Durham University
Wolfson Research Institute for Health and Wellbeing

20th Anniversary of Neuroscience North East

Neuroscience North East 2022

9:00–17:30 December 12th, Durham and Online

https://durhamneuroscience.co.uk/conference/
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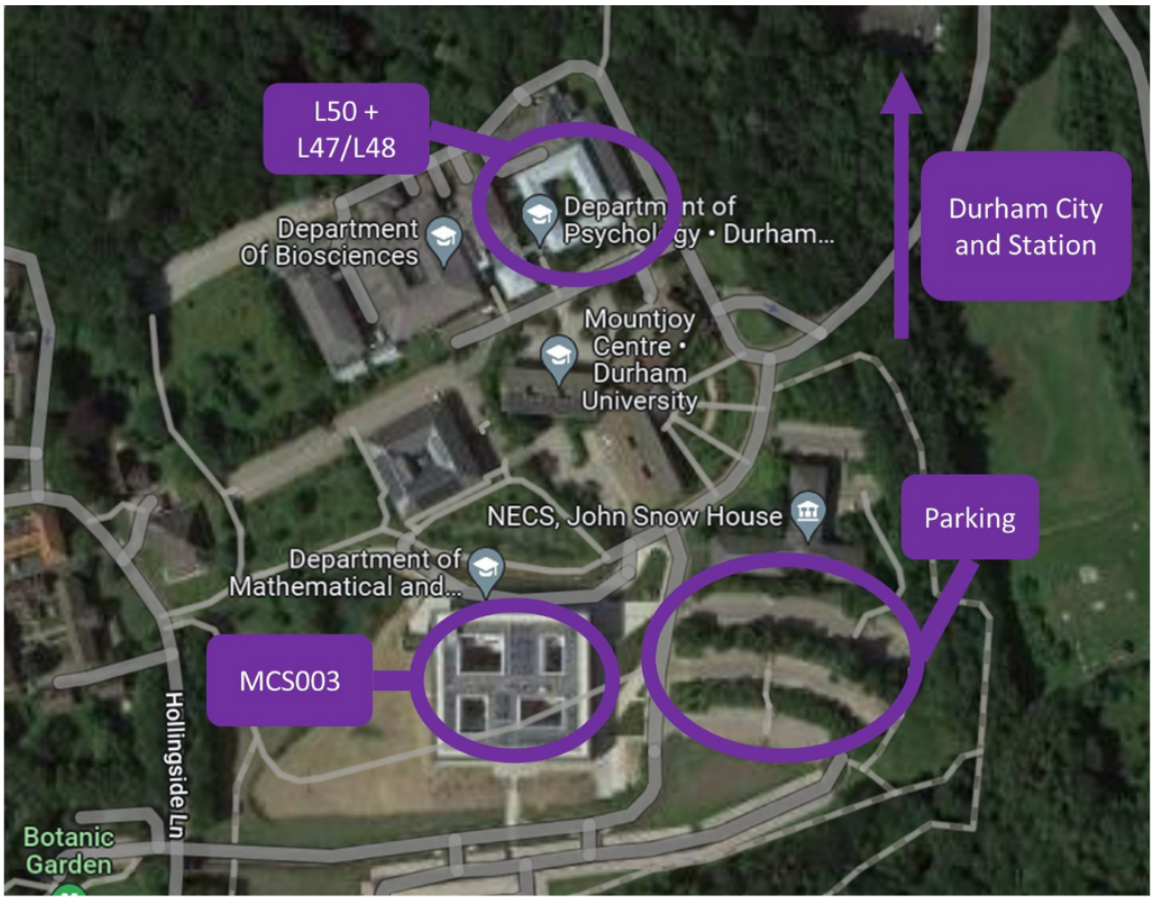

Time Slot	Activity	Room
9:00 - 9:30	Arrival	Biosceiences/Psychology Department
9:30 - 11:00	Symposium 1	L50
11:30 - 11:30	Refreshment Break	Psychology Department
11:30 - 13:00	Symposium 2	L50
13:15 - 14:45	Lunch and poster session	MSC003
14:45 - 16:15	Symposium 3	L50
16:15 - 16:45	Guest Speaker	L50
16:45 - 17:00	Prize and Final thoughts	L50
17:00 ONWARDS	Networking sessoion	Psychology Department

Guest Talk

Living with Parkinson's (20 years) & The value of engaging with clinical trials (GDNF specifically)

Chris Atherton-Proctor

16:15PM - 16:45 PM

Chris Atherton-Proctor was diagnosed with Parkinson's in 2004. 20 years later, she underwent surgery to take part in a Glial Cell Line Derived Neurotrophic Factor (GDNF) study on brain cells. After this, her life significantly improved. At NNE, she will be talking about living with Parkinson's as well as the value of engaging in clinical trials.

More about GDNF:

https://www.parkinsons.org.uk/research/gdnf-glial-cell-derived-neurotrophic-factor#:~:text=What%20is%20GDNF%3F,these%20cells%20to%20grow%20again.

PROGRAM

Symposium 1

Chaired by: Timothy Wise and Marco Bocchio

Symposium 2

Chaired by: Jonathon McPhetres and Penny Lawton

Symposium 3

Chaired by: Daniel Glassbrook and Michal Halicki

Posters

O1 - Circuit mechanisms of multi-neuron synchrony in the developing and adult hippocampus

Marco Bocchio, *Department of Psychology, Durham University*

The synchronous recruitment of multiple neurons is an important neural mechanism underlying various cognitive processes (for instance, memory consolidation and decision making). In addition, multi-neuron synchrony is altered in many brain disorders, for example epilepsy. Despite the physiological and pathological importance of multi-neuron synchrony, the circuit mechanisms allowing the brain to orchestrate neuronal co-activity remain unclear. I will present electrophysiological, calcium imaging and anatomical data showing how inhibitory neurons and specific neural pathways can regulate neuronal co-activity in the neonatal and adult hippocampus.

In the neonatal CA1 hippocampus, neuronal synchrony is high. A special set of inhibitory neurons born very early in development ('hub neurons') are key controllers of network bursts. This is achieved through widespread projection targets enabling these neurons to synchronise vast portions of the hippocampus. In the adult hippocampus, neuronal synchrony is low, but small network bursts associated with sharp-wave ripples occur during rest. Hub neurons remain morpho-physiologically distinct from other inhibitory neurons, displaying a remarkable correlation with pyramidal neurons' co-activity. This strong link with network activity may be linked to their long-range projection targets and a preference for excitatory inputs from local sources.

Next, I will show that neonatal network bursts are also controlled by glutamatergic inputs from the entorhinal cortex and the ventromedial thalamus, the two main excitatory inputs innervating CA1. While entorhinal inputs are able to control both sensory-driven and internally-generated network bursts, the thalamic inputs only control the latter. This is achieved via different circuit motifs, with the entorhinal inputs innervating both pyramidal neurons and interneurons, whereas the thalamic inputs are selective for the latter neuron type.

Finally, I will present all-optical data (2-photon calcium imaging and targeted single-cell optogenetics) demonstrating that in the adult CA1 hippocampus inhibitory interneurons favour pyramidal neurons' correlations and network bursts. These results challenge previous theoretical and experimental work claiming that inhibition exerts decorrelating effects on neural networks. This paradoxical action of inhibition

O2 - Defining the nuclear genetic architecture of a maternally-inherited mitochondrial disorder

Róisín M. Boggan

Mitochondrial function is under bi-genomic control; pathogenic variants in the nuclear and mitochondrial genomes (mtDNA) can result in clinical mitochondrial disease. The most common cause of multi-system adult mitochondrial disease (mtDNA variant m.3243A>G; NC_012920.1) is associated with extensive unexplained clinical heterogeneity. Variant m.3243A>G allele level, age and sex explain only a small proportion of this variability (pseudo-R^2 range = 0.05-0.26), whereas high to moderate estimates of heritability for some m.3243A>G-related phenotypes provide evidence for the influence of unidentified nuclear factors.

