UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN

Neuroscience Program

COLLEGE OF LIBERAL ARTS & SCIENCES

SfN Night Abstract Booklet

Fall 2021 - October 26, 2021

4:00 PM – 6:00 PM

Beckman Institute for Advanced Science and Technology

Schedule of Events:

4:00-4:30pm: Introduction and Welcome—Martha Gillette in 2269 Beckman

4:30pm-5:30pm: Presentations

Animal Models in Neuroscience I, Room 2269

4:30pm: Amara Brinks
4:40pm: Elli Sellinger
4:50pm: Zoë MacDowell Kaswan
5:00pm: Coltan Parker
5:10pm: Ashley Otero

Animal Models in Neuroscience II, Room 3269

4:30pm: Maltesh Kambali
4:40pm: Muxaio Wang
4:50pm: Rajasekar Nagarajan
5:00pm: Grace Lyu
5:10pm: Alex Armstrong

Human Models in Neuroscience, Room 5602

4:30pm: Evan Anderson
4:40pm: Liran Ziegelman
4:50pm: Rafay Khan

5:30-6:00pm: Refreshments and Awards, Neuroscience Lounge

Abstracts

Animal Models in Neuroscience I, Room 2269

Effects of Adolescent Methamphetamine Exposure on Perineuronal Net and Parvalbumin+ Cell Density in the Rodent mPFC

A.S. Brinks, L. C. Carrica, D.J. Tagler, J. M. Gulley, J. M. Juraska

Adolescence is a time of enhanced vulnerability to several psychiatric disorders, including substance use disorder. While there are likely social factors that contribute to this vulnerability, ongoing maturation of brain regions critical for cognitive function may also contribute. Across adolescence, the medial prefrontal cortex(mPFC) undergoes significant reorganization, with parvalbumin+ (PV) inhibitory interneurons gaining their fast-spiking phenotype and perineuronal nets (PNN's) aggregating primarily around PV cells. Previous studies have shown PNN's are influenced by female, but not male, puberty with post pubertal females having fewer PNN's than prepubertal littermates. PNN's are also influenced by drug administration, though this is highly specific with heroin resulting in fewer PNN's and cocaine resulting in more PNN's. To assess the effects of meth on PV cells and PNNs rats were dosed with meth around female puberty (EA), male puberty (LA), and early adulthood. Male and female Sprague Dawley rats were exposed to 3mg/kg meth via intraperitoneal injection from either postnatal day (P) 30-38 (EA), P40-48 (LA), or P60-68 (Adult). Brains were collected one day after dosing and fluorescently labeled for PNN's and PV for density quantification. Preliminary results show that meth differentially effects PNN density in males and females, with males having increased PNN density at all timepoints females having increased PNN density at only the EA and adult timepoints. PV density was increased in both males and females in the EA timepoint, but decreased in late adolescence. While these results indicate an effect of meth exposure on both PV cell and PNN density, further results will include measures of mPFC volume to control for changing volume over adolescence. This will allow for further comparisons across age and sex.

Developmental cell death in the hippocampus and related cognitive behaviors are altered by perinatal exposure to phthalates

E.P. Sellinger, H. Fenton, A. Brinks, J.M. Juraska

The plasticity of the perinatal period leads to increased susceptibility to environmental insult from endocrine-disrupting chemicals such as the plasticizers known as phthalates. There is an association between developmental phthalate exposure and impaired cognitive and emotional processing outcomes in children (Radke et al., 2020), however their mechanism of action remains unclear. Using a rat model, our lab has demonstrated exposure to an environmentally relevant mixture and dose of phthalates during the perinatal period results in fewer neurons in the adult medial prefrontal cortex that correlates with impaired cognitive flexibility (Kougias et al. 2018). More recently, we've determined this reduction in neurons is due, at least in part, to elevated cell death both pre-and postnatally (unpublished observations). The mPFC forms connections with the hippocampus, a brain

