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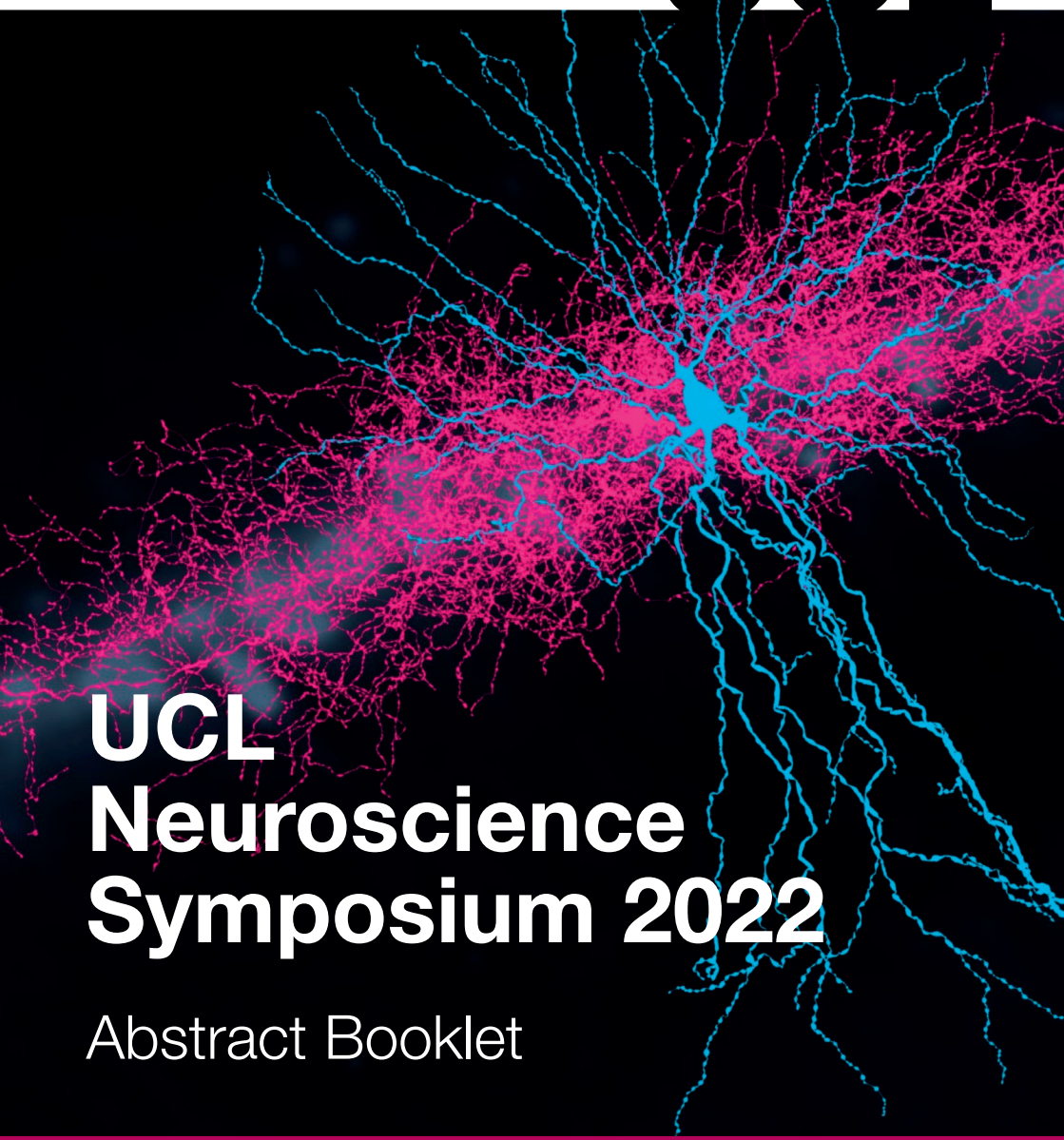

# UCL Neuroscience Symposium 2022

## Abstract Booklet

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The 10 posters shortlisted for the 2022 Research Poster Prize are highlighted in blue and will all be displayed in the Jeffery Hall.

## Cognition and Behaviour | Elvin Hall

### 1. Emma Clark - Cell and Developmental Biology

**POSTER TITLE**
The role of male-specific interneurons in memory retrieval

**AUTHORS**
Clark E, Molina-García L, Colinas-Fischer SR, Barrios, A.

**ABSTRACT**
The ability to integrate sensory stimuli with previous experience to form distinct behavioural outputs allows animals to adapt to their ever-changing environment. One factor which can influence the way sensory information is processed is biological sex. Sexual differences in learning and behaviour have been demonstrated in the free-living nematode Caenorhabditis elegans. Whilst both sexes of C. elegans show repulsion to the odorant benzaldehyde if associated with starvation, only males become attracted to the odorant if conditioning takes place in the presence of mates. Our lab has previously shown that this behavioural switch, known as sexual conditioning, requires a class of male-specific interneurons, the Mystery Cells of the Male (MCMs) (Sammut et al., 2015). However, MCMs do not show significant activation during sexual experience. Here we tested whether MCMs are required for memory retrieval rather than memory formation. We generated transgenic C. elegans expressing the fluorescent calcium indicator GCaMP in MCMs to monitor neuronal activity upon re-exposure to benzaldehyde. We found that there was significant difference in MCM activation upon benzaldehyde exposure in sexually conditioned C. elegans compared to pre-exposure, suggesting that the MCMs are specifically required for memory retrieval during sex-specific learning.

### 2. Susana Colinas Fischer - Cell and Developmental Biology

**POSTER TITLE**
Circuit and molecular mechanisms of an associative learning task

**AUTHORS**
Colinas-Fischer S, Molina-García L, Lin L, Barrios A

**ABSTRACT**
The ability of neural circuits to be changed by experience, optimising an organism's behaviour, is key to survival. We are dissecting the role of the neuropeptide PDF in mediating aversive olfactory learning to benzaldehyde in C. elegans. When benzaldehyde is paired with starvation, an aversive experience, C. elegans' response to benzaldehyde switches from attraction to repulsion (Lee 2010, Lin 2010). Here we show that both PDF-1 and PDF-2 mediate this form of aversive learning and seek to describe the underlying circuit.

Benzaldehyde is sensed primarily by the AWC neuron, which synapses onto first-level interneurons AIB, AIY and AIA to regulate naïve chemotaxis (Bargmann 1993, Chalasani 2007). We know that the AWC-AIB synapse is important for aversive learning (Cho 2016), but that learning can also occur elsewhere in the circuit. Therefore, we are looking to find which neurons are the relevant source of and target for PDF signalling in aversive learning. For this we are exploiting the strength of the Cre-Lox system to systematically test the role of PDF ligand and receptor-expressing neurons in aversive learning. We will then use calcium imaging to record the activity of implicated neurons and describe how learning changes the flow of information through the circuit.

### 3. Magda Dubois - Max Planck UCL Centre for Computational Psychiatry and Ageing Research; Wellcome Centre for Human Neuroimaging

**POSTER TITLE**
The role of exploration in impulsivity

**AUTHORS**
Dubois M, Hauser T.

**ABSTRACT**
Deciding whether to forgo a good choice in favour of exploring a potentially more rewarding alternative is a challenging arbitration in human reasoning and artificial intelligence. Humans show substantial variability in their exploration. In particular, one can distinguish between complex exploration strategies, (i.e., take expectations as well as the uncertainties of choice options into account), and heuristic strategies (i.e., require relatively less computation). The cheapest such strategy, value-free random exploration, deliberately ignores all available information, in effect choosing entirely randomly. Even though such mechanism can be suboptimal, humans occasionally rely on it due to its low computational demand. Theoretical but only limited empirical work has suggested that excessive exploration is a critical mechanism underlying the psychiatric dimension of impulsivity, but little is known about the specific exploration strategy which is at play. Supported by previous findings that impulsivity is associated to increase avoidance of mental effort, we hypothesized that it is specifically value-free random exploration which is associated with impulsivity. We put this theory to test using a large online sample (N=580 healthy adults), dimensional analyses, and computational modelling in a pre-registered study. We used a novel exploration task which allows to assess the contribution of distinct exploration strategies in human decision-making. We demonstrate that impulsivity is associated with value-free random exploration ($r=0.26$, $p<0.001$). Our results allow to shed light on the mechanisms which go awry in impulsive subjects.

### 4. Samuel Failor - UCL Queen Square Institute of Neurology

**POSTER TITLE**
Visuomotor association orthogonalizes visual cortical population codes

**AUTHORS**
Failor SW, Carandini M, Harris KD

**ABSTRACT**
The response of a neuronal population to a stimulus can be summarized by a vector in a high-dimensional space. Theoretically, the brain should be most able to associate distinct behavioural responses to two sensory stimuli when the rate vectors they evoke are close to orthogonal. To investigate whether and how the formation of distinct visuomotor associations modifies visual population codes, we measured the orientation tuning of 4,000-neuron populations in primary visual cortex before and after training on a visuomotor association task, where two stimuli were associated with opposite behavioural responses. Visuomotor association suppressed responses to the stimuli associated with motor actions, most strongly amongst weakly-tuned neurons. This suppression reflected a simple change at the population level: sparsening of population responses to motor-associated stimuli, resulting in the orthogonalization of their rate vectors. The magnitude of population response sparsening to the motor-associated stimuli dynamically varied trial-by-trial and was well explained by a model of F-I curve modulation.

**5. Karolina Farrell - Experimental Psychology**

**POSTER TITLE**
VTA dopamine neurons signal phasic and ramping reward prediction error in goal-directed navigation

**AUTHORS**
Farrell K, Lak* A, Saleem* AB

**ABSTRACT**
The predominant theory of ventral tegmental area (VTA) dopamine neuron function is that they signal reward prediction error (RPE) in their phasic activity. A recent study observed ramping dopamine release during goal-directed navigation, but its relationship to RPE signalling is currently under debate. We set out to explain the function of this ramp and its relationship to phasic RPEs experimentally and theoretically.

We characterised VTA dopamine neuron activity by performing calcium imaging as mice learned to perform a goal-directed navigation task in virtual reality. Across learning, phasic responses resembling RPEs developed, as well as a slow pre-reward ramp in activity. This ramp was modulated by learning stage and task engagement.

To explain whether this ramp could represent RPE, we devised a Q-learning model that incorporated noisy state inference. This model recapitulated our behavioural findings and produced simultaneous phasic and ramping prediction error. The model predicted that a ramp should improve task performance, which we confirmed in our experimental data, indicating that the ramp played a teaching role in the selection of accurate location-specific action during navigation. Our findings provide neural evidence and a theoretical framework to explain ramping dopamine neuron activity as a form of RPE that improves goal-directed navigation.

**6. Dwaynica Greaves - UCL Institute of Cognitive Neuroscience**

**POSTER TITLE**
Exploring theatre neuroscience: using portable technology to measure an actor’s sense of self and interpersonal coordination

**AUTHORS**

Greaves DA*, Pinti P*, Din S, Hickson R, Diao M, Lange C Khurana P, Hunter K, Tachtsidis I, Hamilton A F de C

**ABSTRACT**

Collaborations between neuroscientists and the theatre industry enables research on social cognition to be conducted in ecologically valid settings with replicable realistic stimuli. Here researchers present the first proof of principle to firstly investigate the technical limitations of measuring real-life social interactions in theatrical settings and how to overcome those. Secondly, the effects of being in character on an actor's sense of self. Thirdly, whether interpersonal coordination can be measured across various modalities (neural, physiological, and behavioural). Participants were six actors from Flute Theatre who were rehearsing an extract from Shakespeare's A Midsummers Night's Dream. Actors completed a walking (control), speaking (control) and acting task where their names or fellow actors' names were called out during the rehearsal. Measurement devices included functional near infra-red spectroscopy (fNIRS), motion capture (MOCAP) and a physiological monitoring belt. Findings revealed suppression of prefrontal cortex regions when actors heard their own names whilst acting compared to control conditions. In addition, there was significant interpersonal coordination across the three modalities. Researchers concluded that theatre neuroscience, portable multimodal technology/datasets as well as hyperscanning paradigms are effective in the study of real-world neuroscience and show a promising direction for the ecological validity of research within the field.

**7. Benedict Greenwood - UCL Institute of Cognitive Neuroscience**

**POSTER TITLE**

Which ADHD traits modulate the control of attention to task-relevant and task-irrelevant emotional stimuli?

**AUTHORS**

Greenwood BM, Garfinkel SN

**ABSTRACT**

Many individuals with attention-deficit hyperactivity disorder (ADHD) have difficulties regulating their emotions, potentially due to differences in controlling attention to emotional stimuli and/or altered emotional reactivity. It is unclear whether differences in controlling attention to emotional stimuli relate to the inattentive or hyperactive/impulsive features of ADHD. In this online study, adults from the general population (N=119) completed a self-report assessment of ADHD traits and an executive function task. On each trial, participants were presented with a happy, angry or neutral face and had to identify the expression (emotion is task-relevant) or gender (emotion is task-irrelevant). The main performance measures were percent correct responses and parameters (mu, sigma and tau) describing the distribution of response times. Increasing inattention traits were associated with reductions in the speed advantage (lower mu) for task-relevant happy over neutral stimulus features. Greater overall ADHD symptomatology was associated with reductions in the accuracy advantage for task-relevant happy and angry faces over neutral faces. Responses to task-irrelevant emotional stimulus features were unrelated to any ADHD traits. The results suggest that, in the general population, difficulties in controlling attention to task-relevant

emotional information are driven more by the cognitive mechanisms underlying inattention traits than the those driving impulsivity.

### 8. Marta Huelin Gorriz - Experimental Psychology

**POSTER TITLE**
The role of prior experience in the replay of both novel and familiar contexts

**AUTHORS**
Huelin Gorriz M, Bendor D.

**ABSTRACT**
The sequential reactivation of place cells (i.e. hippocampal replay) during sleep, is postulated to be a central mechanism for memory consolidation. Here we investigate how memories are prioritised for sleep replay by varying two key factors influencing memory consolidation: (1) the temporal duration of an experience and (2) its familiarity arising from the amount of prior experience.

Rats were trained to run on two novel tracks, each track limited to a fixed but different number of laps (varying experience duration). Following a post-run sleep session, rats were re-exposed to both tracks again, but for the same amount of time (varying familiarity).
We found that in both novel and familiar environments, the number of awake replay during the most recent behavioral episode was the most accurate predictor of the rate of sleep replay (events/s) occurring during the subsequent sleep session.

### 9. Alexane Leclerc - UCL Queen Square Institute of Neurology

**POSTER TITLE**
How do visual perception and imagination overlap in the brain?

**AUTHORS**
Leclerc A, Dijkstra N, Kok P, Fleming S.

**ABSTRACT**
Background. How imagination and perception interact within the brain remains poorly understood. Recently, in a behavioural study, Dijkstra, Mazor, Kok & Fleming (2021) found that imagining a stimulus increased the likelihood of detecting that same stimulus at threshold. Moreover, participants with more vivid imagery were more likely to report the presence of an external stimulus, suggesting interactions between imagery and perception.
Aim. In a neuroimaging study, we aimed to ask at what locus in visual processing imagination and perception overlap, by asking subjects to imagine one grating orientation and presenting, at perceptual threshold, either a congruent or incongruent grating.
Methods & Results. During piloting, we found that the psychological manipulation of imagery-perception congruency fluctuated too slowly to be detectable after high-pass filtering the BOLD response. To combat this issue, we designed an online behavioural experiment in which congruency fluctuated 4x as rapidly. However, we failed to replicate the psychological congruency effect found in Dijkstra, Mazor, Kok & Fleming (2021) in this faster design. The challenge is therefore to find an optimal trade-off between a faster design necessary for analysing BOLD signal dynamics and a slower design that may be important for revealing psychological effects of imagery. I will present the results of behavioural

experiments conducted across a range of congruency alternation frequencies that are designed to address this issue.