Using Haseman-Elston regression-based genetic linkage analysis in a cohort of 208 individuals from 83 pedigrees, we explored the nuclear genetic architecture of eleven phenotypes related to the m.3243A>G variant. For three phenotypes (migraine, cardiovascular involvement, and gastro-intestinal disturbance), no regions of interest were identified; simulation results suggest that any nuclear genetic contribution is highly polygenic in origin.

For seven phenotypes (cerebellar ataxia, chronic progressive external ophthalmoplegia, diabetes, myopathy, psychiatric disturbance, ptosis, and stroke-like episodes), at least one region of interest (LOD > 1.8) was identified. Seven regions of interest were identified for encephalopathy, including two (LOD > 3.3) on chromosomes 7 and 11, suggesting that a small number of nuclear factors play a key role in the development of this severe neurological phenotype.

This work describes the genetic architecture of the nuclear factors that influence m.3243A>G-related disease, revealing that different phenotypes are influenced by nuclear variation in different ways. Using the results of this work to inform future studies will enable the further elucidation of the underlying genetic architecture of this complex disease via genome-wide association studies, polygenic scores, and whole-genome sequencing. This work will build a better understanding of disease development and progression, and will have a tangible impact on patients and patient care.

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O3 - In vivo toxicology studies of retinoid acid receptor modulators drugs (RAR-Ms)

Lorenzo Croce, MSc, MSci, Professor Andrew Whiting, PhD and Professor Peter McCaffery, PhD
The Vitamin A Lab and Nevrargenics Ltd.
Institute of Medical Sciences
University of Aberdeen and Durham University

Retinoic acid (RA) is the active metabolite of vitamin A, a necessary micronutrient coming from both plant and animal sources. The main physiological function of RA is via the 'genomic pathway': activating expression of thousand of different genes through its nuclear retinoic acid receptor (RAR), a ligand-gated transcription factor.

In the past two decades RA, in addition to its key role as a developmental factor, it has emerged as a necessary mediator of major adult brain mechanisms, including neural plasticity and synaptic scaling.

Most interestingly, RA has proven a potent neuroprotective factor which can support axon regeneration. However, to achieve this outcome, not only does RAR need to activate the typical 'genomic pathway' but it also requires to act on the more recently discovered 'non-genomic pathway'.

The above properties of RA have great potential in neurodegenerative disease drug development, because neuroregeneration has always proved elusive throughout decades of pharmaceutical research.

Now, Aberdeen's Vitamin A lab is partnering with the company Nevrargenics ltd., in its goal to develop neuroregenerative small-molecule drugs based on Vitamin A: the retinoic acid receptor modulators (RAR-Ms). These drugs have been shown to activate both the genomic and non-genomic pathway in vitro, as well as inducing axon regeneration.

The first year of my PhD has focused on the first in vivo testing of the drugs to probe whether they would hit target RA genes and induce the genomic pathway. This goal was carried out together with the identification of a non toxic dose of the drugs.

After examining different dosages, results have proven positive showing no significant expected side effects (skin irritation) in mice treated with a dose still sufficient to activate RA reporter genes significantly in the cerebral cortex. The exception for side effects was the final highest dose, but for only one of the three drugs.

Specifically, the drugs have elicited a transcriptional response in the RA reporter gene Cyp26b1, the final catabolic enzyme in RA metabolism, which is know to have a direct expression response

to RAR activation. For this gene the highest doses of treatments elicited upregulation which exceeded 10 fold in RNA expression.

The Cyp26b1 gene has also shown an interesting time course pattern in its response to treatment. It showed upregulation (often >7 fold) in the cerebral cortex samples at the 2.5 hours after drug treatment, but this effect would decrease, cease or even reverse in the samples from the 24 hours after treatment.

Moreover, the effect size of the 2.5h upregulation and the amount of the ‘rebound’ at 24h was shown to be RAR-M dose dependent.

O4 - Investigating the role of dietary protein in cognition across the lifespan using *Drosophila Melanogaster.*

Sophie Waldron

In humans, sufficient intake and quality of dietary protein have been linked to preserved cognitive ability in ageing. Relatedly, epidemiological studies in humans and work with rodent models have isolated low dietary protein as a risk factor for dementia, implying that insufficient protein intake throughout the lifespan may cause disease. It is hypothesised that reduced levels of several neurotransmitters, whose precursors are often amino acids, may be the cause of these cognitive defects. Here, we used *Drosophila melanogaster* to investigate the consequences of protein deficiency on memory across the life course. Using defined culture media which allows precise control of amino acid concentrations, we showed that, despite decreased survival rates, cognitive abilities did not seem to be impaired by protein deprivation. This finding, which contrasts with existing findings in humans and other model organisms, suggests the existence of mechanisms to efficiently recycle neurotransmitters in deprivation states. Taking advantage of the numerically simple and genetically tractable brain of the fly, we are now researching the key genetic and molecular mediators of the interaction between diet, ageing, and cognition. I will present our latest results.

O5- **Mitochondrial dysfunction in parvalbumin cells tiggers juvenile-onset severe neurological dysfunction in vivo**

Elizaveta Olkhova

Mitochondrial diseases comprise the largest group of inherited metabolic disorders. Neurological symptoms include epilepsy, ataxia, and cognitive impairment. Previous *post-mortem* neuropathological studies implicated severe oxidative phosphorylation (OXPHOS) deficiencies in GABAergic inhibitory neurons accompanied by neurodegeneration in mitochondrial disease, including Purkinje neurons of the cerebellum. This study aims to test the hypothesis that underlying hyperexcitability may arise due to neuronal network disinhibition and that metabolically demanding fast-spiking parvalbumin-expressing (PV+) neurons are highly susceptible to mitochondrial dysfunction.

A novel mouse model of mitochondrial DNA (mtDNA) depletion selectively within the PV+ cells was generated by a conditional knockout of mitochondrial transcription factor A (*Tfam*) gene via *cre-loxP* system. Mice were characterised at behavioural, electrophysiological, neuropathological, and molecular levels. A battery of behavioural tests was used to phenotype the mice, including open field, rotarod, novel object recognition, elevated plus-maze, and visual cliff tests. *In vitro* electrophysiology was performed in acute hippocampal slices CA3 by inducing gamma oscillations via carbachol (cholinergic agonist) and kainate (glutamatergic kainate receptor agonist).

Mutant mice exhibited a progressive phenotype, initiating at 8 weeks of age with tremor, cognitive impairment (in the novel object recognition test) and anxiety-like behaviour (in the elevated plus-maze test). Hyper-locomotion and stargazing (absence-like seizures) were detected at 10 weeks, with severe ataxia observed by 12 weeks. Hippocampal electrophysiology demonstrated a deficit in gamma oscillations in the knockout group upon cholinergic agonism, and aberrantly high area power of gamma oscillations upon stimulation with glutamatergic agonist kainate. Concomitantly with these data, a loss of calbindin-expressing inhibitory interneurons was detected in hippocampal CA3 region. Taken together, hyperexcitability is implicated as a feature of this mouse model. OXPHOS complexes I, III and IV within the PV+ cells of the knockout mice had differential deficiency levels which were brain region dependent. PV+ neurons demonstrated an upregulation of anaplerosis enzyme pyruvate carboxylase, demonstrating metabolic remodelling in response to OXPHOS deficiency. Moreover, we detected an upregulation of activity-dependent PV calcium-buffering protein in Purkinje neurons and deep cerebellar nuclei neurons, corroborating c-Fos neuronal activity marker upregulation in these regions, providing evidence for hyperexcitability within the cerebellar loop. Purkinje neurons showed a reduction in mtDNA copy number and modest cell loss. Cerebellum exhibited reactive microgliosis and astrogliosis. Knockout mice had reduced weight and severely shortened lifespan. The novel mouse model recapitulates key features of neurological phenotype associated with mitochondrial dysfunction and could be used as a powerful translational preclinical mode

O6 - Glowing Glomeruli: Improving protocols for imaging bumblebees brains

Timothy Wise, Iman Muktar, Carolina Gomez Ramirez, Lena Riabinina
Insect Neuro Lab, Department of Biosciences, Durham University

Bumblebees (*Bombus spp*) are key global pollinators supporting agriculture and economies yet are facing widespread population declines due to habitat changes and industrialisation (Cameron and Sadd, 2020; Soroye, Newbold and Kerr, 2020). For pollination and mating, bumblebees use olfaction. This vital sense is reliant on the antennal lobes, formed of bunches of glomeruli, within the brain which process signals coming from the antennae. Despite research into the olfactory coding by the glomeruli, there are no studies covering their morphology or comparing across *Bombus spp*.