region that also undergoes protracted development. The present study aims to investigate how phthalates alter the normal course of cell death in the dorsal and ventral hippocampus and to assess whether early exposure results in immediate cognitive behavioral changes. To expose developing pups to the phthalate mixture, dams were fed0, 0.2, or 1 mg/kg/day on a cookie from gestational day 2 through 25 days post-partum. One male and one female pair per litter were sacrificed on P5 and another on P10 for analysis of cell death using a TUNEL label. A third male/female pair from each litter was tested on the elevated plus maze (EPM) on P27 followed by the Morris Water Maze (MWM) beginning on P29. A preliminary analysis (n=4-6/group) reveals a significant increase in cell death in dorsal CA1 ($p=0.045$) in both sexes on P5 after phthalate exposure and a similar, though non-significant, increase in the dentate. A significant effect of phthalate exposure is also seen in males only (n=5-6/group) on the percent of open arm entries measured on the EPM ($p = 0.04$). Males exposed to 1mg/kg also show a decreased latency to enter the open arm compared to controls ($p = 0.02$). Finally, no apparent effects of phthalate exposure were seen in preliminary analyses (n=5-6/group) of the MWM. Increased N and more sampled days for apoptosis cell death and behavior will be added.

Ido2 deficiency is protective against acute seizures and hyperactivity in a kainic acid model of ictogenesis

Z.A. MacDowell Kaswan, M. Hurtado, E.Y. Chen, R.H. McCusker

Neuronal hyperexcitability, particularly in association with neuroinflammation, can trigger the development of acute seizures (ictogenesis), putting patients at risk of subsequent pathologies such as epilepsy and chronic behavioral changes. Neuroinflammation induces expression of indoleamine 2,3-dioxygenase (Ido) 1 and 2within the central nervous system. The Ido's are the first and rate limiting enzymes of the kynurenine pathway, by which tryptophan is converted into kynurenine and subsequently into neuroactive metabolites. Kynurenine metabolites, some of which are ictogenic, directly interact with glutamate receptors in the brain to modulate neural activity. Ido1 and Ido2, therefore, may provide a mechanistic link between neuroinflammation and ictogenesis. In the kainic acid (KainA) model of ictogenesis, systemically administered KainA crosses the blood brain barrier to activate glutamate receptors and cause seizures. We used this model to explore the effect of Ido1 and Ido2 deficiencies on acute seizure susceptibility. Mice were injected intraperitoneally with five doses of 4.5-5 mg/kg KainA or saline control at intervals of 30 minutes and observed for seizures throughout the injection period and for an additional30 minutes after the final dose. We found that mice deficient for Ido2 (Ido2KO) are less likely to experience seizures following injection of KainA compared to wild-type (WT)C57BL/6 mice. In contrast, mice deficient for Ido1 (Ido1KO) have equivalent seizure incidence compared to WTmice.Ido2KOmice are also protected from KainA-induced hyperactivityassessed8 days post-injection. Gene expression was quantified in hippocampi collected 30 min after the final injection. Unexpectedly, hippocampalIdo1 andIdo2expression is reduced by KainA treatment regardless of seizure incidence. However, KainA increased expression of the proinflammatory cytokines TNFαand IL-1β. Cytokine expression is higher in the hippocampi of mice that experienced seizures relative to those that did not, indicating higher levels of hippocampal neuroinflammation. Surprisingly, TNFα expression is higher in Ido2KOmice compared to WT or

Ido1KOmicedespite their lower seizure incidence. Our data indicate that the low seizure incidence of Ido2KOmice makes Ido2 a putative candidate for new anti-seizure therapeutics.

Novel sexually-differentiated cell populations in the preoptic area of a sex-changing fish, *Amphiprion ocellaris*, characterized by single-nucleus RNA sequencing

C.G. Parker, Z.V. Johnson, B.E. Hegarty, G.W. Gruenhagen, J.T. Streelman, J.S. Rhodes

