INTERNATIONAL SOCIETY FOR BEHAVIOURAL NEUROSCIENCE

MEETING SCHEDULE

ISBN 2018 Anchorage, AK: Organizer Patrick Forcelli

**Denotes prospective members*

SUNDAY, JUNE 24

6:30-9:30 PM: *Opening Reception* on the Green (Lakefront Anchorage Hotel)

MONDAY, JUNE 25 (All talks to be held in Lakefront Anchorage Hotel, Lake Spenard Room)
Coffee, Tea, Water available all day.

AM *free time to explore*

1:00 PM – 4:00 PM: *Symposium I: The motor-cognitive interface – motor system contributions to cognition.* Organizers: Cherie Marvel and Jutta Peterburs

- 1:00-1:30 Gary Turner
- 1:30-2:00 Karin Schon*

2:00-2:30 *Coffee Break*

- 2:30-3:00 Ana Daugherty*
- 3:00-3:30 Cherie Marvel
- 3:30-4:00 Jutta Petersburs

4:15-5:00 *Works in Progress*

- 4:15-4:30 Jonathan Peelle
- 4:30-4:45 Joshua Ewen
- 4:45-5:00 Philip Servos

TUESDAY, JUNE 26

10:30 AM- 6:30 PM: *All day excursion to glacier turn tour* (meet at hotel lobby 10:15)

WEDNESDAY, JUNE 27

9:00 AM – 12:00 PM: Symposium II: *Individual Difference factors in Neural Modulation and Adaptive Plasticity in Normal and Pathological Aging.* Organizers: Nancy Dennis and Kristen Kennedy

- 9:00-9:30 Natasha Rajah
- 9:30-10:00 Nancy Dennis

10:00-10:30 *Coffee Break*

- 10:30-11:00 Kristen Kennedy
- 11:00-11:30 Karen Rodrigue
- 11:30-12:00 Mark Mapstone

INTERNATIONAL SOCIETY FOR BEHAVIOURAL NEUROSCIENCE

12:00-1:30 *Lunch*

1:45-3:00 *Traditional Talks and Work in Progress*

1:45-2:00 Yi-Shin Sheu*
2:00-2:15 Rosanna Olsen*
2:15-2:30 Patrick Forcelli
2:30-2:45 Ludise Malkova
2:45-3:00 Simon Overduin (*WIP)*

3:00-3:30 *Coffee Break*

3:30-4:45 PM *Presidential Lecture:* Dr. Kelly Drew, Professor, Institute of Arctic Biology, "Hibernation, thermoregulation and the consciousness of cold"

6:00-9:00 PM *Banquet Dinner* (located at Reddington Ballroom, Lakefront Anchorage)

THURSDAY, JUNE 28

9:00-10:00 AM *Works in Progress*

9:00-9:15 Christine Smith
9:15-9:30 Dominic Cheng
9:30-9:45 Victor Santos*
9:45-10:00 Brittany Aguilar*

10:00-10:30 *Coffee Break*

10:30-12:00 *Business Meeting*

12:00 – *Lunch and Conference Concludes****

****For those who are staying longer and interested in booking an additional excursion, contact Salmonberry Tours https://www.salmonberrytours.com.****

Work in progress

Title: Looming threat as an ethological stimulus for use in anxiety studies
Presenting Author: Brittany Aguilar (ba438@georgetown.edu)
Affiliation: Department of Pharmacology & Physiology, Georgetown University
Co Authors: Forcelli, Patrick A; Malkova, Ludise
Affiliations: Department of Pharmacology & Physiology, Georgetown University

Rapidly approaching visual stimuli (looming objects) are known to evoke unconditioned defense responses across species. From lampreys to monkeys, such responses to predator approach are important for species survival and appear to be highly evolutionarily conserved. A subcortical visual threat processing pathway containing the superior colliculus (SC) has been described in rodents as a structure important for visual loom response. The SC receives multimodal sensory information, including visual information from the retina, and mediates reflex-like behaviors, orienting, avoidance, cowering, escape, and defensive vocalizations. Response to visual loom falls under the umbrella of threat reactivity in which the SC appears to play a critical role. Although components of the circuitry underlying unconditioned response to a looming stimulus have been elucidated, pharmacological studies showing modification of the behavior itself have yet to be completed. Similarly, aside from a single study investigating an autism-like mouse mode, no behavioral outcomes from disease or disorder models have been described. Here we describe a modified version of the looming threat task, Forced Loom, where no escape route is available. In addition to describing the task, we characterize several variables of interest: stimulus specificity, habituation, context-dependence, pharmacological sensitivity (anxiogenic/ anxiolytic drug effects), ethological threat effects (cat odor). Testing was conducted in male Sprague-Dawley and Long Evans rats, which display strain differences in their responses in this task.