Hence, this research aims to understand the morphological differences between antennal lobe glomerular structure across *Bombus spp* to study interspecific differences and assess the connection to possible flower preference. Concurrently, progressive protocol improvements to the brain visualisation protocol are being made and assessed focusing on both the immunostaining and slide mounting stages.

Bumblebee species collected around Durham and then DNA barcoded for identification were dissected to isolate their brains which were then double immunostained to label Nesprin1 using cy3 tags, with some undergoing an additional tissue-clearing procedure adapted from murine systems. Afterwards, samples were mounted using different techniques (including tape and broken glass sides) to maintain 3d structure before confocal fluorescent imaging. Z-stacks were then processed using AMIRA (Thermo Fisher, 2019)to obtain volumetric data for comparative analysis.

Initial results indicate that glomeruli quantity and size vary across individuals and species. Regarding protocol, additional tissue-clearing protocol and alternate mounting techniques both provided improved image quality and visualisation. Future research needs to be done to further optimise these techniques and assess their relative benefit against cost.

References:

Cameron, S.A. and Sadd, B.M. (2020) ‘Global Trends in Bumble Bee Health’, *Annual Review of Entomology*, 65(1), pp. 209–232. Available at: https://doi.org/10.1146/annurev-ento-011118-111847.

Soroye, P., Newbold, T. and Kerr, J. (2020) ‘Climate change contributes to widespread declines among bumble bees across continents’, *Science*, 367(6478), pp. 685–688. Available at: https://doi.org/10.1126/science.aax8591.

O7 - Aphasia

Virginia Hehlert

People speak seeing and yet understanding nothing....
Moving their mouths and yet no one understands ...

Aphasia is a condition that turns life upside down after a stroke. Language is our favourite means of communication. Aphasia manifests itself in various ways, both the reception and the reproduction of speech can be disturbed, for example Broca's aphasia and Wernicke's aphasia. As individual as the patients are, as diverse can be the subtle differences of the respective aphasia. To enable the best possible cure, brain waves are being researched and have already shown a lot about language processing in each case in healthy people and in those with the disease.

At the conference I would like to give an overview of the dynamics of language reorganisation embedded in a system of neuroscience in aphasia. If there is still time, I would like to mention Van de Sandt-Koenderman's fMRI study in subacute and chronic aphasia.

About me:
I am an exchange student from Germany and currently enrolled in a double master in linguistics and media studies. During my bachelor thesis, I wrote about aphasia with a focus on aphasia during childhood. Currently, my research focus is on artificial intelligence.

Bibiography:

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O8 - Understanding the function of solitude in arousal regulation processes

Thuy-vy Nguyen, *Assistant Professor, Psychology, Durham University*

Solitude is commonly defined as either a physical experience of being alone or subjective experience of being alone. Instead of being a negative experience like loneliness, solitude is a regular event of everyday life. Across the lifespan, the amount and frequency of spending time alone increases with age, leading to solitude being studied most among older adults. While social capitals and socioeconomic factors can contribute to feelings of loneliness and isolation experienced in solitude, adults across age groups reported that time spent solitude is particularly beneficial for rest. However, how solitude provides such opportunity has not been well-understood. At most, previous literature presented contradicting evidence that makes it challenging to determine when solitude is restful. In this talk, I will discuss a few experimental works that might shed light on future research that can look at biological mechanisms that explain the regulatory function of solitude. Specifically, in my previous works, I identified a pathway through which solitude immediately impacts our emotions, and that is through arousal; when social stimuli are reduced, people's emotional arousal dropped in solitude. This means that we can begin to look at other biological and physiological processes connected to emotional arousal to explore further how we can cultivate solitude for health and well-being.

O9 - High resolution retinal imaging using an AOSLO to enable precision eye tracking

Penny F. Lawton a , Allie C. Hexley b , Hannah E. Smithson b , Laura K. Young a
a Biosciences Institute, Newcastle University, Newcastle, NE2 4HH, UK
b Department of Experimental Psychology, University of Oxford, Oxford, OX2 6GG, UK

The Adaptive Optics Scanning Laser Ophthalmoscope (AOSLO) is a retinal imaging system allowing us to image the cells in the retina with high resolution by correcting
for monochromatic aberrations in the optics of the eye. When using the AOSLO, participants are asked to fixate on a target to reduce eye movements, which cause distortions in the images. However, the eye is continually in motion, due to small-scale fixational eye movements, which are fundamental to vision [1]. While these have long been considered a nuisance for imaging, more recently distortions in AOSLO images have been exploited to provide high spatial and temporal resolution measurements of eye movement, well beyond the limit of traditional video-based eye trackers [2,3]. This allows precise investigation of fixational eye movements to shed new light on their role in vision. Accurate imaging and motion tracking, therefore, are key in investigating both the retina and eye movements. However, external factors such as beam wander, instability in the AO system, temperature fluctuations, bench movements, and other sources of vibration and turbulence may significantly impair these measurements. Importantly, these may be confounded with real movements of the eye, and this has so far not been considered. We have introduced a calibration technique involving imaging of a model eye placed after the scanning system and before the AO system. Thus, the real scan position is known independently, and any deviations due to external motion may be removed from the AOSLO imaging data. We will describe our AOSLO tracking method, the impact of external factors on the accuracy of these measurements, and how this compares to typical eye movements we may measure during a visual fixation task.

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Annual Review of Vision Science, 1, 499-518 (2015).
[2] Mulligan, J. B., “Image processing for improved eye tracking accuracy,” Behavior
Research Methods, Instruments, & Computers. 29, 54–65 (1997).
[3] Stevenson, S. B. & Roorda, A., "Correcting for miniature eye movements in high-
resolution scanning laser ophthalmoscopy," Proc. SPIE 5688, Ophthalmic
Technologies XV (2005).

O10 - Does Empathy equal Empathy? Comparing the Empathy Quotient and Interpersonal Reactivity Index

Isabel Nemec

The Empathy Quotient (EQ) (Baron-Cohen & Wheelwright, 2004) and the Interpersonal Reactivity Index (IRI) (Davis, 1980) are the most frequently used self-reports to measure empathy. Both measures define empathy in terms of cognitive and emotional empathy. An important difference exists between the EQ and the IRI, however, as the former measures empathy as a unidimensional trait and the latter as a multidimensional one. This study acts as a comparison between the EQ and IRI and aims to ascertain how affective they are at measuring the same construct by evaluating their convergent validity. Furthermore, this study investigates the scoring of sex differences in empathy on the EQ and IRI. In order to reach a broader target group, an English and a German version of both measures were used in an online survey: the original version of the EQ (Baron-Cohen & Wheelwright, 2004) and IRI (Davis, 1980), as well as the German version of the EQ (de Haen, n.d.) and IRI (Paulus, 2019).

18 participants (11 females, 7 males) completed the online survey in English and 76 participants (44 females, 31 males, 1 divers) completed the online survey in German. To evaluate the validity of the EQ and IRI, the data was first analyzed using a Pearson correlation analysis, a Bayesian paired samples t-test and a graphical comparison of the z-scores. Subsequently, the mean scores of the female and male participants were compared and an independent samples t-test was conducted, to evaluate whether both measures score equally in empathy in spite of the differences in their sex.

The results of the Pearson correlation analysis showed low correlation between the EQ and the total IRI score, as well as two IRI subscales (r ranging between 0.399 and 0.304, $p < 0.01$). A moderate correlation was found between the EQ and EC subscale ($r = 0.65$, $p < 0.001$). The graphical comparison of the z-scores of each participant revealed that half the participants were classified differently by the EQ and IRI. The results of the independent samples t-test showed only minimal differences in effect size for measuring sex differences in empathy for the EQ ($d = 0.615$, $p < 0.05$) and IRI ($d = 0.477$, $p < 0.05$). The results of this study suggest that the EQ and IRI present no sufficient concurrent validity and should therefore find limited application.