Across vertebrate species, sex differences in cell number and phenotype in the preoptic area of the hypothalamus (POA) are essential to regulating sex-specific reproductive physiology and behavior. In mammals, male POA differentiation can be traced back to the presence of gonad-derived androgens, while female POA differentiation (feminization) does not have a clear trigger to mark its beginning and proceeds without gonadal influence. As such, POA feminization is less amenable to laboratory manipulation in mammal models, and is generally not as well understood. In anemonefish like the common clownfish *Amphiprion ocellaris*, POA feminization follows a clear trigger and proceeds without gonadal influence, providing a complementary model for the study of POA feminization. Anemonefish display natural male-to-female sex change, and sex change is easily induced in the lab. Previous work in A. ocellaris is identified a sexually-differentiated cell population in the anterior POA that is more numerous in females than males. In order to identify potential phenotypes for this cell population, and identify other sexually-differentiated characteristics in the anemonefish POA, we carried out single nucleus RNA sequencing on POA-containing brain tissue from mature male (n=6) and female (n=6) A. ocellaris. Libraries were prepared from pooled samples and individual fish were recovered (demultiplexed) using scSplit. Clustering produced 49 clusters, which were then classified as representing major cell classes (e.g., excitatory neurons, inhibitory neurons, radial glia, microglia) using canonical markers. After recovering individuals from pooled samples, we tested which clusters differed significantly between the sexes on the basis of cell number. We found 12 clusters to be sexually differentiated, of which 7 were female-biased and 5 were male-biased. One of the male-biased clusters was found to be strikingly differentiated (prominent in males and almost absent in females) and contained a high proportion of cells expressing an androgen receptor gene, suggesting a potential role in brain-pituitary-gonad signaling. Possible homology of the identified sexually dimorphic cell populations in the fish POA with mammalian POA will be evaluated by statistical comparisons with mouse POA single cell data (publicly available). Results provide clear cellular composition endpoints for sexual differentiation of the POA that is accomplished during sex change. Further studies will explore the time-course, gonad-dependence/independence, signaling cascades, and epigenetic programming involved in active feminization of the POA in the novel anemonefish model.

Murine influenza A virus disrupts immune profiles in the maternal gut and placenta but not the fetal brain

A.M. Otero, A.M. Antonson

Maternal immune activation (MIA)during pregnancy is linked to neurodevelopmental disorders, such as schizophrenia and autism, in offspring. The majority of animal models initiate MIA using pathogen mimetics, which induce a controlled innate immune response. In this study, we use a mouse model of live H3N2 influenza A virus (IAV), which is moderately pathogenic and activates both innate and adaptive immune responses. As respiratory IAV infection is known to cause downstream immune dysregulation in the intestine, we hypothesized that this would contribute to inflammation in the fetus. Small intestine, placenta, and fetal brains were collected from C57BL/6NTacmiceongestational day 17, seven days post inoculation (dpi) with IAV(n=17) or saline(n=15), across four identical replicates. Despite no detectable virus in the small intestine, respiratory IAV infection upregulated the gene encoding RORγt, the main transcription factor for TH17 and ILC3 cells of type III immunity. RORγt+type III immune cells releasepro-inflammatoryIL-17 cytokines, which are implicated in MIA-driven developmental abnormalities. However, transcription of Il17a, Il17f, and Il17rawas unaltered in maternal intestinal tissue regardless of treatment, as was production of IL-17Aprotein.To investigate if IAV-induced MIA impacted the fetus, we looked at immune profiles in the placenta and fetal brain. The placenta, which acts as a physical and immune barrier between dam and fetus, demonstrated altered immune profiles in infected dams. However, neuroinflammatory genes in the fetal brain were not significantly different between groups. Our results demonstrate that a moderately pathogenic IAV infection upregulates type III immune cells in the maternal gut at seven dpi with no significant difference in IL-17 production. Furthermore, changes in the placental immune response, but not fetal, suggest the placenta remains a resilient barrier during moderate maternal infection. Our data confirm the necessary use of live pathogens in MIA modeling to evaluate the complete immune response and improve translation to the clinic.

Animal Models in Neuroscience II, Room 3269

Evidence for a potential role of an increased copy number of the gene encoding glycine decarboxylase (GLDC) in the pathophysiology of psychosis

