Carrie Poon   Research Advisor: Frank Barone

Delayed administration of thrombopoietin improves long-term outcome from ischemic stroke

Ischemic stroke is a major cause of long-term sensory, motor, and cognitive deficits. Only 5% of stroke patients are able to meet the 4-hour time window for tissue plasminogen activator (tPA) thrombolysis, the only current FDA approved treatment for ischemic stroke. Our lab has previously shown that thrombopoietin (TPO), a hematopoietic platelet growth factor, has acute protective effects. TPO administration up to 4 hours after middle cerebral artery occlusion (MCAO) significantly decreased the degree of stroke-induced brain infarction, edema, inflammatory cytokines and blood brain barrier injury. TPO-treated rats also exhibited significantly improved post-stroke sensory-motor performance. Here we explore the delayed and long term effects of TPO. Male Sprague-Dawley rats underwent 2 hours of MCAO and monitored for 4 weeks. Rats received either 2 intravenous administrations of phosphate buffered saline (PBS) or TPO (optimum protective dose of 0.1ug/kg). The first administration was 24 hours after MCAO (i.e., after the stroke infarct is fully developed) and the next administration was on day 4 after MCAO. Neurological deficits 4 weeks post-stroke were improved significantly in the TPO-treated group compared to the PBS-treated group (p<0.01). Active place avoidance learning was utilized to measure post-stroke cognitive performance. The TPO treated group received significantly fewer shocks across trials and exhibited improved place avoidance learning, compared to the PBS group that did not learn (p<0.01). Preliminary immunohistochemistry studies for neurogenesis and angiogenesis suggest increased neuronal and vessel development in the area adjacent to brain infarction. My goal is to investigate peri-infarct neurogenesis, angiogenesis and the (re)myelination of demylinated axons post-stroke in order characterize the mechanisms responsible for the post-stroke restored functioning due to delayed TPO intervention.

Lilei Chan   Research Advisor: Jennifer Baxter

What Interventions can be Implemented to Reduce the use of Physical Restraints in the Elderly Requiring Long Term Nursing Care?

Physical restraints, devices used to restrict patients' mobility, are used widely in long term care institutions to reduce the risk of falls and potential injury. It has been suggested that physical restraints cause physical and psychological suffering to the patient. In addition, the use of physical restraints has been linked to injury and death. The aim of the present study was to explore interventions that can be utilized in lieu of physical restraints in the elderly requiring long-term nursing care. A review of the literature on physical restraints used on older adults living in long term care and the possible interventions aimed to minimize their use was conducted. A total of 12 articles were collected from CINAHL, EBSCO, and Pubmed databases using the search criteria "physical restraints" and "patient safety". Nine of the 12 articles were selected for this review. The results revealed the use of physical restraints can be significantly reduced by the following interventions: meaningful and supportive patient-staff interaction continuing education of nursing staff in geriatrics (n=3), utilization of advanced practice nurses for consultation purposes, policy change (n=3), availability of alternative interventions, surveillance technology, and the utilization of a fall management program (n=2). There is a need in knowledge and application of interventions and alternatives to physical restraints. Restraint-free environments improve both the health outcomes of the patients and provide the basis for good clinical practice.

Natalia Grin'kina   Research Advisor: Peter Bergold

A single head impact in adult mice immediately produces two persistent patterns of neurological and behavioral deficits

In clinical TBI, single closed head impact (CHI) produces a heterogeneous pattern of behavioral and neurological deficits. We have developed a CHI animal model that reliably produces two injury syndromes (CHI-1 and CHI-2) by a single impact to a closed head of an adult C57/Bl6 mouse. Differences in restoring spontaneous breathing and righting reflex indicate that the CHI-1 and CHI-2 syndromes arise immediately after the injury. Both CHI-1 and CHI-2 mice had transient motor deficits that were no longer present 7 days after CHI. At seven days, sham, CHI-1 and CHI-2 groups were trained on an active place avoidance task, a test of cognition and memory. Sham and CHI-1 animals were able to acquire the task while CHI-2 animals were not. Also, sham mice could lower time to 1st entrance, a parameter of task retention, while CHI-1 mice could not. The same retention deficit was seen on the subsequent day on the active place avoidance task with the shock zone location rotated 180°. These data suggest that CHI-1 mice are deficient in task retention, while CHI-2 mice are deficient in task acquisition.

A second set of sham, CHI-1 and CHI-2 mice were returned to their home cages for one month before behavioral testing. The sham, CHI-1 and CHI-2 mice tested at one month had similar performance on the active place avoidance as mice tested at one week. These data suggest that the behavioral deficits produced by CHI were long lasting. The persistence of the behavioral effects correlates closely with the patterns of histological damage seen in CHI-1 and CHI-2 mice (Sangobowale, et al., adjacent presentation). This model is presently being used to test drugs that limit injury in CHI-1 and CHI-2 mice.

Michael Sangobowale   Research Advisor: Peter Bergold

A single head impact in adult mice produces differing patterns of grey and white matter injury

The heterogeneity of brain injuries is a hallmark of TBI. This heterogeneity provides a substantial barrier to finding effective therapies. Our laboratory has developed a closed head injury (CHI) animal model that reliably produces multiple patterns of brain damage. Two injury syndromes (CHI-1 and CHI-2) are reproducibly produced after a single closed head impact to adult mice. The two injury syndromes differ in righting reflex, and cognitive and memory deficits (Grin'kina, et al., adjacent presentation). They also differ in structural damage to the brain. At 14 days, grey matter, NeuN staining shows little difference between the hippocamppi of CHI-1 and CHI-2 mice. In contrast, immunostaining for MAP2 shows a striking loss of dendrites in the CA3 and hilar regions in CHI-2, but not CHI-1 mice. At one month, white matter injury was assessed for myelin content using luxol fast blue and axonal content using a pan-neurofilament antibody. CHI-2 had widespread myelin and neurofilament loss in multiple white matter regions. CHI-1 mice had more selective loss in cingulum and corpus callosum. The more widespread grey and white matter damage in CHI-2 correlates with the more severe behavioral deficits. These data strongly suggest that CHI-2 mice have a more severe TBI than CHI-1 and CHI provides a model for the clinical heterogeneity of human TBI.

Alexander Coltoff   Research Advisor: Stacy Blain

p27 [58-106] Competitive Inhibition of Brk Phosphorylation of p27 in vitro

The proliferation of several breast cancers has been associated with the expression of the tyrosine kinase Brk. Brk is responsible for the phosphorylation of p27, a cell cycle regulator that increases the kinase activity of CDK4/6, which drives the cell cycle forward. Brk binds to p27 through the interaction of its SH3 domain with three possible sites - k1 [90-96], k2 [107-120], and k3 [182-195] - present on p27. My research will determine if p27 [58-106], a truncation mutant with residues 58-106, will bind to Brk in vitro. I will also determine if p27 [58-106] can competitively inhibit in vitro p27 phosphorylation by interacting with SH3 domain of Brk.

I have created and purified p27 [58-106] using ANTI-FLAG M2 affinity gel protocol. In addition to purifying p27 [58-106], I have purified wild type (wt) p27, p27 [10-86], p27 [22-106], p27 [25-59], and Alt Brk, an alternative splice variant of Brk. These proteins either have been, or will be, used to further elucidate the interaction between p27 and Brk.

It is hypothesized that p27 [58-106] will competitively inhibit the in vitro phosphorylation of p27. To test this, I will perform a competition assay with p27 [58-106], wt p27, and Brk. I will examine the assay for phosphorylation on the Y88 and Y74 sites of p27.

I have also created inducible pTRE3G vectors that contain DNA encoding the various p27 truncation mutants. This DNA is to be transformed into mammalian cells in order to elucidate in vivo interactions between Brk and p27.

The hyperactivity of Brk in breast cancers should result in the hyper-phosphorylation of p27. CDK4/6, which acts to drive the cell through the G1/S phase transition, is maintained in its active state through the hyper-phosphorylation of p27. The creation of competitive inhibitors of p27, like p27 [58-106], could have a possible anti-proliferative effect in breast cancers by down regulating the phosphorylation of p27 by Brk.

Lindsay Hill   Research Advisor: Stacy Blain

Toward the creation of an in vitro 3D culture model for the study of Multiple Myeloma cell plasticity and dormancy

Multiple myeloma is the second most common hematological malignancy, yet systems for studying this disease, including 2D cell culture and animal models, lack biological structure and are difficult to manipulate, respectively. In my current study, I aim to create an in vitro 3D model of the bone marrow microenvironment to study primary and immortalized myeloma cells. Previous studies in our lab and others have identified two myeloma cell phenotypes: stem-like CD38+, CD138- progenitor cells and differentiated CD38+, CD138+ cells. Initial studies using fluorescent activated-cell sorting of CD38 and CD138 stained NCI-H929 myeloma cells are consistent with these findings, identifying 2-3% of cultured cells with the stem-like phenotype. Our group has further demonstrated that CD138+ cells can dedifferentiate back into their CD138- progenitor, suggesting an inherent plasticity. Initial work will require sorting the two cell populations based on CD138 status and additional population-specific biomarkers. Population-specific expression levels of transcription factors and other intracellular proteins will be analyzed using qPCR. The de-/differentiation interconversion of myeloma cells is observed in 2D culture without a structural niche or support cells, suggesting an autocrine or paracrine secreted cytokine is responsible. We will perform cytokine arrays to identify the putative cytokine(s) involved. These studies will be replicated using primary myeloma cells. We will subsequently study cell-cell interactions in an in vitro 3D alginate hydrogel matrix by co-culturing primary and immortalized human myeloma cells with bone marrow stromal cells, mimicking the in vivo niche. Alginate hydrogel provides ease of conjugation of neutralizing antibodies or siRNA, based on our findings, to potentially block interconversion. We propose that manipulation of our 3D model will allow us to alter cell fate and will advance our understanding of myeloma cell plasticity and treatment targets.

Danielle Joseph   Research Advisor: Stacy Blain

The Plasticity Potential of the Putative Multiple Myeloma Cancer Stem Cell

Multiple myeloma (MM) is characterized by a clonal proliferation of the plasma cell within the bone marrow. Patients with this malady have a median survival rate of between 3-5 years from initial diagnosis. Though MM patients may undergo chemotherapy and autologous stem cell transplant, relapse is often inevitable. This suggests that there are MM cells that exhibit stemness characteristics that enable them to evade chemotherapy and reinitiate tumor growth. Stemness is defined by four characteristics: the ability to self-renew, to differentiate, to remain in a slowly proliferating or quiescent state and to be chemoresistant. The maturation of the MM cell is characterized by the acquisition of the CD138 marker. Previous data proposes that the MM cancer stem cell is the CD138- cell because it has the potential to self-renew, differentiate, and when compared to its CD138+ counterparts, to proliferate slower and to be more chemoresistant. However, our data unexpectedly demonstrates that the CD138+ mature tumor cells may also be able to dedifferentiate. As this happens in culture in the absence of supportive accessory cells or a niche, we believe that cytokines produced by the CD138+ cell are responsible for this plasticity in an autocrine or paracrine manner. The aims addressed here are: 1) to characterize both the CD138- precursor and the mature CD138+ cell from the RPMI 8226 cell line for its ability to self-renew, differentiate, remain quiescent and chemoresistant, 2) to determine which cytokines and signal transduction pathways are responsible for the plasticity that permits a tumor cell to gain or lose the stemness phenotype, and 3) to determine whether other MM cell lines also exhibit a similar plasticity. Our data implies that the notion of a phenotypically defined cancer stem cell in multiple myeloma may not be applicable. Instead differentiated, mature CD138+ MM tumor cells may be able to obtain a stem-like phenotype, enabling them to recapitulate tumors.

Inamul Kabir   Research Advisor: Stacy Blain

Sphingomyelin Synthase-related (SMSr) deficiency has no effect on tissue ceramide levels

Sphingomyelin Synthase-related (SMSr) belongs to sphingomyelin synthase (SMS) gene family. However, it has no SMS activity but ceramide phosphoethanolamine synthase (CPES) activity. SMSr is an ER resident enzyme and is expressed in almost all tested tissues including liver, small intestine and macrophages. Evolutionarily speaking, SMSr is more ancient member than other two in this family, SMS1 and SMS2. Both SMS and SMSr use ceramide as a substrate. The former deficiency increases ceramide levels and the later deficiency would also be expected to increase ceramide levels. It has been reported that SMSr gene knockdown in HeLa cells dramatically increases cellular ceramide levels damaging the early secretory pathway. Based on this observation, we hypothesized that SMSr deficiency in vivo would increase ceramide which may initiate a series biological processes including apoptosis and inflammation. In this study, we prepared SMSr gene knockout (KO) mice. We measured CPES activity in mouse tissues and found that macrophage CPES is barely detected, but other tested tissues still have reduced or normal CPES activity since SMS2 also has CPES activity. We measured ceramide phosphoethanolamine (CPE) levels and found that CPE is decreased in the liver, macrophages, and plasma. Interestingly and mystically, we did not find ceramide changes in the liver, macrophages and plasma of the KO mice compared with controls. We also measured plasma cholesterol, triglycerides, phospholipids, apo-lipoprotein levels, and did not observe any change due to the genetic ablation of SMSr. In conclusion, our results demonstrate that CPE production by SMSr has minimal effect on ceramide level in tested tissues and SMSr deficiency does not have observable influence on lipoprotein metabolism.

Priyank Patel   Research Advisor: Stacy Blain

Breast cancer related kinase (Brk) and its alternative splice variant (Alt-Brk) regulate G1-S phase progression of cell cycle in breast cancer

Breast cancer is the leading cause of cancer related death in women. Benign breast tumor can be diagnosed easily and if treated, it has a high survival rate. Thus, inhibiting proliferation of tumor cells to prevent tumor progression would drastically increase the window of opportunity to treat the patient. G1 phase is the only 'responsive' phase of cell cycle which can be manipulated to inhibit cell proliferation. In early G1 phase, p27 forms a ternary complex with cyclinD-cdk4. When in ternary complex, 3-10 helix of p27 blocks the ATP binding pocket of cdk4 resulting in the inhibition cdk4 kinase activity. When p27 is phosphorylated on Y88/89 residues, the 3-10 helix vacates the ATP binding pocket of cdk4 and activates it. Once activated, cyclinD-cdk4 phosphorylates pRb and cell progresses from G1 to S phase of cell cycle. The identity of kinase that phosphorylates p27 was unknown. We show that Brk phosphorylates p27 in vitro and in vivo. p27 protein levels increase but it's phosphorylation decreases in contact arrested cells as compared to proliferating cells. We found that even though p27 phosphorylation decreases in contact arrested cells as compared to proliferating cells, Brk protein levels are similar. This could be explained by the presence of catalytically inactive alternative splice variant (ALT-Brk) of Brk. ALT-Brk inhibits WT Brk activity by competitively binding to the substrates. We show that ALT-Brk is expressed in breast cancer cell lines. Moreover, ALT-Brk inhibits cell proliferation. The mechanism by which ALT-Brk inhibits the cell cycle is unknown. Our hypothesis is that ALT-Brk competitively inhibits the phosphorylation of p27 by WT Brk preventing activation of cdk4 activity and in turn inhibits phosphorylation pRb. Thus, ALT-Brk acts as an endogenous inhibitor of the cell cycle in breast cancer.

Elina Shteyn   Research Advisor: Stacy Blain

Establishing the Role of CDK4 in Pancreatic and Breast Cancer.

Proper regulation of the cell cycle is vital for error-free cell division. The cyclinD-cdk4 complex is responsible for progression of the cycle from the G1 to S phase by inactivating the G1 checkpoint. Deregulation of cdk4 (k4) contributes to the abnormal control of the checkpoint and is seen in many types of cancers. Thus, we want to examine how unregulated k4 activity affects the G1 checkpoint in cancer cells.

Brk, a kinase, is overexpressed in 60% of breast cancers. It indirectly activates k4 by phosphorylating (-phos) p27 on Y88, which in turn activates the CyclinD-k4 complex. Using stable cell lines overexpressing wild type (WT) and catalytically inactive (KM) Brk we showed by IF that p27 Y88 -phos increases in the WT Brk cells. To show that the increase in p27 Y88 - phos translates into increased k4 activity, we treated the cells with PD0332991 (PD), a specific inhibitor of k4. The IC50 value for the mock and the KM cell lines was 150 nM, but WT Brk had an IC50 value of 500 nM. The data shows that Brk increases p27 Y88 -phos, which in turn increases k4 activity. It suggests that PD sensitivity is correlated with k4 activity.

Deregulation of k4 activity might contribute to the development of Pancreatic Ductal Adenocarcinoma (PDAC) and inhibition of k4 would block the proliferation of pancreatic cancer cells. We tested a panel of pancreatic cell lines from different tumor grades to determine their sensitivity to PD. We detected two classes of cells: a sensitive group with IC50 values 1μM - 2.3μM and a resistant group with IC50 values 9.7μM -25.8μM. We hypothesis that cells with high IC50 values will either have much higher levels of k4 that can't be inhibited by the drug or the resistant cells may have evolved from a requirement for k4. In the latter case, PD would not be an effective therapy in the treatment of PDAC. We are currently analyzing PD treated cells for direct k4 and cdk2 activity by in vitro kinase assay to distinguish between the two mechanisms.

Shahnaz Miri   Research Advisors: Ivan Bodis-Wollner/ Eric M. Shrier

The foveal avascular zone in Parkinson disease

Background and objective: Foveal vision impairment, foveal thinning and remodeling have been demonstrated in Parkinson disease (PD). Despite the relationship between foveal pit morphology and foveal avascular zone (FAZ), no information is available regarding FAZ and microvascular structure of the retina in PD. This study aimed to quantify the size of the FAZ in PD.
Methods: This cross-sectional study is performed at the Departments of Ophthalmology and Neurology of SUNY Downstate Medical Center. Twenty-one PD patients (42 eyes; mean age 67.38 ± 8.0 years) and 11 healthy controls (22 eyes; mean age 68.50 ± 2.4 years) were enrolled. There was no significant age or gender difference between the two groups. Retinal fluorescein angiography and photography were performed on each subject using the Heidelberg Spectralis. Retinal images were analyzed using Image J software (version 1.45) to calculate the FAZ area and diameter. The FAZ area was compared between PD and controls. At the same visit, patients' retina was evaluated using spectral domain optical coherence tomography (OCT) (Heidelberg Spectralis) to evaluate the correlation between FAZ area and foveal thickness. The statistical analysis was performed using SPSS software (version 21.0) and P-value less than 0.05 was considered statistically significant.
Results: FAZ area in PD patients (0.304 ± 0.118 mm2) was significantly smaller than healthy controls (0.369 ± 0.107 mm2) (P=0.03). There was no significant correlation between age and FAZ area (R=0.04, P=0.74). The FAZ area had a significant negative correlation with foveal inner retinal (IRL) thickness (R=-0.613, P=0.0001).
Conclusion: This is the first study of the retinal microvasculature in PD. The results demonstrate smaller FAZ area in PD patients than in age matched controls. Microvascular changes of the retina were noted in the monkey MPTP model of human PD. Our human results may be relevant for further neurobiological studies.

Rachael Jennings-Charles   Research Advisor: Mohamed Boutjdir

Role of CaV 1.3 L-type Ca2+ channel in Congestive Heart Failure

Cardiac contraction results from the introduction of calcium into the cell via L-type Ca2+ channels, resulting in calcium induced calcium release. Research has shown that disorders in cardiac function often result from improper handling of Ca2+. L-type Ca2+ channels in the heart are composed of CaV 1.2 and CaV 1.3. Unlike CaV 1.3, the role of CaV 1.2 in heart failure has been extensively characterized. While CaV 1.2 is ubiquitously expressed in fetal and adult hearts, CaV 1.3 is highly expressed in fetal myocytes but not in adult heart ventricles. In the adult heart, CaV 1.3 is expressed in atria only. Previous research has shown that select fetal genes are re-expressed in adult ventricles during post myocardial infarction induced hypertrophy. One such re-expressed gene is the T-type calcium channel gene CACNA1G. During heart failure, additional Ca2+ influx into the sarcolemma may be able to off-set the loss of functioning of myocardial tissue. The aim of the present study is to test the hypothesis that CaV1.3 is re-expressed in the ventricles of failing hearts. For this study human normal and failing ventricular myocardial tissues were obtained. The tissue was then assessed by RT-PCR and western blot to observe the potential re-expression of CaV1.3 transcript and proteins in failing heart ventricles compared to normal ventricles. Post MI mouse whole cell lysate was also assessed for the presence of CaV 1.3. Preliminary RT-PCR results show that CaV1.3 is re-expressed in adult ventricular myocytes of hypertrophic human hearts but not in normal hearts. The highest fold up-regulation of CaV 1.3 was observed in the human right ventricle. Transcript levels were 23 times that of normal un-diseased tissue. Future research will involve the use of rodent models of heart failure. A state of hypertrophy will be induced in mice by LAD ligation. Research into CaV1.3 may lead to the identification of new markers for heart failure as well as potential therapeutic approaches.

Laura Brana   Research Advisor: Meriam Caboral-Stevens

Laparoscopic vs. da Vinci® Hysterectomy: A Cost-Effectiveness Study

Introduction: Hysterectomy is the second most frequently performed surgical procedure in women in the United States (US). Advances in robotic technology have allowed the development of the Da Vinci® robotic system for surgical procedures, which gained Food and Drug Administration (FDA) approval for hysterectomy in 2005. Advantages of the robotic technique include less blood loss, less pain, and a faster recovery. An analysis of overall cost in relation to the various components of both the laparoscopic and da Vinci ® hysterectomy must be studied to determine the cost-effectiveness of each technique.

Is the Da Vinci® Robotic technique more cost-effective compared to laparoscopic technique in women between 40-50 years of age undergoing hysterectomies for non-malignant condition? Using a predictive modeling of cost-effectiveness, this is a quantitative, retrospective study comparing the cost between Da Vinci® robotic and laparoscopic technique for hysterectomies of nonmalignant conditions performed at a hospital in NY. A convenient sample of 60 charts of women between 40-50 years of age with American Association of Anesthesiologists (ASA) Classifications 1 and 2 who underwent hysterectomies (30 robotic hysterectomy and 30 laparoscopic hysterectomy) for non-malignant conditions will be included in this study. Non-malignant conditions include but are not limited to, endometriosis, vaginal prolapse, uterine fibroids, pelvic adhesions, unusually heavy bleeding and pelvic pain. Cost will be measured by the length of stay of each procedure.