Work in progress

Title: PTSD and Eyeblink Conditioning
Presenting Author: Dominic Cheng (dcheng@auburn.edu)
Affiliation: Auburn University
Co Authors:
Affiliations:

A significant number of active duty soldiers and veterans acquire posttraumatic stress disorder (PTSD) associated with combat. PTSD is a debilitating illness that is preceded by a traumatic event that produces neurological changes. Symptoms include high anxiety, re-experiencing traumatic memories, hypervigilance, hyperarousal, and memory deficits. Identifying these neurological changes could facilitate the diagnosis, prevention, and treatment of PTSD. The goal of this project is to achieve a better understanding of structural and functional changes in the brains of subjects with PTSD. Most PTSD classical conditioning studies have used fear conditioning and although this is a valid approach, the emotional component may complicate interpretation from a pure learning standpoint. For this reason, we chose to use eyeblink classical conditioning (EBC) as our model system. This paradigm involves the temporal pairing of a neutral conditioned stimulus (CS; e.g., a tone) with an unconditioned stimulus (US; e.g. a corneal airpuff). In trace conditioning, there is a stimulus-free period between CS offset and US onset. This form of learning provides a unique approach to study multiple brain structures affected by PTSD (e.g. cerebellum and hippocampus). Behavioral studies report that PTSD subjects show abnormal trace acquisition and extinction. To date there have been no neuroimaging or neuromodulation studies of PTSD subjects during eyeblink conditioning, leaving significant gaps in our knowledge about which neural components underlying the CS-US association are most affected by PTSD. We plan to use functional magnetic resonance imaging (fMRI) and transcranial direct current stimulation (tDCS) to study functional connectivity in PTSD participants in order to better understand the neural bases of PTSD-related activations during EBC.

Symposium - The motor-cognitive interface – motor system contributions to cognition

Title: Neural Correlates of Aerobic Exercise Benefits to Episodic Memory: A Randomized Control Intervention Study in Older Adults

Presenting Author: Ana Daugherty (adaugher@illinois.edu)
Affiliation: Beckman Institute for Advance Science and Technology, University of Illinois Urbana-Champaign
Co Authors: Burzynska, Agnieszka (2); Ehlers, Diane (3); Salerno, Elizabeth (4); Fanning, Jason (5); Voss, Michelle (6); McAuley, Edward (1,3); Kramer, Arthur (1, 7)
Affiliations: (1) Beckman Institute for Advanced Science and Technology, University of Illinois at Urbana-Champaign; (2) Department of Human Development and Family Studies, Colorado State University; (3) Department of Exercise Science , University of South Carolina; (4) National Cancer Institute, National Institutes of Health; (5) Department of Health and Exercise Science, Wake Forest University; (6) Department of Psychological and Brain Sciences, University of Iowa; (7) Departments of Psychology and Mechanical & Industrial Engineering, Northeastern University

Several intervention strategies have been considered to promote maintenance of memory function in older age. We examined the potential effects of aerobic exercise (walking), and combined aerobic exercise with social and cognitive engagement (contra dancing) as compared to non-aerobic, active control in a six-month randomized intervention. At pre- and post-intervention, healthy, sedentary older adults (N=247, 60-79 years) completed a word recall task that included four repeated trials and a short-delay recall following an interference list. All intent-to-treat analyses were completed in a latent modeling framework that included memory performance curves, changes in regional brain volume and cardiorespiratory fitness, and intervention group comparisons. Across all individuals, trial 1 recall increased ($p<0.001$) and interference cost on delayed recall decreased ($p=0.01$) at post-intervention. Across intervention conditions, gains in cardiorespiratory fitness (VO2max) were indirectly related to better memory outcomes via regional brain volumes. Specifically, while accounting for individual differences at pre-intervention, gains in word recall were partially explained by larger volumes of insula cortex ($p<0.01$) and a trend for hippocampus ($p=0.09$) at post-intervention, and these regions mediated the effects of higher cardiorespiratory fitness ($p<0.04$) on memory performance. When comparing the prescribed interventions, walking, but not dancing, produced greater improvements in word recall ($p=0.04$) and greater gains in cardiorespiratory fitness ($p=0.09$) as compared to active control. Taken together this suggests long-term retention and better resiliency to interference in episodic memory over the course of the intervention, and aerobic walking produced control-adjusted gains in performance. The effect of cardiorespiratory fitness was dependent upon regional brain volumes, and older adults with larger insula cortex and hippocampus demonstrated greater cognitive benefit.