### 10. Alexis An Yee Low - UCL Queen Square Institute of Neurology

**POSTER TITLE**
Self-Esteem depends on beliefs about the rate of change of social approval

**AUTHORS**
Low AAYL, Hopper WJT, Angelescu I, Mason L, Will G-J, Moutoussis M

**ABSTRACT**
A major challenge in understanding the neurobiological basis of psychiatric disorders is to rigorously quantify subjective metrics that lie at the core of mental illness, such as low self-esteem. Self-esteem can be conceptualized as a 'gauge of social approval' that increases in response to approval and decreases in response to disapproval. Computational modelling approaches have shown that learning signals that represent the difference between received and expected social approval drive changes in self-esteem. However, it is unclear whether self-esteem based on social approval should be understood as a value updated through associative learning, or as a belief about the self, updated by new evidence depending on how strongly it is held. Our results show that belief-based models explain self-esteem dynamics in response to social evaluation better than associative learning models. Importantly, our findings suggest that in the short term, self-esteem signals the direction and rate of change of one's beliefs about approval within a group, rather than one's social position.

### 11. Lennart Luettgau - Max Planck UCL Centre for Computational Psychiatry and Ageing Research

**POSTER TITLE**
Behavioral and computational evidence for compositional reuse of experience in humans

**AUTHORS**
Luettgau L, Moran R, Stachenfeld KL, Kurth-Nelson Z, Dolan RJ

**ABSTRACT**
Interacting processes produce our everyday experiences, e.g., meeting friends in the park in summer is a product of community structures and cyclic seasonality. Decomposing factors underlying experience allows reusing knowledge in similarly structured environments. We tested this ability in a paradigm featuring two cyclic graph factors (4 and 6 states), presenting trajectories through two-state compositions. Participants experienced 12 of 24 possible product-states but could recombine graph factor knowledge to infer unexperienced compositions. We assessed graph factor knowledge by asking participants to predict upcoming experienced (Sequence Probes) and unexperienced states (Inference Probes). We found above-chance performance that increased over time – with higher Sequence Probe than Inference Probe accuracy. Inference accuracy was higher for the 4-state than the 6-state graph. Computational simulations showed that a successor feature model learning product state predictions performed poorly during Inference. Another successor feature model, learning expectations about features constituting product states, showed above-chance accuracy in Inference Probes, which remained stable over time. Additionally,

Sequence and Inference Probe accuracy were indistinguishable. A hybrid model captured features of human behavior but predicted no difference between both graph factors' Inference Probe accuracies. Our results suggest that humans factorize state spaces underlying their experience, allowing for compositional reuse of knowledge.

### 12. Karyna Mishchanchuk - Neuroscience, Physiology & Pharmacology

**POSTER TITLE**
Computational strategies and neural correlates of probabilistic reversal learning in mice

**AUTHORS**
Mishchanchuk K, MacAskill AF

**ABSTRACT**
When faced with a changing, uncertain environment it is necessary to infer its underlying structure to guide behaviour. This has often been formalised as a value updating problem – where actions are chosen based on the weighted average of past reward. Activity of midbrain dopamine neurons is commonly associated with the error in such value prediction, and is proposed to be crucial for learning and updating of values to inform decision making. However, it has become increasingly apparent that both humans and animals often use an alternative strategy – inferring hidden states to make predictions and guide behaviour. In this study we hypothesised that mice might also use hidden state strategies during decision making, and that this would be reflected in midbrain dopamine activity.

To investigate this, we used a probabilistic reversal learning task in mice. In this paradigm, for optimal performance it is necessary to continuously integrate past trial outcomes to predict reward contingencies associated with different actions across reversals. Probing animals' behaviour with computational modelling, we found that it was consistently best fit by models that incorporated hidden states. Furthermore, by recording dopamine release in the nucleus accumbens during the task, we found phasic dopamine was most strongly predicted by error associated with hidden state inference strategies.

Overall, we find that mouse behaviour and midbrain dopamine activity during probabilistic reversal learning is best described by a hidden state inference strategy. Ongoing work is investigating the sources of the state prediction that influence dopamine signalling during decision making.

### 13. Laura Molina-Garcia - Cell and Developmental Biology

**POSTER TITLE**
Neuropeptide modulation of aversion and reward during learning

**AUTHORS**
Molina-García L, Colinas-Fischer S, Clark E, Minaur-Ortiz B, Truman R, Lin L, Barrios A.

**ABSTRACT**
To understand how the brain integrates reward and aversion during learning, we are dissecting a circuit for sexual conditioning (SC) in C. elegans. SC is a form of male-specific associative learning by which a rewarding experience with mates overrides an aversive association with starvation, switching the males' behaviour to a stimulus from repulsion to

attraction. Previously, we implicated the MCMs interneurons and the neuropeptide PDF-1 as regulators of SC. Here we show a dual role for PDF-1 in regulating aversive and appetitive learning in C. elegans by acting on different neurons.

Neuropeptides signal extrasynaptically, yet the relative contribution of source specificity versus overall neuropeptide levels is unknown. By performing cell-specific removal of PDF-1, we identified the source of PDF-1 for SC. Specific neurons that receive input from mate-sensing neurons, but not other PDF-1 expressing neurons, are required for SC. Interestingly, PDF-1 from these neurons is not required for aversion, strengthening the importance of source specificity during neuropeptide signaling. Therefore, we have linked a molecule to a set of neurons controlling a behavior that underlies sex differences in learning.

Currently, we are measuring neuronal activity to further understand how sensory information is represented after conditioning and how PDF-1 switches stimulus preferences.

### 14. Annie Morsi - Psychology and Language Sciences

**POSTER TITLE**
Face perception varies systematically across the visual field

**AUTHORS**
Morsi, A
Goffaux, V
Greenwood, JA

**ABSTRACT**
Low-level vision varies predictably across the visual field, with acuity and contrast sensitivity better along the horizontal compared to the vertical meridian and in the lower compared to the upper visual field. In contrast, judgements of facial appearance have been found to vary idiosyncratically across the visual field, suggesting a dissociation between higher-level face recognition and low-level vision. To compare these variations more directly, we developed a face acuity test measuring the smallest size necessary to judge gender at 8 visual field locations. In 3 experiments, we demonstrate a clear horizontal-vertical difference for gender acuity. We also found evidence for an upper-lower difference, which although smaller than the horizontal-vertical difference, was consistently present. In other words, the spatial resolution of face perception varies systematically across the visual field, mirroring patterns seen for low-level vision. Spatial properties are inherited through the visual system, causing location to influence face perception.

### 15. Tara O'Driscoll - Neuroscience, Physiology & Pharmacology

**POSTER TITLE**
Investigating the emergence of neural circuits for navigation in developing rats using wireless technology

**AUTHORS**
O’Driscoll T, Muessig L, Cacucci F, Wills T.

**ABSTRACT**
The neural representation of space is encoded by spatially-modulated neurons including head direction cells (HD cells), place cells, and grid cells. Previous work has shown that these cell types emerge sequentially in rat postnatal development.

Typically, spatial cognition experiments using in vivo electrophysiology are made as a single animal forages in an open-field environment while tethered to an acquisition system. In developmental studies, this requires the removal of the rat pup from its homecage, mother and littermates. Wireless technology is emerging as a promising alternative: neural data loggers permit the recording of single-unit neuronal activity in an animal's homecage, thereby tracking spatial cell development while minimising disruption of early sensory experiences. The first aim of this study was therefore a proof-of-concept that wireless recordings of spatial cells in rat pups are comparable to standard techniques.
The second aim was to investigate whether the maturation of HD cells follows a different trajectory in a naturalistic environment to that previously observed in traditional open-field recordings. To address this, ensembles of HD cells were wirelessly recorded in the homecage from P12 to P16.

By studying the ontogeny of these cells, we hope to better understand the neural basis of spatial learning and memory.

### 16. Jessica Passlack - Neuroscience, Physiology & Pharmacology

**POSTER TITLE**
Role of nucleus reuniens in flexible behaviour dependent on cues and outcomes

**AUTHORS**
Passlack J, Burgess N, MacAskill A

**ABSTRACT**
We must constantly decide how to behave in an environment under different circumstances. The hippocampus (HPC) and prefrontal cortex (PFC) are both necessary to drive such flexible behaviour. However, it is unclear how HPC and PFC interact to support flexible behaviour. To understand what role each structure plays, we first looked to see how they are anatomically connected through their largest bidirectional source of connection: nucleus reuniens (nRE). We found that there are distinct regions of nRE that project to HPC and PFC. To generate hypotheses about the distinct information that is being transmitted to HPC and PFC, we built Bayesian reinforcement learning models representing HPC and PFC. HPC models learn detailed environmental maps in the form of successor representations, whereas PFC models learn outcome-based state-value maps. We found that the models have opposing limitations: HPC models struggle to separate different behaviours during learning, but PFC models cannot utilize predictive cues. Interestingly, utilizing information from PFC models stabilizes learning in HPC models, which can then be used to guide responses to predictive cues. To test our hypotheses about the distinct information transmitted from nRE to HPC and PFC, we ultimately aim to inhibit each projection during flexible behaviour in mice.

### 17. Masahiro Takigawa - Experimental Psychology

**POSTER TITLE**
Experience-Driven Rate Modulation is Reinstated During Hippocampal Replay

**AUTHORS**
Takigawa M, Tirole M, Gorriz MH, Kukovska L, Bendor D

**ABSTRACT**
Replay, the sequential reactivation of a neuronal ensemble, is thought to play a central role in the hippocampus during the consolidation of a recent experience into a long-term memory. Following a contextual change (e.g. entering a novel environment), hippocampal place cells typically modulate their in-field firing rate and shift the position of their place field, providing a rate and place representation for the behavioural episode, respectively. However, replay has been largely defined by only the latter- based on the fidelity of sequential activity across neighbouring place fields. Here we show that dorsal CA1 place cells in rats can modulate their firing rate between the replay of two different contexts, mirroring the same pattern of rate modulation observed during behaviour. This context-driven rate modulation within replay events was experience-dependent, observable during both behavioural episodes and throughout the subsequent rest period, but not prior to experience. Furthermore, we demonstrate that both the temporal order and firing rate of place cells can independently be used to decode contextual information within a replay event, revealing the existence of two separable but complementary neural representations available for memory consolidation processes.

## 18. Ruslana Tymchyk - UCL Division of Psychiatry

**POSTER TITLE**
The effects of a mindfulness-based decentering intervention on momentary changes in self-esteem during social feedback

**AUTHORS**
Tymchyk R, Norbury A, Huys Q.

**ABSTRACT**
Background/Intro
Mindfulness-based therapies improve general mental wellbeing and reduce the symptoms of depression (Fjorback et al., 2011). However, more research is needed to identify which elements of mindfulness-based therapy programmes contribute to reduced depressive symptoms. Multiple factors also contribute to the symptoms of depression. One potential contributory factor is biased updating of self-evaluative beliefs (self esteem) during social feedback (Will et al., 2017).

Methods
This study will investigate whether mindfulness-based decentering interventions contribute to symptom improvement by altering how self-esteem changes in response to social feedback. Specifically, participants will complete a previously characterized social evaluation task (Will et al., 2017) both before and after completing a randomly-assigned intervention (decentering or control condition). Changes in the effects of social feedback on momentary self-esteem ratings will then be compared between conditions.

Hypothesis
We hypothesise that the decentering intervention will decrease the impact of negative feedback on self-esteem, compared to the control intervention.

Results
The abstract only presents design. Data acquisition and analysis will be complete by July.

Implications
Findings may provide insight into mechanisms underlying effective mindfulness-based cognitive therapies for depression.

**19. Paula Wicher - UCL Institute of Cognitive Neuroscience**

**POSTER TITLE**
Copying choice induces liking: an online study of art preferences

**AUTHORS**
Paula Wicher, Antonia Hamilton

**ABSTRACT**
It is widely believed that being mimicked makes us like the person more (Chartrand and Bargh, 1999). Does this phenomenon also hold true for copying choices? In an online interactive study using Zoom, 40 participants had live conversations with confederates who did or did not copy their art choices. They then completed measures of perceived warmth and competence to assess first impressions, whilst their facial behaviour was video recorded. The results showed that confederates who mimicked the participants' art preferences were liked more than those who made dissimilar choices. Moreover, copying preferences increased social perceptions of warmth (e.g., friendliness, attractiveness, similarity), but not competence (e.g., art knowledge). Automated facial analysis using OpenFace showed no significant difference in participants' and confederates' facial expressions between conditions (agreement vs disagreement). In conclusion, copying choice seems to be one of the driving factors in likability judgments.

## Developmental Neuroscience | Elvin Hall

**20. Reem Alkharji - UCL Great Ormond Street Institute of Child Health**

**POSTER TITLE**
Dystrophin mutations affect astrocyte behavior

**AUTHORS**
Alkharji R, Lange J and Ferretti P

**ABSTRACT**
Duchenne Muscular dystrophy (DMD) is a severe neuromuscular illness defined by irreversible muscle atrophy. Mutations cause it in the dystrophin gene (DMD), which has 79 exons and regulates the expression of multiple isoforms with tissue specificity promoters. 30% of DMD patients exhibit cognitive and behavioural impairments. However, unlike muscle, the role of dystrophin in the brain is undetermined. DMD astrocytes exhibit aberrant functional responses to injury and have been implicated in neuropsychiatric, neurodegenerative, and neurological diseases (Lange et al., 2021). To assess whether this was linked to different development stages of normal and DMD astrocytes, we investigated morphological and molecular alterations in DMD astrocytes. To this purpose, human induced

pluripotent stem cell iPSC-derived astrocytes were generated from healthy and DMD68 mutant lines. Exon 68 dystrophin mutations impact all isoforms, including DP71, which is strongly abundant in astrocytes. Anti-dystrophin antibodies confirmed the absence of dystrophin in DMD68 IPSCs, neural progenitors, and astrocytes. However, dystrophin isoforms were found in normal cells, where they were differentially regulated throughout neural differentiation. After six weeks of differentiation, DMD68 astrocytes had less EAAT1, glutamine synthetase, S100B, and NF-KappaB expression than healthy astrocytes. This supports a role for dystrophin in astrocyte formation that deserve further investigation.

### 21. Matthew Bostock - Cell and Developmental Biology

**POSTER TITLE**
Photoreceptors establish a Hedgehog morphogen gradient to diversify precursor cell identities in their target field in Drosophila

**AUTHORS**
Bostock MP, Fernandes VM

**ABSTRACT**
The Drosophila visual system is a tractable model to study how neuronal diversity is established. Each optic lobe is organised into four neuropils, the simplest of which is the lamina, with only 5 neuron types (L1-L5). Photoreceptors secrete Hedgehog (Hh) to induce lamina development, such
that for every unit eye there is a corresponding lamina unit made up of post-mitotic precursors stacked into columns. Differentiated columns each contain one of every lamina neuron type, yet how lamina precursors are diversified was unknown. Here, we found that Hh pathway activity is graded along the distal to proximal lengths of columns. By genetically manipulating Hh signalling activity, we showed that different activity thresholds specify unique lamina identities. Consistent with pathway activity, we identified a Hh protein gradient polarised along lamina columns. Thus, Hh acts as a morphogen to pattern the lamina. Although this is the first such report during Drosophila nervous system development, it shows remarkable similarity to patterning of the vertebrate neural tube by Sonic Hedgehog. Altogether, we show that differentiating neurons can regulate the neuronal diversity of their target fields through morphogen gradients.