Conclusion: This research study will look at one variable to determine the cost of each procedure and to determine if a robotic approach to hysterectomy is a more cost effective choice. This study acknowledges some limitations: small sample size due to the relative newness of the robotic technique, data from one hospital's patient population alone, and only one variable contributing to overall cost being tested.

Natasha Acosta-Diaz   Research Advisor: Geetha Chari

Psychosis in Previously Well-Behaved Children; Recognizing Anti-NMDA Receptor Encephalitis

N-methyl-D-aspartate (NMDA) Receptor Antibody Encephalitis was first described in 2007, having been observed in women with mature teratomas. In this autoimmune encephalitis, NMDA receptor antibodies target the NR1 subunit of the receptor, causing alteration of synaptic function resulting in classic signs and symptoms of this disease process. We now know it is also seen in men, although less frequently, and may also be associated with other tumor types. Patients frequently present with either behavioral changes and/or seizures, in the setting of a history of recent prior illness. Through the course of the encephalitis, they most often have an autonomic instability, fluctuating level of consciousness, and central hypoventilation. Increased case reports are leading to more awareness, enabling earlier intervention for this type of encephalitis. Psychiatric symptoms tend to include: Visual hallucinations, anxiety, aggression, hypersexuality, and catatonia. Other symptoms seen are anterograde amnesia, mutism, speech disorders, rigidity, orofacial and whole body dyskinesias, and generalized tonic-clonic seizures. Cerebrospinal fluid findings are variable. Magnetic resonance imaging may be normal or show hippocampal fluid attenuation inversion recovery hyperintensities. Electroencephalogram findings range from diffuse delta slowing to status epilepticus.

We describe four pediatric patients who presented with acute changes of mental status, three with psychosis and one with status epilepticus to a large university hospital in New York City within a one-year time span, who were found to have antibodies positive for NDMA Receptor Encephalitis. Of the 4 patients, 3 were female and 1 was male. The age of onset was from 5 -19 years old. The initial psychiatric evaluation, workup, treatment, and final outcome will be discussed.

Srinath Gopinath   Research Advisor: Jeremy D Coplan

The Neurobiology of GAD Using 1H-MRSI: Aberrant Neurochemistry of Hippocampus and DLPFC, which Predicts Worry and IQ

Introduction: The neurobiology of GAD remains relatively uncharted. Using 1H-MRSI we sought to examine for aberrant resting state neurochemical connectivity of neurometabolite ratios using hippocampus as a hub. Based on recent studies, we also examined whether ROIs that participate in aberrant neural networks would preferentially predict both anxiety and intelligence in GAD.

Methods: GAD patients (n=16; F =11) and medically healthy volunteers (n=16; F=10) were assessed using proton magnetic resonance imaging applying the Duyn et al method using axial plane 1 (hippocampus) and 3 (dlpfc, central gyrus). Full Scale IQ, Penn State Worry Questionnaire (PSWQ) and Anxiety Sensitivity Index (ASI) were assessed. Metabolites included NAA/Cr, and Cho/Cr.

Results: No group differences for Cho/Cr were noted. Right hippocampal Cho/Cr positively predicted left DLPFC Cho/Cr in GAD distinguishable from controls [$F(1,28) = 15.72$; $p = 0.0004$]. Left hippocampal Cho/Cr positively predicted left central gyrus Cho/Cr in GAD distinguishable from controls in a similar manner. Left and right DLPFC Cho/Cr positively predicted ASI but only left DLPFC Cho/Cr positively predicted IQ. By contrast, IQ in controls positively correlated with left central gyrus Cho/Cr.

Conclusions: We demonstrate aberrant neurochemical connectivity for the Cho/Cr ratio between hippocampus as a hub with central gyrus and DLPFC in GAD, which is significantly absent in controls. An ectopic locus for left DLPFC Cho/Cr is noted by its association to both IQ and anxiety, whereas controls have left central gyrus Cho/Cr association with IQ without anxiety.

Asif Karim   Research Advisor: Jeremy Coplan

Social Rank and CSF Oxytocin (OT) in Maternal Stress: Influence on HPA axis

Background: OT plays an important role in social bonding and in certain psychiatric disorders. We examined CSF OT in the context of maternal social stress, HPA axis regulation, social rank and dyadic distance. We hypothesized differential patterns of maternal OT regulation of maternal HPA axis as a function of maternal stress and posited differential OT concentrations as a function of maternal social rank.

Methods: Twelve socially-housed mother-infant bonnet macaque dyads were studied after variable foraging demand (VFD) compared to 11 unstressed dyads. Dyadic distance was determined. Social ranking was performed blindly. Post-VFD maternal plasma cortisol and CSF OT were compared to non-VFD mothers.

Results: Low social rank was predicted by decreased dyadic-distance in VFD but not in controls ($p = 0.001$). In non-VFD mothers, social rank played no role in determining maternal HPA axis response whereas VFD-exposed subordinate mothers exhibited decreased plasma cortisol levels in comparison to VFD-exposed dominant mothers ($p=0.03$). Maternal CSF OT positively predicted maternal cortisol only in VFD mothers ($p = 0.02$). CSF OT concentrations were higher in dominant versus subordinate mothers irrespective of rearing status ($p=0.02$).

Conclusions: Maternal VFD exposure couples maternal social rank to dyadic- distance presumably reducing maternal contingent responsivity. VFD dichotomizes HPA axis response as a function of social rank. Implicating OT effects as a function of maternal stress, OT regulates HPA axis only under VFD conditions. Consistent with previous studies, social dominance is associated with increased OT. OT interacts with VFD stress in the regulation of maternal HPA axis.

Shariful Syed   Research Advisor: Jeremy Coplan

Relationships between early life stress, GLP-1 and dentate gyrus neurogenesis.

Introduction: We explored relationships between plasma glucagon-like protein-1 (pGLP-1) in adolescent nonhuman primate males and our previously observed inverse correlation between body mass and dentate gyrus neurogenesis in adulthood. Although GLP-1 is associated with weight loss and neurotrophic effects, we explored relationships between physiological levels of adolescent pGLP-1 and subsequent adult body weight and neurogenesis in the context of early life stress (ELS). We used variable foraging demand (VFD) to induce stress in nursing mothers and their infant offspring.

Methods: Morphometry, fasting pGLP-1, insulin resistance and lipid profiles were determined in 14 adolescent bonnet macaque males [10 VFD-reared and four unstressed controls (UCS)]. Later, as mature adults, dentate gyrus neurogenesis rates were counted using doublecortin staining. Using a median split, comparisons between subjects with "high" versus "low" adult neurogenesis were assessed.

Results: Lower BMI, higher pGLP-1, less central adiposity, yet higher insulin resistance in adolescence was associated with "high" adult neurogenesis rates. Whereas pGLP-1 was inversely related to body weight in all adolescents and in ELS adults, it was positively correlated in UCS. Higher adolescent pGLP-1 correlated with lower adult body mass only in subjects with "high" neurogenesis rates.

Conclusions: Higher adolescent pGLP-1 was associated with adolescent insulin resistance and higher adult neurogenesis rates. These findings suggest a developmental adaptive role of pGLP-1 following ELS, reflecting brain-gut interactions between intestinal L-cell-derived GLP-1 and neuronal GLP-1 with its receptors.

Jyothsna Karlapalem   Research Advisor: Daniel Cukor

Trait Anxiety Predicts Risk for Decreased Medication Adherence in Patients with Chronic Medical Illness

Introduction: Non-adherence to prescribed medication is a major issue in all chronically ill patient groups. Predictors of adherence behaviors are multifaceted and include limited time and resources, adverse effects of treatment, severity of illness, beliefs about medication, levels of anxiety and depression. This study aims to explore the association between anxiety, depression and beliefs about medication with adherence in patients with end stage renal disease.

Methods: As part of a larger study, 57 patients with ESRD on hemodialysis completed several psychological measures including the State-Trait Anxiety Inventory, Beck Anxiety Inventory, Beck Depression Inventory, Belief about Medications Questionnaire (BMQ) and the Medication Adherence Rating Scale (MARS), a self-report measure of adherence. These measures were administered again after six months (n=50).

Results: At initial assessment, trait anxiety was significantly associated with elevated (BDI>15) depression (r =.51), beliefs about harmfulness of medications (r= .38) and specific concerns about medication (r = .32). Trait anxiety scores were associated with continued clinical depression(r = .51) and worse adherence scores on MARS (r = -.47) at follow up. Neither the State Anxiety Indexnor BAI were found to have statistically significant association with medication adherence or depression scores at initial assessment or follow up.

Discussion: Patients with higher levels of trait anxiety are more likely to have elevated depression, more concerns about the safety of their medications and have decreased adherence to medication over time. This pattern of associations appears to be specific to trait anxiety, suggesting that an anxious style, more than acute anxiety, may be associated with negative outcomes. Assessment of trait anxiety may be helpful in the identification of patients at particular risk for decreased adherence and would enable us to provide focused interventions.

Lindsay Silva   Research Advisor: Diana Dow-Edwards

Age of Exposure Affects Behavioral Response to Delta-9-Tetrahydrocannabinol During the Peri-Pubertal Period in the Rat

Marijuana is the most commonly abused illicit substance in the United States. Additionally, in 2010, almost 60% of all first time marijuana users were under the age of 18. Research indicates that adolescents who use marijuana are at higher risk of developing anxiety, depression, and other mood disorders. Adolescence is a period during which both physical and behavioral maturations take place. Puberty occurs during adolescence; however, during a more narrowly defined time frame marked by the attainment of sexual maturity, which normally occurs around postnatal day 40 (P40) in male rats and P30 in females. The onset of puberty also coincides with peak cannabinoid receptor 1 (CB1) and endocannabinoid system (ECS) activity which suggests that puberty may be a particular time during development in which the subject is more sensitive to the effects of δ-9-tetrahydrocannabinol (THC), the primary psychoactive substance in marijuana. Our study on the effects of early adolescent (P29-38) THC exposure revealed sex differences in measures of anxiety. Males showed less anxious behavior in the elevated plus maze (EPM) following THC administration whereas females did not exhibit behavioral differences in response to THC exposure. Although THC exposure in this study occurred within adolescence for all the rats, the males could be considered pre-pubertal while the females were pubertal during the administration period. THC was then administered to pre-pubertal (P21-30) females as well as pubertal (P39-48) males. Preliminary data suggest that pre-puberty is a critical time during which THC exposure elicits behavioral differences in measures of anxiety in both male and female animals. Reductions in anxious behavior, similar to those of pre-pubertal males, were observed in pre-pubertal females following THC treatment, whereas in pubertal males, these differences were no longer observed.

Bryan McCarthy   Research Advisor: Helen Durkin

Substance P (SP) Mediated Suppression of CD4+CD3+P38 MAP Kinase+ T Cells, IL-4 and Ragweed Specific Memory IgE Responses by Human Peripheral Blood Mononuclear Cells (PBMC).

Rationale. Magnetic/electrical stimulation of human or rat left, but not right, temporo-parieto-occipital (TPO) cortex transiently increases serum SP levels (~1hr) and blood CD4+ T cell numbers (4 hr) (humans, rats), while suppressing IgE production by B cells in lymph nodes and spleen (48 hr) (rats) and serum IgE levels (4 days) (humans, rats). These effects were prevented by transection of rat spinal cord at T2 or thymectomy. Stimulation of human or rat left TPO cortex activated an epsilon specific pathway because IgM, IgG and IgA levels did not decrease. Others demonstrated that CD4+ T cells and IL-4 are required for human and rodent IgE responses and that p38MAPK is associated with IL-4 which, in turn, is required for IgE production. We previously reported that SP suppresses murine memory IgE responses in vivo and in vitro. This study determined the effect of SP on human CD4+CD3+ p38MAPK+ T cells, IL-4 and memory IgE responses.
Methods. CD45+CD14-p38MAPK+ leukocyte and CD4+CD3+p38MAPK+ T cell distributions of ragweed sensitized IgE+ humans (n=6) were determined ± 15-30 min incubation with PMA ± SP (flow cytometry). The effect of SP on ragweed antigen induced IL-4 and memory IgE responses was determined by culturing PBMC for 0-12 days ± ragweed antigen ± SP. IL-4 in PBMC and IgE levels in supernatants were determined (RT-PCR, ELISA).
Results. CD45+CD14-p38MAPK+ cells and CD4+CD3+p38MAPK+ T cells were detected in PBMC (~30%) and their numbers greatly increased after PMA stimulation (>70%). Inclusion of SP with PMA in culture prevented the increases in p38MAPK+ cells obtained with PMA alone, and decreased background numbers of both subsets. When PBMC were cultured with ragweed antigen, IL-4 production and peak memory IgE responses occurred on day 10. Inclusion of SP with ragweed antigen in culture prevented induction of both responses.
Conclusion. SP mediates suppression of memory IgE responses by suppressing CD4+p38MAPK+ T cells and IL-4 production.

Benjamin Lee   Research Advisor: André Fenton

Out-of-Context Activation Memory: Temporal Gradient of Memory Enhancement

Background: I previously showed that a stressful experience induces consolidated (stable), unrelated memories to become activated (labile), and then enhance the expression of that memory. A 20-min forced-swim induces a stress response that raises serum corticosterone levels to 300%, and the swim environment had no physical, hormonal, or other identifiable feature in common with the learning context.

Rationale: The lingering consolidation hypothesis proposes that an acquired memory progressively undergoes consolidation with time such that the stability of the memory gradually increases and becomes more resilient to disruption in a kind of temporal gradient. The working hypothesis is that there is a temporal gradient that increases the stability of the acquired memory such that swim stress can no longer activate and enhance the memory. I investigated whether there is a temporal gradient within which swim stress can enhance the expression of a consolidated (stable), unrelated memory.

Methods: After learning an aversively-conditioned left/right (L/R) discrimination task in a T-maze, I subjected rats to a 20-min forced-swim 1, 7, 14, or 30 days later. Recall was then tested 1 day after the swim. Since the training establishes a robust memory, retention was measured by switching the safe/shock arms and measuring the number of errors.

Results: Swim stress enhanced the expression of memories that were 7-days-old or younger, as compared to the non-swim control group. However, a swim stress had no impact on memories that were 14-days-old and older. Also, all groups showed persistence of a L/R discrimination memory a month after learning as 20/26 (77%) animals initially chose the arm that they had learned (test of proportions $z=2.016$; $p=0.0438$).

Discussion and Significance: These data suggest that there is a temporal gradient within which swim stress can enhance consolidated (stable) memories, and that the window closes at some point between 1 week and 2 weeks.

John Choi   Research Advisor: Joe Francis

Nonlinear model predictive control for the design of optimal microstimulation patterns for somatosensory neural prostheses

Somatosensory feedback is crucial for the accurate and reliable control of movement and will be an important component in neurallycontrolled limb prostheses. Encoding transducer readings into multichannel electrical patterns to be applied through a centrally implanted electrode array is an open problem. Similar to cochlear implants, an objective for these implants is to recreate naturalistic patterns of activation, or at least to preserve information throughput to the brain. We have previously shown that a linear dynamical model and a model predictive controller could generate pulse patterns in ventral posterior thalamus that roughly recreated natural touch responses (field potentials) in somatosensory cortex (S1). Central to this process is a parsimonious and accurate dynamical model. We have improved our model by incorporating nonlinear elements. These accounted for phenomena such as short-term plasticity and input nonlinearity, which greatly improved the representative capacity and accuracy. A nonlinear optimization method was able to control this model and produce more faithful control over the neural trajectory in S1. We have also shown that using a predictive model, the controller produces responses that maintain most of the natural information on punctate touch parameters such as amplitude and spatial location. This optimization technique could be a way to develop biomimetic encoders for use in next generation neural prosthetic devices.

David McNiel   Research Advisor: Joe Francis

A method for training non human primates to modulate grip force towards development of advanced brain machine interfaces

Partial or complete impairment of the upper limb can result from a number of injuries or neurodegenerative diseases. Repair or replacement of a lost or damaged limb with a device controlled by the user's brain is an elegant solution to this issue. A neurally controlled robotic limb must include a robust control strategy to apply an appropriate level of grip force. This ensures that the object being gripped is neither damaged by excessive force or dropped. Towards the development of a brain machine interface (BMI) capable of reaching, grasping, and transporting an object from one location to another we have developed a method of training non human primates (NHPs) to modulate their grip force. Software was developed which allowed dynamic visualization of the level of grip force applied to a cube. When a trial begins a random target grip force is made visible and the animal must match and hold their applied force to the target force for some amount of time. If the task is completed successfully the animal receives a small juice reward. If the animal fails to complete the task no reward is given and a new trial begins. Two NHPs have been successfully trained in this paradigm; their accuracy in task performance is currently greater than 90%. This is an effective method of training NHPs in the modulation of grip force and will allow for further development of BMIs capable of providing various forms of dynamic feedback. In the future we plan to implant relevant brain regions to test various control strategies that ultimately will allow the animals to control the grip force exerted by a robotic hand.

David Daniel   Research Advisor: Nagaraj Gabbur

A Survey of Contraception Knowledge among Incoming Interns and Medical Students

Introduction: Contraception is an important topic that is taught in medical school. The objective of this study is to assess contraceptive knowledge in incoming interns who have just graduated compared to students just entering medical school.
Methods: A cross-sectional study was performed using a survey regarding 9 methods of contraception (Natural Family Planning (NFP), Condoms, Depo-Provera, Patch, OCPs, IUD, Diaphragm, NuvaRing, and Implanon). The survey was handed out during resident and student orientation, with a response rate of 145 (54.1%) and 99 (52.6%). Results were analyzed using 2-sided Mann-Whitney U tests, Spearman's rank correlation, Student t-tests, and a Bonferroni correction.
Results: Interns had a significantly higher overall score compared to students ($p<.001$). Additionally, interns had more knowledge regarding NFP($p<.001$), Depo-Provera ($p<.001$), OCPs($p<.001$), IUDs($p<.001$), and Diaphragms($p<.001$). Women had a significantly higher overall score ($p=.0003$). Respondents who regularly attended religious service had a lower overall score ($p=.0027$). Age was positively correlated with a higher score ($p<.001$). Graduation from a US medical school resulted in a higher overall score ($p<.001$). US graduates were comprised of a younger population, yet still scored significantly higher than international graduates.
Conclusion: Gender, religious attendance, age, and type of medical school were all related to contraception knowledge. However, specific knowledge regarding Condoms, NuvaRing, Implanon, and Patch should be emphasized in medical school curricula. Although age correlated positively with score, this was not true for type of medical school. US medical schools are more effective at teaching contraception than international schools.

Ioannis Alagkiozidis   Research Advisor: Yi-Chun Lee

Survival impact of cytoreduction to microscopic disease for advanced stage cancer of the uterine corpus

Objective:To assess the impact of cytoreduction to no gross residual disease (RD) on overall survival (OS) in patients with stage III-IV uterine carcinosarcoma (MMMT), papillary serous/clear cell (UPSC/CC) and endometrioid carcinoma (EC).
Methods:We identified 168 patients who underwent surgery for advanced uterine cancer between 1984 and 2009 in 2 teaching hospitals in Brooklyn, New York. Epidemiologic and surgical characteristics were collected. OS was calculated using the Kaplan-Meier method. Predictive factors were compared using the log rank test and Cox regression analysis.
Results:Our cohort included 54 patients with MMMT , 54 patients with UPSC/CC and 60 patients with EC. Complete gross resection was achieved in 64% of patients with MMMT, in 53% of patients with UPSC/CC and in 68% of patients with EC. There was no interaction between pathology type and feasibility of complete cytoreduction (p=0.390). No gross RD was associated with a median OS of 25 months versus 13 months in patients with gross RD (p=0.037). Within each pathology type the absence of gross RD was associated with a trend for improved survival. OS was 21 months for patients with MMMT when complete gross resection was achieved, versus 9 months for those with gross RD. OS was 22 months for patients with UPSC/CC and no gross RD, as compared to 12 months for patients with gross RD. Lastly, for patients with EC, OS was 36 months if no gross RD, versus 21 months for patients with gross RD. On multivariate analysis, predictors of increased mortality were gross RD (HR=2.0 during 1st year post-surgery, p=0.019), stage IV, p=0.025) and age (HR=1.04 per year of age, p=0.002).
Conclusion:Cytoreductive surgery to no gross RD is associated with improved OS in advanced uterine cancer. This effect is uniform among histologies. There is no interaction between pathology type and feasibility of complete cytoreduction.

Weerasinghege Jayasekara   Research Advisor: Cathryn Galanter

Human Trafficking

Background: Human trafficking, which includes sexual and labour exploitation has received increasing global attention over the past two decades and continues to persist affecting nearly 27 million people worldwide. It is difficult to quantify the victims due to its sensitive and hidden nature. It has been estimated that approximately 800,000 people are trafficked across international borders annually. Of those, 80% are women or girls; 50% of these females are minors. In the United States alone, 50,000 persons are trafficked into the country every year, and approximately 400,000 domestic minors are involved in trafficking.
Objective: The principal objective is to pilot a specific screening tool to identify victims of human trafficking, and thereafter develop a standard protocol for referral to counselling and preventive services.
Method: We will survey 20 consecutively admitted patients from our inpatient child and adolescent psychiatric units ranging in age from 6-23years old. We will administer a 26-item questionnaire, which covers psycho-social and economical aspects of human trafficking. We will ask patients about their understanding and the relevance of the questionnaire. Institutional Review Board approval is pending.
Results: Results are forthcoming.
Discussion: Future studies will examine rates of exposure to human trafficking on our inpatient unit and will inform our development of a protocol for referral for counselling and services after discharge.