Work in progress

Title: No evidence for enhancement in visual featural attention
Presenting Author: Joshua Ewen (ewen@kennedykrieger.org)
Affiliation: Kennedy Krieger Institute, Johns Hopkins University
Co Authors: Cunningham, Corbin; Egeth, Howard
Affiliations: Johns Hopkins University

We had previously assumed that featural attention in the visual system operated by enhancing the attended feature. In our first experiment (Moher, Egeth and Ewen, 2014), we used the P1 ERP component as an index of attention while performing a task that involved attending to and acting upon one color and ignoring another. Comparing to the P1 response from a task-irrelevant color, we were surprised to find that the P1 to the ignored color differed from that of the task-irrelevant color, whereas the P1 to the ignored color had a decreased amplitude compared with the others. In a follow-up experiment, we repeated the task, now with two to-be-ignored colors. Again, the amplitude of the P1 response to attended and task-irrelevant colors did not differ, while the P1 amplitude to the combination of the ignored color was relatively suppressed. It remains a challenge to demonstrate whether the brain suppresses both or only one of the to-be-ignored colors. Finally, to tax the inhibitory function further, we rapidly cycled the to-be-ignored condition across trials. Again, the P1 amplitudes to task-irrelevant and attended stimuli were similar. The P1 amplitude to the to-be-ignored colors differed--though this time was greater than that of attended and task-irrelevant colors, despite good behavior performance (i.e., the ignored stimuli were not acted upon). We look forward to discussing possible interpretations.

Traditional paper

Title: Mediodorsal Thalamus Is Required for Discrete Phases of Goal-Directed Behavior in Macaques

Presenting Author: Patrick Forcelli (paf22@georgetown.edu)
Affiliation: Georgetown University
Co Authors: Wicker, Evan; Turchi, Janita; Malkova, Ludise
Affiliations: Georgetown University (EW, LM); National Institute of Mental Health (JT)

Reward contingencies are dynamic: outcomes that were valued at one point may lose value. Action selection in the face of dynamic reward associations requires several cognitive processes: registering a change in value of the primary reinforcer, adjusting the value of secondary reinforcers to reflect the new value of the primary reinforcer, and guiding action selection to optimal choices. Flexible responding has been evaluated extensively using reinforcer devaluation tasks. Performance on this task relies upon amygdala, Areas 11 and 13 of orbitofrontal cortex (OFC), and mediodorsal thalamus (MD). Differential contributions of amygdala and Areas 11 and 13 of OFC to specific sub-processes have been established, but the role of MD in these sub-processes is unknown. Pharmacological inactivation of the macaque MD during specific phases of this task revealed that MD is required for reward valuation and action selection. This profile is unique, differing from both amygdala and subregions of the OFC.

Symposium - Individual Difference factors in Neural Modulation and Adaptive Plasticity in Normal and Pathological Aging

Title: Within-person brain function variability: Effects of age and difficulty level
Presenting Author: Kristen Kennedy (kristen.kennedy1@utdallas.edu)
Affiliation: Center for Vital Longevity, School of Behavioral and Brain Sciences, The University of Texas at Dallas
Co Authors:
Affiliations:

Current understanding of functional brain activation changes with aging is largely based on examination of mean task-induced blood oxygen level-dependent (BOLD) response between groups of adults of varying ages. However, within-person individual variability in BOLD response across trials has been suggested as a marker of brain circuitry flexibility. Estimating age-related differences in within-person variability to cognitive challenge across the adult lifespan may yield new insight into the function of variability of activation and how this function ages. Here, in a healthy lifespan sample (N=171, aged 20-94) we examined BOLD variability during a parametrically increasing n-back task (0-, 2-, 3-, and 4-digits-back) using mean of the squared successive differences (MSSD) of within-voxel time series variability, with age as a continuous predictor of MSSD. We found that variability evidenced significant nonlinear (quadratic) increase with increasing age at all four WM loads, with an accelerated rate of increase with advancing age. Interestingly, the regions involved expanded with each level of difficulty and included frontal (precentral, middle frontal gyri), parietal (angular gyrus, inferior parietal), cingulate, temporal (parahippocampal, middle temporal, amygdala), and subcortical (bilateral thalamus, insula) regions. Notably, variability predicted task-accuracy only at the hardest level of difficulty, such that higher variability was associated with poorer accuracy. We found no effect of age on variability of de-activation at any WM load. These results indicate that during n-back performance, BOLD variability increases with aging, at an accelerated rate, and at the highest level of difficulty increased variability is detrimental to task performance. While previous findings have interpreted greater variability as a beneficial marker of neural flexibility, we consider here that variability may, at least in these subcortical and association cortical regions, be interpreted as stability and this stability of function is lost with age and has a negative effect on performance.
Supported in part by NIH grants R00-AG-036848, R00-AG-036818, and R01-AG-056535.

Traditional paper

Title: Transient inactivation of the parahippocampal cortex impairs nonnavigational spatial memory in macaques

Presenting Author: Ludise Malkova (malkoval@georgetown.edu)
Affiliation: Georgetown University Medical Center
Co Authors: LaFlamme, Elyssa; Forcelli, Patrick
Affiliations: Georgetown University Medical Center

