

# **24th Annual Meeting of ISBN**

**July 11-15th, 2016**

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**Abstracts**

Session Type: Symposium 1 - Prefrontal network contributions to cognition

Title: How instructions and expectations shape pain and aversive learning

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Higher order knowledge has profound effects on emotion, perception, and well-being. For example, in the case of placebo effects, beliefs and expectations directly influence clinical outcomes. Our work aims to isolate the psychological and neurobiological mechanisms that mediate expectancy effects on affective experience. In this talk, I will present a series of studies that investigate how expectations, verbal instructions, and conditioning modulate responses to pain and aversive learning. We combined quantitative models and experimental approaches, and measured effects on subjective decisions, physiological outcomes, and brain responses during fMRI scanning. Our work indicates that expectations strongly modulate pain, and that instructions have dissociable effects on the brain mechanisms involved in aversive learning. Specifically, we find that instructions modulate activity in the dorsolateral prefrontal cortex, which influences learning-related responses in the striatum and orbitofrontal cortex. However, the amygdala learns from feedback alone, and seems to be impervious to instructions. New results suggest that these factors also lead to dissociable effects on pain and autonomic nervous system responses to painful stimuli. Finally, I will address the implications of our findings for studies of affective learning, subjective pain, and clinical outcomes.

Session Type: Work in progress

Title: Dissociating memory and executive dysfunction in Parkinson's disease

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Executive dysfunction related to fronto-striatal alterations is a hallmark of the cognitive profile in Parkinson's disease. However, it has been suggested that dysfunction in extra-striatal regions, including the medial temporal lobes (MTL), may be associated with a worse cognitive prognosis. In standard clinical practice, MTL integrity is assessed using tests of episodic memory, but our ability to detect true MTL dysfunction with these tools is suboptimal due to the ubiquity of executive deficits in PD which also impact memory performance. To circumvent this limitation, we used principal component analysis (PCA) to derive orthogonal factors from neuropsychological test scores from a large cohort of PD patients (n=221). PCA identified three significant latent components that reflected memory, executive functioning and premorbid skills. We then investigated the neural underpinnings of these components using voxel-based morphometry (VBM) in a subset of patients. We show the executive component to be related to the integrity of the caudate and prefrontal cortex. Although the memory component did not show a relationship with MTL structures, there were correlations with other regions known to be involved in memory retrieval including ventromedial prefrontal cortex and posterior cingulate. Our next step will be to investigate how well these components predict cognitive outcome 5 years following deep brain stimulation surgery.

Session Type: Symposium 1 - Prefrontal network contributions to cognition

Title: Discovering prefrontal function through its interactions

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In rats, the most studied aspects of hippocampal function relate to its role in spatial learning and memory. However, the complexity of its anatomical connections, the effects of selective hippocampal lesions, and electrophysiological activity in behaving animals have made it clear that its role in cognition is much more comprehensive. In this talk, I will review some of our recent experimental findings that shed light on the hippocampus in cognition and behavior. I will focus on the hippocampus and its interactions with the prefrontal cortex and midline thalamus. I will illustrate how some features of hippocampal lesions resemble the effects of prefrontal lesions such as in aspects of behavioral control. In other cases, I'll report features that distinguish them such as in decision making. Most notably, I'll show how midline thalamic lesions enhance cognitive performance along several dimensions that would normally be impaired following prefrontal or hippocampal lesions.

Session Type: Symposium - New perspectives on episodic memory and aging

Title: The influence of gist processing on false memories in aging

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The fuzzy-trace theory posits that memory can be based on retrieval of either item-specific or gist traces. Dependence on gist traces in the absence of item-specific traces has the negative side effect of increasing false memories. I will present evidence from three false memory studies that show aging is associated with an over-reliance on gist processing and that this reliance underlies age-related increases in false memories. I will also present neuroimaging evidence that underscores the role of lateral temporal cortices in modulating gist-based memories across in older adults with a specific focus on the relationship between activity in lateral temporal cortex and behavioral indices of false memories. Finally, I will present data suggesting that age-related increases in false memories arise from an over-reliance on gist-based processing in temporal cortex combined with under-recruitment of monitoring and evaluation processing in prefrontal cortex.