### 22. Dimitri Budinger - UCL Great Ormond Street Institute of Child Health

**POSTER TITLE**
An iPSC-derived midbrain dopaminergic modelling platform reveals a key role for manganese homeostasis in cell survival and mitochondrial function

**AUTHORS**
Budinger D, Alhaque S, Abdul-Sada A, Gonzalez-Mendez R, Park J, Zaki MS, Christodoulou J, Dale RC, Barral S, Kurian MA.

**ABSTRACT**
Manganese (Mn) is an essential trace metal, crucial for normal neuronal cell function. Acquired and genetic disorders leading to Mn imbalance can result in a broad spectrum of neurological phenotypes. Mutations in Mn transporters SLC39A14, SLC39A8 and SLC30A10 have been identified in patients with Mn dyshomeostasis, and are associated

with progressive, often debilitating disorders. The molecular mechanisms underlying Mn dysregulation and neurotoxicity are poorly known, and there are currently no effective treatments. Using patient-derived induced pluripotent stem cells, we developed a midbrain dopaminergic neuronal model of the three inherited Mn transportopathies. We used a range of molecular, cellular and transcriptomic approaches to investigate the physiological role and pathophysiological sequelae of Mn in health and disease. Our results show Mn dysregulation leads to an increase in cellular stress and subsequent neuronal cell death. Mitochondrial function tests highlight dysregulation of OXPHOS complexes at mRNA, protein, and enzymatic activity levels, defects in mitochondrial membrane potential and ATP production. Bulk RNA-sequencing analysis confirms mitochondrial dysregulation in patient lines and highlights pathways associated with collagen, synaptic dysregulation, oxidative stress and cellular death. Our findings provide more insight into the disease mechanisms underpinning Mn transportopathies, highlighting potential avenues for the future development of targeted therapeutic strategies.

### 23. Patrizia Ferretti - UCL Great Ormond Street Institute of Child Health

**POSTER TITLE**
Dystrophin mutations affect astrocyte behavior

**AUTHORS**
Alkharji R, Lange J, Ferretti P

**ABSTRACT**
Duchenne Muscular dystrophy (DMD) is a severe neuromuscular disease resulting in irreversible muscle atrophy caused by mutations in the dystrophin gene (DMD), which has 79 exons and multiple promoters regulating expression of different isoforms with tissue specificity. One-third of DMD patients exhibit cognitive and behavioural impairment. However, the role of dystrophin in the brain is not well understood. Astrocytes have been implicated in neuropsychiatric, neurodegenerative, and neurological diseases. Our aim was to further investigate whether astrocytes are affected in DMD patients. Astrocytes were generated from human induced pluripotent stem cells (iPSCs) derived from healthy and DMD patients. Mutations in exon 68 (DMD68) impact all dystrophin isoforms, including DP71, which is highly expressed in astrocytes. Absence of dystrophin in DMD68 IPSCs, neural progenitors and astrocytes, was confirmed by lack of anti-dystrophin antibody reactivity that, in contrast, positively stained healthy cells. RNA-seq analysis of healthy and DMD68 astrocytes identified dysregulation of genes in diseased astrocytes consistent with behavioural and metabolic defects observed. This was supported by significant reduction in EAAT1, glutamine synthetase, S100B, and NF-KappaB in DMD astrocytes, as compared to healthy ones, detected by immunofluorescence and RT-qPCR after 6 weeks of differentiation. This supports a role for dystrophin in astrocyte function.

### 24. Rebecca Powell - UCL School of Pharmacy

**POSTER TITLE**
Developing aligned engineered tissue constructs using differentiated iPSCs to support peripheral nerve regeneration after injury

**AUTHORS**
Powell R, Phillips JB

**ABSTRACT**
Schwann cells are an integral part of peripheral nerve regeneration, transforming into repair Schwann cells which proliferate and elongate to form a column of aligned cells across the nerve gap. This column of aligned cells supports and guides the regenerating axon across the injured site allowing downstream reinnervation of the muscle. However, this regeneration process is slow and in cases where there is no connection between the damaged nerve ends an autograft must be used which can result in further complications for the patient. Engineered nerve constructs can be developed from cell-seeded biomaterials as an alternative to the autograft. In this project, Schwann cells and Schwann cell precursors were differentiated from human induced pluripotent stem cells and combined with collagen-type I to form an aligned hydrogel. These differentiated cells express genes associated with Schwann cells in addition to those involved in intercellular interactions in the nerve bridge. In an in vitro model of peripheral nerve regeneration, primary rat dorsal root ganglia were co-cultured with the aligned cellular constructs and showed these constructs support directed neurite extension.

### 25. Anadika Prasad - Cell and Developmental Biology

**POSTER TITLE**
Differentiation signals from glia are fine-tuned to set neuronal numbers during development

**AUTHORS**
Prasad AR, Baldaia-Lago I, Bostock MP, Housseini Z, Fernandes VM

**ABSTRACT**
The number of neurons formed during development need to be tightly regulated to form complex neural circuits. Known strategies include regulating the number of neurons that are formed or survive during development. Here, we study how neuronal numbers are regulated in the lamina neuropil of the Drosophila visual system. The lamina consists of ~800 columns. Each column has six precursors; five will differentiate into the lamina neuron subtypes (L1-L5) whereas the extra precursor is killed off by apoptosis. This process is highly stereotyped. How exactly five lamina neuron subtypes differentiate from an equivalent pool of six precursors is unknown. Our results indicate that a glial population, the outer chiasm giant glia (xgo), regulates the L5 neuron numbers in each column. In response to signals secreted by photoreceptors, the xgo secretes multiple ligands to induce L5 differentiation. We uncovered that the extra precursor is capable of becoming an L5, but due to insufficient amounts of differentiation signals, it dies. The newly differentiated L5s act as a sink and limit the availability of these signals. In sum, our work highlights stereotyped patterns of programmed cell death in the lamina arise from extrinsic signals which reliably patterns the development of the nervous system.

### 26. Kimberley Reid - UCL Great Ormond Street Institute of Child Health

**POSTER TITLE**
MED27, SLC6A7 and MPPE1 variants in a complex neurodevelopmental disorder with severe dystonia

**AUTHORS**

Reid KM, Spaull R, Salian S, Barwick K, Meyer E, Zhen J, Girata H, Sheipouri D, Benkerroum H, Gorman K, Papandreou A, Simpson M, Hirano Y, Farabella I, Topf M, Grozeva D, Carss K, Smith M, Pall H, Lunt P, De Gressi S, Kamsteeg EJ, Haack T, Carr L, Guerreiro R, Bras J, Maher E, Scott R, Vandenberg R, Raymond L, Chong W, Sudhakar S, Mankad K, Reith M, Campeau P, Harvey RJ, Kurian MA

**ABSTRACT**
Objectives: To identify and characterize the underlying cause of disease in a sibship presenting with severe developmental delay, generalized dystonia, episodic status dystonicus, chorea, epilepsy and cataracts.
Methods: Whole-exome sequencing was performed followed by functional characterization of candidate genes using structural homology modelling, patient-derived primary cell lines, in vitro overexpression systems, and a zebrafish model.
Results: Homozygous variants were found in: MED27 - c.839C>T (p.Pro280Leu), SLC6A7/PROT - c.1186G>A (p.Gly396Ser), and MPPE1/PGAP5 - c.985A>T (p.Arg329*). The patients had many features of MED27-related disorder, however the SLC6A7 and MPPE1 variants were investigated to determine whether these genes also contributed to the phenotype. Homology modelling predicted p.Gly396Ser to cause loss of protein function with impaired proline recognition; reduced cell-surface expression, decreased proline transport, decreased proline affinity and reduced maximal currents were observed. Zebrafish morpholino knockdown of slc6a7 revealed developmental delay and fragile motor neuron morphology that was rescued by PROT-WT, but not PROT-G396S RNA. Finally, analysis of patient fibroblasts indicated a reduction in cell-surface expression of glycophosphatidylinositol (GPI) anchored proteins, linked to PGAP5 dysfunction.
Conclusion: We report a family harboring a homozygous MED27 variant with additional loss-of-function SLC6A7 and MPPE1 variants, highlighting the importance of blended phenotypes caused by multi-locus pathogenic variants.

## 27. Stephen Terry - UCL Ear Institute

**POSTER TITLE**
A new CRISPR-Tol2 based toolkit for combining gene knockout with long-term tracking of edited cells in chick embryos and primary mouse neuro/glial cultures

**AUTHORS**
Terry S, Zak M, Smith K, Jagger D , Daudet N.

**ABSTRACT**
CRISPR has revolutionised genomic editing, enabling loss-of-function experiments in many organisms. The chick embryo is an instrumental model system for understanding animal development, but its potential has been limited by a lack of robust tools for gene knockdown (1). CRISPR-Cas9 editing has previously been achieved in chick embryos at early stages of development (2), and efficiency improvements made to this system (3), though there has been a lack of tools for efficient editing coupled with long-term tracking of edited cells. To overcome this limitation, we developed an approach using in ovo electroporation of three plasmids – (i) a Tol2 transposon driving the co-expression of a single guide sgRNA and a fluorescent reporter, (ii) Cas9, and (iii) the Tol2 transposase. Our CRISPR system can successfully generate mosaic knockouts of Sox2 and Atoh1, key transcription factors for sensory specification and differentiation in the developing inner ear. To broaden the

accessibly of our CRISPR approach we proved our system works in mouse primary neuro/glila cultures. We validated our system by correlating mutant phenotypes and absence of Sox2 or Atoh1 protein with expression of the fluorescent reporter in edited cells. Our approach combines the power of CRISPR-Cas9 editing with the ability to identify and track edited cells in an otherwise normal tissue at late stages of embryonic development.

## Disorders of the Nervous System | Elvin Hall

**28. Amanda Almacellas - UCL Queen Square Institute of Neurology**

**POSTER TITLE**
Gene Therapy for Focal Cortical Dysplasia type II

**AUTHORS**
Almacellas Barbanoj A, Maffei B, Hoke J, Carpenter J, Chimonides C, Kullmann DM, Magloire V, Lignani G

**ABSTRACT**
Epilepsy is a devastating neurological disease, affecting 1% of the world's population. Focal Cortical Dysplasia (FCD) is a group of focal cortical malformations due to somatic mutations in the neuronal progenitors. FCD type II is caused by mutations leading to the hyperactivation of the mTORC1 pathway in more than half of the reported cases. FCD II is commonly associated with drug-resistant epilepsy, for which surgical resection of the focal brain area where the seizures arise remains the best hope to achieve seizure freedom. The mean age of seizure onset in FCD patients is of 6.3 years and consequently FCD is the first cause of brain surgery in children. Nevertheless, this procedure is not always effective and often precluded by proximity to eloquent regions which is why gene therapy is currently the most promising candidate replacement for surgical treatment of FCD.

The aim of this project is to validate a gene therapy based on the use of a modified KCNA1 (which encodes the potassium channel Kv1.1) for treating seizures in a mouse model for FCD II. Kv1.1 has been selected as a therapeutic protein not only because it attenuates neuronal excitability but also to reconstitute physiological Kv1.1 levels taking into account the downregulation of KCNA1 translation that occurs due to mTORC1 activation.
This project is based on the use of a FCD II mouse model generated by in-utero electroporation on neuronal progenitors for inducing mTORC1 hyperactivation. A battery of molecular biology and behavioural tests was performed for the characterization of this mouse model, which recapitulates the pathogenesis seen in humans, including cognitive comorbidities. EEG recordings were performed on the mice before and after the injection of the gene therapy, showing promising results in reducing 70% of seizures over 2 weeks and the ictal activity. We also performed behaviour experiments to assess the effect of our innovative treatment on memory and cognition with encouraging results regarding the safety of this treatment.

In conclusion, KCNA1 gene therapy is a very promising innovative approach for the treatment of FCD II as it locally reduces hyperexcitability, treating seizures regardless of the somatic mutation present, while memory and cognition remain unaffected.

**29. Sharifah Anoar - Genetics, Evolution & Environment**

**POSTER TITLE**
Understanding c9orf72 hexanucleotide repeat linked to mitochondrial dysfunction

**AUTHORS**
Sharifah A, Teresa N

**ABSTRACT**
Frontotemporal Dementia (FTD) and Amyotrophic lateral sclerosis (ALS) are neurodegenerative diseases characterised by declining motor and cognitive functions. Even though these diseases present with distinct sets of symptoms, FTD and ALS are two extremes of the same disease spectrum, as they show considerable overlap in genetic, clinical and neuropathological features. Among these overlapping features, mitochondrial dysfunction is associated with both diseases. For example, recent studies have shown that cells derived from patient iPSCs display mitochondrial abnormalities, and similar abnormalities have been observed in a number of animal disease models. C9orf72 hexanucleotide repeat expansion (C9) is the primary genetic cause of both FTD and ALS and has been linked to mitochondrial abnormalities. This research project will investigate mitochondrial dysfunction in a Drosophila C9orf72 model and characterise how mitochondrial genes can modulate C9 toxicity in the Drosophila brain.

**30. Annamaria Balogh - UCL Institute of Cognitive Neuroscience**

**POSTER TITLE**
Exploring individual-level associations between depression and anxiety symptoms and change blindness

**AUTHORS**
Balogh A, Glyn L, Shafran R, Robinson OJ

**ABSTRACT**
Cognitive biases are associated with affective disorders. Since change blindness paradigms are thought to measure attentional biases, they could potentially be used to reveal mechanisms linked to depression and/or anxiety. We conducted two studies to explore the association between depression/anxiety symptoms and performance on a change blindness task.

N=545 participants in the first and N=616 in participants in the second study were recruited online. Participants performed a change blindness task alongside questionnaires measuring depression/anxiety symptoms. We used regression analyses to test for associations between task performance and questionnaire scores. We then conducted a mega-analysis by pooling data across the two studies.

In the first study, higher depression score was associated with faster mean reaction time (B=-27, p=0.034), and in the second study, higher anxiety score was associated with faster mean reaction time (B=-16, p=0.025). In the mega-analysis (N=1161), we found a significant association between mean reaction time and depression symptoms (B=-20, p=0.007) as well as anxiety symptoms (B=-17, p=0.006). These effects were not significant after adjusting for age.

Our results provide preliminary evidence that individuals with higher self-reported depression and anxiety scores are faster at identifying visual changes. However, this observed relationship may be entirely or partially driven by age.

### 31. Zhongbo Chen - UCL Queen Square Institute of Neurology

**POSTER TITLE**
Functional genomics  further characterise and potentially improve diagnostic yield of hereditary ataxia

**AUTHORS**
Chen Z, Cipriani V, Tucci A, Gustavsson EK, Zhang D, Reynolds RH,  Vestito L, Smedley D, Houlden H, Botía J, Ryten M

**ABSTRACT**
80% of hereditary ataxia (HA) patients remain undiagnosed even following whole genome sequencing. We leveraged multi-omics data aiming to characterise the genetic architecture and increase the diagnostic yield of HA.

We generated 284 genic features capturing information about gene structure; genetic variation; tissue-specific, cell-type-specific and temporally-relevant expression and protein products. We categorised 318 HA-associated genes as childhood-onset, adult-onset and those overlapping both. We then compared these genomic features across gene categories and collectively through unsupervised learning.