O11 - Chromesthesia - An examination of synaesthetic elements within Olivier Messiaen's '*Quatuor pour la Fin du Temps*'

Elwyn Rowlands

In this talk, I aim to provide an insight as to how neuroscientific knowledge can shed light on the nature of various musical compositions and forms as a useful interdisciplinary tool within arts and humanities subjects. I shall analyse the compositional output of the french composer, Olivier Messiaen, who was well-known for the synaesthetic elements that feature within his musical output. In particular, I shall examine Messiaen's use of what he perceived to be 'cascades of blue-orange chords' to symbolise his Catholic faith within the second movement of the *'Quatuor pour la Fin du Temps'* entitled *'Vocalise, pour l'Ange qui Annonce la Fin du Temps.'*

O12 - The need for the Oxford Visual Perception Screen (OxVPS) and it's cultural adaptations

Tsz Ying Flora Loh

Many stroke survivors report having visual perceptual impairments, yet most are often left undiagnosed. A review of current practices and challenges in screening for visual perception deficits after stroke was conducted and found that there was an apparently lack of uniformity in current practices for screening. There was also no standardised testing that was easily accessible and suitable for survivors with limited concentration or verbal issues. The Oxford Visual Perception Screen (OxVPS) and it's cultural adaptations aims to fill this gap in diagnosis and help facilitate the identification of visual perception deficits within stroke survivors for early treatment.

O13 - Emotional piloerection is dissociated from psychological experience

Jonathon McPhetres

Nearly everyone has experienced piloerection (goosebumps), and this seems like a very noticeable and obvious physiological event. However, in the present research (N = 71), we compared objective and self-reported goosebumps finding that participants are highly inaccurate at reporting when they experience piloerection during laboratory experiments. This low accuracy rate was not moderated by piloerection intensity, bodily location, or heart rate variability. However, goosebumps were observed on multiple body sites with relatively high frequency. A follow-up survey online (N = 500) found that participants most commonly monitor their forearms for goosebumps, suggesting that many participants are not monitoring their whole body or lack the ability to distinguish piloerection from other sensations. These results suggest that goosebumps are dissociated from psychological experience, perhaps because of their vestigial nature in humans.

O14 - The phenomenology of delirium in Parkinson's disease.

Florence Gerakios

Delirium is a neuropsychiatric syndrome defined by acute changes in attention, level of arousal and cognition. Delirium occurs in over half of patients with Parkinson's disease (PD) in hospital however, the diagnosis of delirium is often missed.

To better understand the phenomenology and natural history of delirium in PD. We will compare how features of delirium differ between participants with and without PD.

Participants with a diagnosis of PD admitted to Newcastle upon Tyne Hospital Trust were invited to take part (the Defining Delirium and its Impact in Parkinson's Disease' [DELIRIUM-PD] study and cross-sectional data from the Identifying Delirium and its Impact in Parkinson's disease [DETERMINE-PD] pilot study). Participants were compared with older adults from the Delirium and Cognitive Impact in Dementia (DECIDE) study. Delirium was diagnosed across consecutive days using the Diagnostic and Statistical Manual (DSM-5) criteria and severity was captured using the Memorial Delirium Assessment Scale (MDAS).

The pooled cohort consists of 241 participants; n=164 with PD and 77 older adults. 38.6% of participants without PD had a diagnosis of delirium (n = 77) whereas 59.1% of the participants with PD had delirium (n=97).

We have shown that delirium is more common in PD compared to older adults. This study will aid in the accuracy of symptom recognition and, subsequently, the prognosis of delirium in PD.

O15 - Targeting Neuromuscular Ageing using Novel Synthetic Retinoids and Chromo-Pharmacological Approaches

Topping, Alistair[1]*, Chazot, Paul[2], Whiting, Andrew[3], Pekovic-Vaughan, Vanja[1]**

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Deterioration in neuromuscular function is one of the main drivers of age-related loss of muscle mass and strength in animals and humans, leading to frailty and a lower quality of life. In addition, muscle atrophy is accelerated in many chronic diseases of ageing and is a key determinant of mortality, thus posing a global health challenge and an unmet clinical need for developing new therapies.

Many promising small molecules have been tested as therapies for age-related muscle atrophy in preclinical models, however, they often fail in clinical trials due to a lack of translational knowledge on drug administration regimens, such as dose, duration and timing of treatment. Retinoic acid derivatives have been shown to have protective effects on muscle and neuronal ageing in preclinical models, however, they have several properties that make them difficult to administer to patients safely and effectively. We, thus, focused on the development of an in vitro drug screening platform using chrono-pharmacological approaches, in order to elucidate the optimal time-of-treatment for several novel retinoid-based compounds.

In order to study the impact of retinoids in a time-of-day manner, we conducted genomic and cellular based assays, namely real-time qPCR and high-throughput real-time bioluminescence imaging, to ascertain retinoid effects on cellular circadian rhythms, a conserved ~24 time-keeping mechanism, governed by positive/negative transcriptional/translational feedback loops. Preliminary data in skeletal muscle cells showed that the treatments with retinoids had profound effects on the clock gene expression, targeting primarily the negative feedback loop of the molecular clock. This result was seen at both gene promoter and mRNA level. Moreover, our data has revealed that chrono-based timing of retinoid treatments had differential effects on clock reporter oscillations. Given that misalignment of circadian rhythms is linked to increased risk of drug toxicity, our findings shed light on the potential of chronotherapy in providing improved understanding of toxicology and efficacy of these novel compounds.

O16 - Probing prodromal biomarkers of Chronic Traumatic Encephalopathy (CTE) in retired rugby players with a history of multiple concussions

Michal Halicki & Paul Chazot, *Department of Biosciences, Durham University*

Over the recent years, several large cohort studies have reported that Traumatic Brain Injury (TBI) is a risk factor in the development of chronic, long-term neurological and psychiatric conditions. TBI has been associated with an increased risk of mental disorder and cognitive impairment as well as an early onset of neurodegenerative diseases, such as Alzheimer's Disease (AD) and Chronic Traumatic Encephalopathy (CTE). Concerns have specifically intensified over the health and well-being of contact sports players and war veterans who are especially prone to TBI and its potential long-term consequences. This problem is exacerbated by the difficulty of diagnosing neurodegenerative diseases. While several biomarkers have been approved for the diagnosis of AD, CTE can only be confirmed by a post-mortem brain autopsy. This study investigated the relationship between TBI and the levels of serum-derived prodromal biomarkers of CTE in our UK Rugby Health Project cohort of retired rugby players with a history of multiple TBIs. We aimed to distinguish biomarkers indicative of early manifestations of CTE, which could be useful in the clinical setting.

We used blood sera collected between 2016 and 2018 from retired rugby players and non-contact sports athletes as a part of the UK Rugby Health Project. We focused on biomarkers that have previously been associated with TBI, such as total Tau (t-Tau) and Serum Amyloid A (SAA). Further, we extended our research to autoimmune Neurofilament Light antibody (anti-Nf-L antibody), which to the best of our knowledge, have not yet been investigated in the context of TBI and CTE, but have been implicated in different neurological conditions. The levels of those biomarkers were quantified using enzyme-linked immunoassays.

Our results show that total Tau is the only analysed biomarker that was significantly elevated in the concussed retired rugby players compared to the non-contact sports control ($p \leq 0.001$, Mann-Whitney U Test). In addition, there was evidence of high autoimmune Nf-L antibodies in some of the concussed group participants, which given its first analysis in concussion, is worth probing further with an increased sample size. The findings about t-Tau are generally consistent with previous studies and suggest that t-Tau might be a reliable biomarker of long-term and chronic consequences of multiple concussions. However, to establish t-Tau as the biomarker of CTE more longitudinal studies that would include post-mortem brain autopsies to confirm the diagnosis are required.