Session Type: Work in progress

Title: MULTIMODAL BRAIN IMAGING INVESTIGATION OF SPATIO-TEMPORAL DYNAMICS OF THE RESPONSE TO EMOTIONAL DISTRACTION

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The link between temporal (when) and spatial (where) aspects of the neural correlates of most psychological phenomena is not clear. Elucidation of this relation requires integration across multiple brain imaging modalities and tasks that reliably modulate the engagement of brain systems of interest. This presentation will illustrate such an integration across 3 imaging modalities: functional magnetic resonance imaging (fMRI), electroencephalography/event-related potentials (EEG/ERP), and event-related optical signals (EROS). Executive tasks with emotional distraction were used, because such dual-task designs can dissociate between large-scale dorsal and ventral brain systems involved in cognitive and affective processing. Pilot data from subjects performing an emotional odd-ball task provided initial validation of simultaneous fMRI-EEG and EEG-EROS recordings, and identified prefrontal and parietal cortical responses consistent with unimodal spatial and temporal evidence. Additional pilot data extended these results to a combined working memory-emotion regulation task with emotional distraction, and showed further spatio-temporal dissociations convergent across the 3 modalities, in fronto-parietal areas. Moreover, EEG-informed fMRI analyses identified links between ERP amplitude at parietal electrodes and fronto-parietal hemodynamic responses when coping with distraction, further supporting the value of multimodal imaging integration. Finally, data resulted from simultaneous fMRI-ERP-EROS recordings will also be discussed.

Session Type: Symposium - New perspectives on episodic memory and aging

Title: Disentangling cognitive control contributions to age-related associative memory impairments

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Associative memory impairments, such as forgetting someone's name, become more common and distressing as we age. Prefrontal cortical (PFC) dysfunction has been cited as a major contributor to these impairments. Existing theories do not specify whether aging impacts particular subregions of the PFC and the cognitive functions they support. Emerging theories of PFC organization differentiate cognitive control functions along dorsal-ventral and rostral-caudal gradients and between hemispheres. These theories are based almost entirely on young adult data and have not been tested in aging. I will present findings from several fMRI and EEG studies from our lab in which we attempted to disentangle the effects of age on different cognitive control contributions to associative memory encoding and retrieval. Our emerging results suggest that age-related changes in the rostral PFC and the control functions it supports, to a greater extent than caudal areas, contributes to age-related associative memory impairments.

Session Type: Traditional paper

Title: Chemogenetic silencing of the midline and intralaminar thalamus blocks amygdala-kindled seizures

Presenting Author: Forcelli, Patrick A.

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Temporal lobe epilepsy is the most common form of medically-intractable epilepsy. While seizures in TLE originate in structures such as hippocampus, amygdala, and temporal cortex, they propagate through a crucial relay: the midline/intralaminar thalamus. Prior studies have shown that pharmacological inhibition of midline thalamus attenuates limbic seizures. Here, we examined a recently developed technology, Designer Receptors Exclusively Activated by Designer Drugs (DREADDs), as a means of chemogenetic silencing to attenuate limbic seizures. Adult, male rats were electrically kindled from the amygdala, and injected with virus coding for inhibitory (hM4Di) DREADDs into the midline/intralaminar thalamus. When treated with the otherwise inert ligand Clozapine-N-Oxide (CNO) at doses of 2.5, 5, and 10 mg/kg, electrographic and behavioral seizure manifestations were suppressed in comparison to vehicle. At higher doses, we found complete blockade of seizure activity in a subset of subjects. CNO displayed a sharp time-response profile, with significant seizure attenuation seen 20-30 mins post injection, in comparison to 10 and 40 mins post injection. Seizures in animals injected with a control vector (i.e., no DREADD) were unaffected by CNO administration. These data underscore the crucial role of the midline/intralaminar thalamus in the propagation of seizures, specifically in the amygdala kindling model, and provide validation of chemogenetic silencing of limbic seizures.