We have previously reported that transient pharmacological inactivation of the hippocampus in macaques severely disrupted performance on the Hamilton Search Task (HST), a self-ordered non-navigational test of spatial memory (Forcelli et al., 2014). In this task animals are presented with an array of eight boxes, each containing a food reinforcer; one box may be opened per trial, with trials separated by a delay. Only the spatial location of the boxes serves as a cue to solve the task. The optimal strategy is to open each box once without returning to previously visited locations. Following hippocampal inactivation animals performed at chance levels on 30 sec delay trials. In accordance with the dorsal-ventral stream hypothesis (Ungerleider & Mishkin, 1982), spatial information enters the hippocampus through a relay in the parahippocampal cortex (PHC). Thus, here we hypothesized that inactivation of the PHC would also disrupt memory performance on the task. Three male rhesus macaques (Macaca mulatta) were pre-trained on the HST prior to implantation of an MRI-guided stereotaxic microinfusion platform. Bilateral microinfusions of the glutamatergic antagonist kynurenic acid (KYNA, 100mM, 1.5µl) were used to transiently inactivate sites in PHC (infusions of physiological saline of the same volume served as controls). Transient inactivation of the PHC impaired HST performance on 30 sec delay trials. The number of trials to complete the task and the repetition index (a measure of the frequency and severity of opening errors) fell to chance levels. The treatment did not impair performance on 1 sec delay trials. Similarly, the performance was not impaired on a variation of the HST, which has color cues in addition to spatial cues, providing the option of a non-spatial strategy. This finding is consistent with our previous data showing impairment after hippocampal inactivation, indicating that both hippocampus and PHC are critical for spatial memory.

Symposium - The motor-cognitive interface – motor system contributions to cognition

Title: Cerebro-Cerebellar Contributions to Working Memory in Early Lyme Disease
Presenting Author: Cherie Marvel (cheriemarvel@gmail.com)
Affiliation: Johns Hopkins University
Co Authors: Creighton Jason, Morgan Owen, Slapik Mitchell, Mihm Erica, Rebman Alison, Aucott John
Affiliations: Johns Hopkins University

Lyme Disease is caused by the bacterium Borrelia burgdorferi, which is transmitted by infected deer ticks. Symptoms of Lyme Disease typically include fatigue, joint pain, sleep difficulty, bullseye skin rash, and cognitive complaints. Specifically, cognitive complaints include difficulty in working memory/executive function. However, neuropsychological tests show normal cognitive function in people with Lyme Disease. This can be frustrating news for patients who are struggling cognitively, yet feel they are not supported in the clinic.

We hypothesized that people with Lyme Disease can function cognitively normal, but at a physiological cost, which could be measured as hyperactive brain activity, i.e., the brain needs to work harder to maintain normal performance. To test this, we administered a functional MRI (fMRI) paradigm of working memory to 7 patients (~21 days after initial infection) and 10 healthy controls. In this task, healthy volunteers previously showed activity in secondary motor areas, such as the supplementary motor area (SMA), premotor cortex, and lateral cerebellum, in association with increasing working memory load. Activity in this motor pathway is thought to support working memory by creating a motor trace of online information, to prolong phonological storage, a process that intensifies with cognitive load. We expected that Lyme patients would show a disproportionate increase in this motor pathway during working memory.

Consistent with prior cognitive reports, accuracy and response time did not differ between groups. FMRI data showed that Lyme patients and controls equally activated premotor cortex and SMA in response to cognitive load. However, Lyme patients hyperactivated the lateral cerebellum (Lobe VI) and bilateral prefrontal cortex BA 9, a key working memory area. Creating regions of interest (ROI) from these two hyperactivations, we found that intensity of the fMRI signal in both ROIs inversely correlated with duration of illness, suggesting recovery of function over time.
This study supports the notion that Lyme Disease impacts cognition and the brain, thereby supporting patients' self-reports of cognitive difficulties.

Traditional paper

Title: Under what conditions does the hippocampus contribute to the eye movement repetition effect?

Presenting Author: Rosanna Olsen (rolsen@research.baycrest.org)
Affiliation: Rotman Research Institute, Baycrest
Co Authors: Sebanayagam, Vinoja; Moscovitch, Morris; Grady, Cheryl; Rosenbaum, Shayna; Buchsbaum, Bradley; Ryan, Jennifer
Affiliations: Rotman Research Institute, Baycrest, York University

Evidence of memory for repeated information can be indexed through the monitoring of eye movements. The eye movement repetition effect is characterized by fewer fixations to repeated, compared to novel, stimuli, and may depend on the hippocampal system under some but not all circumstances. This work investigated the relationship between the eye movement repetition effect, subsequent explicit memory, and the hippocampal system (Olsen et al., Cortex, 2016). Eye movements were monitored in a developmental amnesic case (H.C.), whose hippocampal system is compromised, and in a group of typically developing participants while they studied single faces across multiple blocks. The current study found that the magnitude of the repetition effect was not correlated to performance on a surprise subsequent recognition memory test. These findings indicate that, at least under incidental encoding instructions, the eye movement repetition effect reflects a processing change due to experience that does not necessarily reflect a memory representation that is available for conscious appraisal. A follow-up functional magnetic resonance imaging study demonstrated that eye-movement repetition effects which occur after either a single or multiple repetitions may differentially rely on hippocampal and neocortical representations, respectively (Olsen et al., under review). Collectively, this work suggests that eye movement repetition effects are differentially supported by neocortical and hippocampal systems, depending upon the exposure context and the representational nature of the underlying memory trace.

