOV has been isolated in survivors’ eyes and CSF, we set up this study to assess neuro-ophtalmologic and neurocognitive profile in survivors. To contrast neuro-ophtalmologic deficits in EVD survivors to relevant profiles in their IgG+ but free of EVD close contacts, and IgG- controls. findings in Ebola survivors, healthy Ebola IgG+ contacts, and anti-Ebola IgG- controls (N = 120). 2. Determine whether group-differences in neuro-ophtalmologic findings (Aim 1) are mediated by initial EBOV viral load or persistence with discernable IgG antibody responses to EBOV proteins. 3. Enhance and build capacity in neurocognitive assessments, neuro-ophtalmologic evaluation, and EVD immunoprofiling and RT-PCR. 360 randomly selected participants (120 EVD survivors, 120 IgG+ survivors healthy close contacts, 120 IgG- healthy controls) are undergoing longitudinal assessments of motor and sensory systems, neurocognition (Altoida software), mental health (MMSE questionnaire), and anxiety and depression (Goldberg test). Neuro-ophtalmologic assessments include visual function (visual acuity, color vision, contrast sensitivity, tablet-based perimetry), pupillary reflexes, ocular motility, ocular biomicroscopy, indirect ophthalmoscopy, and fundus photography. Immunologic profiling is performed using ELISA whereas virology testing is done by RT-PCR. Concentrations of serum protein biomarkers were determined using the Olink app. The response rate was 98.3%. Among survivors, there were significantly more subjects with than without anxiety symptoms (43.1% vs. 28.8%), depressive symptoms (53.0% vs. 27.5%), and cognitive impairment (46.5% vs. 29.1%). Mean VA was significantly lower in cases (0.93±0.18) than positive (0.98±0.09) and negative controls (0.98±0.08). Seven patients had neuro-ophtalmologic disease (4 with optic nerve disease, 2 with ocular motility deficits, 1 with optic nerve melanocytoma), 3 with chorioretinal scars. Survivors tend to have a lower contrast sensitivity than all controls. Iris atrophy was associated with survivor status. Preliminary analyses showed no difference in protein biomarkers concentrations between treatment groups. This preliminary analysis showed that anxiety, depression, and cognitive impairment are frequent among survivors. A small group of them have neuro-ophtalmologic disease. Subsequent analyses will determine whether neurocognitive deficits and neuro-ophtalmologic disease are mediated by immunologic profiles.

Pardo-Villamizar, Carlos, Neuroinfections Emerging in the Americas Study (NEAS): A Research Network to Establish the Role of Emerging Infections in the Incidence of Acute Neurological Problems in Colombia

In response to the increased incidence of GBS in Colombia during the ZIKV outbreak in 2016, a multidisciplinary team of clinicians, researchers, and public health specialists from different university-based hospitals across Colombia established the Neuroinfections Emerging in the Americas (NEAS) network, a multicenter-based observatory of acute neuroinflammatory disorders (ANIDs) focused on the investigation of the role of emerging infections in neuroinflammatory diseases. Our project aims 1) to evaluate the relationship between emerging or re-emerging infections contributing to the burden of acute neuroinflammatory disorders (ANIDs) in Colombia and 2) to characterize Guillain Barre Syndrome (GBS) as a model to examine the interaction of infection as a triggering factor of ANIDs. We conducted a combined retrospective and prospective, longitudinal cohort study of newly diagnosed patients (<30 days of symptom onset) who fulfilled established criteria for GBS, encephalitis, myelitis, meningoencephalitis, or cranial nerve disorders of unknown etiology, accrued between January 2020 and December 2022 (COVID-19 epidemic period). Using a case-control study design, we matched cases
of GBS with household and/or hospital controls to determine infections as risk factors for disease. During the COVID-19 epidemic surveillance period, 439 patients with ANIDs were recruited. The median age of the subjects was 39 (IQR 21-58) years, and 54% were male subjects. The most common preceding events during the 4 weeks before the onset of neurological symptoms were upper respiratory tract infection (13%) and gastroenteritis (11%), although most of the population (70%) denied preceding events. The most frequent ANIDs were GBS (46%), facial nerve palsy (17%), and optic neuritis (11%). The diagnosis of encephalitis (8%), myelitis/encephalomyelitis (8%), and meningitis (3%) were less frequent. There was no evidence of an upsurge of ANIDs during the period of COVID-19 as compared with the pre-COVID-19 period (2016-2019).