Session Type: Traditional paper

Title: Accelerated long term forgetting in children with epilepsy

Presenting Author: Gascoigne, Michael

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This study examined long-term memory formation in 20 children with idiopathic generalised epilepsy (IGE), 23 children with temporal lobe epilepsy (TLE) and 58 control children. Participants completed two learning tasks (verbal list and spatial-location) which both involved learning to a criterion before recalling information following short (2-min and 30-min) and long (7-day) delays. A two-way ANCOVA revealed an interaction ( $p < .05$ ) on the verbal list, but not on the spatial-location task. Compared to controls, children with IGE and those with TLE showed a reduction in word recall at a 7-day delay, relative to 30-min delay ( $p < .01$ ) but not from a 2-min to 30-min delay. Our study shows accelerated long term forgetting for verbal material in children with epilepsy, irrespective of epilepsy focus.

Session Type: Symposium - New perspectives on episodic memory and aging

Title: Cross-Cultural Differences in Memory with Age

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Recent research indicates that culture can shape cognitive processes, including the use of different mnemonic strategies. I will discuss two studies in which we investigate the ways in which culture impacts memory and the use of strategies with age. Relating information to the self facilitates general and source memory for both younger and older Americans. A self-referencing strategy, however, may be less effective in interdependent cultures in which the self is conceptualized in relation to others rather than as an independent entity. We compared the effectiveness of a self-referencing strategy in younger and older adults in the US and Taiwan. Although memory in younger adults from both cultures benefits from self-reference, Taiwanese older adults benefit less than American older adults. A second strategy known to differ across cultures is in the use of categories. We compared the tendency to commit categorical errors in memory across younger and older adults from the US and Turkey. Although the rates of false memories are higher in the older adults compared to young, cultural differences in the pattern of memory errors persist across age groups. Taken together, these studies suggest potential preservation of cultural differences with age, as in the case of categorical memory errors, as well as in the exaggeration of cultural differences with age, as in the case of self-referential memory.

Session Type: Traditional paper

Title: Automatic recruitment of the motor cortex by poorly attended graspable objects

Presenting Author: Harris, Irina

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Previous behavioural (e.g. priming) and neuroimaging studies have suggested that the motor properties associated with manipulable objects are automatically accessed when people passively view objects. We directly tested this by measuring the excitability of the motor cortex when participants viewed pictures of graspable vs. non-graspable objects that were presented during a period of disrupted control over attentional and encoding processes (i.e., during the attentional blink). Participants had to identify two briefly presented objects separated by either a short or long SOA. The second picture in the sequence could be a graspable or a non-graspable object. Motor-evoked potentials (MEP; an index of cortico-spinal excitability) were measured from the right hand in response to a single TMS pulse delivered over the primary motor cortex representation of the right hand (left M1) 250ms after the onset of the second target. Behavioural results showed poorer identification of objects at short SOA compared to long SOA, consistent with an attentional blink, which did not differ between graspable and non-graspable objects. However, MEPs measured during the attentional blink were significantly higher for graspable objects than for non-graspable objects, confirming that the motor cortex is automatically activated during recognition of graspable objects.

Session Type: Traditional paper

Title: Frontal modulation supports working memory performance in middle-aged and older adults

Presenting Author: Kennedy, Kristen M. Kennedy

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Increasing working memory load in young adults evokes increased activation to demand. Working memory performance declines with age, but it remains incompletely understood how the aging brain is able to modulate neural activation to meet these demands. We examined modulation of neural activity to demand in working memory across levels of difficulty within the adult lifespan. Healthy adults ages 20-94 (N=173) completed an n-back fMRI block-design task with four levels of working memory load: 0-, 2-, 3-, 4-back on a 3T Phillips Acheiva scanner after training to 80% accuracy prior to scanning. Multiple regression analyses in SPM were conducted with age as a continuous variable and WM load as a linear parametric contrast. In the whole sample, increasing WM load was associated with parametrically increasing activation in bilateral posterior parietal cortex, dorsolateral prefrontal cortex, and cerebellum, as well as parametrically decreasing activation in widespread brain regions including medial frontal/anterior cingulate, visual cortex, posterior cingulate. With increasing age, decreased parametric activation to WM load selectively appeared in right middle frontal gyrus (rMFG). Greater modulation of rMFG was associated with more accurate performance, but in an age-dependent manner. Specifically, younger adults' rMFG activation was unrelated to task performance, whereas middle-aged and older adults showed a positive association between activation and performance, suggesting that maintenance of rMFG activation after young adulthood is in service of facilitating performance. These findings support the notion that contralateral, right hemisphere frontal activation in middle-aged and older adults serves a facilitative role in maintaining cognitive performance.