We found: (i) an unexpectedly high short tandem repeat density within childhood-onset genes suggesting that we may be missing pathogenic repeat expansions in this cohort; (ii) cell-type-specific expression differentiates childhood- and adult-onset ataxias with CNS glial-specific expression in childhood-onset genes; (iii) significant similarities in annotation across the groups using unsupervised clustering analysis suggesting adult- and childhood-onset patients should be screened using a common gene set. We tested the latter hypothesis within the 100,000 Genomes Project by rare variant burden analysis. This demonstrated a significantly higher burden of potentially pathogenic variants in certain childhood-onset HA genes among adult-onset patients.

Our analysis highlights important genetic architecture features investigate in an unsolved cohort and suggests that a broader testing strategy for HA could increase the diagnostic yield.

### 32. Aine Fairbrother-Browne - UCL Great Ormond Street Institute of Child Health

**POSTER TITLE**
Mitochondrial-nuclear cross-talk in the CNS is modulated by
cell type and perturbed under neurodegenerative disease status

**AUTHORS**
Fairbrother-Browne A, Ali A, Reynolds R, Garcia-Ruiz S, Zhang S, Chen Z, Ryten M, and Hodgkinson A.

**ABSTRACT**

Mitochondrial dysfunction contributes to the pathogenesis of many neurodegenerative diseases. The mitochondrial genome encodes core respiratory chain proteins, but the vast majority of mitochondrial proteins are nuclear-encoded, making interactions between the two genomes vital for cell function. Here, we examine these relationships by comparing mitochondrial and nuclear gene expression across different regions of the human brain in healthy and disease cohorts. We find strong regional patterns that are modulated by cell-type and reflect functional specialisation. Nuclear genes causally implicated in sporadic Parkinson's and Alzheimer's disease (AD) show much stronger relationships with the mitochondrial genome than expected by chance, and mitochondrial-nuclear relationships are highly perturbed in AD cases, particularly through synaptic and lysosomal pathways, potentially implicating the regulation of energy balance and removal of dysfunction mitochondria in the etiology or progression of the disease. Finally, we present MitoNuclearCOEXPlorer, a tool to interrogate key mitochondria-nuclear relationships in multi-dimensional brain data.

### 33. Patricia Garcez - UCL Queen Square Institute of Neurology

**POSTER TITLE**
Investigating long-term effects of Zika virus and SARS-CoV-2 infection on brain development

**AUTHORS**
Garcez, P.P., Christoff R.R, Higa M. L., Tanuri A., Magalhães D., Clark J., Reuschl A-K., Magusali, N., Jolly., C., Hardy J., Salih D

**ABSTRACT**
Maternal infections are risk factors for cognitive impairments in the offspring. Some viruses can be transmitted vertically such as Zika virus (ZIKV) and, less frequently, SARS-CoV-2. In the ZIKV congenital infection, the offspring develop a set of birth defects such as microcephaly, ventriculomegaly and corpus callosum dysgenesis. Here we examine the impact of different maternal infections during corticogenesis. Congenital infection of ZIKV isolates lead to a reduction in callosal area and density of callosal neurons. Moreover, axonal tracing revealed that callosal axons are misrouted and midline glial cells, required for midline axon guidance, are reduced. RNA-Seq data from infected brains identified dysregulation of neuroinflammation, axon guidance and axonogenesis related genes. In sum, ZIKV infection impairs critical steps of corpus callosum formation by disrupting not only neurogenesis but also axon guidance and growth. Corpus callosum developmental defects and neuroinflammation could lead to an increase in cortical excitability. Preliminary data show that SARS-CoV2 Spike (S) protein when injected intraperitoneally in pregnant mice results in higher susceptibility to seizures of the offspring. As a perspective, we plan to examine the impacts of different variants of SARS-CoV2 infection during corticogenesis and its long-term effects in gene expression, neuroinflammation and axon degeneration.

### 34. Amy Geard - UCL School of Pharmacy

**POSTER TITLE**
AAV9-mediated gene therapy in a knock-in mouse model of infantile neuroaxonal dystrophy

**AUTHORS**

Geard A, Whaler S, Poupon-Bejuit L, Massaro G, Hughes MP, Lalji K, Waddington SN, Kurian MA, Rahim AA, Krushni Lalji1, Simon N.Waddington2,3, Manju A. Kurian4,5, Ahad A. Rahim1

**ABSTRACT**
Infantile neuroaxonal dystrophy (INAD) is a rare lethal pediatric neurodegenerative disease. It is caused by mutations in PLA2G6, and patients present with neurological symptoms between six months and three years of age. No disease modifying treatments are available and there is an urgent need to develop new therapies. We conducted an in-depth characterization of the pla2g6-inad knock-in mouse model. Following characterization, we investigated the therapeutic potential of an AAV9.hPLA2G6 vector administered by various routes of administration to neonatal pla2g6-inad mice. The average lifespan of the model is reduced to an average of 97 days, with weight loss and behavioural decline from 9 weeks old. Neuropathology studies showed neuronal loss and neuroinflammation in the brain and spinal cord, along with autophagic dysfunction and lysosomal accumulation. AAV9.hPLA2G6 gene therapy resulted in a significant improvement in all parameters measured including survival, weight, locomotor function, and neuronal counts in both the brain and spinal cord. Interestingly, an intravenous administration of the vector had no effect on survival. However, when combined with the intracerebroventricular administration it was able to enhance survival beyond an intracerebroventricular administration alone. This study provides novel insights into INAD disease pathology, and suggests an effective therapy with potential for clinical development.

### 35. Ashling Giblin - Genetics, Evolution & Environment

**POSTER TITLE**
Odd-skipped family members rescue toxicity in a C9orf72 Drosophila model

**AUTHORS**
Giblin A, Niccoli T, Cammack A, Jaure N, Fuentealba M, Grönke S, Da Costa Sousa B, Lopez A, Isaacs AM, Partridge L.

**ABSTRACT**
C9orf72 hexanucleotide repeat expansion (C9) is the primary genetic cause of both amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD), two rapidly progressive neurodegenerative conditions for which there is no cure. C9 repeats generate dipeptide repeat proteins that contribute to driving disease. C9 repeat expansion causes neurodegeneration in Drosophila leading to motor defects and a reduced lifespan, which recapitulates aspects of the human disease. A gene overexpression screen for suppressors of C9 toxicity in Drosophila identified two members of the Odd-skipped family of Zinc Finger transcription factors that can extend C9 survival. Overexpressing the human homologs of Odd-skipped also significantly extended C9 lifespan. Transcriptomic analysis showed an enrichment of genes in categories related to metabolism in flies overexpressing the Odd-skipped gene, bowl. Mass spectrometry revealed significant alterations in lipid species in C9 fly heads versus controls, some of which were prevented or even reversed by bowl overexpression. Furthermore, genetic and pharmacological targeting of lipid metabolic pathways increased C9 survival. In summary, Odd-skipped family transcription factors reduce C9 toxicity, downstream of dipeptide repeat proteins, by regulating lipid metabolism.

This work implicates dysregulated lipid metabolism in C9 ALS/FTD, and highlights lipids as a therapeutic target.

### 36. Talia Gileadi - UCL Great Ormond Street Institute of Child Health

**POSTER TITLE**
Central nervous system expression of dystrophins and antisense therapy in a mouse model of Duchenne muscular dystrophy

**AUTHORS**
Gileadi TE, Siddle M, Fergus C, Mitsogiannis M, Chambers D, Catapano F, Kelly VP, Sokolowska E, Morgan JE, Ferretti P, Phadke R, Montanaro F, Muntoni F

**ABSTRACT**
Duchenne muscular dystrophy (DMD) is a severe neuromuscular disease caused by mutations in the dystrophin gene, resulting in muscle degeneration and a shortened life expectancy. DMD patients have a higher prevalence of intellectual disability, anxiety, and autism spectrum disorder than the general population. Mdx mice lacking the Dp427 dystrophin isoform display an enhanced fear response and increased anxiety-like behaviours. Dystrophin expression can be restored using an exon-skipping phosphorodiamidate morpholino oligomer (PMO) treatment in muscle, and intracerebroventricular injections of PMO have been shown to partially rescue the enhanced fear response. In this study, the expression of dystrophin isoforms was mapped across the mouse brain, and intracisternal injections were identified as a minimally invasive and translationally feasible PMO-administration route. Three PMO injections induced exon skipping and low levels of dystrophin protein restoration across brain regions. However, these low levels did not significantly rescue the enhanced fear response or anxiety-like behaviour in mdx mice. These results indicate that the doses of PMO that we used are not sufficient to rescue DMD behavioural phenotypes when administered using the translational intracisternal injection route, and provide important information on the correlation between levels of restored dystrophin in key brain regions and phenotypic rescue.

### 37. Holly Gregory - UCL School of Pharmacy

**POSTER TITLE**
Trilayered aligned electrospun constructs with encapsulated GDNF and tacrolimus for peripheral nerve repair

**AUTHORS**
Gregory H, Ros H, Williams G, Phillips JB.

**ABSTRACT**
The efficacious repair of severe peripheral nerve injuries is currently an unmet clinical need. The gold standard of surgical repair, transplanting nerve tissue from elsewhere in the body to bridge the gap, is limited by donor site morbidity and graft diameter mismatch. Polymeric electrospun nanofibrous constructs may offer an artificial alternative, by providing guidance for the regenerating nerve and allowing functional recovery. Fabricating these conduits using aligned fibres and encapsulated therapeutics may further improve regenerative outcomes. Here, two constructs were developed with a trilayered wall material formed from randomly-orientated drug-eluting fibre mats sandwiched between two aligned polymer-only fibre

layers. The central drug-eluting layer contained either glial cell line-derived neurotrophic factor (GDNF), a potent neurotrophin, or tacrolimus, an immunosuppressant known to promote nerve regeneration. The encapsulation of GDNF and tacrolimus into polycaprolactone (PCL) fibres was achieved using emulsion and coaxial electrospinning respectively. Fibres were optimised for uniform morphology and sustained release of bioactive drug. The ability of the axon-interfacing layer of the wall material, aligned PCL-only fibres, to guide neurons was also explored. These conduits show promise for nerve repair and may support regeneration across gaps in nerve tissue as an alternative to the current gold standard.

### 38. Amy Hicks - UCL Queen Square Institute of Neurology

**POSTER TITLE**
Investigating the gene regulatory mechanisms underlying NSL complex modulation of Parkinson's disease associated genes and pathways

**AUTHORS**
Hicks A, Reynolds R, Botia J, Plun-Favreau H, Ryten M.

**ABSTRACT**
Genetic variants conferring risk for Parkinson's disease (PD) have been highlighted through GWAS, yet exploration of their specific disease mechanisms is lacking. Two PD candidate genes, KAT8 and KANSL1, identified through GWAS and a PINK1-mitophagy screen encode part of the histone acetylating non-specific lethal (NSL) complex. This complex localises to the nucleus, where it has a role in transcriptional activation, and to mitochondria. In this study, we sought to identify whether the NSL complex has potential regulatory relationships with other genes associated with PD in human brain. Gene co-expression network analysis utilising publicly available transcriptomic data from across brain regions (provided by the Genotype-Tissue Expression Consortium) revealed significant clustering of NSL genes (p-value = 2.61x10-3) along with PD-associated genes (p-value = 4.15x10-4) in a frontal cortex co-expression module. Since this enrichment pattern was no longer visible following correction of gene expression for a neuronal signature, the co-expression relationships appeared to be driven by neuronal content. Finally, reverse engineering of gene regulatory networks generated regulons of the NSL complex which contained PD genes and were enriched for PD-relevant biological pathways. Overall, these findings reveal a potentially wider role for the NSL complex in regulating genes and pathways implicated in PD.

### 39. Megan Jones - Cell and Developmental Biology

**POSTER TITLE**
A genetic variant of the Wnt receptor LRP6 accelerates synapse degeneration during ageing and in Alzheimer's disease

**AUTHORS**
Jones ME, Büchler J, Dufor T, Boroviak K, Metzakopian E, Gibb A, Salinas PC.

**ABSTRACT**
Synapse loss is the strongest correlate to cognitive decline in Alzheimer's disease (AD). Deficient Wnt signalling contributes to synapse loss in AD. Moreover, a variant of Lrp6 (Lrp6-

val), which reduces Wnt signalling, is linked to late onset AD. However, the in vivo impact of Lrp6-val on synaptic connectivity in the ageing brain and in AD has not been addressed. We generated a novel knock-in mouse model carrying the Lrp6-val variant. Mice develop normally and show no obvious morphological abnormalities. We examined Lrp6-val homozygous mice for synaptic changes at different ages. Lrp6-val mice were crossed to the AD KI model, NL-G-F, to examine the contribution of this variant to AD pathogenesis. Mice carrying the Lrp6-val variant exhibit structural and functional synaptic deficits at 7-9 months that are exacerbated at 12-14 months. Synapse degeneration is observed at 16-18 months. Lrp6-val;NL-G-F mice exhibit a significant loss of synapses around plaques. However, no differences in plaque load are observed.

Our work highlights the importance of Wnt-LRP6 signaling in synapse integrity in the ageing brain and uncovers, for the first time, that carrying Lrp6-val confers progressive synaptic defects. Our studies uncover the novel role for the Lrp6-val variant in synaptic vulnerability in the context of AD.

**40. Wenfei Liu - UCL School of Pharmacy**

**POSTER TITLE**
Brain-directed AAV gene therapy corrects lethal neurodegeneration and improves locomotor behaviour in a mouse model of CLN5 Batten disease

**AUTHORS**
Liu W, Geard A, Massaro G, Hughes MP, Smith AJ, Ali RR, Mole SE, Rahim AA

**ABSTRACT**
The neuronal ceroid lipofuscinoses (NCLs), commonly known as Batten disease, are a group of inherited lethal paediatric neurodegenerative lysosomal storage disorders. CLN5 disease is a form of NCL caused by mutations in the CLN5 gene encoding a soluble lysosomal lumen protein of unknown function. Children with CLN5 Batten disease suffer progressive motor dysfunctions, vision loss, seizures and dementia, with variable rates of disease progression leading to death around 14-36 years of age. There is no treatment for CLN5 disease and there is a desperate need for a novel effective therapy. Here we describe a preclinical assessment of an adeno-associated virus (AAV) - mediated gene therapy in a transgenic mouse model of CLN5 disease. We show that neonatal intracerebroventricular injections with AAV9 expressing human CLN5 gene under control of a neuronal specific synapsin promoter prevent neurodegeneration, extend lifespan and improve long-term locomotor function of the CLN5 deficient mice. These data demonstrate that brain-directed AAV gene therapy can be a potential therapeutic strategy for CLN5 Batten disease.

**41. Doug Lopes - UCL Division of Medicine**

**POSTER TITLE**
Chronic Pharmacological Inhibition of Glymphatic Function Exacerbates Propagation of Tau Pathology in an Animal Model

**AUTHORS**
Lopes DM, Wells JA, de Silva R, Lythgoe MF,  Harrison IF.

**ABSTRACT**

The glymphatic clearance system is a brain-wide pathway responsible for the removal of waste solutes. Facilitated by astrocytic aquaporin-4 channels (Aqp4), this pathway has been shown to effectively clear proteins prone to aggregation in neurodegenerative diseases including amyloid-β and tau. The extracellular space, which is cleared by the glymphatic system, defines the major conduit for cell-to-cell propagation of such proteins in the brain due to their 'prion-like' characteristics, such as tau. Here, we tested whether modulation of glymphatic function affects tau propagation in an animal model of Tau pathology. Tau propagation was initiated in young Thy1-hTau.P301S mice (P301S), by intrahippocampal injection of aged P301S brain homogenate or control. Animals then received chronic treatment with the Aqp4 inhibitor, TGN-020 or vehicle for 10 weeks. Behavioural performance was periodically accessed and in vivo structural brain MRI scans were acquired at the end of the study. Mice chronically treated with TGN-020 appeared to exhibit some cognitive impairment, accompanied by intensified brain atrophy (MRI), and a greater extent of tau aggregation. These data suggest that modulation of the function of Aqp4, and consequently the glymphatic system function, is capable of altering the extent to which tau is able to propagate throughout the brain.