Work in progress

Title: Identifying movement phenotypes in the developing immature brain through quantification of spontaneous movements

Presenting Author: Simon Overduin (simon.overduin@medportal.ca)
Affiliation: Michael G. DeGroote School of Medicine, McMaster University
Co Authors: Nassif, Omar (1,2); el Helou, Salhab (3); Reilly, Jim (2); Pugh, Edward (3); Galea, Vickie (1)
Affiliations: (1) School of Rehabilitation Science, Faculty of Health Sciences, McMaster University; (2) Department of Electrical and Computing Engineering, McMaster University; (3) McMaster Children's Hospital/Hamilton Health Sciences, Division of Neonatology, McMaster University

Pre-term infants are at risk of developing conditions such as cerebral palsy (CP) and autism spectrum disorder (ASD). As these children develop, they may exhibit an array of atypical sensorimotor and cognitive phenotypes. Among the earliest clinical signs that may be predictive of these disorders are abnormal movement "complexity", "fluency" and "variation". Identification of these atypical patterns currently requires subjective assessment by a trained clinician, observing video records of movements such as may be captured in a neonatal intensive care unit (NICU). This scoring process is subjective and demanding of both time and expertise.

Here, we present a quantitative method that may enable automatic scoring of abnormal movement quality. It uses kinematic data such as may be recorded from an electromagnetic or video-based tracking system. The method extracts submovement-based motor primitives from these data, each characterized by a small number of dimensions including onset time, peak amplitude, direction, and symmetry. Movement complexity, fluency and variation are then defined in terms of these submovement parameters. Their evolution over time may be predictive both of normally-developing term and pre-term infants.

Later analysis will investigate whether these parameters can also be used to estimate the risk an infant will develop conditions such as CP and ASD. Other ongoing work may apply this method in a near-real-time NICU monitoring environment, to detect other abnormal movement patterns as may be seen in hypokinetic pathologies (like sepsis, necrotising enterocolitis, intraventricular haemorrhage, or anemia), or hyperkinetic pathologies (like myoclonus, seizure, and neurological irritation due to meningitis, severe parenchymal brain bleeds, or hydrocephalus).

Work in progress

Title: Age-related changes in speech perception and/or movement
Presenting Author: Jonathan Peelle (jpeelle@wustl.edu)
Affiliation: Washington University in Saint Louis
Co Authors:
Affiliations:

We set out to investigate age-related changes in processing of single spoken words. We hypothesized that older adults would generally rely more on regions of inferior and dorsolateral prefrontal cortex to compensate for age-related hearing loss. Alternately, we thought we might see equivalent activation in both groups, and that any age differences might appear with more challenging types of linguistic stimuli (such as sentences). We conducted an fMRI study of single word processing in young (n=30) and older (n=30) adults. We played single words in quiet using a sparse imaging fMRI design so that that words could be presented in the absence of significant scanner noise. There were two task conditions: a listen-only condition, and a listen-and-repeat condition (which also allowed us to assess perception accuracy). Initial group comparisons suggest greater activation for young adults than older adults in bilateral superior temporal gyri, counter to our predictions. However, in parallel with these condition-based fMRI analyses, we examined average movement in the two groups, and discovered that (perhaps not surprisingly) the older adults tended to move more than did the young adults. I will present the state-of-the-art-as-of-ISBN description of our approaches to dealing with motion differences across groups and the extent to which this may contribute to our observed group differences in single word perception.

Symposium - The motor-cognitive interface – motor system contributions to cognition

Title: Cerebellar contributions to sequence detection in verbal working memory
Presenting Author: Jutta Peterburs (jutta.peterburs@hhu.de)
Affiliation: Heinrich-Heine-University Düsseldorf, Germany & Johns Hopkins School of Medicine, Baltimore, MD
Co Authors:
Affiliations:

Verbal working memory is one of the most-studied non-motor functions with robust cerebellar involvement. While the superior cerebellum (lobule VI) has been associated with articulatory control, the inferior cerebellum (lobule VIIIa) has been linked to phonological storage. The present study was aimed to further elucidate the differential roles of these regions by investigating whether the cerebellum might contribute to verbal working memory via sequence detection. 19 healthy adult subjects completed an fMRI-based Sternberg task which included repeating and novel letter sequences that were phonologically similar or dissimilar. It was hypothesized that learning a repeating sequence of study letters would reduce phonological storage demand and associated right inferior cerebellar activations and that this effect would be modulated by phonological similarity of the study letters. Specifically, while increased phonological storage demand due to high phonological similarity was expected to be reflected in increased right inferior cerebellar activations for similar relative to dissimilar study letters, the reduction in activation for repeating relative to novel sequences was expected to be more profound for phonologically similar than for dissimilar study letters, especially at higher memory load. Results confirmed the typical effects of cognitive load (5 vs. 2 study letters) and phonological similarity in several cerebellar and neocortical brain regions as well as in behavioral data (accuracy and response time). Importantly, activations in superior and inferior cerebellar regions were differentially modulated as a function of similarity and sequence novelty, indicating that particularly lobule VIIIa may contribute to verbal working memory by generating predictions of letter sequences that reduce the likelihood of phonological loop failure before stored items need to be retrieved. The present study thus supports sequence detection as an overarching cerebellar function.