Session Type: Symposium - New perspectives on episodic memory and aging

Title: Remembering the good and the bad: Emotional memory retrieval across the adult lifespan

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Negative events are often remembered more vividly than positive or neutral events, although this effect can be reduced or even reversed with advancing age. In this talk, I first present evidence that negative valence enhances sensory recapitulation during young adults' retrieval: negative memories are associated with greater encoding-to-retrieval overlap within sensory regions than are positive or neutral memories, and the activity within sensory regions as well as the hippocampus tracks most strongly with the accurate retrieval of negative memories. I then present evidence that age may affect these retrieval processes: Age is associated with decreased processing in sensory regions and with decreased connectivity between sensory processing regions and the hippocampus. Importantly, age also is associated with negative correlations between hippocampal activity and activity within multiple prefrontal regions, specifically during the retrieval of negative events. This negative connectivity corresponds with a reduction in the vividness of negative memories, perhaps suggesting a regulatory function for these connections. Consistent with this regulatory view, recent behavioral evidence has revealed that age is associated with an increased likelihood that positive details of complex, negative events are focused upon, and age also intensifies the links between emotional intensity, surprise, and the focus on positive details. Together, these results begin to reveal how the effects of age on retrieval processes can explain the different phenomenology of negative and positive memories across the adult lifespan.

Session Type: Traditional paper

Title: Accelerated long-term forgetting in children: Is this a seizure related phenomenon?

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It has been proposed that accelerated long-term forgetting (ALF) is a seizure related phenomenon. We have investigated this hypothesis in two studies.

The first, longitudinal study, involved children with idiopathic generalised epilepsy (IGE) whose seizures subsided over time and healthy control (HC) children. The second, cross-sectional study, involved patients who have never experienced seizures: children with traumatic brain injury (TBI) as well as HC children. In both studies children learned a list of words to a criterion (perfect recall on 2 consecutive learning trials). Recall was requested after short (2 and 30-min) and long (7-day) delays. A recognition trial was administered on long delay only. On follow up, children with IGE continued to (i) recall significantly fewer words on long but not short delays, and (ii) recognise fewer words compared to HC children although their seizures subsided. Similarly, children with TBI recalled significantly fewer words on long but not short delays relative to HC children. Overall, both studies provided evidence of ALF.

Taken as a whole, findings of our studies suggest that ALF is not always a seizure related phenomenon. It may be present in patients with other neurological aetiologies. Therefore ALF may be more prevalent than expected.

Session Type: Work in progress

Title: Colliculo-pulvinar pathway to the amygdala: Behavioral effects and anatomical connections.

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The superior colliculus has been extensively studied in the nonhuman primate with respect to visual orienting and eye saccades. Whereas the superficial layers of this structure are predominantly visual, the intermediate and deep layers of the superior colliculus (DLSC) are involved in oculomotor activity and threat-related motor behaviors. Extensively studied in rodents and, more recently by our lab in primates, DLSC, together with other structures including the amygdala, constitutes part of the neural circuitry underlying defensive behaviors. We recently found in the primate that disinhibition of DLSC evokes defensive behaviors similar to those in the rat and these behaviors are modulated by inhibition of the amygdala. In addition, the superior colliculus constitutes a node in the pathway of detecting threat. Neuroimaging data in human subjects, as well as anatomical tracing studies in rodents and the tree shrew, suggest functional and anatomical connectivity between the superior colliculus, pulvinar, and the amygdala as a subcortical pathway that is involved in fast and non-conscious perception of emotional stimuli (e.g. facial expressions). However, this pathway has not been yet confirmed by anatomical studies in primates. Our anatomical data based on retrograde tracers placed in the amygdala and anterograde tracers in the colliculus showed a region of sparse overlap of these two projections within the medial pulvinar. Our ongoing experiments concentrate on the effects of pharmacological manipulations of the colliculus - pulvinar - amygdala pathway on processing of emotional stimuli (including fear-provoking stimuli, e.g. snakes). Behavioral effects resulting from reversible pharmacological manipulations within the circuitry together with anatomical data will be reviewed.