Christian Trentacosta   Research Advisor: Cathryn Galanter

**Identification of Childhood Trauma in an Urban Child and Adolescent Psychiatric In-patient Population:
Findings from Prospective Study**

Background: In the last two decades, trauma in children and adolescents has been identified as a growing concern in United States. Havens et al found that Post Traumatic Stress Disorder (PTSD) was underdiagnosed in inpatient psychiatric setting.
Hypothesis: The addition of the UCLA PTSD Index screening tool to our routine clinical assessment process will lead to increased identification of PTSD at admission. With the PTSD Civilian Checklist, we hypothesize that PTSD symptoms will be decreased at time of discharge.
Methods: All patients admitted to the child and adolescent psychiatric inpatient services, ages five to seventeen, will be given the UCLA PTSD Index. Patients identified by the UCLA PTSD Index as traumatized will receive trauma-focused group therapy as part of their treatment. In addition to the UCLA PTSD diagnostic instrument, we will track the change of symptoms, during this study, from admission to discharge, using the PTSD Civilian Checklist. Also, participants can opt out of group therapy but continue within the study. The severity of their symptomatology, as marked by the PTSD Civilian Checklist, at the time of discharge, will be compared with scores of the PTSD Civilian Checklist of those who remained in group therapy. Finally, we will compare the rates of PTSD in children and adolescents admitted after the introduction of routine screening to those rates of those with the diagnosis prior to the implementation of screening. We will examine rates based on admission and discharge diagnosis in the electronic medical records.
Expected Results: We expect increased identification of PTSD at admission with the implementation of the UCLA PTSD Index. We expect decrease in symptoms of PTSD at time of discharge in those who remain in the therapy group and those who opt out of therapy, with a greater decrease in symptoms in those who remain in therapy.

Jinu Thomas   Research Advisor: Laura A. Geer

**Maternal exposure to EDCs from consumer products:
Comparison of levels in a Caribbean immigrant population in the U.S. to national and global Levels**

Endocrine-disrupting chemicals (EDCs) are frequently found in consumer products despite the fact that these substances have been known to adversely affect fetal development and birth outcomes. EDCs have been suspected in the increased incidence of infertility, genital tract abnormalities, obesity, and early onset of sexual maturation. The purpose of this study is to determine if exposure rates of EDCs in expectant mothers of immigrant origin in the US differ from those in other countries. Exposures to EDCs were derived from maternal urinary samples from a sample in a hospital-based cross-sectional study in a predominantly Caribbean immigrant population in Brooklyn, New York. Tracking trend levels in exposure and product usage will inform exposure prevention strategies.

We employed liquid chromotography/tandem mass spectrometry (LC-MS/MS) to quantify bioactive contaminants in urine samples from pregnant women. Exposure levels of comparison countries are derived from various biomonitoring studies. The list of target EDCs includes propylparaben, ethylparaben, and triclosan.

For triclosan, preliminary results indicate the Brooklyn samples had a mean urinary concentration of 8.55 μg/L which is higher than median urinary concentrations in the US (7.60 μg/L), Belgium (2.55 μg/L) and China (3.77 μg/L). For ethylparaben, preliminary results indicate the Brooklyn samples had a mean urinary concentration of 11.0 μg/L which is lower than median urinary concentrations in Korea (38.0 μg/L) but higher than the US (1.0 μg/L) and France (4.1 μg/L). For propylparaben, preliminary results indicate the Brooklyn samples had a mean urinary concentration of 68.0 μg/L which is significantly higher than median urinary concentrations in the US (22.8 μg/L), Japan (20.2 μg/L) and Spain (29.8 μg/L).

Expectant mothers of predominantly Caribbean immigrant origin in the US may suffer increased potential EDC-induced health outcomes compared to populations within the US and abroad.

Andrew Chang   Research Advisor: Alan Gintzler

Sub-Cellular localization of mu-opioid receptor Gs signaling

Long-term opioid administration for pain management leads to a reduction in its effectiveness to treat pain known as tolerance. Many cellular mechanisms have been proposed to explain tolerance such as opioid receptor desensitization and adenylyl cyclase superactivation.

The Gintzler laboratory has previously shown that morphine tolerance results, in part, from an increased association between the stimulatory G protein alpha subunit (Gαs) and the μ-opioid receptor (MOR), which would mitigate traditional inhibitory effects of MOR activation.

In the current study, we investigated the membrane microdomains in which these adaptations were taking place. Caveolae, the structurally distinct, flask-shaped invaginations maintained by caveolin proteins, have been known to be platforms for many signal transduction events. Our model system employed Chinese Hamster Ovary (CHO) cells stably transfected with the rat μ-opioid receptor (MOR-CHO).

In co-immunoprecipitation studies, acute MOR activation with sufentanil increased the association of Gαs and adenylyl cyclase (AC) with caveolin-1 in the Triton insoluble membrane fraction. Furthermore, the lesser-phosphorylated form of Gαs, which preferentially associates with MOR, was found to be concentrated in caveolae. This emphasizes the relevance of caveolae to MOR-Gαs signaling, which increases during tolerance. The trafficking and activity state of other signaling molecules such as adenylyl cyclase into caveolae following chronic morphine is also currently being investigated.

The ability of acute exposure to sufentanil to increase the association of AC and Gαs with caveolin, as well as the translocation of signaling molecules into caveolae following chronic morphine treatment suggests that downstream molecules related to acute and chronic opioid sequelae may be localized in the caveolae microdomain of cell membranes.

Arjun Kumar   Research Advisor: Alan Gintzler

Sexual Dimorphism in the Regulation of Spinal Endomorphin-2 Release

There is considerable evidence that males and females differentially utilize mu-opioid receptor (MOR) antinociceptive systems. MOR-selective opioids are more effective as analgesics in male rats than female rats (Barrett et al., 2002; Cicero et al., 1997). Furthermore, K+-evoked release of spinal cord endomorphin-2 (EM2), the endogenous substrate for MOR, is significantly greater in male rats than female rats (Gupta, von Gizycki, & Gintzler, 2007). The overall hypothesis of the current study is that regulation of the EM2-MOR system in spinal cord shows sexual dimorphism. Specifically, this report aims to examine the regulation of spinal EM2 release by spinal opioid receptors. In this study, I utilized the content of EM2 in intrathecal perfusate from rats to reflect the activity of spinal EM2. First, I validated the method used both to perfuse the intrathecal space in vivo, and to intrathecally administer opioid receptor agonists and antagonists. I also validated a plate-based radioimmunoassay (RIA) to measure EM2 release during these pharmacological manipulations. My data show that this RIA accurately quantifies EM2 in intrathecal perfusate, and that activation of MOR by the exogenous opioid Sufentanil increases endogenous release of EM2. Moreover, spinal MOR regulation of EM2 release appears to be sexually dimorphic, such that MOR activation facilitates EM2 release in males but not females (in either proestrus or diestrus phase of the estrus cycle). This sexual dimorphism is consistent with previous studies showing the importance of the MOR-EM2 system in male antinociception. This study will facilitate a better understanding of sex-specific mechanisms for regulating spinal EM2 release, aiding the development of sex-specific medications for the clinical management of pain.

Emiliya Storman   Research Advisor: Alan Gintzler

CNS Aromatase: Local Estrogen Production and Its Role in Nociception

Differences in pain perception between men and women, as well as between menstrual cycle phases, have been extensively studied (e.g., women experience more severe levels of pain and pain of longer duration than men; more pain during premenstrual and menstrual phases of menstrual cycle). Our laboratory, focusing on mechanisms underlying those differences, has demonstrated the importance of local estrogen availability in the spinal cord of females to analgesic effects of morphine. Aromatase, a membrane-bound enzyme that synthesizes estrogen in various tissues (including CNS) has been suggested to partake in relevant analgesic pathway(s).

We hypothesized that local aromatase activity determines the amount of local estrogen, which could vary between genders and menstrual cycle phases, producing the observed pain differences. This study focused on aromatase and variation of its spinal cord levels between male and female rats and between female rats in different estrous cycle stages. I compared, using quantitative Western blot analyses, the amount of aromatase present in crude membrane preparations from male, proestrous (high systemic estrogen levels), and diestrus (low systemic estrogen levels) rat spinal cords.

No significant differences in levels of aromatase were observed between male, proestrous, and diestrous rats. However, changes in aromatase activity resulting from covalent modification (e.g., phosphorylation) and not its protein content might underlie the difference in CNS estrogen availability. A number of aromatase activity (AA) assays exist to measure peripheral and brain AA. However, to date, no one has been able to detect AA in mammalian spinal cord. I modified a tritium-based AA detection method in rat hypothalamus and am currently pursuing further refinement of the assay to enable rat spinal AA detection.

Understanding of the mechanisms responsible for the observed pain differences might provide better pharmacological target(s) for pain alleviation.

Jeffrey Chang   Research Advisor: Stephen J. Glatt

Quantitative Review and Synthesis of Blood-Based Transcriptomic Biomarker Studies of Autism Spectrum Disorders

Autism spectrum disorders (ASDs) comprise a group of phenotypically similar disease states that affect 1 in 88 children. Efforts to discern clinically useful biomarkers have been demonstrated at many levels of potential pathophysiology, and gene-expression microarray analysis of samples obtained via peripheral blood have provided promising evidence implicating a variety of dysregulated genes. However, each study has identified and implicated different genes and pathways, and as a result the literature suffers from a lack of consensus.

In this study we pooled data from six microarray datasets in order to identify a list of genes that serve as better predictors of the diagnosis of ASD. In addition to our own data, we identified five publicly available datasets of expression microarray data from whole-blood or peripheral blood lymphocyte samples of children with ASDs and typically developing comparison subjects.

The top 5% (by p-value) of dysregulated genes from each of the six datasets was identified by analyses of covariance. Upstream regulators for each study's candidate biomarker set were determined by Ingenuity Pathway Analysis (IPA). Top concurrent upstream regulators were then matched to the top 1% of dysregulated genes across all six datasets. Top biomarker genes to emerge from this analysis included TCF3, CD44, MAPT, STK4, and TBX2, among others. Analysis of the top canonical pathways of implicated genes suggested their involvement in TGF-beta signaling, glucocorticoid receptor signaling, and acute phase response signaling.

These results suggest immune system dysregulation at the gene expression level among children with ASDs. This result bolsters work from other studies performed at the post-transcription, protein, hormonal, and tissue levels in implicating an association of immune system dysregulation with ASDs.

Anupriya Gogne   Research Advisor: Chella Kamarajan

Reduced P300 amplitude in individuals at high risk for alcoholism

Objective: Alcoholism has been considered to be part of a spectrum of disinhibitory disorders, with impulsivity being an important trait. Previous studies have shown a correlation between impulsivity and cognitive deficits in alcoholics and in offspring who are at high risk (HR) to develop alcoholism. Event-related potentials (ERPs) have been used as an effective tool to study cognitive deficits in these populations. Our objective in the present study was to investigate the P300 component of the ERP as well as impulsivity in high risk subjects with a heavy loading of family history of alcoholism using an auditory oddball paradigm.

Methods: Offspring from HR families (N=1785) from the multi-site Collaborative Study on the Genetics of Alcoholism (COGA) and offspring of low risk (LR) control families (N=152) were assessed with an Auditory Oddball Paradigm; P300 amplitudes to target stimuli were measured at midline frontal (Fz), central (Cz), parietal (Pz) and occipital (Oz) regions. Barratt Impulsiveness Scale (BIS) was used to evaluate impulsivity in subjects in both groups. Subjects were further grouped for gender and age (12-15 and 16-25 years).

Discussion: Younger HR subjects showed statistically significant lower P300 amplitudes in the posterior (Oz) region (p=0.042), while the older HR group had lower amplitudes in the central (CZ) region (p=0.033). Females showed higher P300 amplitude than males. Further, HR subjects showed increased impulsivity in all subscales and total BIS scores. Our results demonstrate significant cognitive deficits as reflected by lower auditory P300 amplitudes in subjects from HR COGA families, i.e. families that have a high density of alcoholism. The finding of higher P300 amplitudes in females compared to males is consistent with previous research in this area. Higher impulsivity in HR subjects further establishes the view that alcoholism and its vulnerability may be due to impulsivity and/or underlying neurocognitive disinhibition.

Diana Kurlyandchik   Research Advisor: Chinmoy Gulrajani

Gun violence, Mental Illness, and Public Policy - Where is a rational medium?

Following a number of mass shootings in the USA, the public has turned to the mental health field, demanding an explanation and an understanding, of whether there is an association between the mentally ill and violence. As a result of ongoing firearm violence, much attention has turned to the concept of restricting firearm access to those with mental health history. In the 15 months following the tragedy at Sandy Hook Elementary School in December 2012, there have been at least 66 gun bills introduced to limit gun ownership by individuals suffering from mental illness (Gold, 2013.) Proponents of such restrictions argue that the mentally ill have a higher risk of violence, and that restricting access will prevent such tragedies, in addition to a number of other firearm related suicides and homicides. Opponents of such gun policy dispute this, noting that implementing such laws will divert resources from more crucial preventative programs such as education and research, and will prevent clients from seeking help or from disclosing pertinent information, for fear of threatening confidentiality and interfering with the therapeutic alliance (Gold, 2013.) In this poster, we will debate both sides of this crucial public policy issue, in an attempt to stimulate inquiry and discussion. We also hope to heighten the public's awareness of firearm violence in general, which has accounted for over 250,000 deaths in the last 10 years, compared to 547 deaths in public mass shootings in the past 30 years in the United States. In 2010 alone, there were reported 31,076 firearm deaths in the United States, of which, 62% were suicides (Gold, 2013.) As gun legislature moves forward, it is crucial not to get lost in the sensationalism of mass murders, but to focus on education and prevention of this major public health issue.

Hemananda Muniraman   Research Advisor: Ivan Hand

Premedication practice prior to non-emergent intubation in the United States

Background: Premedication prior to elective intubation has been recognized to decrease adverse physiological effects associated with intubation. Despite this fact, a survey conducted in 2006 in the United States reported only 44% of neonatal units routinely use premedication before intubation. In 2010, an AAP clinical report recommended that except for emergent situations, premedication should be used for all endotracheal intubations in newborns.

Objective and methods: To ascertain the current practice of premedication prior to elective intubation and to assess for practice variation of premedication among different levels of neonatal units. An online survey based questionnaire on the current practice of use of drugs for premedication was distributed via e-mail to neonatologist members of the AAP.

Results: Responses were obtained from 693 neonatologists. 34% of the responders report frequently premedicating prior to intubation with significant variation among the neonatal units (46% among level 4 units and 27% in level 3 and 2 units) p=.000. 44% of responders report having a written protocol or guideline on premedication which significantly correlated with the use of premedication p=.000. Sedation with analgesia (38%) was the most common regimen used for premedication. About 25% of neonatologists report not being aware of the recent AAP policy statement on premedication whereas 33% report changing their practice on premedication following the AAP recommendations.

Conclusions: Despite a recent AAP clinical report recommending use of premedication prior to non- emergent endotracheal intubation, only one third of neonatologists report frequent use of premedication and less than half of the neonatologists have a written protocol on premedication. Our study shows a significant correlation between having such policy with use of premedication and also shows a significant difference in the use of premedication among the different levels of neonatal units.

Ramy Abdel-Naby   Research Advisor: Chongmin Huan

Extracellular signal-regulated kinase (ERK)-dependent p21 (WAF1/Cip1) expression is associated with gemcitabine resistance in pancreatic cancer cells

Introduction: Pancreatic cancer is among the leading causes of cancer-related death in part due to its chemoresistance. Understanding the mechanism of chemoresistance is needed to develop effective chemotherapy. Studies have shown that increased cellular ERK activity drives the chemoresistance to gemcitabine, the drug of choice for pancreatic cancer. Interestingly, ERK was found to transcriptionally upregulate p21 in multiple other cancers, and cytoplasmic levels of p21 determined cisplatin resistance in testicular cancer. This implies that p21 is a mediator of chemoresistance downstream of ERK. Therefore we investigated whether in pancreatic cancer cells p21 expression is regulated by endogenous ERK, and studied if this regulation is associated with gemcitabine resistance.

Methods: Human pancreatic cancer cell lines, PANC-1 and MIA-Paca-2 which respectively possess high and low levels of ERK-mediated gemcitabine resistance, were used in the study. The rat pancreatic tumor cell line, AR42J, was included for comparison. Cells were cultured with the ERK1/2 inhibitor PD98059 (15μM) for 24 to 48 hrs and cell lysates were prepared for the detection of p21 by Western blot. To test chemosensitivity, gemcitabine (0.04 mg/ml) was added to the culture with PD98059 for 72 hrs and surviving cells were quantified by measuring cellular dehydrogenase activity.

Results: Parallel to ERK, in PANC-1 and MIA-Paca-2 cells, p21 levels positively correlated with gemcitabine resistance. ERK inhibition reduced p21 expression and enhanced proliferation of PANC-1, MIA-Paca-2 and AR42J cells (p<0.05). Gemcitabine eliminated 50% more chemoresistant PANC-1 cells (p<0.05) when p21 was reduced via ERK inhibition.

Conclusion: ERK-controlled p21 expression is relevant to gemcitabine resistance in pancreatic cancer cells, supporting that p21 regulates chemoresistance downstream of ERK. Further studies may enable the development of new strategies to overcome the chemoresistance of pancreatic cancer.

Liye Zhou   Research Advisor: Mahmood Hussain

A Novel ELISA-based Method Assesses Differences in the Catabolic Rates of Human ApoA1 and ApoB between Healthy and CAD Patients

The LDL- and HDL-cholesterol concentrations are commonly used as indicators of coronary artery disease (CAD) risk. However, recent studies highlight the need for a method to assess lipoprotein functionality rather than concentrations. We hypothesized that clearance of lipoproteins from normal and CAD subjects might be dissimilar indicating functional and physiological abnormalities. To test this, we developed a simple, rapid method to determine catabolic rates of human apoB-(LDL) and apoAI-(HDL) lipoproteins in mice. Few microliters of human plasma were injected in normal, chow-fed, male C57BL6 mice. Human apoB and apoAI concentrations were measured in mouse plasma by ELISA, plotted against time, and half-lives were deduced using Prism. The half-lives of fresh normal plasma apoB and apoAI were 110 and 219 minutes, respectively. Storage at 4°C for one week increased apoAI half-life to 467 min; but 4 cycles of freeze-thaw had no effect. In contrast, storage at 4°C and repeated freeze-thaw reduced apoB clearance rates. Thus, both normal and patient plasma should be subjected to similar freeze-thaw cycles for comparisons.

Next, we compared the half lives of apoB and apoAI from three CAD [Male/Female 2/1; Age 68±8 years; Cholesterol 142±17 mg/dL; Triglyceride 144±31 mg/dL; LDL-C 93±15 mg/dL; HDL-C 27 mg/dL] with 4 normal [Male/Female 1/3; Age 48±15; Cholesterol 159±57 mg/dL; Triglyceride 144±136 mg/dL; LDL-C 118±41 mg/dL HDL-C 44 ±16 mg/dL] subjects recruited at the University Halle, Germany during 2008-2010 . Half-lives of apoB (57±8 min vs. 0.66±0.15 min, p=0.0025) and apoAI (318.1±17.6 min vs. 78.8±14.1 min, P=0.0024) from CAD subjects were significantly shorter indicating for their faster clearance. It is likely that this method might be useful in routine screening and early-stage diagnosis of CAD. Further studies are needed in a bigger cohort to investigate by which mechanisms plasma lipoproteins from CAD subjects are cleared faster.

Hui Jiang   Research Advisor: Xian-Cheng Jiang

Phospholipid transfer protein (PLTP) deficiency in adipose tissue decreases plasma high density lipoprotein levels

Objectives: Adipose tissue is abundantly expressing phospholipid transfer protein (PLTP), and dysfunction of adipose tissue is associated with cardiovascular disease, diabetes, and obesity. The effect of PLTP adipocyte deficiency in the plasma lipid metabolism and nascent HDL production was examined.

Methods and Results: We took advantage of Cre-loxP system by crossing PLTP-Flox mice to adipocyte protein 2 (aP2)-Cre transgenic mice and created PLTP-Flox/aP2-Cre mice. We found that there are a 90% and a 50% reduction of PLTP mRNA levels in adipose tissue and macrophages, respectively. Moreover, aP2-Cre-mediated PLTP deficiency in mice significantly decreases plasma PLTP activity (22%), cholesterol (21%), phospholipids (20%), mainly on high density lipoprotein (HDL), and apoA-I (35%).

To eliminate the effect from macrophages, we transplanted bone marrow cells from wild type mice to lethally irradiated PLTP-Flox/aP2-Cre mice and PLTP-Flox mice and created adipose tissue-specific KO (WT to PLTP-Flox/aP2-Cre) and control (WT to PLTP-Flox) mice. Theadipose tissue- PLTP KO mice also showed significant reduction of plasma PLTP activity (19%), cholesterol (18%), phospholipids (17%), and apoA-I (26%) levels.

To further investigate the mechanisms, we cultured epididymal fat pats from PLTP-Flox/aP2-Cre and control mice. The apoA-I-mediated cholesterol efflux from the explants was monitored with or without recombinant PLTP. We found that recombinant PLTP significantly increases cholesterol efflux from control or PLTP KO adipose tissue explants. Moreover, PLTP KO adipose tissue explants have significantly less ability for cholesterol efflux than that of controls.

Conclusions: PLTP in the adipose tissue played a minor but significant role PLTP activity in the circulation and in plasma HDL production via promoting cholesterol efflux from adipose tissues.

Kanwaljit Brar   Research Advisor: Rauno Joks

Association of bathing habits to pruritis and allergic disease.

Rationale: Traditionally, physicians caring for patients with pruritis have advised limiting bathing frequency and bathing time. We have anecdotally found in our patient population, comprised primarily of people of Afro-Caribbean descent, that frequent baths are common cultural practice thought to stave off heat in the tropical climate. In the cooler climate of Brooklyn, we have anecdotally found these continued habits lead to pruritis and xerosis.

Methods: IRB approval was obtained. Patients were asked to complete a survey of demographic information as well as information related to bathing habits, medical history, and environmental history. Pruritis was measured using a 5-D itch scale, a validated tool used to measure pruritis.

Results: Seventeen patients were recruited into the study. Among the 17 patients, 16 (94%) were female. Eleven patients (65%) were originally from outside the United States, originating from the Caribbean Islands, or South America. Fifteen (88%) patients reported taking showers only, with only 1 patient (1%) taking a bath only, and 1 patient (1%) taking both. Twelve patients (71%) reported the present of concomitant allergic disease, such as asthma, allergic rhinitis, or urticaria. Average bath exposure time was 34 minutes. Patients who had a bath exposure time of 10 minutes or less had a mean pruritis score of 10, as compared with patients who had a bath exposure time of 10 minutes or more who had a mean pruritis score of 12.75

Discussion: We report preliminary findings of this first study to evaluate bathing habits as they relate to patient complaint of pruritis. Bath exposure time is a novel method of quantifying bathing duration and bathing frequency of patients. The study did not include a correlation with bath exposure time and pruritis score; the findings are limited by the small sample size. This is an ongoing study.