M. Kambali, M. Wang, R. Nagarajan, J. LYU, J. Liu, E. Engin, G. Homanics, U. Rudolph

Genomic copy number variants (CNVs) have been implicated in the etiology of schizophrenia (SCZ) and bipolar disorder. In two patients with psychosis, a rare 9p24.1 CNV, a 1.8 Mb duplication/triplication involving multiple genes, including the GLDC gene encoding the glycine-degrading enzyme glycine decarboxylase, has been found by others. Our goal was to determine whether this CNV is sufficient to induce biochemical or behavioral phenotypes in mice and which gene(s) would be underlying these phenotypes. We hypothesized that an increased copy number of Gldc would lead to increased degradation of glycine, eventually resulting in NMDA receptor hypofunction and schizophrenia-like phenotypes. To address this, we developed mouse models with a triplication (4 copies) of the 9p24.1 genes, or a duplication (3 copies) or a triplication (4 copies) of Gldc alone or of all other 9p24.1 genes. These mice were subjected to qRT-PCR (n=5 each genotype), Western blot (n=10 each genotype) and behavioral studies (n=10 each genotype) at 2-4-month of age. In all genetic mouse models with increased copy numbers of Gldc we found an increase in GLDC protein in hippocampus (Hip), prefrontal cortex (PFC) and amygdala. The microRNA mir132 which has been linked to density of dendritic spines and which is downregulated in patients with schizophrenia was reduced in Hip and increased in PFC. In addition, BDNF mRNA was reduced in Hip and PFC of mice with 4 Gldc copies. However, expression of CREB, p-CREB and BDNF proteins was unaltered. MicroRNA mir137, the product of a risk gene for SCZ as evidenced by GWAS studies was increased in PFC. Furthermore, only in mice with increased Gldc copy number but not in mice with increased copy numbers of the other 9p24.1 genes, we found key behavioral deficits, i.e., startle habituation impairment, absence of latent inhibition to conditioned freezing, working memory deficits in both the Y-maze spontaneous alternation test and T-maze forced alternation tests and sociability deficits, along with social novelty preference deficits. Thus, an increase in the copy number of the Gldc gene is sufficient to induce molecular and behavioral features consistent with a schizophrenia-like phenotype. Our results suggest that in the patients with the 9p24.1 duplication/triplication the increase in GLDC copy number may be an important contributing factor to pathophysiology. The results are in line with our still to be tested overall hypothesis that an increased copy number of Gldc results in increased glycine degradation in astrocytes, leading to deficits in glycine-dependent activation of excitatory glutamate receptors of the NMDA type in neurons and NMDA receptor hypofunction.

Reversal of schizophrenia-like phenotypes in mice engineered to harbor additional copies of the glycine decarboxylase (Gldc) gene

M. Wang, M. Kambali, R. Nagarajan, J. Lyu, J. Liu, E. Engin, G. Homanics, U. Rudolph

Genetic factors have been shown to increase the risk of developing psychosis. Two patients with bipolar disorder with psychotic features and schizoaffective disorder, respectively, have been found by others to harbor a small supernumerary marker chromosome, which contains multiple genes from the 9p24.1 chromosomal region, including the gene encoding glycine decarboxylase (GLDC). GLDC is an astrocytic enzyme that degrades glycine, which is a co-agonist at the NMDA receptor. NMDA receptor hypofunction has been implicated in the pathophysiology of schizophrenia. In these patients, glycine augmentation of antipsychotic therapy with clozapine led to improvements of psychotic and mood symptoms. In order to elucidate the potential mechanism of such reversal of symptoms with glycine, we have generated copy number variant (CNV) mice with increased copy numbers of either the entire 9p24.1 region or of Gldc alone. These mice were developed by introducing loxP sites into the genome followed by trans-allelic recombination in vivo. CNV's were confirmed by comparative genomic hybridization. The goal of the current study was to determine whether glycine alone is sufficient to reverse schizophrenia-like phenotypes in these CNV mice harboring extra copies of the human 9p24.1 region or just of Gldc. Our hypothesis was that glycine alone would be sufficient to reverse at least some schizophrenia-like phenotypes in the CNV mice modeling the patients with the 9p24.1 CNV. In our studies, we included both male and female mice with 4 copies of the 9p24.1 region or with 4 or 2 copies (equivalent to wild type) of Gldc ($n \geq 8$). Mice were administered glycine in their drinking water for 21days.Threehours before behavioral experiments they received glycine (or vehicle) by gavage. To assess glycine delivery, blood samples were analyzed with LC-MS/MS. Furthermore, glycine levels were also determined in hippocampus and prefrontal cortex. Behavioral testing included acoustic startle experiments to determine prepulse inhibition and pulse habitation, latent inhibition to conditioned freezing and working memory in the Y maze. The density and morphology of dendritic spines was assessed with Golgi staining. Experiments to date suggest that glycine has differential effects in different behavioral paradigm. Our results indicate that chronic administration of glycine in mice with an increased copy number of Gldc, thus presumably with higher rates of glycine degradation in astrocytes, may be sufficient to reverse at least some of the schizophrenia-like phenotypes observed.