Symposium - Individual Difference factors in Neural Modulation and Adaptive Plasticity in Normal and Pathological Aging

Title: Age and performance-related brain activity patterns associated with successful context encoding and retrieval: an adult lifespan fMRI study

Presenting Author: Natasha Rajah (mnrajah@gmail.com)
Affiliation: McGill University
Co Authors: Ankudowich, Elizabeth; Elshiekh, Abdel; Pasvanis, Stamatoula
Affiliations: McGill University & Douglas Hospital Research Centre

Age differences in brain activity have been reported at both encoding and retrieval. Yet, it remains unclear whether these differences are due to age, performance of age*performance effects. In the current presentation, I will discuss our results from an event-related fMRI study of spatial and temporal context encoding and retrieval in the adult lifespan in which we examined age and performance effects.

In our initial analysis we used multivariate contrast-based, partial least squares (PLS) to examine between group differences in brain activity during easy (low encoding load; high performance) vs. hard (high encoding load; lower performance) versions of spatial context memory tasks. This analysis only identified group similarities in brain activity during easy vs. difficult tasks at encoding and retrieval. However, a parallel analysis conducted in the temporal context memory tasks identified group differences in performance-related activity at retrieval in young and older adults. Specifically, older adults activated lateral temporal and occipital areas to a greater degree during hard vs. easy temporal context retrieval, compared to young adults.

We then conducted a behavior partial least squares (B-PLS) to differentiate age (as a continuous variable), performance (accuracy) and age*performance effects on brain activity across the adult lifespan. This analysis identified three significant effects: 1) activity in fusiform, middle occipital-temporal and inferior parietal cortices increased with age and decreased with performance; 2) Dorsolateral prefrontal cortex and limbic activity increased with age at encoding, and increased with performance at retrieval; and 3) Right ventrolateral prefrontal and bilateral hippocampus increased with age during retrieval and was differentially related to performance during encoding versus retrieval. We concluded that activity in occipito-temporal and inferior parietal exhibited an age/performance trade-off. In contrast, age-related differences in prefrontal and medial temporal cortices exhibited more complex patterns.

Symposium - Individual Difference factors in Neural Modulation and Adaptive Plasticity in Normal and Pathological Aging

Title: Modifying effects of Alzheimer's disease risk factors on functional brain activation in cognitively healthy adults.

Presenting Author: Karen Rodrigue (krodrigue@utdallas.edu)
Affiliation: University of Texas at Dallas
Co Authors: Kristen Kennedy
Affiliations: University of Texas at Dallas

Recent work investigating age-related differences in the ability of the human brain to dynamically modulate BOLD activation to increasing cognitive challenge has illustrated both decreases in the ability to positively modulate cognitive control networks, and a decreased ability to negatively modulate or deactivate regions associated with the default mode network. This reduced dynamic range of activation in healthy lifespan samples appears to be detrimental as it is associated with poorer task performance during scanning and with lower cognitive performance measured outside the scanner. However, significant individual variability in dynamic range is present among older adult samples and may partly be driven by unspecified risk factors that potentially modify brain function in a subsample of older adults. Here we present data from two FMRI studies examining the impact of two Alzheimer's disease (AD) risk factors, the APOE epsilon4 polymorphism and extracellular β-amyloid deposition, on functional activation to cognitive challenge. Participants carrying risk factors for AD, as well as control participants, were selected for analysis from a parent sample of 171 well-screened, healthy adults ranging in age from 20-94 years. Using an n-back working memory task (including 0-, 2-, 3-, and 4-digits-back) and a spatial-distance judgement task with three levels of difficulty, we show that both the APOE epsilon4 polymorphism and the presence of elevated β-amyloid deposition (quantified by Amyvid PET imaging) modify the extent of age-related differences in BOLD activation on two tasks. Together, these results suggest that the pattern of functional changes in the human brain during cognitive challenge that are typically attributed to the normal trajectory of the healthy aging process, may be partly driven by an increased risk for AD in some adults.

Work in progress

Title: Cellular heterogeneity in the anti-seizure effect of optogenetic activation of the pedunculopontine nucleus.