Edward Kleiman   Research Advisor: Rauno Joks

Effect of Duration of Residence in Brooklyn on IgE responses of Immigrants

Rationale: Inner city areas including Brooklyn, New York suffer disproportionately from allergies and asthma. Brooklyn has ongoing immigration from regions of low allergy/asthma prevalence; currently about 40% of Brooklyn residents are foreign born. We previously reported that ethnicity and history of hepatitis and other infections significantly affected development of new asthma and seasonal allergies in immigrants to Brooklyn. Whether residence in Brooklyn is associated with increasing IgE response has not been determined.

Methods: Immigrants to Brooklyn (n-298) were interviewed about early life living conditions, previous infections, and total IgE (fluoroimmunoenzymeassay), and HSV1 (ELISA) were determined. A generalized linear regression model was constructed, with dependent variable log10 (total IgE). Predictors were history of hepatitis, Herpes simplex 1 IgG, number of children in house, age, sex, rural/town/city and region of origin (4 groups). Tests of utility of polynomial terms in continuous predictors were conducted. Model residuals were examined for skew and for outliers. Model-generated means with standard errors are reported. Analysis of effect included generation of Chi-Square value and degrees of freedom in order to determine significance.

Results: While IgE levels decreased with increasing age, residence in Brooklyn was associated with annual increases in serum IgE (p=0.0003 and 0.016, respectively).

Each additional year of age decreases IgE by 2.0% (95% CI 0.5, 3.1). Each additional year in Brooklyn increases IgE by 1.5% (95% CI 0.3, 2.6). No other predictor was significantly associated with IgE (p=ns).

Conclusions: The decline in IgE levels with age is countermanded by local immune stimuli which stimulate development of IgE responses in previously non-allergic immigrants residing in Brooklyn. These local stimuli may contribute to initiation and persistence of allergic disorders/asthma in immigrants.

Edan Sarid   Research Advisor: Rauno Joks

Targeted Intervention in Adult Patients at risk for Non-Adherence with Asthma Therapy in an Inner City Cohort

Rationale: Non-adherence to prescribed medications contributes to the high prevalence and significant morbidity and mortality of asthma in inner city adults. By measuring risk of non-adherence through the Adherence Estimator (AE) (Merck), we investigated the effects of targeted intervention using the three parameters of concern, commitment and cost.
Methods: We collected AE scores for outpatient adults with persistent asthma treated in our allergy and asthma clinic. 32 patients were included in the study, 13 were found to be at-risk and received targeted intervention and 28 were available for follow up. The AE is a questionnaire that assigns a weighted numerical score for concern regarding medication harm, commitment based on perceived need of medications, and financial burden due to out of pocket expenses. Patients at risk for non-adherence received counseling regarding their specific risk and received a written informational sheet including basic information and resources for the patient. At 30-60 days after the intervention the patients were reassessed with the AE.
Results: There was a significant decrease in total AE score between visit one (mean=11, median=11) and visit two (mean=5, median=0) in patients found to be at risk for non-adherence (p=0.004). There was a significant decrease in patients non-adherent due to concerns about their medication from visit one (mean=8, median=7) to visit two (mean=3, meadian=0) (p=0.008). Decreases in non-adherence due to commitment and cost were not statistically significant.
Conclusions: The risk for problems in asthma medication adherence decreased significantly after targeted intervention addressing specific variables that were identified by the AE. Our findings suggest that the AE may be useful in identifying problematic areas in patients at risk for non-adherence. Targeted intervention may significantly curb patients at risk for non-adherence and improve overall morbidity and mortality in the inner city population.

Helen Zhou   Research Advisor: Rauno Joks

Seasonal Increase in Angioedema in an Inner-City Hospital Center

Rationale: Previously, our group was able to find a statistically significant seasonality in the presentation of angioedema a predominantly African American cohort. However, the cause for this seasonality has yet to be found.
Methods: An IRB approved retrospective EMR chart review was conducted of pediatric and adult patients treated in the emergency department or as an inpatient at Kings County Hospital Center for angioedema, from January 2007 to July 2012. The dates of occurrence of angioedema were obtained in order to determine whether there was a seasonal distribution in presentation and further chart review for the cause of angioedema was undertaken.
Results: We reviewed the charts of 108 patients (73 women, 35 men, mean age 56 years) who were diagnosed with angioedema and presented in either the summer months of June, July, and August, or the winter month of January. Upon identifying causes of angioedema, 78 were attributed to medications, 17 were attributed to foods, and the remaining 13 cases had unknown causes. Of these, 12 (11%) occurred during the summer months.
Conclusions: While there is no difference in presentation of angioedema caused by medications or foods between the summer and winter months, there was a third group where the cause was unidentified. All but one of these unexplained cases occurred during the summer months, and the underlying pathogenesis is yet to be found.

Zerin Kashem   Research Advisor: Michael A. Joseph

Promoting Preconception Health by Recruiting and Training High School Students

Brownsville had the second highest infant mortality rate (7.4 per 1,000) from 2010-2012 among all Brooklyn, NY community districts; a rate that is considerably higher than that of NYC (4.8) as a whole. Preconception health encourages women to engage in healthy lifestyles before they become pregnant. Based on a model developed by the Office of Minority Health, the Brooklyn Perinatal Network designed a Preconception Peer Educator (PPE) program at a high school in Brownsville that recruits high school students to serve as peer educators and mentors for other students within their schools and in the community. We sought to evaluate the effectiveness of this PPE program on the knowledge of preconception health among high school students. High school students (n=7) participated in a three day interactive training session conducted at the school that provided information on healthy eating and active living as well as on the effects of tobacco and drug use during pregnancy. Each training session provided factual information regarding preconception health in the form of handouts, skits, role-play, discussions, and exercises. A pre-post survey design was used to assess changes in students' knowledge before and after training. Scores improved significantly (p < 0.05) from pre-training (38%) to post-training (78%). Additionally, students expressed a high degree of satisfaction in the curriculum content and delivery. While our results indicate improved knowledge of preconception health, routine PPE training sessions and evaluations with larger cohorts of high school students are warranted to assess the acceptability and feasibility of our approach over time.

Ho Ki Mok   Research Advisor: Michael A. Joseph

Financial Strain and Depression in a Sample of Heterosexual Black Men in Brooklyn, New York

Black men in the U.S. have a high level of untreated depression. Past studies of Black men have focused on income and employment status as risk factors for psychological distress, with mixed findings. These studies have not focused, however, on the more proximal determinant of perceived financial strain. We present preliminary baseline data collected as part of an HIV risk reduction program for at-risk heterosexual Black men. Between 11/12-11/13, 141 men were recruited from 12 barbershops in Brooklyn, NY. Financial strain measured men's perception of the degree to which they had adequate money for (1) food, (2) medical care, (3) bills and (4) making ends meet. Responses across all four questions were collapsed to form a dichotomized variable of financial strain such that one group contained men who reported no financial strain across all four categories, and the other group contained men reporting financial strain across any of the categories. Symptoms of depression were assessed using the PHQ-9. Almost all (92%) reported experiencing financial strain and 15% were classified as having depression (PHQ-9 > 7). In a multivariable linear regression model, men experiencing financial strain had marginally higher depression scores than men not experiencing financial strain (p= 0.079), after controlling for insurance and income. In this population, a high prevalence of financial strain and depression was found, indicating a strong need for focused interventions to screen for and support treatment of mental illness in under-resourced areas.

Daniel Anikwue and Alison Seales   Research Advisor: Mary Valmont

Strategies Used by Black, Inner-city Cardiac Surgery Patients to Cope with Health-Related Stress

Background: Over the past two decades, the number of cardiac procedures increased by nearly 70% in the United States. Many patients preparing to undergo cardiac surgery (CS) are often stressed due to the invasiveness of the procedures. Studies show that over a quarter of the black patient population suffer from depressive symptoms before and after CS. The coping strategies of this patient population are not yet well understood.
Objectives: To determine the coping mechanisms of the patient population and to quantify the uses of adaptive and maladaptive coping mechanisms among these patients.
Methods: This project is a retrospective analysis of a larger study. Twelve to 24 hours before CS, 20 patients were administered the Brief Cope, which determines coping mechanisms used when stressed. The Brief Cope consists of 28 questions separated into 14 dimensions. Each dimension is deemed adaptive or maladaptive. Responses range from "Never Used" to "Often Used." Descriptive statistics determined the four most and least frequently used coping mechanisms. Also, the uses of adaptive versus maladaptive coping mechanisms were compared.
Results: The most used coping strategy was Emotional Support (Mean= 6.50) and Acceptance (Mean= 6.50) followed by Positive Reframing (Mean= 6.30). The next most used adaptive strategy was Religion (Mean= 6.20). The least used coping strategy was Substance Use (Mean= 2.30) followed by Behavioral Disengagement (Mean= 2.5), Self-Blame (Mean= 3.20) and lastly, Venting (Mean= 3.35) . The seven most used coping strategies were all adaptive whereas the six maladaptive coping strategies comprised the least used strategies with Substance Use being the rarest
Conclusion: Findings of this study suggest that while adaptive coping strategies are used by patients, a substantial proportion nonetheless use methods that are dysfunctional (i.e. maladaptive). Further data is needed to improve the precision of our estimates and to permit hypothesis testing about the association between coping strategies, adherence, and clinical outcomes after CS.

Amna Hussain and Cassandra Saint Louis   Research Advisor: Mary Valmont

Probiotics Role in Influencing Levels of Indoxyl Glucuronide for Dialysis Patients

Background: Chronic Kidney Disease (CKD) is a serious illness that hinders proper kidney function and eventually progresses to End-Stage Renal Disease (ESRD) in which patients undergo hemodialysis to replace the kidneys function of filtering blood. Indoxyl glucuronide (IG), a uremic toxin beneficial in precise amounts, accumulates to high levels in the blood requiring hemodialysis treatments. RenadylTM is a probiotic supplement shown to significantly reduce levels of toxic metabolites in ESRD patients.
Objectives: 1) to compare our sample mean IG level to the U.S ESRD population; 2) to determine if length of time on dialysis affects IG levels; and 3) if patients with lower IG levels before treatment show the least change in IG levels after treatment.
Methods: IG levels pre- and post-probiotic treatment were taken from thirteen ESRD patients. Simple linear regression and correlation determined the strength and direction between variables. A Student's T-test compared our sample mean IG levels to the US ESRD population.
Results: There was a weak negative correlation between time spent on dialysis and baseline IG levels (R^2= 0.219, p= 0.11). There was a negative correlation between baseline levels and IG change (R^2= 0.762, p= .002). These equations describe the relationship between variables: Baseline IG = 0.761+ 0.214 x Time on Hemodialysis, and Change in IG levels = 0.372+ 0.515 x Baseline IG. Also, there was a significant difference between our samples' mean IG levels and the overall ESRD patient population (Student's t-test: t= 39.28, df=12, 95% CI (0.59, 0.94), p<0.001).
Conclusion: The African-American/Afro-Caribbean population is known to have a high prevalence of CKD and ESRD, which was also evident in our sample population; however, our sample had lower IG levels than the general population. Determining the relationship between IG and the three variables, doctors and patients will better understand the role of probiotics in the progression of CKD.

Yadiry Lagombra, Ehijie Ine and Jameela Harrington   Research Advisor: Mary Valmont

**The Effects of Anxiety and Depression on Behaviors and Attitudes toward Adherence to Treatment
in End-Stage Renal Disease Patients**

Background: End Stage Renal Disease (ESRD) affects approximately 500,000 US adults, with the greatest prevalence in Blacks, Hispanics, and the elderly. ESRD treatment includes hemodialysis three times a week, medications, and dietary restrictions. Non-adherence to ESRD treatment may result in hospitalization, and ultimately death. The effects of psychosocial factors such as anxiety and depression affects adherence to ESRD treatment.
Objective: To determine whether high anxiety and depression are related to decreased treatment adherence in ESRD patients in a predominantly Black patient-population.
Methods: We utilized data collected by our mentors on psychosocial factors and treatment adherence from 57 ESRD patients at SUNY Downstate's Parkside Dialysis Center. Patients were given a series of surveys measuring the relationship between anxiety and depression levels and adherence to treatment (e.g., fluid intake). Scores from the Beck Anxiety Inventory and the Beck Depression Inventory measured psychosocial impact. The ESRD Adherence Questionnaire (ESRD-AQ) provided composite scores for behaviors and attitudes toward adherence. A median split of all scores categorized respondents as high, or low/moderate anxiety, depression, and adherence - both attitude and behavior. An Odds Ratio was determined whether anxiety and depression levels affected patients' attitudes and behaviors toward adherence.
Results: Of 57 respondents, 16% showed below median adherence, 51% had higher anxiety levels and 56% had higher depression. Patients with high anxiety have 25% increased odds of low behavior adherence. Patients with low depression have four times greater odds of low attitude adherence. No statistically significant association exists between anxiety and attitudes adherence, or depression and behavior adherence.
Conclusions: Results supported our hypothesis that anxiety and depression play an important role in self-reported adherence behaviors and attitudes to ESRD treatment.

Genesis Smith, Andre Fouchong and Likowsky Desir   Research Advisor: Mary Valmont

The Impact of Experiencing Side Effects on Asthma Control

Background: Approximately 16.3% of residents in North and Central Brooklyn are diagnosed with asthma. Non-adherence to inhaled corticosteroid therapy, which is the main treatment, is a major issue among patients; leading to four times as many hospitalizations and five times as many deaths in blacks than whites. Non-adherence can be attributed to barriers such as misunderstood instructions, medication cost or potential side effects.
Objective: To determine if there is a relationship between experiencing side effects of asthma medication and asthma-symptom control in an inner city, black patient population.
Methods: A self-developed survey on asthma medication side effects was administered to 32 asthma patients from SUNY Downstate Medical Center (19 adults, 13children), along with two standard asthma questionnaires, the Adherence Estimator (AdEstTM), Merck, Inc., and the Asthma Control Test (ACTTM). Average ACT scores of patients who experienced side effects and those who did not were compared using an Independent Samples Student's t-test.
Results: Sixty-nine percent of the sample population reported not experiencing side effects, and received a mean ACT score of 18.86 ± 5.592. Those experiencing side effects had a mean ACT score of 12.4 ± 4.7. Patients who reported not experiencing side effects scored, on average, 8.31 points higher on the ACT test than patients who experienced side effects (Independent Sample t-test: $t = 3.175$, $df = 30$, 95%CI (2.79, 10.71), $p = .003$).
Conclusions: Patients who experienced side effects did not have their asthma as well controlled as those who did not, supporting our hypothesis. These results give insight into how experiencing side effects can affect a patient's asthma adherence and control. Future and expand research results may aid doctors in tailoring their approach to patients, especially to the African-American/Afro-Caribbean population, concerning medication pros and cons.

Jinyang Liu   Research Advisor: Ira S. Kass/Daisy Lin

The Effect of Sevoflurane on: Learning/Memory and Long-Term Potentiation

Volatile anesthetics impose risk to learning/memory behavior in neonatal and elderly patients. Evidence supporting the underlying mechanisms has started to emerge, however our knowledge is inadequate. We investigated sevoflurane (sevo), a commonly used volatile anesthetic. This study examines (1) the effect of neonatal sevo exposure on adolescent learning/memory behavior and its associated molecular mechanisms, (2) the effect of sevo on long-term potentiation (LTP) in hippocampal slices.

The active place avoidance test was used to study spatial learning abilities of adolescent mice (P27-P28) anesthetized with sevo neonatally (P7). The data showed that sevo treated mice had significantly more entries into the shock zone compared to control mice (no sevo). Hippocampal tissue was taken from these mice at adulthood and analyzed for gene expression changes. We examined two genes associated with the molecular mechanisms underlying learning and memory, mTOR and PKMζ. Our western blot hybridization analysis showed that sevo treated mice had significant decreases in both mTOR and PKMζ expression compared to untreated mice.

LTP was induced by high frequency stimuli (HFS), and field excitatory postsynaptic potentials (fEPSPs) were recorded in the hippocampal CA1 region. If sevo was present before, but not during the HFS there was no difference between the fEPSP slopes of the sevo and untreated slices, both showed robust LTP. However if sevo was present during the HFS, then fEPSP slope was significantly decreased in the sevo treated slices.

Our data suggest (1) sevo exposure during the neonatal period impairs learning/memory behavior during adolescent, a potential mechanism that involves the regulation of mTOR and PKMζ expression, (2) Sevo can block the formation of LTP if it is applied during the HFS, but if it is washed out before the HFS it does not alter LTP. This suggests that sevo has no persistent effect on synaptic plasticity in hippocampal slices from adult mice.

Kobkul Chotikanatis   Research Advisor: Stephan Kohlhoff

In Vitro Tumor Necrosis Factor Alpha responses to Chlamydia pneumoniae infection of PBMC from Asthmatic Children

Background: Infection with Chlamydia pneumoniae (Cpn) can lead to exacerbations of asthma. Cpn can also cause persistent infection, to which asthmatics may be more susceptible. Innate immune responses may have a significant role in susceptibility to persistent Cpn infection. There are no data on innate cytokine responses such as TNF-α in persistent Cpn infection in asthmatics.
Objective: To study the innate immune responses to persistent Cpn infection in asthmatics and non-atopic healthy controls.
Methods: Peripheral blood mononuclear cells (PBMC) from stable allergic asthmatics (n=17) and healthy non-atopic controls (n=9) were mock infected or infected with Cpn AR-39 at MOI of 0.1 and cultured up to 10 days. TNF-α and interferon gamma (IFN-g) were assayed in supernatants by ELISA. Cytokine levels of uninfected were subtracted from those of infected PBMC in each subject. Quantitative PCR for Cpn was performed on nasopharyngeal swabs. Suggestive evidence of persistent Cpn infection was a presence of Cpn- specific effector memory T lymphocyte response (INF- g) and no Cpn DNA detection.
Results: None of subjects had Cpn DNA detected. 59% of asthmatics had suggestive evidence of persistent Cpn infection compared to 0% of healthy controls (p=0.012). In vitro Cpn-induced production of TNF-α was found in 30% of asthmatics with characteristics suggestive of persistent Cpn infection compare to 77.8% of healthy controls (p=0.037).
Conclusion: Suggestive evidence of persistent Cpn infection is associated with diminished Cpn-induced innate cytokine responses in asthmatics. TNF-α may play a critical role in increased susceptibility to persistent Cpn infection in asthmatics. This could be explained by its contribution to intracellular killing of Cpn or interaction with adaptive immune responses.

Aviva Szigeti   Research Advisor: Stephan Kohlhoff

Seroprevalence of C. trachomatis in a pediatric population - implications for vaccine development

Background: Prevention of Chlamydia trachomatis (CT) genital infection is an ideal application for a vaccine program. Similar to the HPV vaccine, immunization with a future CT vaccine would ideally be before infection is acquired. However, there are no current epidemiologic studies of CT infection in children since universal screening and treatment of pregnant women was implemented in the U.S. in 1993.
Objective: To determine current seroepidemiology of CT infection in children.
Methods: Anonymized serum samples were obtained from a pediatric population (0-20 years) in two hospitals in Brooklyn, NY, during 2013. IgG antibodies to CT were determined using microimmunofluorescence (MIF), (Ani Labsystems, Finland). The following age strata were used: <1, 1-3, 4-6, 7-9, 10-12, 13-15, 16-18, 19-20 years (y) of age.
Results: A total of 316 sera were obtained from 316 children; the mean age was 10.9 y and 49% were male. The seroprevalence of anti-CT IgG antibody in infants <1 year was 22.2% (4/18). No antibody was detected in children 1-15 y (0/204), but the seroprevalence was 6.7% (7/104) for children 16-20 y. CT antibody was only found in females >1y. Overall seroprevalence of CT in hospitals 1 and 2 was 1.9% and 5.1%, respectively. The cumulative probability of infection by age 20 years was 12.5% (95% CI 3.1%, 38.6%).
Conclusions: The high prevalence of anti-CT antibodies in infants < 1 y likely represents maternal IgG, as supported by its disappearance after one year of age. Overall seroprevalence in this study is lower than that reported in historic cohorts from the 1980s (prior to universal screening in pregnancy) as well as current data reported from high risk populations. Post-infancy, antibodies are not detected until ≥16 years of age, suggesting it is related to the onset of sexual activity. These data are critical in informing potential CT vaccine strategies, especially the timing of a primary vaccine series (i.e. prior to acquisition of CT infection).

Rafael Flores-Obando   Research Advisor: Charles Abrams

The roles of mutations in connexin47 (Cx47) in myelinating cells of the central nervous system (CNS)

Connexin47 (Cx47) forms homotypic gap junction communication channels between oligodendrocytes (OLs), the myelinating cells of the CNS and can form heterotypic channels with Cx43 expressed in astrocytes. Pelizaeus-Merzbacher-like disease 1 (PMLD1) arises in patients with mutations in GJC2, encoding Cx47; PMLD1 causes nystagmus, cerebral ataxia, and spasticity within the first 6 years of life. One mutation (p.Ile33Met) has been associated with a much milder phenotype - hereditary spastic paraplegia type 44 (SPG44). In cell lines, PMLD1 mutants such as Cx47P87S cause defective protein trafficking, intracellular retention in the endoplasmic reticulum (ER) and loss-of-function, but these studies have not been conducted in OLs, where ER retention of Cx47 mutant protein could lead to cell type-specific cellular stress, activation of unfolded protein response (UPR) pathways and apoptosis. We hypothesize that mutations in Cx47 associated with severe phenotype (Cx47P87S) cause toxic gain of function compared to the milder Cx47I33M mutation. To this end, we have optimized the isolation and culture of primary OLs from neonatal Cx47 knockout pups using immunomagnetic beads. OLs were lentivirally transduced to express Cx47WT and mutants. Next, the pattern of expression of Cx47WT and mutants was determined by immunofluorescence (IF) staining where Cx47P87S showed diffuse cytoplasmic staining compared to the puncta staining of Cx47WT. Conversely, Cx47I33M exhibited puncta staining similar to that of Cx47WT. Next, the subcellular localization of Cx47 mutants was determined by IF staining for Cx47 and ER resident chaperone Grp94 showing that Cx47P87S staining colocalized with Grp94 as compared to Cx47WT and Cx47I33M. These results indicate that in primary OLs Cx47P87S but not Cx47I33M protein is retained intracellularly, specifically in the ER. Ongoing studies will determine if ER retention of Cx47P87S activates the UPR pathway and apoptosis in primary OLs.