### 42. Naciye Magusali - UCL Queen Square Institute of Neurology

**POSTER TITLE**

Genetic variability associated with OAS1 expression in myeloid cells increases the risk of Alzheimer's disease and severe COVID-19 outcomes

**AUTHORS**

Magusali N, Graham A. C, Piers T. M, Panichnantakul P, Yaman U, Shoai M, Reynolds R. H, Botia J.A, Brookes K.J, Guetta-Baranes T, Eftychia B, Sevinc B, Dimitra S, Mina R, Frigerio C.S, Escott-Price V, Morgan K, Pocock J.M,

**ABSTRACT**

GWAS of late-onset AD risk have highlighted the importance of gene variants expressed by the innate immune system. Recently we have shown genes that confer risk for AD are significantly enriched in transcriptional networks expressed by amyloid-responsive microglia. Identifying this transcriptional network allowed us to predict new risk genes for AD, including oligoadenylate synthetase 1 (OAS1). However, the function of OAS1 within microglia and its genetic pathway were not known.

We show SNP rs1131454 within OAS1 is associated with AD by genotyping. The rs1131454 allele associated with increased risk for AD acts an eQTL and results in decreased expression of OAS1. By analysing single-cell RNA-seq data from isolated microglia from individuals with AD and from lung macrophages from individuals with severe COVID-19 we identify genetic networks that contain OAS1, and show a significant overlap in the genes engaged by AD and COVID-19 pathology in human samples. Human iPSC-microglia with knockdown of OAS1 expression using siRNA and stimulation with interferon-gamma show an exaggerated pro-inflammatory response. Our data support a link between genetic risk for AD and susceptibility to critical illness with COVID-19, and that OAS1 coordinates the pro-inflammatory output of innate immune cells in response to elevated interferon levels.

### 43. Nuria Martin - Cell and Developmental Biology

**POSTER TITLE**

Dkk3 Wnt antagonist: a novel contributor to synaptic defects and memory impairment in Alzheimer's disease

**AUTHORS**
Martin-Flores N, Podpolny M, McLeod F, Escott-Price V, Salinas PC

**ABSTRACT**
In Alzheimer's disease (AD), cognitive decline correlates with synapses loss. Increasing evidence suggests that deregulation of the Wnt pathway contributes to synapse vulnerability in AD. Recent studies showed that the secreted Wnt antagonist Dkk3 is increased in plasma and CSF of AD patients and accumulates in Aβ-plaques. However, the function of Dkk3 in the brain remains unexplored. Here, we investigated the contribution of Dkk3 in AD.
Our results show that Dkk3 secretion is increased before plaque formation and accumulates at Aβ plaques in the J20 and NLGF AD models. DKK3 levels are also increased in the hippocampus of AD patients. RNAseq revealed that increased DKK3 expression is associated with AD. Importantly, our gene and SNP-based analyses demonstrate a link between DKK3 gene and AD. Gain-of-function experiments show that Dkk3 decreases excitatory synapse number and function but increases inhibitory synapses in the hippocampus. Importantly, in vivo Dkk3 loss-of-function ameliorates synaptic changes in the hippocampus at early and late stages and improves memory in J20 mice.
Our findings demonstrate a novel role for Dkk3 with opposing effects on excitatory and inhibitory synapses. We propose Dkk3 as a target to reduce synapse dysfunction and cognitive deficits in AD.

### 44. Carlos Mena - UCL Institute of Cognitive Neuroscience

**POSTER TITLE**
Failure to replicate stress-potentiated Pavlovian bias in mood and anxiety disorders in the fMRI environment

**AUTHORS**
Mena C, Liu E, Goer G, Aylward K, Robinson O.

**ABSTRACT**
Previous work suggests that highly anxious individuals display a heightened Pavlovian avoidance bias to withhold action in the face of potential losses. However, this effect has yet to be replicated, and its neural correlates have not been explored. In this study, a group of patients with mood and anxiety disorders (MA, N=33) and healthy controls (HC, N=35) completed the same approach-avoidance task under induced stress as used by Mkrtchian et al. (2017) during fMRI scanning. RL models were fitted using Hamiltonian MCMC. No difference in avoidance bias was found between groups during induced-stress (95% HDI lower-bound=−0.192, upper-bound=1.234) or safe trials (95% HDI lower-bound=−0.6, upper-bound=0.654), failing to replicate the effects reported by Mkrtchian et al. (2017). However, MA patients seemed to exhibit a heightened action bias (95% HDI lower-bound=−1.981, upper-bound=−0.0604) and lapse rate parameters (95% HDI lower-bound=−0.267, upper-bound=−0.051) during induced-stress. These results do not provide evidence supporting previous reports of a heightened Pavlovian avoidance bias in patients with anxiety and mood disorders. However, this study was less well powered and was conducted in an fMRI

environment which is known to induce a sample bias towards less anxious individuals. These potential confounds should be considered when interpreting this null result.

### 45. Christopher Minnis - UCL Great Ormond Street Institute of Child Health

**POSTER TITLE**
Mole laboratory - Batten disease

**AUTHORS**
Minnis C, Zhang H, Gardner E, Clemente-Ramos J, Mole S

**ABSTRACT**
The Mole Laboratory's focus is researching the neuronal ceroid lipofuscinoses (NCL, Batten disease) part of a group of lysosomal storage diseases. These are monogenic inherited neurodegenerative diseases characterised by the accumulation of autofluorescent lipofuscin-like (age pigment) material in lysosomes and neuronal loss, mostly affecting children. Those affected suffer from a progressive disease decline which includes seizures, visual failure, declining mental and motor skills, and premature death. The age of onset ranges from birth to late in adulthood, and is characteristic for the underlying genetic defect. Thirteen genes have been identified, and over 530 mutations which are stored in our curated database, "The international NCL mutation database".

We have 4 main current research interests: (1) Genotype-phenotype correlation, and diagnosis; (2) Transcript variation and link with phenotype; (3) Molecular and cellular basis of disease; (4) Therapeutic development through identification of new therapeutic targets and drugs, and gene therapy, to treat the brain, eye and periphery. We work closely with UCL and EU colleagues towards all aims, and make extensive use of systematic approaches, in particular the genetic tractability of the simple cell model organism fission yeast Schizosaccharomyces pombe.

### 46. Beena Mistry - UCL Queen Square Institute of Neurology

**POSTER TITLE**
Interactions of amyloid-beta and tau with the cellular prion protein

**AUTHORS**
Mistry BN, Purro SA, Wadsworth J, Collinge J.

**ABSTRACT**
Alzheimer's disease (AD) is a progressive neurodegenerative disorder that is the most common cause of dementia in the elderly. The pathological features of AD include the presence of extracellular amyloid-beta plaques, intracellular neurofibrillary tangles composed of hyperphosphorylated tau. Recent observation have shown that interactions between the cellular prion protein (PrPC) and Aβ and tau oligomers are important in mediating some of the toxicity of these proteins in AD (Corbett et al., 2019). PrPC is an ubiquitously expressed cell surface glycoprotein whose normal function remains largely unknown. We use multiple knock-in mice lines that express higher amounts of humanised Aβ peptide and/or humanised tau protein than wild-type mice and differing amounts of PrPC and examined the interaction between PrPC, Aβ and tau using biochemical, cellular and structural techniques. Initial results show the accumulation of Aβ and tau with age in these mice by western blotting and immunohistochemistry. This increase is exacerbated in mice that have been intracerebrally inoculated with human AD brain homogenates compared to vehicle-inoculated animals.

These results and those from future experiments will help elucidate the mechanistic role of PrPC in AD and how its interactions with Aβ and tau affect their toxic properties.

### 47. Hemanth Ramesh Nelvagal - UCL School of Pharmacy

**POSTER TITLE**
Developing gene therapy for Niemann Pick Disease Type C Disease

**AUTHORS**
Hughes MP, Nelvagal HR, Coombe-Tennant OWS, Smith DA, Smith C, MassaroG, Poupon-Bejuit L, Platt FM, Rahim AA.

**ABSTRACT**
Niemann-Pick type C1 disease (NPC) is a lethal neurodegenerative lysosomal storage disorder. The clinical course is dominated by progressive neurodegeneration in the brain leading to premature death, with the cerebellum being particularly vulnerable. Having previously demonstrated the efficacy of AAV9 vectors in ameliorating disease in an NPC1 mouse model, we now have compared efficacy of different promoters expressing the NPC1 gene and found that a novel truncated version of the endogenous human NPC1 promoter fulfilled these criteria and significantly enhanced the therapeutic efficacy in vitro and in vivo in both the Npc1nih and Npc1nmf164 mouse models. Our findings show significant improvements behavioural and neuropathological outcome measures following neonatal intracerebroventricular injections. This optimised AAV vector provides a major step forward towards effective clinical translation of gene therapy for NPC.

## 48. Suran Nethisinghe - UCL Queen Square Institute of Neurology

**POSTER TITLE**
Interruptions in the FXN GAA repeat tract delay age at onset of Friedreich's Ataxia

**AUTHORS**
Nethisinghe S, Kesavan M, Ging H, Labrum R, Polke JM, Garcia-Moreno H, Callaghan MF, Cavalcanti F, Pook MA, Giunti P.

**ABSTRACT**
Friedreich's ataxia (FRDA) is the most common inherited ataxia, primarily caused by the homozygous expansion of a GAA trinucleotide repeat in intron 1 of the FXN gene. GAA repeat expansion causes gene silencing and consequent deficiency of the frataxin protein leading to mitochondrial dysfunction, oxidative stress, and cell death. The GAA repeat tract may be impure and have sequence variations called interruptions. However, large interruptions, determined by abnormal MboII digestion, are infrequent. We used triplet repeat primed PCR (TP PCR) assays to identify small interruptions at the 5' and 3' ends of the GAA repeat tract through alterations in the electropherogram trace signal.
Contrary to large interruptions, we found that small interruptions are more common, with 3' interruptions being the most frequent. Based on the detection of interruptions by TP PCR assay, our patient cohort (n = 101) was stratified into four groups: 5' interruption, 3' interruption, both 5' and 3' interruptions or lacking interruption. Those patients with 3' interruptions were associated with shorter GAA1 repeat tracts and later ages at disease onset. The age at disease onset was modelled by a group-specific exponential decay model. Based on this modelling, a 3' interruption is predicted to delay disease onset by approximately 9 years relative to those lacking 5' and 3' interruptions. This highlights the critical role of interruptions at the 3' end of the GAA repeat tract in modulating the disease phenotype and its impact on the patient's prognosis.

## 49. Daman Rathore - UCL Queen Square Institute of Neurology

**POSTER TITLE**
Characterisation of seizure-SD interactions in awake-headfixed mice using multisite graphene solution-gated field effect transistor arrays combined with Ca2+ imaging

**AUTHORS**
Rathore D, Smith A, Masvidal-Codina E, Rossi F, Guimera-Brunet A, Timofeeva Y, Wykes R, Volynski K.

**ABSTRACT**
Cortical seizures are often accompanied by spreading depolarisation (SD), but the relationship between these phenomena remains enigmatic. SD frequently results in suppression of subsequent neuronal activity. While this activity suppression has been linked to seizure termination, reports also demonstrate increased excitability following SD. Previous studies have been restricted to electrode-based recordings from few cortical sites, limiting the ability to resolve event relationships.

To capture the interactions between ictal discharges, seizures and SD, we characterised the propagation and interaction of these events in the cortex of awake mice. We bilaterally expressed GCaMP7f, and recorded picrotoxin-induced seizures and SDs using widefield

imaging. Moreover, we simultaneously utilised transparent, 16-channel epidural graphene transistor arrays (gSGFET), to allow the acquisition of full-bandwidth electrophysiology. We developed an imaging analysis pipeline to characterize seizures and SD based on origin and propagation properties. We utilised the temporal resolution of gSGFETs to gain detailed insight into classified paroxysms. Using these methods, we performed high-throughput event analyses to examine the diversity of ictal-associated DC events and their role in epileptic paroxysms.

We demonstrate that the combined application of calcium imaging and gSGFETs provides unparalleled insights into seizure termination, which will facilitate the development of novel therapeutic avenues.

### 50. Fabio Ribeiro Rodrigues - Psychology and Language Sciences

**POSTER TITLE**
Tauopathy causes increased synchronisation of low frequency rhythms and disruption of stimulus-induced gamma in mouse visual cortex

**AUTHORS**
Rodrigues FR, Papanikolaou A, Holeniewska J, Saleem A, Solomon S

**ABSTRACT**
Tau dysfunction is a prominent feature of neurodegenerative disorders including dementia, causing impairments that should have correlates in the electrical activity in the brain that may facilitate diagnosis and detection.

We chronically recorded local field potential (LFP) signals from layer 4 visual cortex (V1) in the rTg4510 mouse model of tauopathy, at 5 months (early in degeneration) or 8 months (more advanced degeneration). LFP measurements were recorded in awake head-fixed male (1) rTg4510 mice, (2) rTg4510 mice in which mutant tau expression was suppressed, and (3) wildtype littermates, in the presence and absence of visual stimulation, while monitoring their locomotion and pupil dimensions. We used multitaper analysis to measure the power spectra of the LFP in each condition.

We observed a decrease in gamma at more advanced stages of tauopathy, that was accompanied by a reduction in stimulus-induced gamma oscillations (ca. 75-85Hz). We also found substantially increased low frequency power (2-10Hz) in both 5m and 8m tauopathic animals during resting states, associated with high cortical synchronisation and coupling of low frequency rhythms.

We conclude that early during tauopathy, neuronal ensembles in V1 enter periods of increased cortical synchronisation, likely reflecting reduced drive to the local network.

### 51. Julia Rodriguez-Sanchez - Computer Science

**POSTER TITLE**
Modelling 40 Hz auditory steady-state responses indicates NMDA receptor dysfunction in emerging psychosis

**AUTHORS**
Rodriguez-Sanchez J, Grent-'t-Jong T, Uhlhaas P J, Adams RA

**ABSTRACT**
Cortical inhibitory interneurons and pyramidal neurons have been proposed as key players in the aetiology of schizophrenia. However, it is unclear which of these cell types is primarily responsible, and more work is needed to understand the exact nature of their dysfunction. We analysed MEG data collected during a 40 Hz auditory steady state response (ASSR) paradigm from participants at clinical high-risk for psychosis (CHR-P, n=116), patients with first-episode psychosis (FEP, n=33), controls with nonpsychotic disorders (n=38) and healthy controls (n=49), first reported by Grent-'t-Jong et al (2021, Biol Psych). Dynamic causal modelling was used to investigate interneuron and pyramidal cell function, including contributions of NMDA receptors. DCM analyses revealed decreased NMDAR-mediated connectivity between the medial geniculate nucleus and primary auditory cortex in both CHR-P and FEP. We also found reductions in pyramidal cell (but not interneuron) NMDA conductance in both CHR-P and FEP (vs controls). Our results support the hypothesis that pyramidal neuron hypofunction – mediated in part by NMDA receptor dysfunction – is a primary deficit in emerging psychosis. Consistent with previous findings, we found altered thalamocortical connectivity. These findings highlight the potential of using MEG and computational modelling to probe excitatory/inhibitory circuit change in psychosis.