Presenting Author: Victor Santos (victorrsantos@gmail.com)
Affiliation: Georgetown University
Co Authors: Forcelli, Patrick
Affiliations: Georgetown University

Epilepsy is the second most prevalent neurological disorder. One form of epilepsy, absence epilepsy, is characterized by typical absence seizures (ASs). ASs are brief (3-30 second) nonconvulsive epileptic events that consist of sudden impairment of consciousness accompanied by a generalized synchronous, bilateral, 2.5-4 Hz spike and slow-wave dischargers (SWDs) in the electroencephalogram (EEG). Various subcortical structures play a critical role in modulating seizures, including substantia nigra pars reticulata (SNpr) and superior colliculus (SC). These structures display broad-spectrum anti-seizure effects. Both structures provide input to pedunculopontine nucleus (PPN), a brainstem nucleus that is a critical part of the ascending reticular activating system. Activation of the PPN can trigger potent desynchronization of the cerebral cortex. Thus, the PPN is both anatomically and functionally positioned to mediate the anticonvulsant effects of SNpr and SC. The PPN contains a variety of cell types, including cholinergic projection neurons, GABA neurons and glutamatergic neurons. Here, we evaluated the anti-absence seizure effects of optogenetic activation and silencing in each different neuron populations in PPN. Absence seizures were evoked by systemic administration of γ-butyrolactone - GBL (SWD-thalamocortical/absence seizures model) and electrographic seizures were recorded on a within-subject basis (i.e., with and without optogenetic activation/silencing). Optogenetic activation (5 Hz) of ChAT+ neurons suppressed cortical SWD absence seizures. However, inhibition of cholinergic neurons had no effect on absence seizures. Meanwhile, optogenetic activation of GABAergic neurons of PPN increased absence seizures, whereas optogenetic silencing of GABAergic neurons was without effect on absence seizures. Finally, activation or inhibition of glutamatergic neurons from the PPN have no effect of the number of absence seizures. These data indicate that different populations of neurons in the PPN exert diverse effects in the modulation of seizures. Using optogenetic neuronal activation in cholinergic neurons from PPN is a promising target for seizures control of epilepsy.

Symposium - The motor-cognitive interface – motor system contributions to cognition

Title: Fitness and exercise as modulators of the medial temporal lobe memory system in young adults

Presenting Author: Karin Schon (kschon@bu.edu)
Affiliation: Boston University
Co Authors: Nauer, Rachel; Dunne, Matthew; Kern, Kathryn; Storer, Thomas; Stern, Chantal
Affiliations: Nauer, Dunne, Kern, Stern: Boston University; Storer: Brigham and Women's Hospital, Harvard Medical School

Animal models highlight upregulated adult hippocampal neurogenesis in the dentate gyrus (DG) subfield of the hippocampus as the primary plasticity mechanism through which aerobic exercise enhances learning and memory. In humans, randomized clinical trials have shown that aerobic (i.e. endurance) exercise has a positive impact on multiple cognitive domains including learning and memory, resting-state functional connectivity, and hippocampal volume. However, the majority of this research has focused on older adults, and it is unknown how exercise and fitness modulate hippocampal function and structure at the subfield level. First, we examined modulation of effective connectivity between the hippocampus and default mode network (DMN) regions by aerobic fitness cross-sectionally using conditional granger causality analysis (CGCA). Second, we examined whether change in aerobic fitness predicted change in volume of the DG/CA3 region and performance on a hippocampal-dependent behavioral pattern separation task requiring disambiguation of similar stimuli. Healthy young adults (aged 18-35 years) participated in a twelve-week, trainer-supervised exercise intervention three times per week. Participants were randomly assigned to either an endurance training intervention or a resistance training intervention. Aerobic fitness was determined using submaximal treadmill testing. CGCA of our cross-sectional resting-state data showed that aerobic fitness modulated the difference of causal influence, i.e. effective connectivity, between the hippocampus and DMN regions and between DMN nodes. Further, our exercise intervention data demonstrated a positive association between change in aerobic fitness following exercise training and change in both anterior DG/CA3 volume and pattern separation task performance in initially low-fit individuals. Improving fitness in young adults may lead to enhanced function and increased volume of specific subregions of the medial temporal lobe memory system consistent with animal models. Our data extend these models by suggesting aerobic exercise may enhance communication between the hippocampus and large-scale brain networks in young adults, which is a focus of our ongoing research.

Work in progress

Title: ERP Correlates of the Midas Touch
Presenting Author: Philip Servos (pservos@wlu.ca)
Affiliation: Wilfrid Laurier University
Co Authors: Cruickshank, Katrina
Affiliations: Wilfrid Laurier University

Although the midas touch (brief, interpersonal touch leading to a range of positive outcomes) has been described rather extensively in the psychology literature little is known about its neural underpinnings. In this study, neural signatures were explored when couples completed a conjunction search task. One individual (the signaler) was responsible for conveying to their partner (the responder) the number of targets being searched for, through the use of tactile (human or inanimate) or auditory (voice or electronic beep) communication. A range of event-related potential components were examined. In particular, the N2 component was enhanced during the tactile communication trials whereas the P3 component was enhanced during verbal communication. Finally, all communication types elicited similar N1 signatures.