Eli Lazar   Research Advisor: Richard Kollmar

Extracellular Activity of the Superior Laryngeal Nerve in the Rat

Our aim was to test the feasibility of extracellular recording from the superior laryngeal nerve (SLN) in the rat and to relate SLN activity to breathing. Access to the SLN is technically difficult due to its anatomical location at the base of the rat skull where it splits from the vagus nerve right after its emergence from the skull. In two deeply anesthetized rats, the SLN was surgically isolated. Extracellular nerve activity was recorded from the SLN in conjunction with thorax motion. Data was acquired with Spike2 software at a sampling rate of 2 kHz for 10 minutes. The raw SLN recording revealed pulsatile nerve activity in synchrony with thorax motion. Power-spectrum analysis of the full-wave-rectified envelope revealed that SLN activity and thorax motion had a an identical mean frequency of 1.6 Hz. Plotting the normalized SLN activity against thorax motion revealed that the two were nearly completely out of phase. Peak thorax expansion corresponded to troughs of SLN activity and vice versa. Cross-correlation analysis revealed that maximum SLN activity lagged behind maximum thorax expansion by 246 ms or 143 degrees. We concluded from these results that the SLN is maximally active near the end of thorax contraction or the end of expiration. According to most textbooks, the SLN innervates the cricothyroid muscle, which tenses the vocal folds, leading to adduction towards the end of expiration. Recent evidence, however, suggests that the SLN also innervates other laryngeal muscles, such as the thyroarytenoid (adductor) and posterior cricoarytenoid (abductor), that receive their primary innervation from the recurrent laryngeal nerve (RLN). This may explain why damage to the RLN does not necessarily lead to complete vocal-fold paralysis. Having established in this study a procedure to record from the SLN, a more difficult target than the RLN, we are now in the position to carefully investigate patterns of laryngeal reinnervation by either nerve upon RLN injury.

Ayush Sutaria   Research Advisor: Richard Kollmar

The Optimal Recurrent Laryngeal Nerve Crush in the Rat, and Spontaneous Recovery

A major complication of thyroid surgery is unilateral vocal-fold paralysis from trauma to the recurrent laryngeal nerve (RLN). The injury to the RLN leads to a unilateral vocal-fold paralysis: loss of tone in the intrinsic muscles of the larynx causing a bowing of the vocal folds, lack of glottic closure, dysphonia, dyspnea, and a risk of aspiration. Current treatments for RLN injury restore muscle tone, but reinnervation is inefficient and takes many months. With incomplete recovery, purposeful movement of the vocal folds and complete glottic closure are not restored due to aberrant reinnervation and synkinesis. However to test treatment options initially a proper RLN crush had to be established.

Before performing surgeries where the RLN was crushed, recordings of the rats using multiple modalities had to be done. A program on matlab was created that would record the EKG, the air flow rate using a plethysmograph, the chest wall expansion using a voltage rubber band, and the vocal fold motion using a pediatric laryngoscope attached to a video camera all in unison. These recordings were done on rats with the use of 4 different anesthetics due to the different effects of anesthetics on breathing patterns. Once sufficient recordings had been recorded, RLN crush surgeries were performed and recordings were repeated a week post surgery. Next the rats were euthanized with euthasol and perfused with formalin. The larynx, trachea and esophagus were dissected out to be cut and stained for histology to determine the severity of the crush and regeneration. Due to the very long protocol for each rat, there was only enough time to perform 5 RLN crush surgeries. From the dissection of the larynx, trachea and esophagus, measurements and observations of the anatomy of the rat were obtained.

Aryeh Dienstag   Research Advisor: Vilayannur Rao

Clozapine Induced Cardiomyopathy - a Case Report and Literature Review

Case: Our patient was a male in his late 20s with a history of schizophrenia. He was brought in by EMS to our hospital with a fever, tachycardia, head, neck and chest pain. He became unresponsive in ED and was admitted to the medicine service for a workup of FUO. The patient had been started on clozapine 2 weeks prior to admission and titrated up to 250mg daily. After all standard investigate procedures had been negative - it was noted that patient was tachycardic and displayed some minor irregularities on EKG, including PVCs and QTc elongations. A cardiology consult was called and an echocradiorgram showed 15% ejection fraction. The patient was started on ACE inhibitors and beta blockers and clozapine therapy was switched to olanzapine. Subsequent to stopping clozapine, the patient needed to be involuntarily admitted to a psychiatric inpatient unit.

Discussion: A review of the literature examining reports from 1970 to 2004 of cardiac side effects in patients on clozapine concluded that clozapine is associated with a low risk (0.015%-0.188%) of potentially fatal myocarditis or cardiomyopathy (Merrill 2005). Clozapine induced cardiomyopathy is typically of the dilated type and sinus tachycardia may be accompanied by fatigue, dyspnea and tachypnea. EKG are typically non-specific. A cardiomyopathy is confirmed by an echocardiogram and should lead to prompt discontinuation of clozapine (Nielson 2013).

The leading hypothesis is that of an IgE-mediated hypersensitivity reaction. Supported by observations of peripheral eosinophilia and eosinophilic inclusions within endomyocardial biopsy samples of affected patients (Layland 2009). Clozapine related cardiotoxicity remains difficult to diagnosis as many of its manifestations -particularly fever, tachycardia, and fatigue- are common during clozapine titration. Fever occurs in 20% of the patients commencing treatment with clozapine and is considered a "benign, self-limited phenomenon" (Merrill 2006).

Michael Maloney   Research Advisor: Ketan Shevde

Myoclonal and Hypertensive Response to Etomidate during Induction of Anesthesia

Objective: The purpose of the initial study was to compare the hemodynamic response to induction of anesthesia with etomidate in hypovolemic vs. normovolemic ASA 3 and 4 patients.

Background: Etomidate is used for induction of anesthesia in cardiac patients because of its reputation as a stable hemodynamic agent. Myoclonal activity is a well-documented side effect of the drug. We developed an IRB-approved study to validate etomidate's hemodynamic profile in hypovolemic ASA 3 and 4 patients. We terminated the study after three of the first four enrolled patients developed adverse reactions.

Methods and Results: Patients were induced with etomidate pretreated with lidocaine. Because the pure effects of etomidate were under investigation, no additional general anesthetic agents were used for induction. As per an IRB-approved protocol, we planned to monitor hemodynamics for a 6-minute period following etomidate administration, after which other drugs would be given and the patient intubated. Three out of four patients developed severe myoclonal activity and hypertension, and two of these patients became tachycardic. This called for deviation from the protocol, as patients required immediate administration of muscle relaxant and general anesthetics.

Conclusion: Etomidate may possess inherent hypertensive and tachycardic properties in ASA 3 and 4 patients, in addition to previously documented myoclonal activity. To mitigate myoclonus and an elevated hemodynamic response, we recommend that etomidate be used in conjunction with muscle relaxant and additional general anesthetic agents for induction.

Ryan Mooney   Research Advisor: Erich Lang

Secondary Pelvic Congestion Syndrome: Description and Radiologic Diagnosis

Introduction and objective: Pelvic Congestion Syndrome (PCS) is an often under- and misdiagnosed condition of the pelvic venous system leading to nonspecific pelvic pain that was initially described in females alone. Our primary aim was to describe our findings of Secondary PCS as a distinct entity from Primary PCS in that it has an identifiable vascular etiology and is gender nonspecific. We also aimed to assess the adequacy and reliability of late-arterial phase CT Urography (CTU) as the initial imaging modality in diagnosing and evaluating Secondary PCS.

Methods: We retrospectively reviewed 59 patients with PCS, 36 males and 23 females ages 24 to 63, from 2000-2011. To maximize opacification, CTU images were taken in the late-arterial phase with a 35-50 second delay after contrast administration.

Results: Review of our cases revealed multiple etiologies for PCS, including: Nutcracker syndrome (19 cases), cirrhosis (17), retroaortic left renal vein (11), tumor thrombosis of the IVC (5), portal vein thrombosis (4), renal cell carcinoma with left renal vein thrombosis (2), and left kidney AVF (1). The most common symptom was unexplained chronic pelvic pain. The patients in our series had clearly identifiable vascular flow abnormalities leading to the development of PCS, and were therefore diagnosed as having Secondary PCS. All cases were easily identified utilizing CTU to visualize and measure dilation of the left gonadal vein and pelvic varices. This modality also proved valuable in the identification and management of the various underlying causes of Secondary PCS.

Conclusions: Secondary PCS is distinct from Primary PCS in that it arises from clearly identifiable vascular flow abnormalities and occurs in both males and females. The diverse set of underlying etiologies, as well as the resulting congested varices, can be reliably and adequately visualized using CTU as the initial imaging modality.

Andrew Beck   Research Advisor: Jason Lazar/Louis Salciccioli

Determinants of the Blunted Carotid-Radial Pulse Wave Velocity Decline to Hyperemia in Patients with Congested Heart Failure

Carotid-radial pulse wave velocity (PWV) decreases during hyperemia induced by upper arm occlusion in healthy subjects. This decrease is blunted in patients with congested heart failure (CHF). This hyperemic response has been proposed as an indicator of vasodilation reserve and possibly endothelial function. The determinants of the blunted response in CHF are unknown. We investigated the contributing factors to this blunted response in CHF.

57 patients (61±14 years old) with clinically stable CHF were studied. Patients on dialysis, with inability to obtain PWV, or a non-sinus rhythm were excluded. Demographics and clinical variables were obtained by interview and chart review. Ejection fraction (EF) was measured via echocardiography. Baseline blood pressure was measured. Baseline pulse wave velocity (PWV) and augmentation index (AI) were measured using SphygmoCor. Upper arm occlusion was applied for 5 minutes by Hokanson inflator, with cuff pressure held 50 mmHg above the systolic pressure. Hyperemic PWV was measured 1 min post cuff deflation. Percentage change of PWV (hyperemic PWV-baseline PWV)/baseline PWV) was calculated and correlated with clinical variables, augmentation index (AI) and level of serum brain natriuretic peptide (BNP).

The hyperemic change of PWV significantly correlated with age (r= 0.36; p=0.006), systolic blood pressure (r=0.55; p<0.001), BNP level (r=0.29; p=0.03), New York Heart Association classification (r=0.27; p=0.04) and baseline PWV (r= -0.31; p=0.02), but not with EF (r=0.14; p=0.32) or AI (r=0.17; p=0.23). Multivariate analyses demonstrated systolic blood pressure (r= 0.46; p<0.001) and baseline PWV (r= -0.29; p<0.01) to be independent predictors of the hyperemic response, with a trend found for BNP level (r= 0.20; p=0.09).

Systolic blood pressure and baseline PWV are independent predictors of a blunted hyperemic PWV response in CHF. Elevated BNP levels may reflect abnormal vascular reactivity and merits further study.

Shahid Khan   Research Advisor: Jason Lazar/Louis Salciccioli

Comparison of Macrovascular and Microvascular Responses Evaluated by Hyperemia and Passive Leg Raising in Diabetic Patients

Diabetes mellitus impairs macro- and microvascular function. Flow-mediated dilation (FMD) of the brachial artery (BA) post upper arm occlusion evaluates macro function. BA occlusion induces distal microvascular dilation, which upon deflation evokes hyperemia and BA (macrovascular) dilation. We previously found passive leg raising (PLR) to elicit BA dilation with no increase in microvascular perfusion using laser Doppler flowmetry (LDF) in healthy subjects. This study compared macro- and microvascular responses in 43 diabetics and 37 controls. Baseline BA mean flow velocity (MFV) and diameter were measured by ultrasound. PLR and BA hyperemia were performed and MFV, FMD and LDF measured after each intervention. PLR increased BA MFV (p=0.030) and FMD (p<0.001) in diabetics and controls with no change in LDF. While PLR induced increases in MFV were similar between the two groups (p=0.31), PLR-induced FMD was lower in the diabetic group (p<0.001). Hyperemia increased MFV (p<0.001), FMD (p<0.001) and LDF (p<0.001) in diabetics, however all responses were blunted in this group (p<.03 for all).

MFV and LDF hyperemia induced changes was similar in diabetics(r=0.62, p=<.001) and controls (r=0.61 p= <.001). Hyperemia induced FMD and LDF correlated in controls (r=0.35, p=0.030), but not in the diabetics (r=0.13, p=0.40). There was a trend in hyperemia induced FMD with MFV changes in controls (r=0.31, p=0.06), but not in diabetics (r=0.27, p=0.11). PLR induced FMD did not correlate with MFV in either group (p=ns).

In summary, PLR changes in FMD did not correlate with MFV in diabetics or controls. Hyperemia induced FMD correlated with LDF in controls, but not in diabetics. Thus, hyperemia induced FMD appears related to both macro and microvascular function. Uncoupling of changes in microvascular flow and hyperemia induced FMD in diabetes as well as the significance of PLR induced changes in FMD and MFV without concomitant changes in LDF merit further study.

Yang Liu   Research Advisor: Jason Lazar/Louis Salciccioli

Determination of the Stiffness Index Via Applanation Tonometry in Bonnet Macaques

Although non-human primate models are used to study cardiovascular disease and aging, measures of arterial stiffness such as pulse wave velocity are not easily obtained in these animals. The Arterial Stiffness Index (SI) is a recently proposed measure of arterial stiffness that is obtained from a noninvasively recorded arterial pressure waveform. This measure, calculated as the time delay between the systolic and diastolic peaks of the peripheral pulse divided by subject height, is analogous to pulse wave velocity. We determined SI using applanation tonometry and its correlates in Bonnet Macaques, a commonly used species of monkey in experimental models.

In a cohort of 34 healthy female Bonnet Macaques (age 12 ± 5 yr; weight 5.4 ± 1.5 kg; crown rump length 44 ± 2 cm) femoral artery applanation tonometry was performed using the SphygmoCor device (AtCor Medical, Australia) during anesthesia with ketamine. The SI was calculated has crown-rump length/time delay between systolic and diastolic peaks of the arterial pressure waveform. The derived SI was correlated to monkey demographics, blood pressure and the central augmentation index (augmented pressure/pulse pressure).

SI was obtained in all animals. The mean SI was 11.3 ± 5 m/sec. The SI correlated with age (r= 0.40, p=0.02), mean peripheral pressure (r= 0.43, p=0.01), augmented pressure (r= 0.50, p=0.003), augmentation index (r= 0.65, p<0.001), and inversely with heart rate (r= -0.39, p=0.02). On multivariate analysis the augmentation index was the only independent predictor of SI (B= 0.55, p=0.02).

The SI can be readily obtained from applanation tonometry in Bonnet Macaques. The SI correlates with age, blood pressure, augmentation index, and inversely with heart rate. The relation between SI and augmentation index suggests the SI to be a promising measure of arterial stiffness that is obtained from one arterial site in the non-human primate model.

Ravi-Inder Mann   Research Advisor: Jason Lazar/Louis Salciccioli

Effect of Baseline Mean Flow Velocity, Carotid-Radial Pulse Wave Velocity and Laser Doppler Flowmetry on the Hyperemic Response

Hyperemia induced by release of arm occlusion to assess flow mediated dilation of the brachial artery by ultrasound is used to assess vascular function. Although the baseline brachial artery diameter affects the degree of dilation during hyperemia, the effect of the baseline values of mean flow velocity (MFV) by vascular ultrasound, carotid-radial pulse wave velocity (CRPWV) and laser doppler flowmetry (LDF) on the respective hyperemic responses are unknown. We analyzed the influence of the baseline values on these measurements.

The hyperemic response to CRPWV was tested in 288 subjects with and without cardiovascular disease/risk factors. In a second group of 43 diabetic patients and 40 healthy controls, hyperemic MFV and LDF were measured. Percentage changes in CRPWV, MFV, and LDF were calculated as: % change = (hyperemic index-baseline index)/baseline index x 100%.

%CRPWV inversely correlated with the baseline CRPWV value ($r= -0.20$, $p=0.001$). On multivariate analysis this effect remained with age, systolic BP and gender included in the model. Similarly, %MFV significantly correlated with the MFV baseline value in the normal controls ($r= -0.73$, $p<0.001$) and the diabetic patients ($r= -0.44$, $p=0.007$). The %MFV difference between the normal and diabetic groups ($403.0\pm303.9\%$ vs. $294.6\pm328.5\%$; $p=0.024$) was strengthened after adjustment for the baseline MFV ($p=0.008$). %LDF significantly correlated with the baseline value in the normal controls ($r= -0.88$, $p<0.001$) and the diabetic patients ($r= -0.71$, $p<0.001$). Similarly, the %LDF difference between the normal and diabetic ($247.4\pm250.9\%$ vs. $150.6\pm170.5\%$; $p=0.045$) was strengthened after adjustment for the baseline LDF ($p=0.035$).

Hyperemic changes in MFV, CRPWV and LDF are related to baseline values of these indices respectively. For all 3 measures, larger baseline indices are associated with a smaller hyperemic % change. Failure to account for baseline differences might affect group comparisons.

Amit Bhanvadia   Research Advisor: David Lee

Variations in colonoscopy quality and adherence to accepted guidelines between Private Gastroenterologists, GI fellows, and Colorectal Surgeons

Colonoscopy is the gold standard for colorectal cancer screening and for the diagnosis of various colonic disorders. Our objective was to compare the quality, adenoma detection rate (ADR) and adherence to guidelines (ATG) formulated by American Gastroenterological societies among the colonoscopies performed by private screening GI physicians (group 1), colorectal surgeons (group 2), and fellows under supervision (group 3).

This is a retrospective analysis of all outpatient colonoscopies performed between 2007 and 2013 at an inner city teaching hospital. Patients' age, indication for colonoscopy, and quality indicators; including ADR and ATG in post-procedure recommendations were recorded. Patients with known IBD, previously known colonic lesions, abnormal abdominal imaging, poor prep, and incomplete colonoscopies were excluded. Statistical analysis was performed using Pearson chi square test and ANOVA.

752 charts between September 2007 and April 2008 were reviewed. 410 patients fit the inclusion criteria: 76 patients (group 1), 157 (group 2), and 177 (group 3). Median age was 66, 59 and 53 years ($P<0.001$) and total procedure time was 28+/- 11.7, 27+/- 9.5 and 38.4+/- 17 minutes respectively ($P<0.001$). ADR was 11.8%, 17.8% and 11.3% in respective groups ($P=0.192$). ATG for post-procedure recommendations was significantly higher amongst fellows (83%) compared to screeners (34.2%) or surgeons (47.1%) ($P<0.001$). Separate analysis was done including incomplete procedures but keeping other exclusion criteria and the rate of incomplete colonoscopies was 27.6%, 8.7 % and 4.3% respectively ($P<0.001$).

ADR and ATG are critical measures of high quality endoscopists. Disparities amongst groups relate to level of experience, available completion time, and motivation/pressure to comprehensively detail appropriate recommendations. As a learning process, fellows take the longest time but appear most motivated to achieve completion and provide the most detailed recommendations.

Rachelle Dugue   Research Advisor: Douglas Ling

Parvalbumin-expressing GABAergic Interneurons in Traumatic Brain Injury and Post-Traumatic Epilepsy

Traumatic brain injury (TBI) is the leading cause of chronic disabilities worldwide. Post-traumatic epilepsy is a notable complication, occurring in 7.6 per 100 persons for moderate and 13.6 per 100 persons for severe TBI. A controlled cortical impact model of moderate TBI in the rat was used to further evaluate cellular changes associated with post-traumatic epilepsy. Previous studies in our laboratory have shown significant neocortical neurodegeneration and evoked epileptiform events via intracellular recordings from regular spiking pyramidal cells and hyperexcitability within the first week of injury. However, the cellular changes behind such hyperexcitability are unknown. Several proposed mechanisms suggest that a reduction in GABAergic neurons can lead to epileptogenesis. Therefore, parvalbumin immunohistochemistry was performed to examine potential changes in parvalbumin-expressing GABAergic interneuron populations related to previously observed epileptiform activity; no significant changes were observed in the somatosensory cortex within the first 5 days after injury. However, additional time points following CCI, as well as additional interneuron populations must be considered to better assess cellular changes underlying epileptiform activity in CCI-injured animals.

Anna Bulanova   Research Advisor: William Lytton

Integrating Systems Biology Markup Language (SBML) with NEURON

The NEURON simulator software is widely used by the computational neuroscience community for electrophysiology modeling. We have recently extended it to provide support for reaction-diffusion dynamic (RxD class). Many reaction simulations, written for a variety of different cell types in various organs, have been developed in the Systems Biology Markup Language (SBML), a standard XML-based format supported by over 200 software packages. We therefore have developed routines to import SBML simulations into NEURON, enabling NEURON users to import a large number of previously developed cell biology models and use them in computational neuroscience research. These can then combine with NEURON's electrophysiological simulation capabilities, and with other intracellular reaction models written in the new RxD syntax. This allows combined use of 2 extensive collections: the neuroscience ModelDB (http://senselab.med.yale.edu/modeldb/) and the SBML BioModels (http://www.ebi.ac.uk/biomodels-main/) databases.

Import and export of SBML models is handled using the libSBML library (http://sbml.org/Software/libSBML). A critical feature is a method to match state variables across the different models and different modeling levels. We also needed to extend this tool to make sure that matching parameters are identified across models and and to permit central facilities to allow the user to manage parameters, regardless of their origin. The importation procedure is as follows: 1) electrophysiology model is loaded from ModelDB or constructed de novo; 2) NEURON loads SBML data and instantiates appropriate RxD objects: rxd.Region, rxd.Species, rxd.Reaction; 3) user interactively or preemptively matches state-variable names across the combined models; 4) SBML models do not include diffusion so diffusion constants can be added to provide the spatial element of the combined model; 5) user can adjust the parameters and make simulation runs of the model.