## 52. Helena Ros - UCL School of Pharmacy

**POSTER TITLE**
Aligned Nanofibrous Biomaterial Optimisation for Supporting Peripheral Nerve Repair

**AUTHORS**
Ros H, Phillips JB, Gregory H.

**ABSTRACT**
Peripheral nerve injury is a debilitating condition for patients and there is currently an unmet clinical need for effective treatments. The clinical 'gold standard' approach for repairing nerve gaps is the nerve autograft which is effective but has limitations. Nanofibrous biomaterials may offer a promising alternative to the autograft by mimicking the extracellular matrix through which nerves can regenerate. This work aims to optimise a novel formulation of aligned nanofibrous biodegradable polymeric biomaterial for use in a peripheral nerve repair conduit and investigate the response of relevant cell types to this substrate. A polycaprolactone solution containing a surfactant was electrospun into fibre mats and collected on a rotating mandrel or disk collector. Both solution flow rate and collector speed were optimised to generate uniform fibres with a high degree of alignment. Biocompatibility was confirmed using a resazurin-based metabolic assay, which verified the biomaterial to be non-toxic to a rat Schwann cell line. Subsequent work includes physical characterisation of the biomaterial and the use of rat primary neurons to assess whether nanofibre alignment encourages directional and accelerated neurite outgrowth. The results of the study will assist in developing a novel conduit for supporting peripheral nerve regeneration.

## 53. Marco Sancandi - UCL School of Pharmacy

**POSTER TITLE**
Diabetes drugs activate neuroprotective pathways in models of neonatal hypoxic-ischemic encephalopathy

**AUTHORS**
Poupon-Bejuit L, Geard A, Millicheap N, Rocha-Ferreira E, Hagberg H, Thornton C, Rahim AA.

**ABSTRACT**
Hypoxic-ischemic encephalopathy (HIE) is a serious complication of labour caused by reduced blood flow and oxygen supply to the neonatal brain, potentially resulting in mortality for the infant or lasting brain damage. GLP1-R agonists are a class of drugs that are used clinically to treat type 2 diabetes but have also been shown to be neuroprotective in various models of neurodegeneration and brain injury such as HIE. In this study, we demonstrate that both exendin-4 and semaglutide can significantly improve the neurological outcome in the mouse model of HIE at short- and long-term time points with improved neuropathology, survival and locomotor function. We also investigate the mechanisms behind how GLP1-R peptide agonists exendin-4 and semaglutide trigger neuroprotective and anti-inflammatory mechanisms in cell and mouse models of neonatal HIE. We show that the PI3/AKT signalling pathway is upregulated and levels of cAMP are increased by activation of GLP1-R leading to a host of pro-survival and anti-apoptotic outcomes. This study provides a mechanistic insight into the neuroprotective and anti-inflammatory properties of GLP1-R agonists in HIE that may also be relevant for other neurological conditions that these peptides have been shown to be effective in.

**54. Javier Sanchez Bautista - UCL Queen Square Institute of Neurology**

**POSTER TITLE**
Progranulin deficiency causes mitochondrial bioenergetic defects in frontotemporal dementia

**AUTHORS**
Bautista JS, Falabella M, Lu S, Plun-Favreau H, Wray S, Pitceathly RDS

**ABSTRACT**
Mutations in the progranulin (GRN) gene are one of the main causes of frontotemporal dementia (FTD), resulting in haploinsufficiency of the soluble protein progranulin (PGRN). Mitochondrial dysfunction is considered a key mediator in the pathogenesis of several neurological disorders, including amyotrophic lateral sclerosis and Parkinson's Disease. However, the effect of PGRN on mitochondrial activity has not been explored. We hypothesise that mitochondrial dysfunction may play a role in GRN-related FTD pathogenesis.

A GRN knockdown was generated in H4 cells using a lentiviral shRNA vector. In this model, PGRN deficiency induced a decrease in the mitochondrial biogenesis regulator PGC1α and a decrease in the mitochondrial transcription factor TFAM. In addition, we observed a decrease in mitochondrial DNA, mitochondrially-encoded transcripts and protein expression as measured by qPCR and Western Blot analysis. Finally, a bioenergetic impairment was observed in PGRN deficiency H4 cells using the Seahorse assay.

These preliminary results suggest that PGRN may maintain mitochondrial homeostasis via PGRN-PGC1α-TFAM signalling. Future work will involve characterising the mitochondrial mechanism, and validating these findings in FTD human brain samples and patient-derived iPSCs to potentially identify novel therapeutic avenues.

### 55. Dunxin Shen - Genetics, Evolution & Environment

**POSTER TITLE**
Identifying neuron clusters vulnerable to C9orf72 mutation via single-cell RNA sequencing

**AUTHORS**
Dunxin S, Alec V, Carlo SF, Teresa N

**ABSTRACT**
FTD and ALS (Frontotemporal Dementia and Amyotrophic Lateral Sclerosis) are both devastating neurodegenerative diseases having no cures. A hexanucleotide repeat mutation in the C9orf72 gene is the most common genetic cause of those two diseases. Like many other neurodegenerative diseases, ALS and FTD display selective neuronal vulnerability: only some neuronal populations succumb to disease, even though the toxic species are ubiquitously expressed. However, why and how different types of neurons react differently in the disease progression remain unclear. In order to identify which neuronal populations are selectively depleted in response to the disease onset and analyse which pathways are activated in vulnerable and resistant neuronal population, we carried out single-cell RNA sequencing on the brains of a fly models of expressing 36 repeats. We have analysed the transcription profile of single brain cells following induction over a time, to allow us to understand how neuronal responses to the repeats develops as disease progresses.
We are in the process of identifying neuronal clusters which are depleted and those which are maintained following induction of the repeats. We are also looking into pathways differentially activated in different neuronal clusters.

### 56. Poppy Smith - UCL School of Pharmacy

**POSTER TITLE**
Production of aligned endothelial cell tissue engineered repair constructs for peripheral nerve regeneration

**AUTHORS**
Smith PO, Jat PS, Phillips JB

**ABSTRACT**
Traumatic peripheral nerve injury, which impacts 1 in 1000 people and costs $150 billion annually in the US alone, poses a serious clinical challenge. The autograft, the current ‘gold standard’ for peripheral nerve repair, is limited by donor tissue availability and results in donor site injury. Artificial nerve repair constructs, generated by tissue engineering, provide a promising alternative in which aligned cellular biomaterials can support neuronal regeneration. Here, the incorporation of endothelial cells into collagen hydrogels to form stabilised, anisotropic, engineered neural tissue was developed through the application and optimisation of a novel technique. This technique was shown to rapidly and simultaneously stabilise and align hydrogel-based nerve repair constructs through the controlled aspiration of cellular collagen gels. The magnitude and duration of the negative pressure applied in this

technique was explored to maximise endothelial cell viability and alignment. Cell viability in the engineered neural tissue was corroborated by cell staining and lactate dehydrogenase assays. Moreover, cell alignment in the nerve construct, assessed by confocal imaging of cytoskeletal cell staining, was significantly improved compared to the starting hydrogel. Future work will evaluate the potential for the constructs to support Schwann cell migration and neurite outgrowth, critical aspects for successful nerve regeneration.

### 57. Audrey Ker Shin Soo - UCL Great Ormond Street Institute of Child Health

**POSTER TITLE**
PLA2G6-Associated Neurodegeneration (PLAN): A Natural History Study

**AUTHORS**
Soo KSA, Barwick K, Kurian MA on behalf of PLAN Natural History International Study Group

**ABSTRACT**
AIM: To define PLAN disease course through an international multicentre natural history study.

METHODS: Patients with biallelic PLA2G6 mutations were identified through a British Paediatric Neurology Association national surveillance unit study (2017-2020) and collaboration with 20 international centres. Clinical details were obtained through standardised, anonymised proformas.

RESULTS: 296 PLAN cases were identified. There were 3 phenotypes: Infantile Neuroaxonal Dystrophy (INAD), atypical Neuroaxonal Dystrophy (aNAD) and adult-onset dystonia-parkinsonism (DP). The median age at symptom onset differed significantly according to phenotype (INAD=1.2years, aNAD=3years, DP=20years $p<0.01$). The commonest presenting symptoms were developmental regression(49%), gait abnormalities(22%), developmental delay(11%) and eye abnormalities(9%). All aNAD and DP patients learnt to walk independently but most INAD patients(63%) did not; those who achieved it lost ambulation earlier than the aNAD group (median age 2vs6.5years). There were significant differences in age at motor regression, death rate and Kaplan-Meier survival curves between groups. Genotype-phenotype correlations were evident. Nearly all the aNAD and DP cases harboured 2 missense variants.

CONCLUSION: This is the largest ever PLAN natural history study, improving the understanding of the disease natural history and phenotypic differences for this ultra-rare, neurodegenerative condition. Given the lack of biomarkers, this data will aid evaluation of upcoming novel precision therapies.

### 58. Dora Steel - UCL Great Ormond Street Institute of Child Health

**POSTER TITLE**
Identifying and understanding rare movement disorders through whole-genome sequencing

**AUTHORS**
Steel DBD, Barwick KES, Reid KM, Kurian MA

**ABSTRACT**
Many people with genetic movement disorders never receive a specific diagnosis. One reason is that many disease-causing genes have yet to be identified. Another is that some genes have complex or variable phenotypes which are incompletely understood. We used whole genome sequencing (WGS) to identify novel genetic causes of movement disorders and to understand existing ones better.

Triome WGS was performed on people with childhood-onset movement disorders believed likely to be genetic. Participants underwent detailed clinical phenotyping. If no recognised diagnosis was identified using a broad gene panel, a shortlist of candidate pathogenic variants was created using in silico tools and examination of genes' physiological function and expression. Strong candidates were investigated using functional laboratory work and/or case-finding through collaborators and gene-matching services.

Several novel genetic cause of movement disorders have been identified so far, including VPS16, VPS41 and DRD1, with over one novel disorder found per 50 triomes analysed. Additionally, several diagnoses of ultra-rare disorders were made which expand or clarify the reported phenotype.

WGS combined with detailed phenotyping allows both identification of novel genetic causes of movements disorders and improved understanding of existing rare phenotypes. Our results suggest that a large number of monogenic disorders still await discovery.

### 59. Catherine Turnbull - Institute of Prion Diseases

**POSTER TITLE**
Comparison of tau pathology in three different mouse models following inoculation with tissue from Alzheimer's disease (AD) patients

**AUTHORS**
Turnbull C, Ravey J, Purro S, Collinge J.

**ABSTRACT**
Amyloid beta (Aβ) and tau are the two key proteins associated with Alzheimer's disease (AD), the leading cause of dementia worldwide, which are both thought to have prion-like properties with seeded propagation and spread of disease-related assemblies. We have been investigating mouse models containing humanised versions of these proteins to further our understanding of how AD progresses, as well as deciphering the prion-like properties of both Aβ and tau, after the inoculation of Aβ or tau assemblies or seeds. However, a mouse model containing both humanised Aβ and tau has not been previously studied in the context of AD. Here we show that a mouse model containing both the Swedish and Iberian mutations (NL-F) in the amyloid precursor protein and expressing human Aβ42, as well as exhibiting all six isoforms of human tau, shows earlier tau seeding of typical AD cases compared to its retrospective TauKI and NLF mouse models in vivo. Our results suggest that the NLF_TauKI double knock-in mouse may be a superior model for studying the role of prion-like behaviour of Aβ and tau assemblies in AD. We anticipate that this model will also prove useful in future characterisation of putative Aβ and tau strains which will require in vivo serial passages to characterise.

**60. Aikaterini Vezyroglou - UCL Great Ormond Street Institute of Child Health**

**POSTER TITLE**
Diagnosing ATP1A3-related Disorders. Are our Clinical Criteria Sufficient?

**AUTHORS**
Vezyroglou A, Akilapa R, Barwick K, DDD Study Group, Balasubramanian M, Sisodiya SM, Kurian MA, Cross JH

**ABSTRACT**
OBJECTIVES
ATP1A3 is associated with a spectrum of phenotypically diverse neurological disorders, making evaluation of variant pathogenicity challenging. In this study, we have endophenotyped a new patient cohort with detailed analysis of ATP1A3 genetic variants.

METHODS
Thirteen patients with ATP1A3 variants were identified from the Deciphering Developmental Disorders (DDD) study, with additional 11 cases contributed by international collaborators. A Pubmed literature search was undertaken, for all publications containing “ATP1A3” from 2004 to 2021. CADD-scores were calculated and missense constraint analysis performed.

RESULTS
Twenty-four patients with a neurological phenotype were found to carry 21 different ATP1A3 variants. Notably, many patients had little phenotypic overlap with classical disease and most did not fit the clinical criteria for common ATP1A3 phenotypes. 1108 patients have been previously published carrying 168 different ATP1A3 variants. Common recurrent variants are associated with well-defined phenotypes, while rare variants often result in rare symptom combinations, like in our study. Pathogenic/likely pathogenic variants had significantly higher CADD scores and clustered within 4 main regions of constraint.

CONCLUSION
The established clinical diagnostic criteria do not always capture ATP1A3-mutation positive patients. Further analysis of genetic criteria, such as CADD score and variant location can also aid the diagnosis of an ATP1A3-related condition.

**61. Rania-Iman Virjee - UCL Queen Square Institute of Neurology**

**POSTER TITLE**
Direct stimulation mapping and intraoperative localisation of the thalamocortical tract in tumours affecting sensory pathways

**AUTHORS**
Virjee RI, Sefcikova V, Samandouras G.

**ABSTRACT**
Introduction: Description of monitoring and stimulation mapping of sensory pathway tracts remain absent in brain tumour surgery. This is vital as damage to superior-thalamic-radiation/thalamocortical-tract (TCT) can result in sensory ataxia/motor apraxia leading to disability and poor patient quality-of-life. Only two cases were reported (cortical and subcortical) in asleep patients. Here, the objective is to describe the anatomo-functional and

neurophysiological technique in locating and preserving the TCT in three tumour resection cases.

Methods: Over three months, two patients (37-years-old/43-years-old) underwent an awake-resection with dual clinical and neurophysiological monitoring, and one patient (58-years-old), underwent asleep-resection with neurophysiological-monitoring only. These were primary brain tumours involving the somatosensory-cortex and superior-thalamic-radiations. The ulnar nerve and ulnar/median nerves were stimulated in three and two cases respectively. A bipolar probe was used in the presumed TCT anatomical locations to detect its precise location.

Results: TCT and complete tumour resection, were detected in all three cases. Pathology demonstrated either IDH-mutant-astrocytoma, WHO-grade-2, or IDH-negative-astrocytoma WHO-grade-4.

Conclusion: Peripheral stimulation of the ulnar or median nerves with subcortical bipolar probe recording is an accurate and feasible method for TCT localisation and protection, thereby ensuring maximum-safe-tumour-resection from tumours affecting the sensory pathways. Further cohorts should be analysed allowing standardisation of mapping paradigms.