O17 - Expression of the schizophrenia associated gene FEZ1 in the early developing fetal human forebrain.

Maznah Alhesain, Hannah Ronan, Fiona LeBeau, Gavin J Clowry

Newcastle University Biosciences Institute and Centre of Research Excellence in Neuroscience, Newcastle upon Tyne, NE2 4HH, the United Kingdom.

The protein fasciculation and elongation zeta-1 (FEZ1) is involved in axon outgrowth but potentially interacts with proteins whose roles range from intracellular transport systems to transcription regulation. Gene association and other studies have identified FEZ1 as being directly, or indirectly implicated in schizophrenia susceptibility. To test for a role in early human brain development, we mapped FEZ1 expression by region and cell type in the normally developing forebrain. All tissues were collected with appropriate maternal consent and ethical approval by the Human Developmental Biology Resource (HDBR.org). RNAseq data was obtained from previously published sources. Thin paraffin sections 8-21 post-conceptional weeks (PCW) were used to perform RNAScope in situ hybridization and immunohistochemistry against FEZ1 mRNA and protein and other marker proteins, sometimes in combination. Tissue RNAseq data revealed that FEZ1 is highly expressed in the human cerebral cortex between 7 and 17 PCW (top 5% of protein coding genes), and single cell RNAseq at 17-18 PCW in cortex and thalamus confirmed its high expression, predominantly in maturing excitatory neurons, but also in GABAergic neurons and non-dividing progenitor cells. Histological approaches confirmed, in the cerebral cortex, strong expression of mRNA and protein in post-mitotic neurons. At 10 PCW, in the progenitor zones, an increasing gradient of mRNA expression was seen from lateral to medial in both cortex and the ganglionic eminences, with high expression also in the thalamic progenitor zone. Protein expression was increasingly observed in axon tracts at older stages, co-localised with GAP43. FEZ1 has different expression patterns and potentially diverse functions in discrete forebrain regions during prenatal human development.

O18 - Delineating the neurodegenerative mechanisms underpinning epilepsy in Alpers' syndrome.

Dr Laura Alexandra Smith

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Background: Alpers' syndrome is a rare paediatric mitochondrial disease characterised by super-refractory epilepsy which is associated with severe neurodegeneration, rapid neurological decline and premature death. It is typically caused by bi-allelic pathogenic variants in the DNA polymerase gamma gene (POLG) resulting in mitochondrial DNA (mtDNA) depletion, consequent mitochondrial oxidative phosphorylation (OXPHOS) deficits and neural impairment. The precise neurodegenerative mechanisms underpinning the occipital-predominant epilepsy in Alpers' syndrome remain unclear. However, the dysfunction and degeneration of inhibitory interneurons, in conjunction with astrocytic abnormalities, are hypothesised to contribute to seizure-associated alterations in cortical activity.

Methods: We performed a detailed quantitative neuropathological investigation of inhibitory interneuron subtypes (parvalbumin+, calretinin+, calbindin+ and somatostatin+ interneurons) and reactive astrocytes (GFAP+) in post-mortem cortical tissues from 13 patients with Alpers' syndrome, 9 neurologically-normal controls and 5 sudden unexpected death in epilepsy (SUDEP) patients (to control for generalised epilepsy-associated pathology).

Results: In control brain, parvalbumin+ interneurons were more abundant within the occipital cortex when compared with other cortical regions and other interneuron subtypes. In contrast, we identified a severe loss of parvalbumin+ interneurons in Alpers' syndrome brain tissue, with decreased abundance of OXPHOS proteins in the remaining parvalbumin+ interneurons. Severe reactive astrogliosis was also evident in the occipital cortex of these Alpers' syndrome brains. This was characterised by an accumulation of abnormal hypertrophic astrocytes, which demonstrated both mitochondrial OXPHOS protein deficiencies and altered expression of key astrocytic proteins including glutamine synthetase (an enzyme responsible for metabolising the excitatory neurotransmitter glutamate), Kir4.1 (potassium ion channel subunit) and aquaporin-4 (astrocytic water channel).

Conclusions: The high relative density of parvalbumin+ interneurons in the occipital cortex is reversed in Alpers' syndrome brains and remaining interneurons exhibit severe mitochondrial dysfunction. This differential loss of parvalbumin+ interneurons may underpin the occipital-predominant epilepsy of Alpers' syndrome. Changes to crucial astrocytic proteins involved in recycling neurotransmitters and buffering ions, suggests that dysfunctional astrocytes have an important role in the pathophysiology by exacerbating the neuronal hyperexcitability in Alpers' syndrome.

O19 - Resting and post-sport information processing performance in athletes at risk of concussion

Dr Daniel Glassbrook, *Department of Biosciences, Durham University*

Mild traumatic brain injuries (mTBI) are one of the mostly commonly reported injuries in contact sport athletes, and pose a significant long term health risk (2). A mTBI is commonly known as a concussion, and is the result of a sudden movement of the brain within the cranium. Suffering a concussion can result in a range of symptoms for example, headaches and nausea, and has been linked to persistent cognitive decline and long-term neurodegeneration (1, 3). Concussion is however currently difficult to objectively assess. The Integrated Cognitive Assessment (ICA) is a newly developed method for the assessment of brain function, and may be applicable to the assessment of concussion in athletic populations. The ICA is a short test of cognitive function via an assessment of information processing speed, and is completed on a handheld device such as an iPad. The aim of this project was to determine changes in information processing performance after taking part in sports specific training. ICA Index, ICA Speed, and ICA Accuracy were assessed pre- and post-participation in contact and non-contact sports. Statistically significant changes were observed from pre- to post-sport in all variables, except for ICA Index in the non-contact group. ICA Index and ICA Speed increased (positive) in all groups after participation in sport, and ICA Accuracy decreased (negative) in all groups after participation in sport (Figure 1). Overall, the ICA test is able to measure changes in cognitive ability after sport. The improvements in ICA Index and ICA speed may be due to positive physiological benefits of sport participation, and the reduction in ICA Accuracy post-sport due to a speed-accuracy trade-off effect.

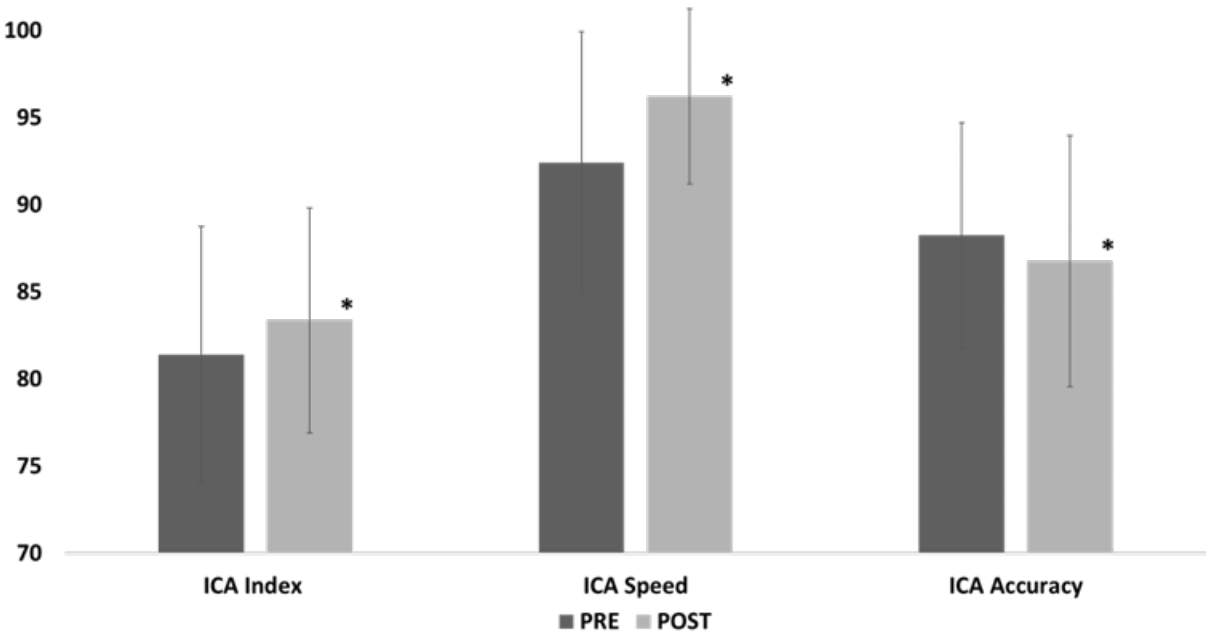

Figure 1. ICA results pre and post sport for all groups. Data are presented as mean ± standard deviation. *, Statistically significant $p < 0.001$.