Session Type: Traditional paper

Title: Identifying the Neurocognitive Determinants of HIV-Risk Behaviors

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HIV-risk behavior is often motivated by the possibility of immediate reward (e.g., unprotected sex). Moreover, reward stimuli co-opt one's attention. Our previous study showed that attention to reward was stronger in HIV+ individuals with vs. without a drug history. In this preliminary follow-up study, we have tested 10 HIV+ individuals (5 with and 5 without a drug history), using fMRI combined with a task that measures the ability to learn a stimulus-reward association and then, subsequently, to ignore that reward when presented in a novel, irrelevant context.

The basal ganglia (BG), a key target for damage by HIV infection, play a central role in reward processing and addiction. We hypothesized that if reward salience was high and difficult to ignore, BG activity would increase in response. This effect would be greater for those with a drug history.

HIV+ individuals with a drug history showed hyper BG activity when task demands required them to ignore the reward information, indicating reward salience was high. HIV+ individuals without a drug history showed no such BG activity. Thus, HIV+ individuals with a drug history may face the greatest challenge in ignoring reward information and, consequently, controlling risky behaviors in pursuit of that reward.



Session Type: Traditional paper

Title: Accelerated Longer Term Forgetting in Patients with Focal Epilepsy: Rates and Underlying Causes

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Accelerated Longer Term Forgetting (ALF) is defined as a memory impairment that is seen only at long delays (e.g., after days or weeks) and not at standard, shorter (e.g., 30 min) delays. Research indicates that ALF occurs in some patients with epilepsy, but the prevalence rates and underlying causes have not been established. As a first step, we tested recall in 60 normal control subjects (aged 18-65) for lists of words and abstract drawings [Rey Auditory Verbal Learning (RAVLT) and Aggie Figures, respectively] at 30 min and 7 day delays. These scores were used to determine cut-offs for diagnosing both ALF and a more standard (earlier) memory impairment (Miller et al., 2015). Next, we assessed 45 patients with focal epilepsy (20 left-, 20 right- and 5 bilateral-epileptic foci; mean age = 43) in the same way. The prevalence rate of ALF was three times higher than normal (approximately 15%) on the RAVLT, but no different from normal (approximately 6%) on the Aggie Figures. In contrast, a much higher proportion of these patients showed earlier memory deficits at the 30 min delay (31% on RAVLT, 18% on Aggie Figures). There was a significant hemispheric specificity effect only at the 30 min delayed recall of the RAVLT (patients with left-hemisphere foci worse than those with right-sided foci;  $F=4.63$ ,  $p<.05$ ). Presence of a hippocampal lesion was associated with ALF. Previous work has indicated that the presence of interictal discharges is also a predictor of ALF. Knowing how to identify ALF and appreciating that hippocampal pathology and interictal discharges contribute to its manifestation are important for clinical practice. Such results could help determine treatment and also substantiate the complaints of some patients (who perform normally on standard testing).

Session Type: Traditional paper

Title: On the outskirts of cognition: highlighting the functional role of the mediodorsal thalamus

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In many ways, the underdog in aspects of cognition is the mediodorsal thalamus. It is reciprocally connected to the prefrontal cortex – seen as the superstar of the cognitive domain – yet, very little is known about the functional role of the mediodorsal thalamus in cognitive processes. Its' role is likely linked to critical inputs received from the amygdala and basal ganglia. Previous research from my lab has demonstrated that the mediodorsal thalamus (especially the magnocellular subdivision that is interconnected with the ventral striatum and the orbitofrontal cortex) has a key role in learning new information and adaptive decision-making. More recently, our studies have provided causal evidence for its critical importance in allowing the rapid updating of information to guide optimal decisions. Understanding the influence of the mediodorsal thalamus for learning and within the decision-making network will likely offer new insights into conditions in which these processes break down. Essentially, all neuropsychiatric disorders involve abnormal decision-making, and it's a core symptom in addiction, eating disorders, obsessive-compulsive disorders and schizophrenia. The mediodorsal thalamus may also provide an avenue for helping cognitively able people get a mental boost.