2) Fifty-seven patients with GBS, 67% male, with a median age (IQR) of 52 years (24–64) were matched with 77 controls. The associations of GBS with male sex (OR, 4.4; 95% CI 2-9.7; p<0·0001), preceding diarrhea (OR, 5.5; 95% CI 1.6-19.4; p=0·008), and history of recent upper respiratory tract infection (OR, 8.25; 95% CI 2.4-28.3 p=0·001) were of substantial magnitude and statistically significance. Recent specific infections did not significantly differ between cases and controls, but recent exposure to C. jejuni, M. pneumoniae, and Chikungunya virus showed elevated odds ratios of 2.72, 1.76, and 4.97, respectively. ANIDs continued to present during the recent COVID-19 pandemic in Colombia. However, we did not observe a significant increase in the incidence of GBS or other ANIDs in our centers compared to the ZIKV epidemic (2015-2016) or endemic phase (2017-2019). SARS-coV2 did not significantly impact the incidence of ANIDs in Colombia.

Paul, Robert, Mental Health Phenotypes of Well-Controlled HIV in Uganda
HIV and mental health (MH) disorders, particularly depression, anxiety, and post-traumatic stress disorder (PTSD), are among the top 10 causes of disability among people with HIV (PWH) in Uganda. Most studies of PWH have focused on MH disorders as unidimensional constructs. However, the phenotypic expression and clinical course of MH conditions among PWH in Uganda and worldwide are heterogeneous. Accordingly, there has been a shift towards identifying MH phenotypes using data driven methods capable of identifying novel insights into mechanisms of divergent MH phenotypes among PWH. This study leveraged the analytic strengths of machine learning combined with inferential methods to identify novel MH phenotypes and the underlying explanatory features among PWH. 277 PWH (46% female, median age=44; 93% undetectable viral load [<50copies/mL]) were included in the analyses. Participants were enrolled in an observational community-based cohort residing in the Rakai region of Uganda. Participants completed the Patient Health Questionnaire-9 (PHQ-9), Beck Anxiety Inventory (BAI), and the PTSD Checklist-Civilian (PCL-C). Hierarchical clustering was used to identify MH subtypes using total symptom scores on the questionnaires. Inferential statistics (with false discovery rate) compared demographic and clinical factors between clusters (e.g., ELS). We identified four MH phenotypes. Cluster 1 (n=76; PTSD phenotype) endorsed clinically significant PTSD symptoms, with an average PCL-C total score >33. Clusters 2 (n=32; anxiety phenotype) and 3 (n=130; mixed anxiety/depression phenotype) reported minimal PTSD symptoms, with modest elevations on the BAI (Cluster 2) and PHQ-9 (Cluster 3). Cluster 4 (n=39; normative MH phenotype) reported no clinically relevant elevations in MH symptoms. The frequencies of childhood physical and sexual abuse were highest among individuals in the PTSD phenotype. Individuals in the anxiety phenotype were older and primarily female with elevated physical but not affective symptoms, most likely reflecting menopausal
symptoms. Successful identification of discrete MH phenotypes and unique risk determinants has potential to guide the development and deployment of tailored prevention and intervention strategies. Results also underscore the importance of item-level analysis of mental health assessments to allow more deep and accurate phenotyping and risk assessment.

Post, Kristi, Neuropsychiatric Genetics of African Populations: Building the Research and the Researchers Together
An estimated 1.3 million individuals in sub-Saharan Africa and millions more in other low-and-middle-income countries are living with a psychotic disorder. However, limited research focuses on these populations and even less focus on neuropsychiatric genetics research. Genomic studies have yet to adequately represent the entirety of the global population. The Neuropsychiatric Genetics of African Populations-Psychosis (NeuroGAP-Psychosis) study aims to address this gap. NeuroGAP-Psychosis is a case-control genetics study which collected genetic and environmental risk factors for psychotic disorders across Ethiopia, Kenya, South Africa, and Uganda. Alongside the research, we focused on the importance of integrating interdisciplinary training into research programs to ensure sustainability of research in underrepresented settings. This paper reports on the aggregated baseline demographic and clinical characteristics of the 42,953 participants (50.3% cases) recruited from the multi-country study from 2018 through March 2023, as well as comparisons of these characteristics by country and case status. It also shares lessons learned in establishing, maintaining and sustaining collaborative research capacity development programming. These findings suggest the importance of ongoing evaluation of cross-cultural differences to explore clinical implications and patterns of symptoms amongst geographically and culturally diverse populations, and future analyses should also evaluate within-country differences to better explore these variations. We will highlight why integrating training with research is vital to any equitable collaboration and will ultimately lead to a wider reach for scientific impact and amplification of underrepresented voices in scientific communities. Our team has begun to re-contact participants in Kenya and Uganda to investigate other mental health conditions, including PTSD, OCD, and suicidality. Further, the success from this initial study has spurred further new collections in Kenya and Uganda to further genetics research on PTSD. As before, capacity building programming will be of utmost importance for all future research programs.