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P1 - Can cognitive tests differentiate Progressive Supranuclear Palsy from Parkinson's disease?

Alexis Cheviet, Alison Lane, Anthony Atkinson & Daniel Smith

Progressive Supranuclear Palsy (PSP) is a common public health problem affecting about six people per 100 000. This neurodegenerative disease is characterized by a wide range of symptoms including falls proneness, mobility and swallowing difficulties, akinesia, axial rigidity, and vertical paralysis of the gaze. Owing to the large overlapping of these clinical signs with those reported in the common idiopathic Parkinson disease (PD), PSP is often mistaken as PD, at least during the early stages of the pathology. Existing research, including a pilot study we ran from 2015-2019, suggests that people with PSP have problems with visuospatial attention and short-term memory as compared to PD patients but these factors are not routinely used during diagnosis. Hence, the aim of this study is to analyse several cognitive functions on a large cohort of PSP and PD patients to verify the relevance of such tests as a diagnostic tool. Visual attention ability has been assessed thanks to three visual search tasks in which participant must identify a target among distractors (differing by its colour, its orientation, or a conjunction of both characteristics). Short-term memory task has been adapted from a change detection task in which each

volunteer has to recall the colour or the position of one among several objects. Additionally, we used an emotion recognition task to assess social cognition and three eye tracking-based tests to explore the integrity of oculomotor system (saccades, smooth pursuit and reading). Overall, preliminary results suggest that the assessment of these cognitive functions can be used as a cheap and effective way to differentiate PSP and Parkinson's disease.

P2

Laura Boylan

Examining the impact of interventions and support for adults with ASD Autism Spectrum Disorder (ASD) is a life-long neurodevelopmental condition characterised by persistent struggles in social communication and social interaction across multiple situations. Such struggles can have a negative impact on psychological and social wellbeing and may be associated with a range of negative consequences. Literature suggests that struggles associated with ASD continue into adulthood and quality of life for autistic adults is lower than for non-autistic adults. Autistic adults remain dependent upon others for everyday support, yet there is a lack of research examining the support that is needed for these adults. Research investigating support and interventions for autistic adults mostly focus on social skills training (SST). However, SST often run in contrived settings with immediate benefits. There is need for further research to examine if such support can be transferred to more naturally occurring settings, for more sustained improvements for autistic adults. There has also been increased interest in researching the benefits of music interventions for autistic people, although again, such studies tend to occur in contrived settings with a focus on adolescents. This research aims to address the gap with regards to interventions and support for autistic adults by exploring socially supportive interventions in a more naturally occurring setting; developing an understanding of the possible psychological and social benefits this will have. The research will work with the award-winning, international project, Aukestra: an ensemble that brings together autistic and non-autistic adults to share a common interest of making music and having fun. Using both qualitative and quantitative methods, the benefits of such informal, naturally occurring support can be ascertained. A template/model/resource can then be created for use by other support services working with autistic adults with the longer term goal of enhancing psychological wellbeing and overall quality of life for autistic adults.

P3- Small Molecule Inhibitors to Control Interferon-I Induced Neuroinflammation

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Though type-I interferons play a role in regulating the innate immune response, evidence shows they can exacerbate neuroinflammation.1 The key role of neuroinflammation in neurodegenerative diseases is becoming increasingly clear,2-4 and so it is accepted that aberrant IFN-I signalling contributes to the progression of diseases such as Alzheimer's Disease.5 As such, the interferon-I signalling pathway (Figure 1) is an attractive therapeutic target. Current IFN-I modulating drugs are JAK inhibitors, since they are "druggable". However, this leads to broad and unselective effects. Selective modulation of type-I interferons by targeting another point in this pathway has therefore become an area of great interest for drug discovery.

This poster will detail a phenotypic pathway approach to the discovery of new small molecule inhibitors of IFN-I signalling. Through this approach, we hope to uncover molecules that can modulate less commonly manipulated targets in the IFN-I pathway, validating where along the cascade provides an optimal balance between anti-inflammatory activity and undesirable side effects, such as susceptibility to infection.

Following hit identification (high-throughput screening) and validation, new compounds were designed to allow exploration of structure-activity relationships. Once synthesised using chemical techniques, these compounds were tested for their percentage inhibition of the IFN-I response and profiled via western blotting and fluorescent imaging methods. Results indicate an increased potency, along with what appears to be almost full knockdown of the IFN response in some cases. These findings provide evidence to support that the modulation of a target within the IFN-I pathway (other than the JAK protein) is possible and can lead to inhibition of the IFN-I response. They also contribute to our understanding of how this pathway can be manipulated to bring new medicines to patients.

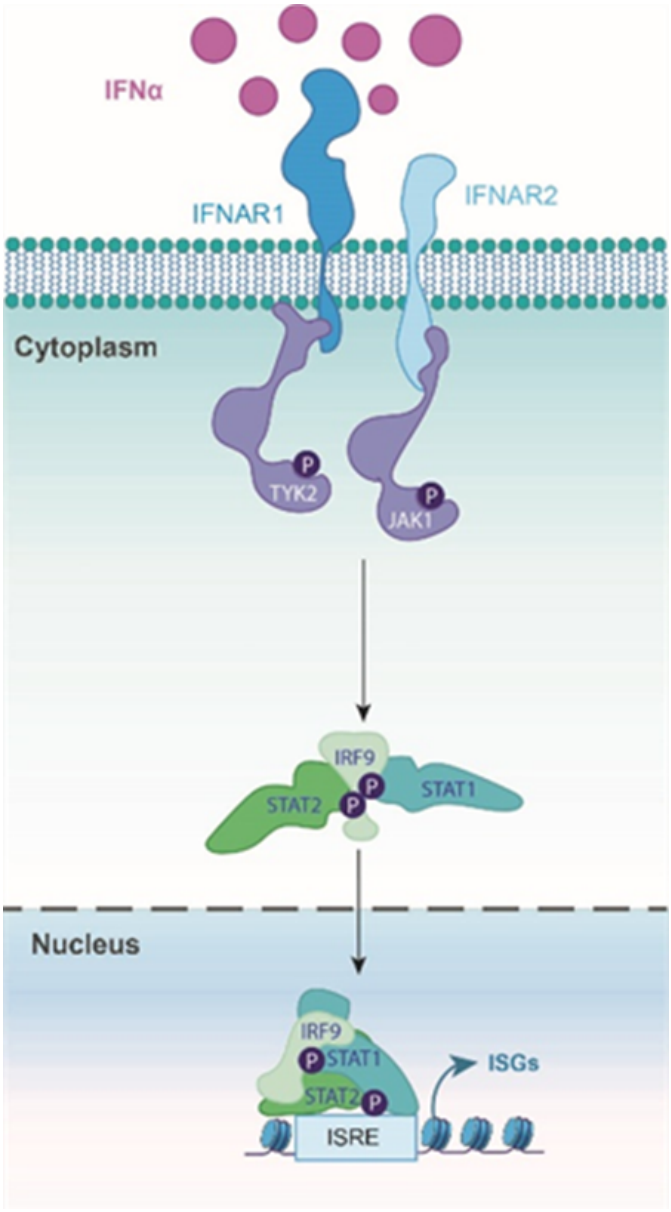

Figure 1: The IFN-I pathway

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P4 - Fixation Eye Movements- "Eye Tracking to Study if Fixational Eye Movements Improve Vision”

Varun Padikal

Our eyes continually move, even when we fixate our gaze on a target. These micro-movements are called fixational eye movements (FEM) and are classified as microsaccades, drifts, and tremors. Microsaccades are rapid ballistic movements up to 1° in amplitude with a frequency of 1 Hz. Drift is a slow, random walk with an amplitude between 0.04° and 0.13° and speeds around 1°/sec. Tremor is a tiny oscillatory or wavelike movement (amplitude less than 0.01°) with a frequency of around 90 Hz, although the existence of tremor is still debated. FEM are crucial to our visual perception, as they maintain gaze on a stimulus while counteracting perceptual fading. They also transform the spatial luminance pattern on the retina into a spatio-temporal neural signal, and there is evidence, at least in the case of drift, that this is beneficial for extracting visual information. It is also evident that the characteristics of these micro-eye movements change with ophthalmic disease.