Session Type: Traditional paper

Title: Understanding left and right in the brain

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Functional hemispheric asymmetries affect many cognitive, sensory and motor systems in humans, but their ontogenesis and neurophysiology are poorly understood. Classic ontogenetic theories assume that handedness and language lateralization, probably the best known examples for functional hemispheric asymmetries in humans, are determined by a single gene. In my research program, I investigate the ontogenesis and neurophysiology of hemispheric asymmetries using different methodological approaches. The evidence from these studies indicates that a single gene view on the ontogenesis of functional hemispheric asymmetries likely is incorrect. Instead, different genetic and epigenetic influences determine these complex phenotypes.

Session Type: Work in progress

Title: Under watchful eyes: The impact of social observation on performance monitoring in social anxiety disorder

Presenting Author: Peterburs, Jutta

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Intense fear of (social) performance situations, negative evaluation and failure is a core symptom of social anxiety disorder (SAD). Evidence for altered error and feedback processing in SAD has recently been accumulating, pointing to enhanced performance monitoring in anxious individuals. However, despite the relative specificity of SAD psychopathology little is known about the impact of social context on performance monitoring in SAD. In this talk, I am going to present findings from ongoing electroencephalography (EEG) studies aimed to determine if behavioral proxies and electrophysiological correlates of error processing and probabilistic feedback learning are altered in patients with SAD as a function of social context, that is, by presence (or absence) of an observer.

Session Type: Work in progress

Title: Non-Invasive Neuromodulation Combined with Intensive Cognitive and Physical Rehabilitation Induces Neuroplastic changes In Patients with Multiple Sclerosis - an fMRI study

Presenting Author: Ptito, Alain

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### Objective

To study the effects of non-Invasive tongue stimulation (using the Portable Neuromodulation Stimulator (PoNSTM) combined with Intensive Cognitive and Physical Rehabilitation on gait, balance, working memory and concomitant changes in the brain of Multiple Sclerosis (MS) patients.

### Participants and Methods

Fourteen MS patients: randomized to 7 Active Stimulation (means: age=48; education=14.7 yrs; IQ=111; Female=4) and 7 In Sham Stimulation groups (age=50; education=16.7 yrs; IQ=113; Female=4). Subjects received 2 hours of intensive physical therapy and 20 minutes of working memory training 5 days a week for 14 weeks. Task-related functional MRI (fMRI) using motor imagery and working-memory tasks were completed before, and following therapy. Comprehensive Sensory Organization (SOT), functional walking performance measures (DGI), and extensive neuropsychological testing were administered pre and post therapy.

### Results

All subjects improved on motor tasks. However, on the SOT, only those in the Active group showed significant improvement from baseline. fMRI showed significant blood oxygen-level dependent (BOLD) signal-changes in the primary motor cortex for the Active group, while the Sham group had increased activity in bilateral premotor cortices. Diffusion tensor imaging revealed decreased mean diffusivity (MD) and radial diffusivity (RD) in the left cortico-spinal tract of the Active group only. Performance was improved for both groups on working memory tasks, but increased dorsolateral prefrontal cortex activity was seen in the Active group.

### Conclusions

These promising results suggest that PoNS stimulation combined with focused therapy enhances motor performance and working memory while driving neuroplasticity. A larger study is warranted to explore these findings further.

Session Type: Symposium - New perspectives on episodic memory and aging

Title: Family history and APOE-4 risk for Alzheimer's Disease impact the neural correlates of episodic memory at midlife

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Episodic memory impairment is a consistent, pronounced deficit in pre-clinical stages of late-onset Alzheimer's disease (AD). Individuals with risk factors for AD exhibit altered brain function several decades prior to the onset of AD-related symptoms. In the current study we tested the hypothesis that episodic memory-related brain regions exhibit functional and structural changes in early middle-aged adults (MA; 40-58yrs) with a family history of AD (MA+FH) and in MA with both +FH status and an apolipoprotein E  $\epsilon$ 4 allele (MA+FH+APOE-4), compared to MA controls. Subjects participated in an event-related fMRI study of spatial context memory and were scanned during encoding and retrieval. Between group multivariate behavior partial least squares (PLS), task PLS analysis and univariate region-of-interest activation analyses of the fMRI data were conducted. In addition, whole brain voxel based morphometry (VBM) and hippocampal volumes were analyzed. There was no significant group difference in spatial context retrieval accuracy or reaction time; nor were there group differences in VBM and hippocampal volumes. Yet, there were group differences in activity and brain-behavior correlation changes in hippocampus, left angular gyrus and medial prefrontal cortex (mPFC). Additionally, the two risk groups exhibited unique patterns of activation and brain-behavior correlation. We conclude that having +FH and +APOE-4 risk factors for late onset AD alter the functional neural networks important for episodic memory by midlife, and that these functional changes precede structural change.