Salvador Dura-Bernal   Research Advisor: William Lytton

Virtual musculoskeletal arm and robot arm controlled by a biomimetic model of sensorimotor cortex

Neocortical mechanisms of learning sensorimotor control involve a complex series of interactions at multiple scales, from synaptic mechanisms to network connectomics. We have developed a multiscale model of sensory and motor cortex consisting of several hundred spiking model-neurons. The model was trained using spike-timing dependent reinforcement learning to drive a simple kinematic two-joint virtual arm in a motor task requiring convergence on a single target. After learning, networks demonstrated retention of behaviorally-relevant memories by utilizing proprioceptive information to perform reach-to-target from multiple starting positions. We utilized the output of this model to drive mirroring motion of a robotic arm. We then intercalated a realistic virtual musculoskeletal arm between the brain model and the robot arm. This virtual musculoskeletal arm received input from neural excitation for each muscle. It then fed back realistic proprioceptive information, including muscle fiber length and joint angles, which were employed in the reinforcement learning process. The limb position information was also used to control the robotic arm, leading to more realistic movements.

This work explores the use of reinforcement learning in a spiking model of sensorimotor cortex and how this is affected by the bidirectional interaction with the kinematic and dynamic constraints of a realistic musculoskeletal arm model. These interactions take place across many spatial and temporal scales that involve both the brain and the arm, requiring the brain model to learn an internal representation of the external limb with its different spatial scales and properties -- torques, elasticity, inertia, etc. The multiscale model paves the way towards a full closed-loop biomimetic brain-effector learning system that can be incorporated in a neural decoder for real-time prosthetic control.

Robert McDougal   Research Advisor: William Lytton

Multi-simulator reaction-diffusion with NEURON

We recently extended NEURON, a widely used tool for in silico studies of biophysically complex neurons and networks of neurons, with semantic and mathematical support for reaction-diffusion studies involving the interaction of cell biology and electrophysiology. In our initial release, we numerically treated the reaction diffusion domain as a branching cable to be simulated deterministically in much the same way as the electrophysiology. That approach offered a familiar structure to experienced NEURON users but it offered no special support for that which makes reaction-diffusion models different and difficult to simulate: widely varying time scales -- from fast calcium buffering to slow calcium waves; small space scales; and the frequent need to handle individual particles stochastically.

Instead of redoing decades of prior work for cell biology simulation, we are developing techniques to allow NEURON to interoperate with established tools such as Neuron Time Warp (a stochastic simulator) and Virtual Cell (a widely used general cellular simulator). As many chemical species, like calcium, play key roles in both electrical and reaction-diffusion dynamics, adjunctive simulators must necessarily be run simultaneously, creating difficulties in terms of combined numerical integrations. In this approach, model specification is done via the existing NEURON reaction-diffusion language. An option is selected to indicate where external tools are to be used to perform the reaction-diffusion calculation. NEURON then launches that tool as a separate process and passes it the model specification. The two tools then synchronize their timesteps and exchange current and concentration information at each time step thereby coupling their dynamics. The required strength of this coupling is a limiting factor in determining how well such external tools can work well together with the central simulator.

Mohamed Sherif   Research Advisor: William Lytton

Calcium waves in neuronal dendrites: a computer model

Background: Multiscale neural models which span both electrical and chemical domains can aid the understanding of the non-linear interactions between drug targets. Calcium (Ca2+) release from internal stores is triggered by many drugs; cytosolic calcium is also augmented by voltage-sensitive channels. Ca2+ spreads within dendrites as a wave. To investigate how variations of different elements affect Ca2+ waves, we developed a multiscale, reaction-diffusion-electrical computer model of an apical dendrite.
Methods: The NEURON simulator was used to model Ca2+ release from endoplasmic reticulum (ER) via IP3Rs in response to binding of both IP3 and Ca2+. Ca2+ was pumped back to the ER by SERCA pumps. We compared the effects of 3 hypothesised patterns of IP3R distribution (continuous ER, IP3R hotspots, ER stacks). We also investigated the effect of synchronous activation of L-type voltage-sensitive Ca2+ channels on the wave behavior.
Results: Different patterns of IP3R distribution could produce Ca2+ waves with a velocity similar to that measured experimentally. A continuous IP3R distribution showed greater sensitivity to IP3R density increase: time to onset was reduced from 220 to 25 ms, speed increased from ~72 to 115 μm/sec, duration at one location increased from 0.85 to 1.1 s, whereas increases in SERCA density resulted in speed reduction. Varying the density of IP3R hotspots vs density of ER affected wave velocity similarly. Adding IL and synaptic bombardment to the simulation provided augmentation of Ca2+ levels but similar wave patterns.
Discussion: Our modeling shows how alterations in IP3R, SERCA, ER or IL modulates Ca2+ wave propagation. Clinically, antipsychotic blockage of IP3Rs altering Ca2+ wave spread, and reducing calcium-induced hyperexcitability, may be one way in which antipsychotics alter schizophrenia pathophysiology.

Vadim Kurbatov   Research Advisor: Laura Martello-Rooney

Visualization of Polymer-based Microparticles in Freshly Harvested Porcine Pancreatic Tissue Post Needle Injection

Systemic side effects are a limitation of chemotherapy for pancreatic adenocarcinoma (PDAC). Poly(lactic-co-glycolic acid) (PLGA) is an FDA approved polymer that can be utilized to create microparticles (MPs). Localized delivery of gemcitabine encapsulated within MPs (GMPs) to the the pancreas was previously explored by our lab in a three phase experiment. In phase I, blank MPs were injected into mouse pancreata to assess for adverse effects. No adverse effects were noted. In phase II, GMPs were injected into nude mouse orthotopic PDAC tumors. Injected tumors showed evidence of apoptosis compared to control. In Phase III, endoscopic ultrasound guided fine needle injection of GMPs was attempted into a live pig pancreas. MPs were not identified upon sacrifice of the pigs, calling to question if MPs entered porcine pancreatic tissue after injection. The goal of the study was to assess if MPs can be localized in porcine pancreatic tissue after direct needle injection. Pancreata were harvested from five freshly sacrificed pigs and placed in PBS for transport. MPs were injected utilizing a variety of needles and approaches, aiming to closely approximate injection conditions in the in vivo experiment. The tissue was preserved in formalin, sectioned, and H&E stained for light microscope visualization. Interseptal MPs were visualized. MPs were not visualized in control sections of porcine pancreatic tissue. This is preliminary evidence that needle injection of MPs is feasible, and that MPs enter the pancreas after injection. Further experiments will need to definitively prove that the visualized objects are MPs utilizing a differential stain. Alternately, a fluorescent marker can be encapsulated within the MP and visualized with fluorescent microscopy. Visualization of the particles in the porcine pancreas provides rationale for repeat phase III experimentation, with the goal of developing a practical methodology for localized chemotherapy delivery for pancreatic tumors.

Larry Siu   Research Advisor: Laura Martello-Rooney

Classification of pancreatic cysts through cytokine profiling of cyst fluid fine-needle aspirate

Pancreatic cyst detection rate has increased due to the use of cross-sectional imaging. Pancreatic cysts can be divided pathologically into pseudocysts, non-neoplastic cysts, and pancreatic cystic neoplasms (PCN). Malignant potential is seen in PCNs, particularly mucinous cystic neoplasms (MCN) and intraductal papillary mucinous neoplasms. Once identified, MCNs require either continual surveillance or evaluation for surgical resection. Currently, standard cyst fluid analyses include CEA, amylase, and cytology. These are often of limited value and new biomarkers need to be defined. Previous studies have used proteomic analyses to improve cyst diagnosis. One candidate set of protein markers are cytokines, a subset of which have been implicated in the carcinogenic process. We hypothesized that the cytokine concentration in pancreatic cyst fluid obtained via endoscopic ultrasound fine-needle aspiration will be differentially detected and could be used as an test to differentiate MCNs and cystadenocarcinomas from pseudocysts and serous cystadenomas. The study protocol was designed to determine pancreatic cyst fluid cytokine levels in mucinous and nonmucinous pancreatic cysts using a slide-based quantitative multiplex cytokine antibody array, which allowed for the quantitative detection of 20 cytokines with the parallel measurement of individual cytokine standard curves. Initial screening of 18 samples (8 mucinous, 10 nonmucinous) demonstrated differential detection of multiple cytokine targets, such as IL-1α and IL-5 that were statistically significant ($P<0.05$). Both cytokines have been linked to protective effects and immune surveillance in the setting of cancer. Additional sample screening will assess borderline non-significant cytokines and validate the preliminary cytokine hits. Cytokines are easily measured by ELISA in a clinical laboratory and would play a role in improving current diagnostic and surveillance strategies.

Laura Palazzolo   Research Advisor: Thomas McIntyre

Burden of Trauma on the Mentally Ill

Background: Given a high prevalence of mental illness and reports of inadequate psychiatric outpatient care in the US, we considered how mental illness may relate to risk for physical trauma. We aimed to characterize the traumatic and psychological profiles of patients who presented with physical trauma in the setting of a previously diagnosed or newly diagnosed psychiatric condition.
Methods: We conducted a retrospective chart review of all trauma patients presenting to Kings County Hospital from 2010 and 2011. Limited comparisons were made between patients with a psychiatric history and patients without a psychiatric history using two-tailed probabilities to determine the significance of the difference between independent proportions.
Results: We identified 109 physical trauma patients with psychiatric illness. The most common psychiatric comorbidities were Major Depressive Disorder (22%), Schizophrenia (17%), and Bipolar Disorder (16%). Psychiatric trauma patients largely sustained blunt trauma (68%), followed by penetrating trauma (30%), and burns (2%). When compared to the trauma population without a psychiatric history, this population was significantly older (40.6 v 32.8, p=0.002), less male (67.3% v 77.7%, p=0.016), had a longer median length of hospital stay (5.5 days v 2.0, p<0.001), required surgical procedures more often (42.7% v 25.8%, p<0.001) and were more likely to have trauma due to suicide (23.6% v 0.3%, p<0.001).
Conclusions: Patients who present with trauma in the setting of a previously diagnosed or newly diagnosed psychiatric condition appear to sustain more severe trauma, reflected by the higher incidence of operative intervention and increased length of stay. This is the first description of how psychiatric illness may affect physical trauma. We hope it may inform stronger mental health policies to prevent physical trauma and protect psychiatric patients after they leave the hospital.

Sergio Angulo   Research Advisor: Herman Moreno

IP3 receptors deregulation in Alzheimer's Disease.

Alzheimer's disease (AD) pathophysiology involves calcium dishomeostasis, nevertheless, it has not been completely characterized to what extent the amyloid and tau pathologies are connected to this process. Although AD calcium deregulation has been for the most part associated with the amyloid cascade, here we demonstrate the association between amyloid toxicity and IP3 receptors overactivation.

Non-ratiometric method for calcium detection (OG1-BAPTA 50µM) was combined with patch-clamp in whole-cell recording configuration in acute brain slices. We studied subicular pyramidal neurons from Wild-Type mice exposed to bath application of acute synthetic oligomeric beta-amyloid 1-42 (oAß42) or the scrambled peptide (Aßscr). Calcium transients were generated by the induction of three action potentials and imaging analysis was performed with a routine built in IGOR. Signals were analyzed from ROIs drawn in the apical dendrites.

Caffeine (10mM) and 2-APB (30µM) reduced the peak calcium transient by 40 and 20% respectively after 30 minutes of bath application. oAß42 (200nM) but not Aßscr increased the peak of calcium transients by 35% after 30 minutes. This effect by oAß42 was prevented by the presence of IP3 receptors blockers (Caffeine and 2-APB).

Amyloid pathologies alter the intracellular calcium dynamics by activation of the calcium stores receptors and this can lead to a molecular cascade of events that finally produce synaptic vesicle release failure and impaired postsynaptic response. Our findings also suggest that modulators of IP3 receptors might be target for pharmacologicals intervention.

Rami Noumi   Research Advisor: Ozgul Muneyyirci-Delale

Urinary Pregnanediol and Pregnanetriol determined by GC/MS analysis revealed lower levels in pregnant patients with preeclampsia

Introduction: Preeclampsia (PE) is a hypertensive disorder that is confined to pregnancy affecting 5-10% of the population, the etiology of which is still under investigation. Kiprono et al (2013) reported significantly lower serum progesterone in PE, suggesting its role in stimulation of elevated endothelin. Gas chromatography-Mass Spectrometry (GC/MS) provides an excellent procedure to evaluate urinary steroid hormones and can be used to determining levels of progesterone (P4) and 17-OH-progesterone (17-OH-P) metabolites in urine. Our goal is to determine these levels in spot urine obtained from PE patients and compare to normal pregnant controls.

Methods: Steroid conjugates from urine were extracted using C-18 columns, hydrolyzed with Glucoronidase-sulfatase enzyme to obtain free steroids, which were further subjected to derivatization to form Methoxime- trimethyl silyl (MO-TMS) derivatives. The MO-TMS derivatives were injected and separated to obtain several urinary steroids and levels of Pregnanediol (PD) the metabolite of P4 and Pregnanetriol (PT) the metabolite of 17-OH-P which are metabolite of P4 and 17-OH-P respectively along with cholesterol.

Results: The PD and PT levels were significantly decreased in PE when compared to normal controls (p=0.003, 0.02) the values being 715 ± 493 and 199 ± 183 GC units respectively. The ratio of PD/Cholesterol and PT/cholesterol were also significantly decreased in PE when compared to normal controls (p=0.003, 0.004) the values being 69.3 ± 60.0 and 11.7 ±12.2 respectively.

Conclusion: Maintaining normal levels of progesterone is critical for the pregnancy. The decreased levels of progesterone in preeclampsia indicate impaired placental steroid metabolism involving progesterone formation from cholesterol.

Mhd Ezzat Zaghlouleh   Research Advisor: Jonathan Perk

Concomitant Neuromyelitis Optica and Non-specific Interstitial Pneumonia with Negative Rheumatologic Studies.

Overlapping of Neuromyelitis Optica (NMO) with other autoimmune disease has frequently been reported, however NMO with Non-specific Interstitial Pneumonia (NSIP) is a fairly rare presentation with few case reports.

Of the autoimmune diseases occurring simultaneously with NMO, Systemic Lupus Erythematosus (SLE), and Sjogren's Disease are more often reported; rarely NSIP was found.

In the following case report, we discuss a patient with an initial presentation of both presumed seronegative Rheumatoid Arthritis and Sjogren's Disease, who was later diagnosed with NSIP. Subsequently, she presented with a transverse myelitis and was found to be seropositive for AQP4 antibodies.

Tzvi Furer   Research Advisor: Aaron Pinkhasov

Post ECT-Expressive Aphasia: An Abnormal Presentation of a Rare Phenomenon

Electroconvulsive Therapy (ECT) has persistently been demonstrated to be a medically safe and effective procedure for prominent depression in elderly patients. Numerous have demonstrated the benefits of ECT sessions in elderly patients as compared to younger patient populations. Among the most prominent side effects, though minor, is transient confusion and memory deficits, the phenomenon of post-procedural aphasia has only been rarely documented and discussed in literature. In this report, we detail an elderly Caucasian woman who demonstrated the phenomenon of post-procedural aphasia lasting from 7 to 32 minutes over the course of nine separate ECT sessions in October 2013. Despite demonstrating symptoms of post-procedural aphasia during all nine ECT sessions, the patient's symptoms of post-procedural aphasia improved when the procedure was modified into a unilateral electrode placement.

Penina Dienstag   Research Advisor: Ketan Shevde

Anesthesia and the Breastfeeding Patient - a Literature Review

Introduction: Patients who are post anesthesia are routinely told to "pump and dump" for 72 hours post-surgery - however it is unclear if this is sound advice

Methods: A narrative literature review was taken utilizing a PubMed search of the terms lactation and anesthesia as well as ABM protocols and anesthesia & toxicology standard references.

Relevant physiology: Passage of medication into breast milk is governed by the same factors as transfer into any other body compartment with passive diffusion accounting for most transfer along with active transport in most cases. Plasma concentration is the most significant factor with intrinsic properties of the medication primarily the lipophilicity, percentage of protein binding and pKa accounting for the degree of diffusion.

Recommendations: One must consider the age and stability of the infant, length of lactation and ability of the infant to clear medication. Women with term healthy infants or older infant can generally resume nursing as soon as mentation has resumed (a hallmark that medication has left the plasma/milk compartment)

Induction agents have a short period of time in plasma and are generally not problematic for resumption of nursing.

Epidural local anesthetics are generally poorly absorbed orally and as such are not problematic

Morphine is considered ideal as it is poorly absorbed orally and has limited transfer into milk

Pethidine/Meperidine - should be carefully monitored due to case reports of sedation

Remifentanyl/Sufentinil as assumed to be ok as they are shorter acting; Fentanyl - at two hours shows extremely low levels

Nabuphine and butorphanol - low milk levels but unique indications

Hydrocodone has been used in breastfeeding mothers but requires close observation

Codein and oxycodone should be used with caution as there have been case reports of adverse events in special circumstances.

Doses of opioid should be carefully monitored and kept to the minimum necessary to maintain maternal comfort

Rishi Gautam   Research Advisor: SK Rasania

Anxiety Level Amongst Medical Students

Research Question: What are the anxiety levels amongst Medical Students?

Objectives: 1.To study the levels of Anxiety amongst Medical Students 2.To compare these levels with different variables and causative factors.

Study Design: Cross Sectional study in a medical college using a standard anxiety questionnaire. Setting: Vardhman Mahavir Medical College, Safdarjung Hospital, New Delhi. Participants: 310 medical students of all the batches currently studying in the college. Results: Out of the 310 medical students who participated in the study, 150(48.4%) were found to have high anxiety levels. The prevalence of abnormally high anxiety levels was maximum in students belonging to the 3rd (66.1%), 5th(47%), 9th (49.3%) semesters. Anxiety levels were significantly higher amongst female students (61.3%) as compared to male students (43.2%) who were having high anxiety levels(p< 0.05). Students living in the hostel had higher anxiety levels(56.1%) than students living at home(38.9%). 66.7% students cited Examinations as most important cause of high anxiety amongst them. No significant relationship was found between anxiety levels and their medium of schooling, or age.

Conclusion: The findings point towards very high prevalence of anxiety amongst medical students, with female students being more prone. Also, examinations instill enormous amounts of stress and anxiety which is clearly evident from very high anxiety levels amongst the students who had their examinations coming up (students belonging to the 3 rd,5th and 9th semesters).

Ankuri Desai   Research Advisor: Edward Quadros

Characterization of folate receptor autoantibodies

Despite decades of research, the pathogenesis of autism spectrum disorder (ASD) continues to remain unknown. It is believed the pervasive condition may have varying pathologies; one is the presence of autoantibodies against the folate receptor alpha (FRα). FRα autoimmunity has been implicated in numerous developmental disorders in children, including cerebral folate deficiency (CFD) syndrome, Rett syndrome, low functioning autism with neurological deficits, and ASD. In a previous study in our laboratory, it was found that more than 75% of children with ASD were positive for serum FRα autoantibodies. FRα autoantibody prevalence in other conditions have been previously examined, demonstrating the presence of both IgG and IgM in neural tube defect (NTD) pregnancies and in cerebral folate deficiency (CFD) patients. Specifically IgG1 and IgG2 antibodies were found in mothers with NTD pregnancy, while in children with CFD the predominant subclasses found were IgG1 and IgG4, which may link its pathogenesis to a GI-mediated milk allergy. The prevalence of FRα autoantibody immunoglobulin isotype, as well as the specific IgG subclass in the ASD population is unknown. Hence, to better understand the pathogenesis of FRα autoimmunity in ASD, the immunoglobulin isotype and subclass of antibody in serum samples from ASD patients positive for FRα autoantibodies were examined using ELISA assays. The study will report on the outcome of this analysis as well as production of recombinant FRα in mammalian cells to further study the binding properties of these autoantibodies.

Stephanie Ishack   Research Advisor: John Ricci, Bruce Cronstein

The Use of 3-D Printed β-Tricalcium Phosphate/Hydroxyapatite to Understand Regulation of Adenosine Receptors in Bone Regeneration

Using specialized 3-D printing technology, combined with bioactive molecules, we can design custom 3-D scaffolds for bone repair. HA/B-TCP scaffold components provide mechanical strength, conduct bone throughout the scaffold & remodel over time. Dipyridamole (DIPY) increases local adenosine levels by blocking cellular uptake of adenosine & stimulates bone regeneration. We tested the capacity of DIPY, hypothesizing that with a bioactive filler, such as DIPY, these scaffolds may successfully regenerate bone over critical sized bone defects in an in vivo model.15% HA:85% B-TCP scaffolds were designed using Robocad software, fabricated using a Robocasting system, & sintered at 1100°C for 4h. SEM, micro-CT, XRD, FT-IR & ICP were used for material characterization. Vehicle, BMP-2 & combination drug scaffolds (scaffold + PBS, scaffold + drug, scaffold+ collagen + drug) were implanted in C57B6 mice with 3mm critical size defect for 2, 4 & 8 weeks. DIPY release from scaffold was assayed in vitro spectrophotometrically over time. Microstructural evaluation using SEM showed a broader pore distribution for sintered materials. XRD, FT-IR & ICP results showed substantial deviations in the original 15/85% HA/B-TCP formulation with detection of ~10% calcium pyrophosphate. DIPY release assays showed a constant release in collagen for 10 days. Quantitative & qualitative results from microCT showed similar & significant bone formation & remodeling in HA/B-TCP- DIPY & HA/B-TCP-BMP-2 scaffolds when compared to vehicle at 2, 4 & 8 weeks ($P \leq 0.05$, $P \leq 0.05$ & $P \leq 0.01$, respectively). Histology showed increased bone formation & increased remodeling in HA/B-TCP- DIPY & HA/B-TCP-BMP-2 scaffolds. Targeting osteoblasts & osteoclasts via appropriate adenosine receptor blockade or stimulation leads to increased bone regeneration in a murine model. Micro-CT & histology results show that the delivery of DIPY in the 3-D ceramic scaffolds promotes bone formation as effectively as BMP-2 in vivo.

Kamala Anumukonda   Research Advisor: Christopher Roman

Role of TFEB in Macrophage Autophagy

Autophagy is important for macrophage development and their immunological functions. First, monocytes must up-regulate autophagy in order to differentiate into macrophages. Once mature, macrophages also need autophagy for efficient phagocytosis of intracellular bacteria, antigen presentation via MHC II to CD4 T cells, host antiviral defense, antifungal responses and activation of defense against gram-negative bacteria via TLR signaling.