Genetic ablation of dentate hilar somatostatin-positive GABAergic interneurons is sufficient to induce cognitive impairment

R. Nagarajan, J. Lyu, M. Kambali, M. Wang, C.D. Courtney, C.A. Christian-Hinman, U. Rudolph

Aging is often associated with a decline in cognitive function. The molecular and cellular mechanisms underlying these cognitive impairments remain poorly defined, but mounting evidence points to changes in GABAergic function as a major causal factor. Interestingly, a reduction in the number of somatostatin-positive (Sst+) interneurons in the DG has been described in aged cognitively impaired but not in unimpaired rodents. However, it remains unclear whether the reduction in Sst+ interneurons in the DG hilus is directly related to or

even causal for age-related cognitive dysfunction. We hypothesized that hilar Sst+ interneurons play an essential role in maintaining cognitive function and that a reduction in the number of hilar Sst+ interneurons might be sufficient to induce cognitive dysfunction. Hilar Sst+ interneurons were ablated by expressing a diptheria toxin transgene specifically in these interneurons. An AAV-mCherry-flex-dtA construct with the EF1α promoter was stereotaxically injected (bilaterally) into the DG hilus of young adult Sst-Cre mice (2-3 months). The control group was injected with an AAV-mCherry virus. After 21 days, the mice were employed for the novel object recognition test (CA1-dependent), the Morris water maze with reversal learning (learning: CA1-and CA3-dependent; reversal learning: DG-dependent), and a Y-maze test (HP, PFC). Brain tissue was collected for immunohistochemistry (c-Fos, GAD-67, Sst). We found that partial genetic ablation of Sst+ hilar interneurons impaired learning and memory functions as determined in the behavioral test battery. It also significantly increased the number of c-Fos-positive neurons in the DG and CA3 regions. Moreover, the number of Sst+ interneurons in the DG was decreased by 49 %, and the number of GAD-67+ neurons 33%. Our results show that the partial ablation of hilar Sst+ interneurons is sufficient to induce changes similar to those observed in aged rodents, such as reduction of Sst in the DG hilus, hyperactivity in DG and CA3 of the hippocampus, and cognitive impairments. This suggests that the changes elicited by partial ablation of hilar Sst+ interneurons may contribute to the development of cognitive dysfunction in aging animals. Furthermore, mice with a partial ablation of hilar Sst+ interneurons may represent a model for studying mechanisms underlying cognitive decline in aging.

Cognitive dysfunction induced by chronic chemogenetic inhibition of somatostatin-positive interneurons in the dentate gyrus hilus

J. Lyu, R. Nagarajan, M. Kambali, M. Wang, U. Rudolph

The cellular mechanisms leading to cognitive dysfunction in the elderly are not completely understood. In aged rodents, hyperactivity of DG granule cells and CA3 pyramidal cells and hypoactivity of CA1 pyramidal cells have been reported, and a reduction of somatostatin-positive (Sst+) interneurons in the dentate gyrus (DG) hilus correlates with cognitive dysfunction. We wanted to test the hypothesis that chronic but not acute suppression of the activity of hilar Sst+ interneurons causes defined learning and memory deficits. An AAV vector expressing hM4D(Gi) was stereotaxically injected bilaterally into the DG hilus of Sst-Cre mice. The control groups were injected with an AAV vector lacking hM4D(Gi). Clozapine was administered to the mice to activate hM4D(Gi)and thus inhibit hilar Sst+ interneurons. The chronic treatment group received clozapine(0.1mg/kg/day) in the drinking water for 21days before the first behavioral experiment and throughout testing and the acute treatment group was administered clozapine (0.1mg/kg i.p.)30minutes before behavioral experiments. We found that both chronic and acute chemogenetic inhibition (CCI and ACI, respectively) of Sst+ DG hilar interneurons increased the number of c-Fos+ neurons only in the DG hilus, but neither in the DG granule cell layer nor in CA3orCA1. In contrast, SST expression was decreased after CCI but not after ACI. Likewise, compared to ACI, CCI resulted in a decreased recognition index in the novel object recognition test, and an increased path length and increased latency to find the hidden platform in the water maze, both for learning and reversal learning. Our data suggest acausal relationship

between a chronic loss of activity of Sst+ interneurons in the DG hilus region and cognitive dysfunction. Furthermore, our results indicate that chronic suppression of the activity of hilar Sst+ interneurons leads to a reduction of SST expression, which has been observed in aging cognitive dysfunctional rodents. CCI but not ACI thus mimics at least some molecular and behavioral features of aging, which itself is a long-lasting process. CCI of DG hilar Sst+ interneurons may thus be further evaluated as an experimental model of aging-related processes in the hippocampus.