Rai, Sauharda, Promoting gender equity in global mental health research capacity building in Low- and Middle-Income Countries: Efforts and learnings from Nepal
Developing local research capacities in Low-and Middle-Income Countries (LMICs) is crucial for advancing health service, reducing health disparities, and ensuring that research is relevant, ethical, contextual, and sustainable (1, 2). Though LMIC has the highest treatment gap for mental, neurological and substance use disorders (3), investment in mental health research is limited, both in terms of funding and capacity building (1). This has resulted in limited research output with only 6% of total mental health research publication coming from LMIC (4). Thus, there is an utmost need to increase the
research capacity of LMICs. However, as efforts to expand research capacity continue to grow in LMICs, it is crucial that these initiatives pay special attention to addressing gender equity in research. It is essential to address the unique challenges that women may encounter in developing their research careers within LMICs (5, 6). Neglecting this aspect could exacerbate existing gender disparities within the research community, potentially widening the gender gap in research participation and leadership. As a part of NIMH funded R01 - REducing Stigma among HealthcAre ProvidErs (RESHAPE) (7), we are working to increase mental health research capacity of local institutions and individuals to promote greater gender equity and collaboration in mental health research in Nepal. Over the last three years, we have conducted a series of capacity building activities targeting early career mental health researchers in the country. These efforts have included hosting 23 monthly webinars and organizing two global mental health summer courses, which saw participation from nearly three-quarters of female researchers. In addition, we facilitated two networking events aimed at connecting early, mid-level and senior Nepali mental health researchers. Furthermore, as a part of RESHAPE study we conducted a scoping review and qualitative interviews on understanding gender disparity in mental health research (5) and social network analysis of mental health workforce in Nepal (8). We also awarded research grants to two female early career researchers to support their work in the field of mental health. In this presentation, we will talk about some of these activities, our lessons learned and future plans to move ahead in our effort to build local capacity and promote gender equity in global mental health research.

Rohloff, Peter, A Hybrid Implementation-Effectiveness Trial of the International Guide for Monitoring Child Development in India and Guatemala

More than 40% of children under 5 years of age in low-income and middle-income countries are at risk of not reaching their developmental potential. Task shifting early child development interventions to frontline workers is an important strategy for closing this gap. We are conducting a hybrid type 1 effectiveness–implementation evaluation of the international Guide for Monitoring Child Development (GMCD) early intervention package adapted for and task shifted to community health workers in rural India and Guatemala. This trial uses a cluster randomized design, and recruitment is currently at 75% of projected target. In this talk we will give updates on lessons learned to date, especially around the extensive adaptations required to appropriately task-shift this intervention to CHW programs.

Vassileva, Jasmin, Addiction Neuroscience Research in Bulgaria: 20 Years of Global Brain Research