### 62. Katharina Wenz - UCL Queen Square Institute of Neurology

**POSTER TITLE**
Modeling Alzheimer's Disease-Down Syndrome in the Fly

**AUTHORS**
Wenz KC, Wiseman FK, Niccoli T.

**ABSTRACT**
Introduction: Down Syndrome (DS) is a commonly occurring genetic risk factor for early onset Alzheimer's disease (AD). APP, which is triplicated in people with DS significantly contributes to AD development in this population. However, how triplication of genes other than APP affects AD risk is not well understood.
We aim to identify which human chromosome 21 (Hsa21) genes, when expressed at higher levels in people with DS, modulate Aß accumulation and worsen cognitive decline.
Methods: I am using Drosophila melanogaster as a screening tool with two main readouts. Firstly, a negative geotaxis assay to assess whether neuromotor function of Aß expressing flies is modulated by overexpression a Hsa21 orthologues. Secondly, quantification of Aß1-42 levels by ELISA. Genes that are found to modify Aß aggregation in the fly brain will be examined in human post-mortem brain tissue, to determine whether and where expression of these genes is increased in people who had DS compared with euploid individual.
Results: I have so far identified that overexpression of Nnp-1 or loqs with pan-neuronal co-expression of Aß increases Aß1-42 levels in female fly heads at 10 days of age.
Conclusion: Overexpression of some Hsa21 orthologues can increase Aß1-42 accumulation compared with normal expression levels of that gene.

### 63. Kimberley Whitehead - Neuroscience, Physiology & Pharmacology

**POSTER TITLE**
Cortical activity is depressed following hypoxia-ischemia in human neonates, even when the injury is behaviourally silent

**AUTHORS**
Gelegen C, Meek J, Mistry N, Frank MG, Whitehead K

**ABSTRACT**
BACKGROUND
In young mammals, hypoxia-ischemia depresses neural activity, which disrupts experience-dependent synaptic plasticity. In humans, suboptimal outcomes have been reported after perinatal acute hypoxia-ischemia, even when it occurred in the absence of abnormal behaviour such as hypotonia. This association could be mediated by depressed cerebral activity following the insult.

METHODS
Infants who underwent scalp EEG monitoring following perinatal acute hypoxia-ischemia (median blood pH: 6.91) were divided into i) ≥moderate clinical encephalopathy (abnormal behaviour after resuscitation sufficient to qualify for therapeutic hypothermia) (n = 15), and ii) no or mild clinical encephalopathy (n = 14). We compared 0-35Hz overall power of the EEG during the 14 hours post birth to that of the EEG in matched controls (n = 8, median pH: 7.28).

RESULTS
Infants with ≥moderate clinical encephalopathy had lower EEG power relative to controls. Infants with no or mild clinical encephalopathy also had lower EEG power relative to controls, but higher EEG power than the group with ≥moderate clinical encephalopathy.

CONCLUSION
Perinatal acute hypoxia-ischemia depresses cortical activity, even when the brain insult is no longer behaviourally expressed. Future work will also examine cortical activity after chronic hypoxia, associated with placental insufficiency in utero.

### 64. Weicong Zhang - UCL School of Pharmacy

**POSTER TITLE**
An investigation to develop and characterize a pre-clinical mouse model that mimics human Alzheimer's disease pathology

**AUTHORS**
Weicong Z, Tiansheng L, Kirsten H, Afia A

**ABSTRACT**
This project aims to characterize AD progression using physiologically relevant AD models that harbour genes for the microtubule-associated protein tau (MapthTau) and β-amyloid precursor protein App (AppNL-F), which are expected to faithfully recapitulate human AD. Using behavioural experiments, neuroanatomy and molecular biology with whole-cell electrophysiological recordings, we characterised the spatial profile of the lateral entorhinal cortex (LEC) and CA1 region using two knock-in mouse models of AD, APPNL-F/NL-F, and

APPNL-F/MAPTHTAU age-matched (7-9, 12-16 and 18-22 months) to wild-type (WT) control mice

There was a similar significant cognitive deficit in both AD models compared to the aged-matched WT shown by behavioural paradigms. This was associated with the expression of the typical hallmarks of AD, Aβ and tau, together with a down-regulation of Wnt/β-catenin signalling and increased neuroinflammation-associated TREM2 expression more severely affected in LEC than CA1.

Our data show that the hallmarks of AD, including expression of Aβ, tau and neuroinflammation together with dysregulation of canonical Wnt signalling pathway increased in the presence of the MAPT gene, most affecting the LEC than CA1. However, the intrinsic membrane properties and synaptic hyperexcitability were similarly altered in both AD mice models. This suggests that MAPT differentially affects some pathological AD hallmarks.

## Homeostatic and Neuroendocrine Systems| Drama Studio

### 65. Shereen Nizari - UCL Division of Medicine

**POSTER TITLE**
On the mechanisms of CO2-induced increases in cerebral blood flow

**AUTHORS**
Nizari S, Theparambil S, Hadjihambi A, Hosford P, Gourine A.

**ABSTRACT**
The human brain produces a staggering 75 litres of CO2 every day. We recently demonstrated that CO2 actions contribute to neuronal activity-dependent increases in cerebral blood flow via its known effect on brain vasculature. However, the mechanisms underlying cerebrovascular CO2 sensing remain largely unknown.
Our systematic-review and meta-analysis suggested that signalling by nitric oxide and cyclooxygenase (COX) products mediate the actions of CO2 in the brain. In acute brain slices, we found that CO2-induced arteriole dilations are indeed prevented by COX-1 and neuronal nitric oxide synthase (NOS) blockade, but not by inhibition of endothelial NOS. Additionally, we found that CO2-induced arteriole dilations in the cortex are also blocked by purinergic P2Y1 receptor antagonism and inhibition of connexin/pannexin channels.
The role of these channels was then studied in dye loading experiments. CO2 and neuronal activity-induced dye loading was blocked by inhibition of connexin channels in cortical brain slices and in the mouse somatosensory cortex in vivo.

These results suggest that CO2-induced cortical arteriole dilations are mediated by connexin channels, purinergic signalling, nitric oxide and products of arachidonic acid metabolism. A working model of how all these seemingly distinct signalling mechanisms may interact to mediate the effects of CO2 will be presented.

# Neural Excitability, Synapses and Glia: Cellular Mechanisms | Drama Studio

**66. Tinya Chang - Neuroscience, Physiology & Pharmacology**

**POSTER TITLE**
Neuromodulation in periaqueductal grey neurons underlying innate defensive mechanisms

**AUTHORS**
Chang, T, Pavon, O, Branco, T.

**ABSTRACT**
The capability to instinctively respond to threats within the environment is crucially important for survival. The midbrain periaqueductal grey (PAG) matter is central to the initiation of innate defensive mechanisms in rodents and in humans. The dorsomedial (dmPAG) and ventrolateral (vlPAG) divisions of PAG distinctively command escape and freezing, respectively, which are mutually exclusive behaviours. Although the PAG receives a wide variety of neuromodulatory inputs, it is unclear how these affect neuronal and circuit-level activity. Transcriptomic analysis from our group recently revealed that excitatory and inhibitory neurons in the PAG express dopaminergic and noradrenergic receptors with opposing action. Thus, we aim to elucidate the precise effect of neuromodulators on the spontaneous activity and biophysical properties of PAG neurons. We perform whole-cell patch-clamp electrophysiological recordings in acute midbrain slices prepared from mice. We utilise Cre-mediated fluorescent labelling of vesicular γ-aminobutyric acid transporter (VGAT) and vesicular glutamate transporter 2 (VGluT2) to visualise and target inhibitory and excitatory PAG cell types. Our results show that dopamine application increases the spontaneous firing rate of VGAT+ dmPAG neurons and lowers the excitability of VGluT2+ dmPAG neurons. These findings suggest that dopamine signalling in the dmPAG reduces the overall activity of the local escape initiation network.

**67. Timothy Church - Neuroscience, Physiology & Pharmacology**

**POSTER TITLE**
Direct suppression of protein kinase A by calcineurin in synapses

**AUTHORS**
Church TW, Tewatia P, Hannan S, Antunes J, Eriksson O, G Smart TG, Jeanette JH, Gold MG

**ABSTRACT**
Interplay between the ancient and ubiquitous second messengers cAMP and Ca2+ is a hallmark of dynamic cellular processes. A common motif is the opposition of the Ca2+-sensitive phosphatase calcineurin and the major cAMP receptor, protein kinase A (PKA). Calcineurin dephosphorylates substrates primed by PKA to bring about changes including synaptic long-term depression (LTD). AKAP79 supports signalling of this type by anchoring PKA and calcineurin alongside one another. We have discovered that AKAP79 increases the rate of calcineurin dephosphorylation of type II PKA regulatory subunits by an order of

magnitude. Fluorescent PKA activity reporter assays, supported by computational modelling, show how AKAP79-enhanced calcineurin action enables suppression of PKA activity by increasing PKA catalytic subunit capture rate. Experiments with hippocampal neurons indicate that this mechanism contributes towards LTD. This non-canonical mechanism for suppressing PKA activity, that doesn't require any change in cAMP concentration, may underlie many other cellular processes.

### 68. Aoife Cosgrave - Neuroscience, Physiology & Pharmacology

**POSTER TITLE**
Examining the anti-inflammatory and neuroprotective potential of a phytocannabinoid compound in in vitro neuroinflammatory models

**AUTHORS**
Cosgrave A, Costello DA, Pedarzani P/

**ABSTRACT**
The activation of Toll-like receptors (TLRs) plays a key role in the pathogenesis of disorders associated with neuroinflammation and therefore offers an attractive target for therapeutic intervention. Phytocannabinoids, derived from the Cannabis sativa plant, can act as modulators of neuroinflammation, such as the compound Cannabidiol, which has demonstrated both anti-inflammatory and neuroprotective effects. This study examines the properties of a lesser-explored phytocannabinoid, "GL4a" (identity blinded for research purposes), in TLR-mediated models of acute neuroinflammation. We have determined that GL4a attenuates pro-inflammatory responses in microglial BV2 cells exposed to the TLR2 agonist lipoteichoic acid (LTA). Moreover, GL4a mitigates LTA-mediated inflammatory responses in neuronal cell lines. This is indicated by a significant reduction in proinflammatory cytokines TNFα and IL-6 as well as nitric oxide production. We further assessed potential mechanisms of action through targeting of specific signalling pathways, previously reported to play a role in cannabinoid action. To examine the impact of GL4a on neuronal integrity under inflammatory conditions, we used whole-cell patch clamp recordings to measure inhibition of a specific potassium current in acute hippocampal slices. This on-going, exploratory study reveals anti-inflammatory and neuroprotective effects of a novel, plant-based compound, GL4a, and supports further interrogation of its potential neurotherapeutic properties.

### 69. Gerard Crowley - UCL Queen Square Institute of Neurology

**POSTER TITLE**
Chemogenetic activation of perforant pathway induces microglial complement signalling and synapse loss

**AUTHORS**
Crowley G, Turkes E, Ge J, Toneva M, Yang G, Fajardo J, Sala Frigerio C, MacAskill A, Duff K, Hong S.

**ABSTRACT**
Region-specific synapse loss during Alzheimer's disease (AD) correlates significantly with cognitive decline. Regions impacted at the earliest stages of AD pathology include the entorhinal cortex and hippocampus, which are synaptically connected via the perforant path.

However, we lack critical insight into what makes certain synapses vulnerable to loss in AD. Microglia, the tissue-resident macrophages of the brain, use complement to act as cellular mediators of synapse loss in AD mouse models; however, how microglia-synapse interactions are impacted by the neuronal hyperactivity also observed in early AD is unknown. In this study, we aimed to investigate whether DREADD-mediated increase of neuronal activity in perforant pathway of adult wild-type mice could reactivate complement-dependent removal of certain synapses. Enhancement of neuronal activity produced increased complement C1q protein deposition at the hippocampal dentate gyrus termination site of the perforant path. C1q upregulation coincided with loss of excitatory presynaptic marker VGLUT2, but retention of VGLUT1+ presynapses, a process which was C1q-dependent. Spatial transcriptomic analysis of these mice highlighted gene expression changes at synaptic sites in response to enhanced activity driven by DREADD. Overall, this work points to neuronal activity as a key regulator of microglial complement reactivation and resulting synapse loss in mouse models.

### 70. Tom Dufor - Cell and Developmental Biology

**POSTER TITLE**
Synapse vulnerability and resilience in a Wnt signalling deficient mouse model

**AUTHORS**
Dufor T , Rogdakis T, Buechler J , Brar K , Lopes D , Palomer E , Martin-Flores N , Li K.W, Smit G, Salinas PC

**ABSTRACT**
Synaptic degeneration is an early hallmark of neurodegenerative diseases and is highly correlated with cognitive decline in Alzheimer's disease (AD). Studies show that some synapses are more vulnerable than others to amyloid-β toxicity. However, the mechanisms remain poorly understood. Growing evidence suggests a link between deficient Wnt signalling and AD. Dickkopf-1 (Dkk1), an endogenous secreted Wnt antagonist, is elevated in the human AD brain and is required for amyloid-β-mediated synapse loss. Using our inducible transgenic mouse model (iDkk1), we showed that two weeks of Dkk1 expression in the adult brain leads to a 40% reduction in excitatory synapses in the hippocampus, LTP deficit and memory loss without neuronal death, resembling early stages of AD. Importantly, synapse degeneration in iDkk1 mice is not progressive suggesting synapse degeneration is stalled. Proteomic analyses of hippocampal synaptosomes at the peak of synapse degeneration revealed an upregulation of astrocytic markers and 3D super resolution microscopy indicated a greater coverage of the remaining spines by astrocytes. We found that adding astrocytes to hippocampal neurons culture protects against Dkk1-induced synapse loss and that Dkk1 induces the secretion of astrocyte protective factors. Our studies reveal a novel mechanism that triggers synapse protection in the adult brain.

### 71. Vincent Magloire - UCL Queen Square Institute of Neurology

**POSTER TITLE**
Harnessing neurogliaform interneurons to control cortical hyper-excitability in awake mice

**AUTHORS**
Richardson A*, Mercier MS*, Shimoda Y, Graham RT, Muller M, Lieb A, Kullmann DM, Magloire V

**ABSTRACT**
Focal seizures are widely considered to arise from a disturbance of the excitation/inhibition balance, and in particular a failure of the GABAergic inhibitory system. Recent work focusing on parvalbumin-positive and somatostatin-positive interneurons has shown that inhibition mediated by these populations is too weak to suppress seizures effectively. In contrast, neurogliaform (NGF) cells could be much more effective, due to their signalling via “volume transmission”.

Here, we therefore investigate the role of NGF cells in seizure generation and maintenance. For this, we use a mouse line (Ndnf-Cre) that enables targeting of NGF cells and a combination of calcium imaging, electrocorticography and closed-loop optogenetic stimulation in models of acute, focal cortical epilepsy. In vivo calcium imaging revealed that Ndnf+ NGF cells are recruited a few seconds after the onset of ictal discharges. These findings suggest that Ndnf+ NGF neurons are involved in seizure activity but whether they promote or prevent the spread of overexcitation remains unknown. To answer this question, we are using optogenetic activation of NGF cells together with local chemoconvulsant application. Our data indicate a strong reduction in seizure duration during light stimulation. Together, this is the first evidence that Ndnf+ cell photo-activation can have strong anti-epileptic effects.