Recently, a transcription factor we study in the lab, TFEB, has been implicated by others in the regulation of genes involved in autophagy and lysosomal biogenesis. TFEB and its close relative TFE3 belong to the MiT family of transcription factors. They share sequence homology and DNA binding properties.

Given the importance of autophagy to macrophage function, I have been studying the role of TFEB in autophagy in macrophages. One in vitro approach is using transformed RAW 264.7 macrophages in which autophagy and lysosome biogenesis can be activated. A second one is using primary bone marrow (BM) derived macrophages in vitro from mice conditionally deficient in TFEB alone or both TFEB and TFE3 (dko). Using these mice, I studied macrophage differentiation by inducing sterile peritonitis.

My preliminary studies show that in RAW cells, TFEB abundance and nuclear localization is responsive to multiple immunological stimuli that activate autophagy such as pathogen associated molecules like LPS from E.coli, cytokines like IFN-γ involved in antiviral defense, and the mTOR inhibitor Rapamycin. In contrast, using BM cells from conditional TFEB null mice and dko mice, I show that TFEB and TFE3 are dispensable for differentiation of monocytes into macrophages both in vitro and in vivo. I would like to investigate if TFEB/ TFE3 mediated autophagy is important in antimicrobial defense.

Yunona Zaytseva   Research Advisor: Maria Rosario-Sim

Obesity and Self-esteem of Russian Adolescents

Background: The problem of obesity and particularly teenage obesity, has received a lot of attention in the past ten years. Overweight and obesity have been named to a list of 10 U.S. critical health priorities making them a key obstacle to health promotion/disease prevention. About 18.1 % aged 12-19 are obese. Research efforts to discover the effects of obesity on self-esteem are worthwhile.

Purpose: The purpose of this proposed research is to investigate the impact of obesity on the self-esteem of obese 14-16 year-old Russian adolescents.

Hypotheses: Russian adolescents who are obese more likely will have lower self-esteem than those adolescents who are of normal weight. Female obese adolescents will have lower self-esteem scores than the male adolescent counterparts.

Conceptual Framework: The proposed study will be guided by Erik Erikson's psychosocial development theory.

Methods: This is a cross-sectional, comparative, and correlational study to compare the effects of obesity on self-esteem of obese and non-obese Russian adolescents. A convenience sample of 100 Russian adolescents aged 14-18 years old will be recruited from four different public schools in Brooklyn, New York. The sample size will provide 0.8 power and a medium effect size. Measures will include a Demographic questionnaire, the Rosenberg Self-Esteem Scale, and a Body Mass Index Equation.

Data Analysis: Descriptive statistics for means and frequency distributions. Chi-square analysis and analysis of variance ANOVA will be used to determine significant relationships among variables. Multiple regression analysis will be performed to establish the strength of the relationships between obesity and self-esteem.

Research and Practice Implications: Further research is necessary to investigate intervention strategies to prevent obesity and improve self-esteem of obese adolescents. Research findings will help guide advanced nurse practitioners when providing care to this select population.

Maria Rosario-Sim

Reversal Theory and Smoking Initiation in Asian American Adolescents in New York City

Background: Reversal theory is a general theory of human behavior in which individuals possess an innate propensity to change or alternate between opposing states of mind known as "metamotivational" states. These states work in pairs of opposites so that change consists of movement between members of each pair. While many personal variables-such as age, gender, ethnicity and acculturation, and socioeconomic status-are nonchangeable; other personal variables are more changeable and fluctuating, such as moods and metamotivational states. Reversal theory can explain why an individual can be in the same situation at different times but experience and behave in different ways.
Objective: To explore the metamotivational states experienced during first smoking experiences of Asian American adolescents.
Design and Sample: This is a cross-sectional, survey research that investigated the differences among the smokers, resisters, and smoking naives of a convenience sample of 328 Asian Americans, aged 16 -19 in New York City.
Measures: The study used a demographic questionnaire, Temptation Episode Surveys (First Smoking Occasion, First Resisted Smoking Opportunity, and Opinions on First Smoking Occasion), the Telic/Paratelic State Instrument, and the Rebellious State Scale.
Results: Statistical analyses revealed that Asian American adolescents smoked the first time when in paratelic, arousal-seeking states, and when physical and social environments were permissive to smoking initiation opportunities such as peers and friends smoking and where adults are not present.
Conclusions: This study was the first to use reversal theory as a framework for smoking initiation. First smoking experiences of Asian American adolescents parallel that of smoking cessation when individuals lapse in a highly tempting situation. Smoking prevention and intervention programs should consider the importance of the physical, social environment, and psychological states of adolescents.

Matthew Troy-Regier   Research Advisor: Todd C. Sacktor

Regulation and Mobility of PKMζ in Dendritic Spines of Primary Hippocampal Rat Neurons

Protein kinase Mζ (PKMζ) is a persistently active alternate splice variant of the atypical protein kinase Cζ (PKCζ). PKMζ is brain specific, has been shown to be both necessary and sufficient for maintaining long-term potentiation (LTP), and is critical for the long-term (days) maintenance of some types of long-term memory. LTP is the enhanced response of a post-synaptic cell to signal from a pre-synaptic cell after concurrent activity of the two cells. PKMζ maintains this facilitated synaptic function during LTP (and long-term memory) by maintaining increased GluA2-containing α-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors in the posy-synaptic densiry (PSD). ζ inhibitory peptide (ZIP) is a specific inhibitor of PKMζ that mimics the regulatory domain of the full length PKCζ and acts on the catalytic domain of PKMζ. Since ζ inhibitory peptide (ZIP) application to hippocampal slices irreversibly disrupts long-term synaptic enhancement, we hypothesize that the location of PKMζ should be stable at specific synapses in order for the persistent kinase activity to maintain synapse-specific information storage during LTP and memory and that the stability could potentially be maintained by kinase activity-dependent mechanisms. Previous studies in our lab have shown that PKMζ is less mobile than freely diffusing proteins over a time course of 30 seconds. These studies have also shown that PKMζ is only in a subset of spines. In order to characterize the proportion and type of spines that contain PKMζ as well as PKMζ's mobility under longer half lives, a plasmid containing ZsGreen-PKMζ and DsRed under an independent promoter was created.

Gavriel Feuer   Research Advisor: Subrata Saha

Prediction of Point-of-Failure in a High-Energy Femoral Neck Fracture Model with Finite Element Analysis

Few studies have attempted to assess whether finite element analysis (FEA) can accurately predict the location of failure of femurs. The goal of this study was to develop a cortico-cancellous proximal femoral FEA model and compare the locations of peak stress to the actual point of failure seen under biomechanical testing conditions.

Fourteen cadaveric proximal femur samples were harvested. Each sample was CT-scanned from which the material properties were obtained and FEA models generated. FEA models were simulated using the open source software FEBio. Each sample was subsequently loaded in a material testing machine to simulate fracture due to axial load. Maximum force, deformation, stiffness, and energy were calculated from the data. Each femur was divided into four zones which were defined by lines drawn perpendicular to the longitudinal axis of the femoral neck: basicervical, transcervical, subcapital, and supracapital. The location of the fracture seen after biomechanical loading was compared to the peak location of tensile stress observed in the superior aspect of the femoral neck in the FEA model. Correlation analysis with Spearman's Rho was performed to determine whether there was a difference between the two methods of analysis.

Fractures occurred primarily in the subcapital region of the femoral head/neck junction (basicervical: 1, transcervical: 3, subcapital: 9, supracapital: 1). FEA analysis demonstrated correct prediction of the location of greatest tensile stress in 9/13 samples. The location of biomechanical failure and FEA peak stress was significantly correlated (Spearman's Rho = 0.64; p = 0.019).

Finite element analysis utilizing individual donor femora is able to correctly predict the location of fracture in the majority of cases in a vertical shear failure model. These findings demonstrated a significant correlation between predicted location for peak stress of the model and the actual location of fracture observed during biomechanical testing.

Martin Pendola   Research Advisor: Subrata Saha

CAD-system Dental Ceramics Sintering Using Microwaves

Introduction: Dentistry has been constantly improved by the use of many materials. and ceramics are probably one of the most frequently used materials today. Their mechanical properties and esthetics are compatible with the high standards requirements of dental treatments today. In the last years, CAD ceramic systems have been preferred due to their improved precision in the confection of dental treatments. However, their process may take up to 8 to 12 hours, with a high energy consumption.
Microwaves have a wide use in industrial processes of drying and purification, and of course, sintering materials. Our previous research shows that microwave hybrid sintering allows to sinter ceramics (usually transparent to microwaves) with several advantages: shorter times and lower energy consumption when compared with regular sintering. Also, we confirmed that dental ceramics can be sintered using microwaves, and some of their mechanical properties may be improved.
Materials and methods: We used MHS to sinter samples of a CAD system ceramics, IPS+e+max (Ivoclar Vivadent). The samples were sintered in a Microwave Furnace (Microwave Research Application Inc), 2000 W power at 1.45 GHz frequency. The firing profiles suggested by the manufacturer were adapted for the microwave furnace. Density, micro hardness Vickers test, and bending strength were measured for the sintered samples.
Results: Our results show that Hardness measurements with of 646 HV (SD ±125). Bending test results showed a flexural strength average value of 1104 MPa (SD ±119). Sintering produced a small dimensional variation of the samples (12%), lower than other ceramics tested (20%). Processing times for the samples, with all the temperature profiles tested, was about 101 minutes.
Conclusions: MHS improved the mechanical properties of IPS-e+max ceramics when compared with the results available in the literature. The process of sintering is reduced in time and the energy consumed is lower.

Roza George   Research Advisor: Sheryl Smith

Synaptic pruning in the prefrontal cortex of female mice during adolescence

Synaptic pruning during puberty has been implicated in the development and progression of neurological diseases such as autism and schizophrenia (van Spronsen and Hoogenrad, 2010). α4βδ GABARs have been shown to play a role in pubertal synaptic pruning in the CA1 hippocampus (Afroz et al., unpublished data). Previous findings have shown that NMDA receptor activation plays a pivotal role in spine stability (Ultanir et al., 2007) and that the presence of α4βδ GABARs, which increase expression at puberty, inhibits NMDA receptor activation by a shunting inhibition in the CA1 of the hippocampus (Shen et al.,2010). The role that α4βδ GABARs have in synaptic pruning of other brain regions has yet to be examined. The prefrontal cortex is a region of logical focus when development is concerned because it controls executive cognitive functions. By using dendritic spine counts, z-stack imaging, and spine classification, synaptic pruning will be studied in the prefrontal cortex where the possible role of α4βδ GABARs in this process will be examined. For this study, female C57BL6 mice were used soon after puberty onset (vaginal opening, ~PND 35) or post-pubertally (PND 56). Brains were processed using the Golgi method and spine counts obtained using a Nikon Eclipse Ci-L microscope. Preliminary data show that distal dendritic spines are significantly more abundant in the prefrontal cortex during puberty which had an average spine density of 2.96 spines/um, than post pubertally which had an average spine density of 2.17 spines/um (t(12)=-3.89646, P<0.05, SEM= 0.1428). There were no significant differences found in the density of proximal spines across adolescence (average pubertal= 2.76 spines/um, average post pubertal=2.41 spines/um, SEM=0.1538). These findings are in agreement with many published studies demonstrating synaptic pruning in prefrontal cortex (Petanjet et al., 2011). Experiments are underway to determine whether α4βδ GABARs play a role in this synaptic pruning.

David Frumberg   Research Advisor: William P. Urban

The effect of rotation on radiologic measurement of DMAA and IMA angles: Novel Radiologic Validation

Background: The Distal Metatarsal Articular Angle (DMAA) is used as a pre- and post-operative measurement hallux valgus deformity. This angle is measured using an AP radiograph of the foot to gauge a 2-D deformity. Using a cadaveric model, and a novel radiolucent box-protractor device, we intend to show the effect of axial rotation of the 1st metatarsal while keeping the proximal phalanx fixed.
Methods: We obtained 8 paired cadaveric feet (n=16) for our analysis, determined their DMAA and IMA angles from AP radiographs. Using SolidWorks, Dassault Systèmes, Waltham, Massachusetts) we developed a radiolucent protractor/drill guide to allow for rotation of the first metatarsal. At each point, an AP and a down the barrel view of the model is taken and DMAA and IMA angles are measured and recorded at each angle. Differences between different amounts of rotation were evaluated using a repeated measured analysis of variance (ANOVA).
Results: The DMAA Angle had a mean deviation from the true value of 7.7°, 6.9°, 10.9°, and 12.3 degrees when rotated at 15, 30, 45, and 60 degrees, respectively. However, the IMA angle had a deviation from the true value of only 1.1°, 1.9°, 1.4°, and 1.9°, respectively. Repeated measures ANOVA demonstrated that this difference between the two radiographic angles was statistically significant at every point of rotation, (all p values < 0.05; Figure 1). Accuracy of the radiolucent jig was confirmed by a strong correlation (Pearson r = 0.968; p < 0.001) between the true angle and the jig angle.
Conclusion: The DMAA angle displayed significantly higher variability with axial rotation when compared to the IMA angle. Though it may provide some value, the use of the DMAA angle alone does not provide adequate information on the three-dimensional rotational deformity that is often encountered in hallux valgus. The intermetatarsal articular angle is less sensitive to rotational deformities.

Damon Greene   Research Advisor: William P. Urban

Can Meniscal Geometry be Predictive of Meniscal Tears in Patients With or Without Concomitant ACL Injury?

Introduction: Several studies have attempted to describe the relationship between meniscal shape and risk of both meniscal as well as Anterior Cruciate Ligament (ACL) injury. In order to fully identify any possible relationship, we sought to meniscal height, width, slope, and cross-sectional area of the lateral and medial, anterior and posterior horns of the meniscus to determine if there were any relationships with meniscal injury.

Methods: Using the sagittal view we measured the meniscal height, base, and slope of the lateral and medial meniscus at the anterior and posterior surface, and the cross-sectional area. A stepwise logistic regression model to determine which factors were most predictive of either meniscal or meniscal and ACL pathology when compared to normal knees.

Results: When comparing normal knee to patients who had isolated meniscal tears, we observed our model to be significantly different from a constant model (chi-square: 39.784, $p < 0.0001$) with excellent fit of the model (H-L statistic, 0.826). Prediction success was 80.5% overall with a Wald criterion which demonstrated that a larger cross-sectional area of the lateral posterior ($p = 0.004$) and medial anterior ($p = 0.034$) horns of the meniscus was a risk factor for a meniscal tear. In patients who had both meniscal and ACL tears compared to normal knees, our model was significant (chi-sqaure: 29.843, $p < 0.0001$) with excellent model fit (H-L statistic, 0.823) and an overall predictive success of 79.4%. Similarly, a larger cross-sectional area of the medial anterior ($p = 0.022$), although we also observed the lateral anterior horn to have an effect ($p = 0.05$).

Conclusion: We observed that a larger cross-sectional meniscal area in both the anterior and posterior horns of both menisci was a risk factor for having both an isolated meniscal tear as well as a combined meniscal and ACL tear.

Preston Grieco   Research Advisor: William P. Urban

Achilles Tendon Rupture: A Biomechanical Evaluation of Varying the Number of Loops in a Physiological Model

Introduction: Management and treatment of acute Achilles tendon ruptures is a controversial topic. The Krackow locking loop technique has become the gold standard for tendon fixation and has been proven, in previous studies, to be stronger than other surgical techniques. According to Krackow, 2 loops provide the maximum fixation and he suggests using 3 loops as insurance. Nonetheless, since the clinical rupture presents with frayed ends, the surgeon is forced to make a rather long incision in order to place an adequate number of loops in healthy tendon proximally and distally. The purpose of this study is to determine the effectiveness, if any, of suturing through the frayed ends of a ruptured tendon in a biomechanical model.

Methods: Thirty-two fresh frozen bovine specimens were cut to simulate a ruptured Achilles tendon. Eight tendons were placed into four groups: Group 1= 3 Krackow loops in the unfrayed tendon; Group 2= 3 Krackow loops in the unfrayed and 2 stiches in the frayed; Group 3= 2 Krackow loops in the unfrayed and 2 stiches in the frayed segment; and Group 4= 1 Krackow loop in the unfrayed plus 2 stiches in the frayed segment. The two phases of cyclic loading were based off the study done by Lee et al. in 2009.

Results: There was a statistically significant difference in Load to failure force with each additional Krackow loop placed. This relationship was linear. There were no failures during Phase 1 in any of the groups. There were 9 total Phase 2 failures, 2 each in groups 1-3, and 3 failures in group 4. There was no statistically significant correlation between the circumference of the tendons, Phase 1 or 2 failure, or load to failure.

Conclusion: With greater desire to limit incision size in open Achilles tendon repair, it is important to know that the biomechanical load strength correlates directly with the number of Krackow sutures placed. We conclude that the addition of sutures in the frayed segment does not augment the biomechanical strength of Achilles tendon repair.

Diana Lau   Research Advisor: William P. Urban

A Biomechanical Analysis of Tibial ACL Reconstruction in the Case of Graft Length Mismatch

Introduction: In recent studies, the incidence of graft length mismatch was reported to be up to 13%%, with a rate of 20% when using allograft patellar BTB grafts. Multiple techniques have been described to accommodate the long graft including: twisting the graft to shorten it, passing sutures through a bone plug tying over a post, or seating the graft in a trough and securing with screws or staples .The objective of this study was to compare the biomechanical strength of four different surgical techniques as measured by load to failure.

Methods: Thirty two fresh frozen bovine tibiae and patellar tendons were divided into four separate groups based on the method of tibial graft fixation and cyclically loaded using an Instron 5566 Biomechanical Testing Machine. Two outcomes were measured: the tensile strength during cyclical loading and ultimate load to failure. A total of four different dixation methods were analyzed: 1) Sutures tied over a post; 2) Bone Staples; 3) Screws and Washers; and 4) Soft Tissue Conversion with Interference Screw.

Results: The highest mean load to failure was observed in group 3 (direct screws and washers) which was 762N ± 173N. The mean load to failure in groups 1-4 were 453N ± 86N, 485N ± 246N, 762N ± 173N, and 458N ± 128N, respectively. Only group 4 (soft tissue conversion with interference screw) had all 8 grafts intact after 1500 loading cycles while the other three groups each had one graft fail at 338 (group 1), 240 (group 2) and 309 (group 3) cycles.

Conclusion: While there are multiple viable techniques for fixation of a BPTB graft in the case of graft length mismatch, this study demonstrated that direct screw fixation offers the strongest construct in comparison to the use of sutures tied over a post, bone staples, and soft tissue conversion with interference screw. Larger, prospective randomized studies are needed to confirm these findings.

Dante Leven   Research Advisor: William P. Urban

Axial Plane Motion During Gait in Patients With AIS

Introduction: AIS impacts gait and function though the mechanism is poorly understood. Few studies have analyzed gait patterns and compensatory mechanisms in AIS patients compared to unaffected controls. The goal of this study was to compare axial plane motion during gait in patients with scoliotic curves versus a control group without spinal deformity.

Methods: Fifteen consecutive AIS patients were prospectively enrolled (mean age14.5 years, 4:11 M/F, and mean Cobb angle 57°). Analysis was performed in a 6-DOF motion analysis laboratory at a sampling frequency of 100 Hz. Thirty-four reflective markers were placed on each patient who then underwent a straight-line walking trial. Comparisons of axial pelvic and thoracic motion were made between the study group and an asymptomatic control group.

Results: Patients with AIS demonstrated a reduction in the magnitude of pelvic rotation (5.2°) compared to controls (9.3°; p < 0.001; Figure 1). Calculation of the total amount of combined (pelvic and thoracic) rotation throughout the entire gait cycle resulted in a 27% reduction in AIS patients (145°) than controls (199°; p < 0.05). Unlike controls who had normal thoracic and pelvic rotation/counter rotation (which cross each other in the axial plane),AIS patients did not have this pattern. In the control group, pelvic and thoracic axial rotation crossed each other at 24% and 78% of the gait cycle resulting in a normal anti-phase gait pattern, but didnot occur at any point of the gait cycle in AIS patients, resulting in an abnormal in-phase gait pattern.

Discussion: Compared to controls, AIS patients demonstrate a lack of pelvic and thoracic coordination as well as a more rigid gait pattern in the axial plane. Pelvic rotation was qualitatively normal, though the amplitude of motion was significantly less while thoracic rotation demonstrated a decreased amplitude as well as an abnormal pattern in the AIS group. This rigid gait pattern and avoidance of a normal anti-phase pattern is similar to the gait seen in patients with low back pain and spinal pathology.

Aditya V. Maheshwari   Research Advisor: William P. Urban

Can Cementing Technique Reduce the Cost of a Primary Total Knee Arthroplasty?

Introduction: With the recent trends towards greater cost containment and accountability on the part of surgeons and hospitals, intra-operative resource usage is a potential avenue for cost-control. The number of packets of cement used during a total knee arthroplasty represents one potential way to reduce costs. The purpose of our study was to evaluate the outcomes of patients who received a cemented primary total knee arthroplasty and stratify these results based on the quantity of cement (e.g. one bag versus two packets) that was used during each procedure.

Methods: A total of 647 cemented TKAs were identified of which 418 (Group I) used one packet and 229 (Group II) procedures utilized two packets of cement. All patients had similar demographic variables. Patients were subsequently followed clinically for a mean follow-up of 5 years during which clinical outcomes (Knee Society Scores) and radiographic outcomes were measured. The total costs were then compared between the two groups.

Results: Evaluation of implant survivorship at final follow-up for each group demonstrated no significant difference (p = 0.60). There was no difference in Knee Society objective or function scores, or complication rates between the two groups. The total supply cost for Group I (one packet) was $459 while for Group II (two packets) was $889.If the current standard technique were employed, which utilizes two packets of cement, a vacuum cement mixer, and a pressurized cement gun, then the total cost would be $1,550, which represented a 340% increase ($1,091 price difference) in the cost compared to Group I.

Conclusion: We did not observe any difference in clinical outcomes. By eliminating several extra cement mixing products we were able to achieve an approximately $1,000 cost saving per case and had equivalent clinical outcomes at mid-term follow-up. Further prospective studies are warranted to evaluate this potential method of cost control in total knee arthroplasty.