Session Type: Symposium 1 - Prefrontal network contributions to cognition

Title: Neural circuits associated with behavioral flexibility in humans and macaques

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Abstract: The human prefrontal cortex has been associated with the most sophisticated aspects of cognition, including those that are thought to be especially refined in humans. First of all I will first present data obtained using diffusion-weighted magnetic resonance imaging (DW-MRI) and functional MRI (fMRI) in humans and macaques to infer and compare the organization of prefrontal cortex in the two species. Secondly I will focus more specifically on circuits supporting the ability to express adapted behaviors in reversal learning tasks. I will present results on structural and functional changes associated with learning reversal tasks in macaques. In discrimination reversal (DisRev) learning tasks animals learn that one choice leads to reward while another does not. Animals also learn that when the reward assignments are switched, the previously unrewarded choice has become the one followed by reward. Behavioural flexibility in DisRev has often been thought to rely on a brain circuit centered on the orbitofrontal cortex (OFC). This view has been challenged because fiber-sparing lesions do not impair discrimination reversal learning in macaques. On the basis of longitudinal changes in grey matter and activity coupling during DisRev training, we identified a neural network associated with behavioral flexibility.

Session Type: Work in progress

Title: Dissociable effects of perceptual and conceptual fluency on familiarity and recollection

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Previous exposure to a stimulus can cause increased fluency of processing on subsequent exposure to the same stimulus, even without conscious retrieval of the encoding event. Conversely, unexpectedly high perceptual fluency can result in a feeling of familiarity, as when a familiar face seems to pop out of a crowd. Artificially increasing the perceptual fluency of recognition memory test items (via masked repetition priming) can induce an illusion of familiarity, increasing the likelihood that primed items will be judged 'familiar'. Recent studies have found that this process may involve perirhinal cortex, which is also implicated in familiarity and item memory. In contrast to this repetition priming effect on familiarity, we have found that conceptual priming of test cues increases correct recollection. In fMRI, these behavioural priming effects correlate with BOLD priming effects in parietal and medial temporal regions that support recollection. In EEG, conceptual and repetition priming effects are temporally and topographically distinct. Recently, using homonyms, we have found that conceptual priming occurs only when the prime matches the semantic sense activated at encoding. These findings suggest that conceptual priming at test facilitates the retrieval of internally generated features of the encoding context, which is a key component of recollection.



Session Type: Symposium 1 - Prefrontal network contributions to cognition

Title: Prefrontal and mid cingulate neurophysiological markers and cognitive performance are dissociated during slow progressive dopamine lesion

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A common understanding of frontal control of executive tasks holds that performance monitoring in midcingulate cortex, indexed by feedback potentials, provides trial-by-trial information needed to update control on the task, the control being indexed by prefrontal beta oscillations. This update supposedly involves reinforcement learning signals, and dopamine is known to modulate both feedback potentials and prefrontal control signals. Hence these neurophysiological signals in frontal cortex have the potential to act as biomarkers for cognitive symptoms of dopaminergic lesion in Parkinson's disease.

I will describe experiments designed to test this set of hypotheses. We recorded chronic longitudinal frontal electrocorticography in macaques performing a test of cognitive control. We established the properties of the neurophysiological markers, and then followed them during a slow systemic dopamine depletion using the neurotoxin MPTP, up until the development of motor symptoms.

I will demonstrate the power of single trial analysis to reveal the complex nature of oscillatory power modulation by multiple aspects of cognitive control. I will then show how dopamine lesion selectively impairs feedback potentials, yet has no impact on either the performance or the beta oscillatory control signal, both thought to rely upon the system generating those potentials. The results allow us to posit a more nuanced model of how these systems interact within frontal cortex and with dopamine, and question the suitability of such signals as biomarkers.