The main objective of this talk is to review the scientific and research capacity building accomplishments of the program in addiction neuroscience that we have developed in Bulgaria over the past 20 years with the support of the Global Brain Disorders program. Bulgaria is a Southeastern European country that is in the top 5 countries in Europe for production of amphetamine-type stimulants, and a key country for heroin trafficking due to its strategic geographical position on the “Balkan Drug Route”. It has some of the highest rates of substance use disorders in the European Union but very limited resources to address its growing substance misuse crisis, particularly after the withdrawal of the Global Fund in 2017. Its income per capita is the lowest in the EU and its research infrastructure is severely
underdeveloped. To address these gaps, in 2003 we established a program for addiction neuroscience research in Bulgaria, which has been continuously funded by FIC and NIDA with two R21 and four R01 studies. Our program in Bulgaria has followed in “real-time” the geopolitical developments and the changing patterns of drug use in Southeast Europe, which has significantly informed our research questions. In a series of studies, we have conducted one of the most extensive assessments and characterizations of various dimensions of impulsivity and related internalizing and externalizing traits in unique groups of mono-dependent (‘pure’) opiate and stimulant users. We have developed and validated a comprehensive phenotypic assessment battery and have deeply phenotyped over 1,000 and genotyped over 600 Bulgarian participants. Our studies contribute significantly to a growing body of literature that reveals important differences between addictions to different classes of drugs, observable long after discontinuation of drug use. These studies have significantly enhanced the capacity and infrastructure for addiction research in Bulgaria. Some of our key capacity building accomplishments are: (1) Establishing the first neurocognitive research laboratory for the study of addictions in Bulgaria; (2) Conducting the first neuroimaging study in addiction in Bulgaria; (3) Establishing active collaborations with 5 Bulgarian institutions; (4) Adapting for Bulgaria and testing with >1,000 participants 27 self-report questionnaires, 3 structured/semi-structured psychiatric interviews, and 11 computerized neurocognitive tasks that we share widely with the Bulgarian research community; (5) Assembling and training a multidisciplinary team of addiction researchers in Bulgaria, some of whom are now co-investigators on new NIH studies; (6) Establishing clinical research rotations for Bulgarian students at our laboratory in Sofia, where we have trained over 70 Bulgarian graduate and undergraduate students.

Vasudevan, Prabhakaran, Integrating Genomics and Proteomics to Understand the Pathogenesis of Parenchymal Neurocysticercosis

Parenchymal neurocysticercosis (pNCC), brain Taenia solium cyst infection, is a lead cause of acquired epilepsy in low and middle-income countries. Seizures in pNCC result from cyst degeneration-induced brain inflammation, markers of which may manifest in the blood. Next-generation sequencing (NGS) of peripheral white blood cells and liquid chromatography-tandem mass spectrometry (LC-MSMS) serum proteomics was used to identify differences in inflammation associated with pNCC and other brain disorders in patients with seizures living in a T solium endemic region. Peripheral blood (10ml) from 28 pNCC patients and 28 individuals with other brain disorders with seizures (13 epilepsy of unknown etiology, 10 glioma, 5 brain tuberculoma) was collected with consent. Peripheral white blood cell mRNA was subject to NGS using Illumina Hi-Seq 2500. Transcripts significantly associated with pNCC compared to non-NCC groups were analysed with DESeq2 and the Wald test with Bonferroni correction at p <0.05. Serum tryptic digests were subject to LC-MSMS and 375 to 1700 m/z spectra analyzed using MASCOT Daemon (version 2.6.2) to search the UniProt human reference database. Proteins were analysed for significant differences between pNCC and the non-NCC groups by the Mann-Whitney test at p <0.05. Transcripts and proteins associated with pNCC were functionally analyzed using Gene Ontology, Ingenuity Pathway Analysis (IPA), and String analysis. Forty transcripts were significantly upregulated, and 120 transcripts downregulated in pNCC compared to non-NCC subjects. Gene ontology revealed 68% involved with biological functions, 70% with molecular functions and 47% were cellular
components. IPA and network analysis identified transcripts associated with immune, cytokine and cellular signalling pathways, highlighting pro and anti-inflammatory activation in pNCC. On LC-MSMS 20 serum proteins were increased by two or more-fold and 3 proteins decreased more than two-fold in pNCC compared to non-NCC sera. Gene ontology indicated that 86% were involved with biological processes, 74% with molecular functions and 95% were cellular components. String network analysis of pNCC-associated serum proteins indicated activation of inflammatory and anti-inflammatory responses, involving complement and coagulation cascades (34%), acute phase responses (30%), immune regulation (26%) and antioxidant mechanisms (9%). NCC-associated seizures are marked by patterns of inflammation reflected in gene and protein expression in peripheral blood which are different in T solium cyst degeneration in the brain when compared with other seizure-inducing processes. These data suggest that management of brain inflammation that prevents tissue injury in patients with pNCC could be monitored in the peripheral blood of NCC patients.

**Weine, Stevan, Scaling-Up Stepped Care for Women’s Mental Health in Primary Care in an LMIC**

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