Cortical processing dynamics during sensory-guided behavior using a tactile virtual-reality task

A. Armstrong, K. Hu, Y. Vlasov

Our goal is to determine how neuronal populations in the mice barrel cortex are organized in dynamic functional networks that guide behavioral choices downstream during a whisker-dependent task. To enrich the number of activity states that neuronal populations encounter during a task trial, we designed naturalistic tactile virtual reality [1] behavioral experiments that load cortical circuits with difficult yet manageable cognitive tasks and, at the same time, elicit an ethologically relevant behavior. The headfixed animal runs freely on a suspended ball treadmill with movement tracked in a 2-dimensional VR plane. Moveable walls on either side of the animal snout are coupled to the animal run, thus producing an illusion that the animal is running in a winding virtual corridor with programmed left and right turns being guided only by the whiskers touching the walls. Of specific interest for our study is the choice period: the time interval when the animal first senses the approaching wall with whiskers until it makes a choice to change the direction of his run. To record from large neuronal populations during active navigation in a tactile VR, 64channel multi-electrode arrays are acutely implanted into the principle whisker barrel thus recording massive single-unit spiking activity across all cortical layers. Using Scnn1a-TG3-Cre x Ai32 mice, with Cre expression limited to 85% excitatory neurons in layer 4 of the cortex, enables optical tagging of individual L4 stellate cells as well as to manipulate these populations using optogenetics. We observed distinct layer-dependent stratification of spiking activity of neuronal populations recorded simultaneously during naturalistic whisker-dependent behavior in our VR. To uncover latent temporal dynamics of cellular-level interactions in recorded neuronal populations during the choice period we focused on analysis of pair-wise temporal correlations of spike timing. Both classical jitter-corrected crosscorrelograms (CCG) and novel machine learning based analytical approaches reveal distinct dynamics of organization of neuronal populations into functional networks across all layers. The extracted patterns of dynamic connectivity are changing rapidly during the choice period at specific times for stimulus presentation, motor action preparation and choice execution when the running direction is changed. Observed correlation of whisker-guided behavior with dynamics of laminar network connectivity can help to reveal specific dynamic organization of columnar microcircuits and shed light on tactile information flow during perceptual decision making. [1] N.Sofroniew, et al, eLife;4:e12559 (2015)

Human Models in Neuroscience, Room 5602

Global brain connectivity reliably predicts individual differences in intelligence

E.D. Anderson, A.K. Barbey

Individual differences in human intelligence can be predicted from patterns of neurobiological connectivity that span multiple brain networks. Much current theorizing into the neural basis of intelligence, however, has adopted a more localizationist perspective, mapping human intelligence to a single specialized brain region or brain network. Current neuroscience evidence points to the importance of both specialized neurobiological systems and global network topology for predicting individual differences in intelligence, suggesting that purely localizationist theories of intelligence may fail to fully capture or explain important sources of individual variation in cognitive ability. To what extent does neuroscience evidence support either global or localized neurobiological connectivity as a key source of individual differences? To further explore the systems-level neurobiology identified by current neuroscience theories of intelligence, we deployed a connectome-based predictive modeling framework to systematically investigate the predictive power of both localized and global functional connectivity patterns theorized in the literature to underpin intelligence. We administered a comprehensive battery of fluid and crystallized intelligence tasks to a large sample of healthy young adults ($N=297$), including figure series completion, LSAT analogical reasoning, Shipley-2 Vocabulary, and the Adult Decision-Making Competence Battery. Structural equation modeling was used to generate confirmatory factor loadings and produce individual estimates of psychometric g within this battery. Using reproducibly processed resting-state data, connectome-based predictive modeling found that intelligence was best predicted from global, whole-brain patterns of resting functional connectivity. In contrast, we observed low or non-existent performance for predictive models trained only on localized connectivity profiles. Critically, we found that weakly-connected edges known to support functional segregation and small-world organization are important neurobiological predictors of individual differences in intelligence, and that these edges were distributed across the entire connectome. Our results point to a need for neuroscience theories of intelligence that integrate specialized and necessary neurobiological substrates of intelligence within a globally efficient information-processing architecture, suggesting important future directions for research into the neurobiological properties that underlie individual differences in cognitive ability.