Traditional paper

Title: Transcranial magnetic stimulation of the right cerebellum impairs prediction of temporal order of items in verbal working memory

Presenting Author: Yi-Shin Sheu (yishin.sheu@gmail.com)
Affiliation: Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD USA
Co Authors: Liang, Yu; Desmond, John E.
Affiliations: Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD USA

Mounting evidence from neuroimaging and behavioral studies suggest that the right cerebellum plays a major role in verbal working memory (VWM). However, the exact nature of how cerebellum contributes to VWM is still unclear. One prominent theory of cerebellar function in motor control proposes that the cerebellum acts as predictive device that makes state-dependent predictions of motor commands based on prior learning of the sensory inputs. Here, we hypothesized that similar computations occur in non-motor functions, such as VWM. In this model, the cerebellum learns the temporal order of a list of phonemes, and for a given item in the sequence, makes a state-dependent prediction of the next item in the sequence. To test this hypothesis, we used transcranial magnetic stimulation (TMS) to briefly disrupt the neural activity of right cerebellum and visual cortex while the participants performed a VWM task. Participants encoded 6 visually presented letters and, after a brief pause, viewed the letters as they were rapidly presented one at a time until the sequence was interrupted and a probe letter appeared. In half of the trials, TMS was applied immediately before the probe was presented. We found that participants made significantly more errors in identifying if the probe was correct when TMS was administered over the right cerebellum compared to visual cortex. Overall, our results are consistent with the idea that cerebellum supports VWM by making prediction of the next verbal item in order based on the encoded articulatory trajectory. According to this theory, disruption of cerebellar activity during the maintenance of VWM results in a loss of state estimation in articulatory trajectory control, which led the participants making a decision based on out-of-date sequence information.

Work in progress

Title: Understanding the functional and structural neuroanatomy of news event memory in order to identify the cognitive and neural changes associated with Alzheimer's disease

Presenting Author: Christine Smith (cnsmith@ucsd.edu)
Affiliation: Veterans Affairs San Diego Healthcare System; University of California San Diego
Co Authors:
Affiliations:

The study of anterograde and retrograde amnesia in the laboratory and the clinic have provided important information about the structure and organization of memory. Anterograde amnesia refers to difficulty laying down new information into memory. Retrograde amnesia refers to loss of information that was acquired before the onset of memory impairment. The severity of anterograde amnesia is usually correlated with the severity of retrograde amnesia. Nevertheless, individuals with amnestic Mild Cognitive Impairment (MCI --thought to be a precursor to Alzheimer's disease), exhibit retrograde amnesia that is disproportionately severe given their relatively mild anterograde amnesia. I will describe a 4-year study that I am undertaking to examine the functional and structural neuroanatomy of retrograde memory for news events (memory for facts learned in the recent or remote past). One goal of the study is to identify the brain regions that support the ability to retrieve information about the recent and remote past in healthy, older controls (N=40). I will obtain structural and functional measures of brain regions (brain volumes/cortical thickness and functional neuroimaging, respectively) as well as structural and functional measures of connectivity between brain regions (diffusion tensor images and functional connectivity, respectively). The hypothesis is that individuals with MCI (N=40) will exhibit damage or altered brain function in the specific regions (and/or connections between these regions) that support past remembrance. An additional goal is to identify whether a test of news event memory could serve as a novel and clinically useful gauge of the cognitive and neural changes associated with dementia due to Alzheimer's disease.

Symposium - The motor-cognitive interface – motor system contributions to cognition

Title: Sex differences in the impact of cardiorespiratory fitness on brain health in older adults
Presenting Author: Gary Turner (grturner.ca@gmail.com)
Affiliation: York University
Co Authors: Dimech, Christina; Anderson, John; Lockrow, Amber; Spreng, Nathan
Affiliations: York University (CD, JA, GT); Cornell University (AL, NS); McGill University (AL, NS)

Physical exercise improves brain physiology, structure, and function in older adulthood. Exercise has been shown to influence neural growth factors and enhance processes such as angiogenesis, synaptogenesis, and neurogenesis. These changes are also measurable at a systems level, impacting cortical structure and function and have been associated with cognitive gains in older adults. Cardiorespiratory fitness (CRF), a product of physical exercise, is frequently cited as a modifiable lifestyle factor that can improve brain and cognitive health in older adulthood. While it is known that older males and females show differential cognitive benefits from exercise, the neural basis of these sex differences in older adults has not been explored. Here I will present findings from a recent investigation of sex differences in the association between CRF and brain function estimated using resting state functional connectivity. We focused on the default, frontoparietal control, and cingulo-opercular networks, assemblies of functionally connected brain regions known to be impacted by both age and fitness level. Fifty-one healthy older adults (31 female) were scanned to obtain measures of intrinsic connectivity within and across the three networks. We calculated global efficiency (a measure of network integration), and local efficiency (a measure of network specialization) using graph theoretical methods. Across all three networks males had lower levels of local efficiency, considered to be a marker of age-related cognitive decline. Further, the relationship between CRF and local efficiency was more robust in males than females. Our findings suggest that associations between brain network integrity and physical health are sex-dependent in older adults. These results underscore the importance of considering sex differences when examining associations between physical fitness, brain function, and cognitive health in later life.