The objective of our study is to investigate the contribution of FEM to visual acuity and how these micro-eye movements affect the vision of healthy individuals and patients with age-related macular degeneration (AMD). Accurate tracking of eye movements is essential in determining whether these micromovements are random or tuned to the stimulus and characteristics of the photoreceptor mosaic to improve vision. The study will also look into the possibility of using different FEM strategies to improve functional vision in AMD patients. To study these aspects of FEM, a commercially available video-based tracker the EyeLink 1000 Plus, and a custom-built Adaptive Optics Scanning Laser Ophthalmoscope (AOSLO) will be used.

Here in this work, we present our initial result from the EyeLink 1000 Plus on classifying different types of FEM using a widely used velocity threshold method (EK technique). We also describe a technique to correct the systematic gaze error in a video-based tracker through coordinate transformation and discuss the stability of these transformations over the course of the experiment. These techniques will aid in the development of a real-time stimulus stabilising system using a video-based tracker at higher retinal eccentricities.

P5 - Design and implementation of optoelectronic visual prosthesis

Emad Aal-Mullakhudher

Some people lose their vision gradually due to injuries or accidents. Also, losing their sight may be due to retinal degenerative diseases, such as age-related macular degeneration (AMD) or retinitis pigmentosa (RP). One of the most important and powerful solutions to restore vision is using artificial means such as implantable devices to treat this disease. Implantable devices are becoming increasingly important in clinical practice. Biosensors, pacemakers, and visual prosthetics may all utilize optoelectronics neuromodulation. One application of optoelectronics neuromodulation in visual prostheses is to control and record the electrical activities that is existing in the tissue. Therefore, these activities may be used by optoelectrophysiology. Electrical neuromodulation stimulation is effective in stimulating neuronal activity, but because it frequently spreads to nearby tissues, it usually leads to nonspecific stimulation. As a result, it is challenging to activate distinct neural sites. On the other hand, based on top-down methods of optical stimulation, most approaches focus on recording the outputs of stimulation inputs, such as observing muscle contractions as a response to action potentials (APs) in animals. Currently, the performance of neuroprostheses is restricted by the spatial resolution of electrical stimulation. However, optogenetics has been demonstrated to enhance the spatial control of neurons in vivo, but it does not offer the quick temporal mechanisms required for auditory and retinal signalling. Therefore, the purpose of this study is to demonstrate that combining electrical and optical neuromodulation stimulation approaches may address some of the limitations of using electrical and optical stimulation separately. The proposed study aims to build a visual brain prosthesis for blindness using a hybrid stimulating approach that combines electrical and optical stimulation technologies. In this regard, it is expected that the proposed research would contribute towards and may achieve the following; (1) Reduce the optical energy required to stimulate excitable tissues to reduce the possibility of thermal tissue damage, (2) Development of optogenetic-based neuroprosthetics featuring spatial and temporal flexibility, (3) Improving the spectral resolution of neural activation compared to electrical-only and optical-only stimulation, (4) Reducing the optical radiance required for neural activation compared to optical-only stimulation. To achieve the above contributions, this project will build a chip to design a hybrid technique that combines electrical and optical neuromodulation using the Cadence software simulator and this chip will be designed and fabricated based on XFAB technology.

P6 - What are the interactions between methylphenidate and Parkinson's disease?

Abigail Stretch, Dr Vincent Croset, *Department of Biosciences, Durham University*

Parkinson's disease (PD) is a common neurodegenerative disease, with growing prevalence worldwide. PD is characterised by the degeneration of dopaminergic terminals, and the presence of motor symptoms as well as changes in sleep and cognition. Current treatments mostly involve the dopamine precursor L-DOPA, although this is associated with motoric side-effects in early onset-PD and is insufficient at relieving symptoms in later stages. Identifying drugs that could outperform or complement the effects of L-DOPA could significantly improve the life of people living with PD.

Previous work in rodents and humans has shown that the psychostimulant Methylphenidate (MPH), which increases dopaminergic signalling by blocking dopamine reuptake from the synapse and is normally prescribed to patients with ADHD, may help relieve PD symptoms. Here, we aim to elucidate how MPH affects neurodegeneration in a *Drosophila* model of PD.

We used a novel feeding assay to establish that flies show a concentration-dependent preference for MPH, therefore suggesting a potential rewarding effect of this drug. We used this data to optimise delivery paradigms for testing drug effect on PD animals. We are now measuring the role of various concentrations of MPH, delivered on its own or jointly with L-DOPA in improving or delaying the onset of locomotor symptoms. For this, we are recording negative geotaxis, a behaviour previously shown to be affected in fly models of PD and commonly used as a metric for locomotor abilities in control and PD flies.

By establishing *Drosophila* as a robust model to study MPH effects on PD, we will provide a powerful tool to address the molecular and cellular effects of this drug on neurodegeneration, with unprecedented resolution. I will present our latest data.

P7 - Nutrient status-dependent behaviour exhibited by Drosophila is under peptidergic control

Elsa Moon

Fruit flies (Drosophila melanogaster) modulate their feeding their internal physiological state; for example, protein-deprived flies prefer to eat on protein-rich food sources above other resources, whereas protein satiated flies don't. These behavioural switches are essential for survival, and likely to be controlled by peptidergic signaling. Indeed, expression of several peptides in the brain is modulated by internal nutrient status to influence feeding. However, how individual neuropeptides influence preference to individual nutrients remains mostly unexplored.

Here we use a novel feeding assay to quantify food consumption and examine how varying nutrient deprivation states change feeding behaviour. Flies sucrose-deprived for 3 days show significant preference for sucrose-rich food over other rich sources. However, surprisingly, whereas protein-deprived flies prefer yeast over other food sources they do not demonstrate any particular preference for a solution of amino acids, even after long periods of deprivation. Therefore, we hypothesise that chemosensory cues present in yeast are crucial for state-dependent food choice. Next, we aim to further assess the role of insulin-like peptides (Ilps) in state-dependent behaviour by measuring their expression upon nutrient deprivation with qRT-PCR and knock down these peptides with RNA interference to elucidate their role in food choice.

Insulin signalling pathways are evolutionarily conserved across many organisms and have profound effects on ageing and age-related diseases in humans. Genetic modulation of Ilps in Drosophila can model metabolic disorders such as diabetes, hyperinsulinemia and those affecting glucose homeostasis, often age-related diseases, helping further characterise molecular mechanisms behind these disorders, discover drug targets and screen potential therapeutic modes to treat these disorders.

P8

Jacopo Franco

This project focuses on optomyography and the design of a near-infrared light-based sensor as a novel technique to non-invasively detect muscle movement. It is primarily intended as a method to control upper-limb prostheses. The sensor uses two near-infrared light-emitting diodes with different wavelengths. A photodiode placed above the muscle of interest detects the amount of back-scattered light. Tests comparing this technique to traditional electromyography sensors show the sensor has an easy-to-process output and good spatial accuracy. A good response match is obtained from the two sensor modalities, with reduced overall latency when using optomyography as a control signal. The current version of the sensor will be presented, with improved noise immunity and multi-channel capability.