Qais Naziri   Research Advisor: William P. Urban

No Additional Benefit with Use of Fibrin Sealant to Decrease Peri-operative Blood Loss During Primary Total Knee Arthroplasty

Introduction: Perioperative blood loss, which is often managed with blood transfusions, remains a substantial problem associated with total knee arthroplasty (TKA). Due to the conflicting reports of the outcomes of fibrin sealant use in TKA, the purpose of this study was to evaluate the efficacy of a fibrin sealant on (1) peri-operative blood loss, (2) blood transfusion requirements, and (3) length of hospital stay.

Methods: A total of 113 patients were identified who underwent a primary total knee arthroplasty and received a fibrin sealant intra-operatively compared to a cohort of 70 patients who did not. Hemoglobin and hematocrit levels were measured pre-operatively and on each post-operative day until discharge. Other outcomes variables that were measured included the need for a blood transfusions and the number of units transfused.

Results: There was no significant difference in the hemoglobin and, hematocrit levels on each postoperative day. There was also no significant difference in the intraoperative blood loss, postoperative blood loss or the total perioperative blood loss in both groups. Within the fibrin sealant group 48 patients (43%) required transfusions, while 21 patients (30%) in the non-fibrin sealant group were given transfusions, which was not statistically significant (p=0.12). For patients who required a transfusion (range 1 - 4 units), the mean requirement in each patient was 2.5 ± 2.4 units in the fibrin sealant group compared to 2.0 ± 0.8 units in the non-fibrin sealant group (p=0.35).

Conclusion: Our report demonstrated no statistically significant difference in transfusion rates, post-operative drain output, or post-operative decrease of mean hemoglobin or hematocrit levels between the fibrin sealant group and non-fibrin sealant group. These results support several other reports in the literature.

Ashish Patel   Research Advisor: William P. Urban

Gait Changes in AIS Patients: Can Surgical Realignment Improve Sagittal Parameters?

Introduction: Spinal sagittal alignment has been recognized as an important factor in successful clinical outcomes in patients with spinal deformities. Currently sagittal alignment is assessed using spino-pelvic parameters measured on static standing radiographs. The purpose of this study was to determine the dynamic properties of sagittal balance in AIS, and the effects of surgery compared to a control group of healthy volunteers.

Methods: Fifteen consecutive AIS patients were prospectively enrolled (mean age 14.5 years, 4:11 M/F, and mean Cobb angle 57°). Analysis was performed in a 6-DOF motion analysis laboratory at a sampling frequency of 100 Hz. Thirty-four reflective markers were placed on each patient who then underwent a straight-line walking trial. Sagittal marker data including C7, pelvis, and center of mass (COM) were calculated to determine the pre-post sagittal balance. All statistical analysis was performed with a Bonferroni-corrected p value < 0.05 for significance.

Results: In normal patients the position of the C7 marker is a mean 51.9 mm posterior to the center of the pelvis. In AIS patients C7 remained posterior to the pelvis, but shifted from 35 mm posterior pre-operatively to 49.7 mm post-operatively (mean posterior shift of 15 mm). This was significantly different between pre- and post-op AIS patients throughout the gait cycle including heel strike (p = 0.04), two-leg stance (p = 0.02), and toe off (p = 0.01). Cross-correlation of the post-operative sagittal balance during the whole gait cycle demonstrated a pattern that resembled the control group (Rxy = 0.98; p < 0.001; Figure 1).

Conclusion: Post-operative AIS patients demonstrated sagittal gait parameters that significantly resembled controls during ambulation. Furthermore, the dynamic pattern in the sagittal plane post-operatively correlated with the control group. The posterior shift of C7 relative to the pelvis may be indicative of a more efficient gait pattern vs. their pre-operative state.

Alex Tajani   Research Advisor: William P. Urban

Is There a Difference in Meniscal Geometry Between Patients with Normal Knees and Those with Meniscal or Ligamentous Injury?

Introduction: Several studies have attempted to describe the relationship between meniscal size and shape with various knee pathologies. The purpose of our study was to explore any association between meniscal size and geometry in patients with meniscal injury and those with normal knees. In order to fully identify any possible relationship, we sought to determine the meniscal height, width, and slope of the lateral and medial, anterior and posterior, meniscus.

Methods: We retrospectively reviewed MRI studies of 121 consecutive patients. These were separated into 3 groups: 1) with ACL rupture or injury with concomitant meniscal injury, 2) those with meniscal injury but intact ACL, and 3) those without any knee pathology. Using the sagittal view we measured the meniscal height, base, and slope of the lateral and medial meniscus at the anterior and posterior surface. From these measurements, total area of the "triangle" could then be measured. For standardization purposes, we used the sagittal cut with the largest height for the anterior and posterior at each location.

Results: The mean measurements of meniscal height, width, and slope showed no statistically significant difference between patients with and without ACL pathology. However, after calculating the area of the triangle it was found that group 3 (no knee pathology) had a significantly smaller area when compared to the remaining 2 groups in the anterior horn of the medial meniscus ($F_{(2, 115)} = 8.495$, p = 0.000) and the anterior ($F_{(2,113)} = 8.229$, p =0.000) and posterior ($F_{(2,116)} = 4.565$, p = 0.012) horns of the lateral meniscus. In the posterior horn of the medial meniscus ($F_{(2,112)} = 8.278$, p = 0.000), group 3 had a significantly smaller area than group 1 but not group 2.

Conclusion: We were unable to find any stastistcally significant difference in radiologic measurement of meniscal height or slope between patients who sustained anterior cruciate ligament and meniscal injuries, those with meniscal injuries alone, and those with no knee pathology. However, patients with no knee pathology had a significantly smaller cross sectional area than the other two groups. Further studies are needed to determine a causal relationship.

Christie Racine   Research Advisor: Miriam Vincent

Endocannabanoid/cannabinoid use and Metabolic Diseases among Blacks

Introduction: Previous studies have shown endocannabanoid/cannabinoid use to be associated with a decrease in LDL, fasting insulin, glucose and hemoglobin A1c levels. Endocannabanoid/cannabinoid users were also show to have a lower BMI, lower LDL and a smaller waist circumference. We sought to evaluate whether an association exists between endocannabanoid/cannabinoid use and metabolic syndrome exclusively in a sample of our black patients.

Method: A total of 100 patients (age range: 18-70 years) were recruited from Family Medicine Center Suite B (UHB) and Family Health Services at University Hospital SUNY Downstate. Patients completed a confidential and anonymous questionnaire that was de-identified that elicited information on sociodemographics and lifestyle behaviors, including physical activity, drug and tobacco, endocannabanoid/cannabinoid and alcohol history.

Results: Of the sample, 61 of our patients admitted to having a history of endocannabanoid/cannabinoid use, 19 were current (<6 months) users and 42 were past (> 6 months) users. After adjusting for effects of cigarette smoking and age, analysis of covariance showed that current endocannabanoid/ cannabinoid users had significantly lower levels of cholesterol ($F =1.260$; $p < 0.05$) and triglyceride ($F =4.401$; $p <0.05$), relative to non-users . Past smokers (>6 months) of marijuana had lower waist circumference ($F =0.022$; $p < 0.05$) and lower diastolic blood pressure ($F =7.272$: $p < 0.05$).

Conclusion: Our results suggest that endocannabanoid/cannabinoid users were associated with lower cholesterol, triglyceride levels, smaller waist circumference and diastolic blood pressure (DBP). This data is significant because it suggests a role for potential endocannabanoid/cannabinoid targeted therapeutic medications to improve our patients' metabolic profile that are at high risk for cardiometabolic disease.

Shama Patel   Research Advisor: Ramaswamy Viswanathan

Emergence of psychosis after right temporoparietal junction lesion: A case report

Schizophrenia is characterized by a diverse array of symptoms; this includes hallucinations, delusions, impairment in attention, working memory, social cognition and emotional expression. Due to this clinical heterogeneity, current theories suggest that Schizophrenia arises from widespread brain abnormalities. However, these models are unable to explain all symptoms of schizophrenia. This is also in contrast to reports of psychosis arising from lesions in the brain. We consider the case of a young patient with a focal right temporoparietal junction (TPJ) lesion and secondary delusions of persecution, reference, guilt, grandeur, and somatic hallucinations, pressured speech and flight of ideas. No mood disturbances or formal thought disorder could be detected. This case provides critical evidence that contrary to current theories symptoms of schizophrenia can be caused by a relatively circumscribed abnormality in the brain and in particular within the TPJ region. Similar cases have been noted in the literature. Previous studies confirmed lesions with CT which lacks resolution compared with the MRI scanning techniques used here; in addition, the lesion in this case was focal and circumscribed to the right TPJ compared to those previously described in the literature. We support a recent theory that Schizophrenia may arise from abnormalities in social communicative processes that are housed in the TPJ. We provide converging evidence from neuroimaging studies, brain stimulation studies which also confirm right TPJ involvement in symptoms of Schizophrenia. We propose that this evidence provides a more succinct model of Schizophrenia, accounting for all symptoms of Schizophrenia including prodromal, positive, negative, and cognitive symptoms. Further research in this field is crucial for a more concise account disease that despite decades of research still remains inexplicable.

Yekaterina Merkulova   Research Advisors: Keith Williams/Nicholas Penington

Intracellular ATP Has Opposite Regulatory Effects on TRPC4 and TRPC5 Channel Activity

TRPC4 and TRPC5 channels are non-selective, cation channels that flux calcium, and therefore their activity may affect many essential cellular processes. TRPC4 channels have been shown to affect signaling in the heart, vasculature, GI tract and the amygdala. Similarly, TRPC5 affects signaling in the amygdala and the hippocampus. Interestingly, despite high sequence homology between TRPC4 and TRPC5, this lab discovered that intracellular ATP inhibits TRPC5-mediated currents, but potentiates TRPC4-mediated currents. Identifying how intracellular ATP modulates the activity of these channels will provide insight into how ATP can affect signaling in normal and pathological states, possibly including vascular resistance and the innate fear response in which TRPC4 has been implicated. The goal of this project is to investigate the mechanism by which intracellular ATP modulates TRPC4 and to compare this with TRPC5. Whole-cell and single-channel, voltage-clamp recordings were performed on HEK293 cells that were transiently transfected with TRPC4, M1 ACh-receptor and eGFP. Whole-cell recordings replicated and confirmed the lab's previous finding that ATP has opposite effects on TRPC4 and TRPC5-mediated currents. Preliminary single channel data demonstrate TRPC4 channel activity with a conductance of 33pS, activation by GPCR's and blocked activity at the membrane potentials between -20 mV and +20 mV - all characteristics of TRPC4 channels. Intracellular ATP does not affect channel conductance. Further studies will aim to confirm preliminary findings and evaluate ATP's effect on duration and probability of channel opening. Subsequently, residues in the N-terminus of TRPC4 channels that interact with intracellular ATP will be identified by mutagenesis, beginning with amino acid residues that are conserved in TRPC4, TRPC5, and TRPV1 and are known to directly interact with ATP in TRPV1.

Frederique Jean-Baptiste   Research Advisor: Tracey Wilson

An Examination of HIV Knowledge and Testing in a Sample of Heterosexual African-American and Afro-Caribbean Men in Brooklyn, New York

While many studies have examined HIV knowledge and testing behaviors among Blacks in America, few to date have evaluated possible ethnic/cultural variations within this group. Baseline data (N=135) from an HIV risk reduction program for at-risk heterosexual Black men were used to evaluate HIV knowledge differences between African-American (77.8%) and Afro-Caribbean (22.2%) men. Men, aged 19 to 65 years (M= 28.72, SD= 8.67) were recruited from 12 barbershops in Brooklyn, NY between 11/12-11/13. HIV knowledge was measured through 13 questions regarding the HIV virus, transmission and prevention methods. Overall knowledge was computed from responses across 13 questions to form a dichotomized variable (complete vs incomplete knowledge) such that one group contained men who correctly answered all 13 questions and the other group contained men who gave at least one incorrect answer. Overall, only 23.8% had complete HIV knowledge, 46.9% did not know the HIV status of at least one of their sexual partners and 63% had an HIV test in the past year. Similar percentages of African-American and Afro-Caribbean men were classified as having incomplete HIV knowledge (73.5% vs. 85.7%), were unaware of the HIV status of at least one of their sexual partners (49.5% vs. 37.9%), and reported not having been tested for HIV in the past year (35.2% versus 43.3%) (all p-values > 0.05). However, a greater percentage of African-American men (56.7%) felt they were able to make a difference in the health of their family, friends and community when compared to Afro-Caribbean men (33.3%) (p= 0.024). Although not all the results showed significant differences between the ethnic groups in this sample, our findings still highlight low HIV knowledge and a high degree of unawareness regarding the HIV status of men's sexual partners. These are causes for concern and indicate a need for more tailored interventions aimed at increasing HIV knowledge and testing behaviors among Black heterosexual men.

Artak Khachatryan   Research Advisor: Youping Xiao

Functional organization of cone-opponent cells in macaque striate cortex (V1)

Macaque V1 contains various types of color-selective cells, but their spatial organization and roles in color perception are largely unknown. To address these questions, we have recorded from tens of V1 single units simultaneously using multi-channel electrode arrays. Reverse correlation analyses with cone-isolating Hartley stimuli were used to calculate the spatiotemporal profile of different cone inputs to each unit. Each cone-opponent cell's receptive field (RF) was then classified as single-opponent (SO) or double-opponent (DO). A SO RF receives opposing inputs from different cone types, and each cone type provides either excitatory or inhibitory input across the entire RF. A DO RF also receives opposing inputs from different cone types, but each cone type provides both excitatory and inhibitory inputs to different subfields of the RF. The majority of the DO RFs had elongated subfields that were parallel and had opposite cone opponency. Nearby DO cells usually prefered similar orientations, but the polarity of their preferred color borders can be opposite. For instance, one cell might prefer a horizontal red/green border with red above green while a nearby cell prefers green above red. A small population of nearby DO cells preferred orthogonal orientations. Most SO cells had only weak orientation selectivity, and nearby units were usually excited or inhibited by the same cone types. Many pairs of nearby units showed a sharp peak at or near zero lag in the shuffle-corrected cross-correlogram, suggesting that they were directly connected or were driven by a common source. Such correlations were found between the same or different types of cone-opponent cells. Our results suggest that single- and double-opponent cells in V1 are spatially clustered according to different visual features. This difference in organization sheds new light on the roles that each type of cone-opponent cells may play in processing color information.

Karen Wong   Research Advisor: Ming Zhang

The Role of Complement C3 in Programmed Cell Death during Myocardial Ischemia/Reperfusion Injury

Background: Ischemia/reperfusion (I/R) injury results from acute inflammation after periods of I/R such as occur in myocardial infarction or cardiac surgery. This project explores a role in the immune response for complement, at the level of complement component 3 (C3), in modulating cardiomyocyte death. C3 is the central protein in the three complement pathways.
Methods: Myocardial I/R was carried out in wild type (WT) and C3-/- mice. I/R-related cell damage was identified by perioperative infusion of propidium iodide to detect necrosis/loss of membrane integrity. Post-operative cardiac function was evaluated by transthoracic echocardiography and by trichrome staining for fibrotic cells. C3 activation was evaluated immunohistochemically by visualizing deposition of its active fragment, C3d, in cardiomyocytes. C3d-receptor expression was detected using an anti-complement receptor-2 antibody. Apoptosis was evaluated by the TUNEL assay and by immunohistochemical staining for activated caspase-3. Imaging findings were confirmed by Western blotting. The supernatant of heart lysate was subjected to immunoprecipitation for cytosolic C3d-protein complexes, the components of which were identified by mass spectrometry (MS).
Results: C3-/- mice, compared with WT, experienced better post-I/R cardiac function. Their cardiomyocytes showed decreased necrosis and increased apoptosis. Activated C3d was found within WT murine cardiomyocytes. MS data indicated that C3d binds to cytochrome C intracellularly. Imaging data showed that the presence of C3d intracellularly is not due to active transport into the cell.
Conclusions: C3 activation, through fragments such as C3d, mediates the inflammatory response in myocardial I/R injury and modulates subsequent modes of cardiomyocyte cell death. The data suggest that C3d may reduce apoptosis by binding to cytochrome c. C3 may prove to be a novel therapeutic target for myocardial I/R injury resulting from excessive inflammation.

Christine Ghobrial

Cardiac Lineage Protein (CLP)-1 plays a distinct role in stress-induced myocardial infarction

Cardiac disease is one of the leading causes of deaths worldwide. The underlying cause of mortality is due to altered cardiomyocyte function, leading to heart failure. Though the heart has been classified as a terminally differentiated organ with limited regenerative capacity, studies have challenged this paradigm where quiescent stem cells become activated and that there is remodeling in the heart following myocardial injury. Our laboratory has shown that a haplodeficicency in cardiac lineage protein (CLP)-1, a transcriptional regulator of the positive transcriptional elongation factor, P-TEFb, restores proliferation in skeletal myocytes when challenged with low serum. And, other laboratories have suggested that CLP1 may interact with proteins, such as Smad3 and NFkB, are also involved in myocardial infarction. We are investigating whether CLP1 plays a role in cardiomyogenesis and in remodeling of the heart during stress-induced myocardial infarction in mice through the methods of trichrome analysis, and immunofluorescence imaging for the markers ckit, Nkx2.5, pSmad3, and NFkB.

Debapriya Basu   Research Advisor: Weijun Jin

**Hepatic S1P deficiency lowers plasma cholesterol levels in apoB-containing lipoproteins
when LDLR function is compromised**

Objective: Site-1 protease (S1P) controls the activation of several membrane-bound transcriptional factors involved in lipid metabolism, including sterol regulatory element binding proteins (SREBPs). However, its role in plasma apoB-containing lipoprotein cholesterol (Blp-c) metabolism is unknown.
Approach and results: A hepatic-specific knockdown (KD) of S1P using floxed S1P mouse models (S1Pf/f) and hepatic expression of Cre recombinase resulted in a 45% and 38% reduction in plasma total cholesterol (TC) and total triglyceride (TG) levels, respectively. Unexpectedly, hepatic S1P KD had a minimal effect on plasma Blp-c in S1Pf/f mice. However, it significantly reduced Blp-c levels in LDLR+/-S1Pf/f and LDLR-/-S1Pf/f mice, suggesting that the Blp-c lowering effect of hepatic S1P KD in S1Pf/f mice is inversely proportional to LDLR function. Consistently, hepatic S1P KD decreased LDLR mRNA expression in S1Pf/f mice by 50%. In addition, in these mice it resulted in discordance between LDLR mRNA and protein expression, especially under fed conditions. Further assessment of hepatic S1P deficiency revealed that it increased LDLR protein stability. Mechanistically, hepatic S1P KD was shown to decrease the liver and plasma levels of the protein proprotein convertase subtilisin/kexin type 9 (PCSK9), which degrades LDLR protein. This effect was more prominent in the fed condition. Hepatic S1P KD was shown to reduce PCSK9 expression through inactivation of SREBPs.
Conclusion: Hepatic S1P is a physiological modulator of plasma Blp-c metabolism through its regulation of LDLR and PCSK9 mRNA expression. Our study suggests that putative S1P inhibitors could be used to lower Blp-c levels when LDLR function is compromised.

Faria Duja

What is the Nurse's Role in the Prevention of Ventilator Aspired Pneumonia?

Objectives: Ventilator Aspired pneumonia (VAP) is a preventable complication that accounts for 47% of infections developed in critical care units. Articles pertaining to the prevention of VAP were reviewed in order to determine the best evidence-based practice for a nurse in a hospital setting. The review had the following objectives (1) Determine factors that increase the risk of VAP (2) Analyze the role of the nurse in the development of this complication (3) Evaluate the most effective evidence-based practice for a nurse in order to decrease the prevalence of VAP.

Method: Electronic databases were searched, including Medline and Cinahl, for primary research published in peer-reviewed nursing journals after 2007.

Results: Articles were chosen according to objective, methodology, setting, level of evidence, and outcome.

Conclusion: Several evidence-based practices were identified that have a strong correlation with patients on ventilators that do not develop pneumonia. Nurses can decrease the occurrence of VAP through hand washing compliance, glove wearing, elevating the head of the bed, regular oral care, and subglottic suctioning. These articles also address the preexisting factor of bacterial colonization in patients, which is found to contribute to increased VAP risk. Articles which analyze endotracheal tube materials that inhibit biofilm formation in order to prevent VAP are noteworthy, but did not meet review criteria. Significant reduction of VAP can be achieved by hospitals developing protocols that implement these practices.

Haroon Kanram

The Ankle Brachial Index is Dependent On Left Ventricular Systolic Function In Bonnet Macques

A low ankle brachial index (ABI) is a marker of peripheral arterial disease and is associated with higher cardiovascular disease event rates. We previously demonstrated in humans that the ABI may be influenced by left ventricular (LV) systolic function. Non-human primates have been used as models to study cardiovascular disease, but measures of vascular function are limited in these animals. Our objective was to determine whether the ABI is associated with LV systolic function in non-human primates. We studied 24 healthy female Bonnet Macques (age 83 ± 21months;weight 4.2 ± 0.6 kg; crown rump length 0.44 ± 0.01 m; monkey mass index 21.3±2.6 kg/height2) that had ABI determination and LV ejection fraction (LVEF) determined by echocardiography concurrently during anesthesia. The ABI for each extremity was calculated as the respective lower extremity pressure divided by the highest of the upper extremity pressures. The monkey mass index (MMI) is analogous to body mass index and is calculated as weight/height2. The mean value for EF was 73±6%. The mean ABI was 1.03 (range 0.78 - 1.17) with similar values in the right and left leg (ABI (right leg), 1.03±0.10, ABI (left leg) 1.02±0.11; p=0.78). On univariate analysis the ABI was related to EF (r=0.584, p=.003). There was no relationship to age, crown rump length, weight, MMI or age. When divided into ABI quartiles (median 1.03; IQR = .95 - 1.10), the mean EF increased in a step-wise manner in each ABI group from lowest to highest (67±5% vs 74±4% vs 77±5%, p=0.007). Thus, on ordinal regression analysis, ABI status was related to LVEF. On forced multivariate analysis EF was the only independent predictor of ABI after adjusting for age and MMI.

In summary, the ABI is influenced by LV systolic function measured by EF in Bonnet Macques. There was no relationship found between age, height, weight or MMI and the ABI. Left ventricular systolic function should be accounted for when considering ABI measurements.