Characterization of motor impairment rating error of transformed IMU data

L. Ziegelman, T. Harrigan, J. Brasic, M.E. Hernandez

This study aimed to characterize the relationship between level of movement impairment and rater accuracy of the movement impairment during a clinical task. These terms are operationalized using the Unified Parkinson's Disease Rating Scale (UPDRS) motor subscale to characterize level of impairment and the absolute value of the percent error of

the rater's rating of transforms of inertial measurement unit (IMU) data when compared to a clinical gold standard to represent rater accuracy. The rationale for characterizing this relationship is that it allows insight into ways in which transformations of motion data could be compared to a traditional method of diagnosis of movement impairment by a clinician. Additionally, characterizing typical rating error allows for additional necessary information in the creation of machine learning classifiers of UPDRS motor task ratings, which is a meaningful step in the process of creating telemedicine tools for movement disorder specialists. This is done by creating a parent regression model, where the performance of a linear model, cubic model, and exponential decay model are compared, as well as testing the selected exponential decay model for a task effect. The clinical ratings were scored by 35 raters certified to administer the UPDRS on a series of 24 participants diagnosed with Parkinson's Disease (PD) with transformed motion data. The exponential model, which was fit as Y=−0.00291e1.13124+0.44694is shown to have the best fit with all three estimates statistically significant at α=0.05and finds that UPDRS scores between 0 and 2 are harder to accurately rate as compared to a 3 or 4. This means that mild symptoms of motor impairment are more difficult to separate from no impairment as compared to severe symptoms. This parent exponential decay model is tested for a task effect, which is found to be present. All together, these models indicate that transformed data is not equally easy to evaluate, where the movement impairment and task type impact a rater's ability to rate motion accurately. This is a necessary first step in the evaluation of the feasibility of using IMU data ratings to build telemedicine tools.

An investigation into changes in neurotransmitter concentrations associated with tinnitus and hearing loss

R.A. Khan, Z. Wang, F. Lam, F.T. Husain

Cochlear dysfunction, followed by changes in central auditory pathways, is widely assumed to be a causal factor for tinnitus. Numerous animal studies of tinnitus have suggested that imbalance of neurotransmitters in the auditory processing pathway, as a consequence of such cochlear dysfunction, are associated with behavioral markers of tinnitus. Specifically, concentrations of GABA, an inhibitory neurotransmitter which is the most widespread chemical messenger in the auditory pathway, have been seen to be decreased in the primary auditory cortex, medial geniculate body, dorsal cochlear nucleus, and ventral cochlear nucleus. Further, GABA agonists have been seen to be reduced in animals in whom tinnitus has been induced, while intervention studies suggest that the introduction of GABA agonists vigabatrin and taurine appear to reduce behavioral markers of tinnitus in animals. Concentrations of excitatory neurotransmitters such as glutamate are also seen to be impacted in tinnitus. While these promising results have been seen in a range of animal models, this research has been sparsely conducted on human subjects. The only study to investigate tinnitus-related changes in neurotransmitter concentrations has suggested that GABA is reduced in the right auditory cortex of tinnitus sufferers, while choline was seen to be associated with tinnitus severity (Sedley et al., 2015). However, the independent impact of hearing loss, which is seen to be associated with reduced GABA regardless of tinnitus status, has not been investigated. In the present study, we employed a volumetric magnetic resonance spectroscopic imaging (MRSI) method to investigate concentration of GABA in six tinnitus sufferers who had accompanying hearing loss, four

participants with hearing loss and no tinnitus, and four normal hearing controls. The volume of interest acquired during MRSI was an oblique slab covering bilateral regions of auditory cortex, inferior colliculus, and thalamus. Subject-specific ROIs were defined for each of these three regions in each participant. Preliminary analyses underscored the feasibility of the study, and demonstrated that we are able to detect GABA and glutamate in the spectrum of molecular weights from regions of interest within the acquired slab. Because of the small sample size, we have focused on data from individual participants and have refrained from conducting group-level analyses yet. This is an ongoing study, with a goal of recruiting ten participants per group by the end of the study, where we plan to investigate differences in GABA and other neurotransmitters between the three groups. If there are reliable differences in the concentration of inhibitory and excitatory neurotransmitters between the tinnitus and hearing loss groups, it will point to the effect of tinnitus alone; if there are no such differences, it will suggest that hearing loss alone is sufficient to explain changes in neurotransmitters even in individuals with tinnitus.