P9

Cong Ma

With the development of medical technology, there is a growing demand for implantable medical electronics. The medical devices are used extensively for diagnostic, preventive and therapeutic purposes. For these implants, especially electronic implants. How to provide them with continuous function becomes a very important issue. At present, lithium batteries are commonly used in the market. However, disposable batteries such as lithium batteries have a limited storage capacity and need to be replaced frequently and manually when they run out of power, making long-term power supply impossible, this becomes a key issue. Finding new sources of energy is a good answer.

We have found that in the human body, glucose is one of the most important energy substances for many organisms and can be replenished through food intake. It is therefore an ideal raw material for fuel cells. We plan to use glucose in the human body as a fuel to develop a glucose fuel cell that can convert the stable chemical energy in glucose into electrical energy. When this device enters the body it can power electronic medical devices inside the body. The breakdown of glucose is currently carried out in both enzymatic and abiotic metal-catalyzed ways. Although enzyme catalysis has the advantage of high specificity and high reaction rate, its poor stability and short lifetime become fatal flaws. The non-biological glucose fuel cell has the advantage of high stability and long lifetime, and how to enhance its power generation efficiency as much as possible becomes a research problem for our group. We will study how to improve the power generation efficiency from the perspective of cell structure design.

P10 - Exploring a new disease-modifying approach for Alzheimer's disease based on retinoic acid receptor (RAR) modulation

Yunxi Zhang, Lilit Garzayan, Emily Hassard, Andrew Whiting, Paul Chazot

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Alzheimer's disease (AD) is the main cause of dementia around the world. AD is defined based on the presence of amyloid β (Aβ) plaques as well as neurofibrillary tangles consisting of hyperphosphorylated tau. AD Symptoms include cognitive decline, memory impairments and behavioral discrepancies. Previous AD studies have highlighted that oxidative stress, inflammation, cell death, senescence and autophagy are important in the disease. Retinoids and Retinoic acid receptors (RARs) are relevant to all of these mechanisms. NVG645, a synthetic retinoid, is a selective RAR agonist with high predicted specificity for RARβ over RARγ and RARα. In the present research, experiments were performed in the human neuroblastoma SHSY-5Y and Rat C6 glioma cell lines to evaluate the neuro- and glio-protective effects of NVG645 (10 nM). Experiments were also performed in the human fibroblasts (HDFs) and keratinocytes (HaCaTs) to evaluate the on-target side effects of NVG645 in the skin. Our results indicated that NVG645 exhibited a protective effect in SH-SY5Y and C6 cells associated with its antioxidant and anti-inflammatory effects. 4 h pretreatment of NVG645 had clear neuroprotective effects after 24 h of inflammatory or oxidative stress, including attenuating mitochondrial damage, reducing necrotic cell death, reducing inflammatory cytokine release, and increasing autophagy levels. NVG645 also had a significant effect in preventing C6 cell senescence. NVG645 can be considered a candidate drug for the treatment of AD and is worth further research.

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P11- Photobiomodulation therapy (PBMT) 1068 nm for the treatment of neurological complications of COVID-19

Lydia Kitchen

1. Introduction: At this stage of the COVID-19 pandemic, it remains important to find treatments for those with severe complications, including the pro-inflammatory cytokine storm, acute respiratory distress syndrome (ARDS), thrombosis and neurological problems. Photobiomodulation therapy (PBMT) using near-infrared light with the wavelength 1068 nm could be used as a non-invasive, drug-free treatment for COVID-19. PBMT acts via the mitochondrial enzyme cytochrome *c* oxidase to induce inflammatory changes, cytoprotection, nitric oxide release and increase blood flow. It is hypothesised that these effects will benefit the respiratory system and other organs targeted by SARS-CoV-2, including the brain (with neurological symptoms, ranging from anosmia to stroke and delirium, becoming increasingly common.)

2. Methods: Cultures of human neuronal (SHSY5Y) and rat glioma (C6) cells were stressed with SARS-CoV-2 spike peptide, lipopolysaccharides (LPS) or hydrogen peroxide, and treated with PBMT 1068 nm. Responses were measured with MTT assays (to compare mitochondrial activity), lactate dehydrogenase (LDH: a cytotoxicity marker) immunohistochemistry and immunofluorescence. Initial experiments were performed on human dermal fibroblasts (HDFs).

3. Results: PBMT improves (* $p < 0.05$) the viability of mitochondria in human skin cells under inflammatory and oxidative stress, obeying the cytochrome c oxidase theory of activation. In C6 glial cells, PBMT reverses the spike-peptide-induced redistribution of the SARS-CoV-2 receptor ACE2 to the cell membrane, which may be useful in reducing viral attachment.

Starvation with serum free media drastically reduces the number of glioma and neuronal cells, and PBMT was able to increase cell number (**** $p < 0.0001$ and *** $p < 0.001$ respectively) back to control levels. The basis of this was investigated and PBMT was found to have no effect on cell death (using the cytotoxicity marker LDH) but did increase the percentage of proliferating cells expressing Ki-67 in C6 cells (** $p < 0.01$).

4. Conclusions: This research demonstrates promising effects of near-infrared light irradiation against SARS-CoV-2 infection and neurological complications. In future experiments, these techniques will be repeated with human microglial cells to determine if they respond to PBMT in the same manner. ATP determination assays and calcium imaging will be used on all cell types to gain further understanding of the mitochondrial activation caused by 1068 nm PBMT.

P12 - Newcastle Visual Cortical Prosthesis

Yu Liu

The Newcastle Visual Cortical Prosthesis project aims to create an optogenetic form of visual cortical prosthesis. We have been developing several forms of probes - a low-resolution optical probe, a higher-resolution flexible optical probe matrix, and a more adaptive flexible optical probe, for optical stimulation of the cerebral cortex. We also have an interoperable ASIC (which we are developing in our sister project CANDO) for driving these probes. In this work, we would like to make an update to our subcutaneous control unit and information transfer software. Our subcutaneous control unit features wireless power transmission and wireless data transmission, a highly efficient compressed streaming algorithm developed and an image stimulation algorithm that matches the stimulation characteristics of the probe. Our control unit obtains power from external hardware through inductive coupling coils to provide power to various modules on the PCB, and its built-in energy management module also provides driving power for our probes. It receives the real-time image stream transmitted by external hardware through a Bluetooth connection, and after further processing, it controls the optrode array to flash according to the content of each frame of the image. The original image has been processed by methods such as an anisotropic diffusion algorithm, edge detection, pyramid resizing, and stimulator mapping to optimize the recognizability of the image while reducing the resolution. And we used run length coding to encode in the Bluetooth transmission process to further compress the size of the image stream. For each frame of the image to be displayed, the control unit dynamically allocates the power-on time of each LED on the optrode to ensure that the total drive current flowing through the optrode array does not exceed the maximum threshold that the brain tissue can tolerate.

Keywords: Visual cortical prosthesis, Optogenetic, Control system, Image processing.

P13

Peimen Yuan

Visual prosthesis devices are used to restore the vision of visually impaired people, by regulating their remaining healthy neurons in the visual pathway. Electrical stimulation devices are used to change the membrane voltage to regulate neurons. However, our vision is formed by the interaction of multiple types of neurons, but the electric field will affect all the neurons in the target region. Optogenetics can regulate only certain types of cells, but the device to emit light will influence a large region, which makes it difficult to realize a high-precision vision. A hybrid stimulus device that combines electrical and optic stimulation will be developed. The intensity of light and electric field will be controlled subthreshold to make sure that neurons would not release spikes without any of them, as they do when these stimuli work together. Local field potential (LFP) will be recorded as the feedback to monitor the activity of neurons to realize adjusting the stimulus intensity dynamically.

ACKNOWLEDGEMENTS

Thank you Dr. Paul Chazot, Lydia Kitchen, Timothy Wise (DUNE President), and DUNE exec members (Emma Cwiklinski, Elwyn Rowlands, Dilan Philibert, Karina Piotrowska, Winter Hong, Flora Loh) for leading and organising this event.

Thank you to our sponsors PCR Biosystems, Starlab, CRB, SLS, 2BScientific, Proteintech and Promega for your valuable contribution.

And finally, thank you to our speakers and participants for your enthusiastic contributions to neuroscience.