### 72. Kjara Pilch - Neuroscience, Physiology & Pharmacology

**POSTER TITLE**
Involvement of CaV2.2 channels and a2d-1 in hippocampal homeostatic synaptic plasticity

**AUTHORS**
Pilch KS, Dolphin AC.

**ABSTRACT**
In the mammalian brain, presynaptic CaV2.2 channels play a pivotal role for synaptic transmission by mediating fast neurotransmitter exocytosis via influx of Ca2+ into the active zone at the presynaptic terminal. The distribution and modulation of CaV2.2 channels at highly plastic hippocampal synapses remains to be elucidated. Here, I assessed CaV2.2 channels during homeostatic synaptic plasticity, a compensatory form of homeostatic control preventing excessive or insufficient neuronal activity during which extensive active zone remodelling has been described. I show that chronic silencing of neuronal activity in mature hippocampal cultures resulted in elevated presynaptic Ca2+ transients, mediated by increased levels of CaV2.2 channels at the presynapse. In addition, this work focussed on α2δ-1 subunits, important regulators of synaptic transmission and CaV2.2 channel abundance at the presynaptic membrane. Here, I show that α2d-1-overexpression reduces the contribution of CaV2.2 channels to total Ca2+ flux without altering the amplitude of the Ca2+ transients. Finally, levels of endogenous α2δ-1 decreased during homeostatic synaptic plasticity, whereas the overexpression of α2δ-1 prevented homeostatic synaptic plasticity in hippocampal neurons. Together, this study reveals a key role for CaV2.2 channels and novel roles for α2d-1 during plastic synaptic adaptations.

### 73. Kevin Sheng - Wolfson Institute of Biomedical Research at UCL

**POSTER TITLE**
Computational Specialisation of Cortical Dendrites

**AUTHORS**
Sheng K, Bicknell B, Häusser M

**ABSTRACT**
The transformation of synaptic input into action potential output is governed by dendritic physiology. Synaptic potentials are subject to severe attenuation on their way to the soma due to passive cable filtering, yet dendritic active conductances and spatial interactions may compensate, or even enhance the processing of particular input features. Dendritic integration thus presents both fundamental constraints on signal transmission and additional opportunities for computation. Both dendritic morphology and biophysics vary widely across cortical cell types, suggesting that different cortical neurons may be specialised for different computations. However, how the morphology and biophysics of dendrites determine the computational repertoire of neurons remains unclear. Here, we introduce a biophysical modelling and machine learning framework to address this question. We develop a general learning rule with which detailed models of neurons, comprising arbitrary morphologies and active conductances, can be 'trained' to perform sophisticated computational tasks. Applying our rule in experimentally validated models across a benchmark set of tasks, we translate the biology of each model neuron into a measure of its processing abilities. We thus establish a systematic approach for investigating the computational specialisation of single neurons, predicting tight relationships between the functional roles of different cell types, their morphology and biophysics.

## 74. Anna Simon - Wolfson Institute of Biomedical Research at UCL

**POSTER TITLE**
Ultrastructural readout of in vivo synaptic activity for functional connectomics

**AUTHORS**
Simon A, Roth A, Sheridan A, Fişek M, Marra V, Racca C, Funke J, Staras K, Häusser M

**ABSTRACT**
Large-volume ultrastructural mapping approaches yield detailed circuit wiring diagrams, but lack an integrated synaptic activity readout which is essential for functional interpretation of the connectome. We have developed a novel strategy for resolving this limitation by combining functional synaptic labelling in vivo with focused ion beam scanning electron microscopy (FIBSEM) and machine learning-based segmentation. Our approach allows us to generate high-resolution near-isotropic three-dimensional readouts of activated vesicle pools across large populations of individual synapses in a volume of tissue. We combine this method with machine-learning strategies using convolutional neural networks that automate analysis with superhuman performance and provide a predictive tool for measurements of synaptic efficacy. We apply this technique to measure presynaptic activity in an ultrastructural context in synapses activated by sensory input in primary visual cortex in awake head-fixed mice, showing that the numbers of recycling and non-recycling vesicles approximate to a lognormal distribution across a large number of synapses. We also demonstrate that neighbouring boutons of the same axon, which share the same spiking activity, can differ greatly in their presynaptic release probability. This approach therefore

can yield crucial functional information about specific synaptic connections in the intact brain, opening the way for functional connectomics.

### 75. Haojie Sun - UCL School of Pharmacy

**POSTER TITLE**
Unconventional intracellular signaling pathway underlying cholinergic M1 receptor-induced axonal action potential threshold plasticity in hippocampal neurons

**AUTHORS**
Haojie Sun, Mala M. Shah

**ABSTRACT**
Acetylcholine is a neurotransmitter and neuromodulator which plays an important role in cognition and learning. We have found that acetylcholine activates axonal, but not somato-dendritic, muscarinic M1 receptors to persistently enhance axonal T-type Ca2+ channel activity and raise neuronal excitability.The intracellular mechanism coupling muscarinic receptors to T-type Ca2+ channels, though, remains unknown. We have investigated this by making electrophysiological recordings from hippocampal dentate gyrus granule cells present in brain slices obtained from adult mice. Application of the muscarinic receptor agonist, oxotremorine-M, led to a persistent decrease in action potential threshold and increase in their excitability in wildtype, and not CaV3.2 null, granule neurons. These effects were G-protein independent, since they were not inhibited by inclusion of GDP-βS in the patch pipette. Inhibition of CaMKII activation by KN-93 or autocamtide-2-related inhibitory peptide prevented muscarinic receptor-mediated changes in granule cells excitability and AP threshold. Our findings so far indicate that muscarinic M1 receptor activation enhances CaV3.2 Ca2+ channels in axons by activating CaMKII in a G-protein independent manner. This indicates that axonal metabotropic receptors couple to distinct signal transduction mechanisms from those present in neuronal soma/dendrites to exert their effects on cell excitability.

### 76. Shuaiyu Wang - Neuroscience, Physiology & Pharmacology

**POSTER TITLE**
Activation of metabotropic glutamatergic receptor 1 persistently enhances hippocampal granule cell action potential firing

**AUTHORS**
Shuaiyu W, Haojie S, Mala S

**ABSTRACT**
L-glutamate acting on metabotropic glutamate receptors 1 (mGluR1s) present on hippocampal dentate gyrus neurons have been suggested to play an important role in the induction and maintenance of synaptic plasticity.  Less, though, is known about how they affect intrinsic excitability of these neurons. This was the primary aim of this work.
To investigate this, we obtained hippocampal brain slices from adult mice and made electrophysiological recordings from granule cells. Application of the mGluR1 receptor agonist, DHPG (100 □M), onto long axon (> 35 □m) granule cells resulted in resting

membrane potential (RMP) depolarization, an afterdepolarization, increased input resistance and reduced action potential threshold. All effects apart from changes in input resistance and action potential threshold were reversible. Consequently, action potential firing was persistently enhanced. The sustained decrease in action potential threshold induced by DHPG was axon-dependent as DHPG applied onto short axon neurons did not affect the action potential threshold. Further, DHPG-induced changes in RMP, afterdepolarization and input resistance, but not action potential threshold, were G-protein dependent as they were inhibited by GDP-βS. These findings suggest that mGluR1 receptors are located in axons and soma/dendrites, activation of which causes intrinsic excitability plasticity by coupling to distinct cell signaling mechanisms.

### 77. Umran Yaman - UCL Queen Square Institute of Neurology

**POSTER TITLE**
Long-read transcriptome analysis in response to amyloid pathology in the APPNL-G-F knock-in mouse model of Alzheimer's disease

**AUTHORS**
Yaman U, Gustavsson E, Magusali N, Taso OS, Macpherson H, Carmona S, Mumford P, Murray M, Wiseman F, Sala Frigerio C, Soreq L, Hardy J, Salih DA.

**ABSTRACT**
Alzheimer's disease (AD) is a neurodegenerative disease defined by amyloid plaques and neurofibrillary tangles. Risk genes associated with AD form transcriptional networks of genes mostly expressed in microglia. However, these amyloid responsive transcriptional networks have been generated from short-read RNA-sequencing (RNA-seq) hence, we have limited information on splicing patterns and transcript level expression in response to amyloid pathology. Long-read RNA-seq technologies has proven to be extremely powerful to fully appreciate alternative splicing (AS) and transcript expression which were previously impossible to resolve adequately by conventional approaches. In this study, we performed long-read RNA-seq in APPNLGF knock-in mouse models and littermate C57BL/6J controls using Oxford Nanopore Technologies. We saw both AS and transcript-level differences in response to amyloid plaques. Our results confirmed the importance of known risk genes for AD and identified changes in AS in response to amyloid, as well as identifying novel transcript isoforms. Comparing the data from murine isoforms that are amyloid-dependent to human transcripts and SNPs associated with AD may provide new insights into novel mechanisms and effects of gene variants associated with disease. These findings will support disease diagnosis, tracking of disease progression, and will provide hitherto unknown disease mechanisms for new therapeutic avenues.

## Novel Methods, Resources and Technology Development| Drama Studio

### 78. Jonathan Ashmore - Neuroscience, Physiology & Pharmacology

**POSTER TITLE**
Two distinct cochlear outer hair cell operational modes: implications for cochlear tuning at high acoustic frequencies

**AUTHORS**
Ashmore J F

**ABSTRACT**
Outer hair cells of the mammalian cochlea are part of an amplification system that enhances incoming sound. Pharmacological manipulations, a wide range of genetic mutations, the anatomical positioning of the cells and a fast voltage driven motility all provide evidence for involvement in cochlear tuning.. However, the low pass filtering by the OHC membrane potential appears to limit the frequency at which potential driven 'electromotility' could contribute to cochlear mechanics. Limiting OHC motile bandwidths have also shown up in vivo in OCT measurements and in vitro by patch clamp recording of isolated cells. To counter this, considerations based on piezo electric descriptions of the OHCs (Iwasa, 2017) (Rabbitt, 2020) suggest that the OHC membrane capacitance can be a source of power up to high acoustic frequencies.

To clarify such proposals biophysically I have used experimental data which demonstrate inward currents arising from the anion movement associated with deformation of the OHC motor protein prestin/SLC26A5 (Gale and Ashmore, 1994). The resulting models show that this OHC current balance extends high frequency the OHC operating bandwidth and may also explain the two distinct auditory nerve frequency tuning curves seen for high and for low best frequencies.

### 79. Emily Atkinson - UCL School of Pharmacy

**POSTER TITLE**
Peptide growth factor mimetics for the treatment of traumatic brain injury (TBI)

**AUTHORS**
Atkinson EA, Phillips JP, Dickman R, Tabor A, Piersimoni M, Rigden, S.

**ABSTRACT**
Traumatic Brain Injury (TBI) is a leading cause of disability in adults, with limited treatment options. TBI is made up of two stages; primary injury resulting from direct trauma to the head and secondary injury caused by the physiological response to the injury. One promising treatment for secondary injury is neuroprotective growth factors, however their use in the clinic is limited due to in vivo instability. Peptide growth factor mimetics are promising alternatives as they can be stabilised and delivered locally. A dimeric macrocyclic peptide mimetic of hepatocyte growth factor (HGF) has previously been synthesised with comparable potency but has not been tested for application in the central nervous system. This work aims to synthesise this HGF mimetic using solid-phase peptide synthesis and develop an in vitro assay, modelling glutamate excitotoxicity in TBI to test the therapeutic. Cortical neurons were harvested from E14 Sprague-Dawley rats and cultured for 21 days. The assay was characterised using immunocytochemistry, confirming the presence of neuronal cells and the c-met receptor, complimentary to HGF. Future work includes determining an optimal time-point for glutamate addition in the assay, developing a second assay to investigate the glial cell response and formulating the peptide into a controlled-release hydrogel.

### 80. Neela Codadu - UCL Queen Square Institute of Neurology

**POSTER TITLE**
In vivo characterization of a novel hybrid array of graphene stimulating electrodes and micro-transistors

**AUTHORS**
Codadu NK., Iaizzo ME., Prokop M., Masvidal E., Guimera A., Garrido JA., Wykes RC.

**ABSTRACT**
Graphene probes have multiple electrophysiological advantages over metal based alternatives. We are characterising in vivo a novel hybrid array that encompasses the excellent stimulating properties of graphene electrodes with the wide bandwidth high-fidelity recordings enabled by graphene micro-transistors.

Cortical spreading depolarisations (CSDs) are a neurophysiological phenomenon characterized by an abrupt widespread disruption of ion homeostasis followed by a depression in neural activity. CSDs are associated with various neurological diseases such as migraine with aura, brain ischemia and epilepsy. Importantly, traditional electrophysiological tools are poorly suited to detect and map these events in vivo. We have assessed the properties of these hybrid arrays to induce and detect CSDs in awake head-fixed mice. Tetanic stimulations (100 Hz-5 s) through the graphene electrodes induced CSD whose propagation could be mapped across the cortex using graphene micro-transistors. Importantly, graphene micro-transistors allow us to detect the ultraslow potential shifts associated with CSD and are less sensitive to stimulation artefacts.

The use of novel technology capable of inducing, detecting and modulating CSDs with high spatiotemporal resolution will improve our understanding of these pathological events. Further development of this technology will allow us to evaluate closed-loop neuromodulation strategies in vivo.

**81. Philip Coen - UCL Institute of Ophthalmology**

**POSTER TITLE**
Lightweight, reusable chronic implants for Neuropixels 2.0 probes

**AUTHORS**
Bimbard C, Takacs F, Robacha M, Carandini M, Harris KD, Coen P.

**ABSTRACT**
[Aims] Neuropixels probes have dramatically increased the number of neurons acquired in a single experiment. With chronic recordings, these neurons can be tracked across days, but this typically requires cementing the probe to the skull. There is thus substantial interest in developing chronic implants that are recoverable and light enough for use in mice.
[Methods] Here, we present the “Apollo Implant”, a device for reversible chronic implantation of Neuropixels 2.0 probes. The implant comprises two modules: the payload module accommodates two probes and is recoverable (~£6), and the docking module is cemented to the skull during implantation and is not recoverable (~£2). The implant weighs ~2.0 g, is open source, and can be adjusted to change the angle of insertion or distance between probes.

[Results] We used the Apollo Implant to insert the same probes across at least 4 mice with no noticeable reduction in recording quality. We successfully tracked neurons across weeks,

allowing us to explore changes of sensory responses and correlation patterns over time, and during a behavioural task.

[Conclusions] The Apollo Implant provides a cheap, lightweight, and flexible solution for chronic recordings in head-fixed mice. We are developing versions for Neuropixels 1.0 probes and freely moving animals.

### 82. Steven Devenish - UCL Queen Square Institute of Neurology

**POSTER TITLE**
Improving the suitability of chemogenetic gene therapies by repurposing non-prescription agents as actuators

**AUTHORS**
Devenish SO, Almeida Silva L, Kaserer T, Goff O, Ussingkaer L, Patel S, Lieb A, Kullmann DM

**ABSTRACT**
Disorders of excessive neuronal excitability represent an enormous disease burden. Approximately 200,000 patients suffer from pharmacoresistant epilepsy in the UK alone, which has not noticeably improved with the development of new drugs in recent decades. Gene therapy is arguably one of the best options for fulfilling this unmet need. Our lab and others have shown that Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) provide on demand control of seizures in both acute and chronic models of epilepsy in rodents. One limitation for clinical advancement of this therapy is in the poor availability of approved medications as activating ligands, which is currently limited to the antipsychotics clozapine and olanzapine. Through further mutation of the muscarinic DREADD hM4Di, we have repurposed the over the counter drug diphenhydramine as an actuator. This agent shows potent and efficacious activation of our modified hM4Di both in multiple in vitro assays, and in mice virally expressing this construct as determined by the amphetamine induced rotation test. This technology, which we refer to as G protein-coupled Receptors Activated by Non-Prescription Agents (GRANPA), is currently being validated in rodent models of epilepsy in the hope of eventual implementation in human clinical trials.

### 83. Ryan Dowsell - Neuroscience, Physiology & Pharmacology

**POSTER TITLE**
Development of a high-throughput assay for identifying regulators of adenylyl cyclase transmembrane domains

**AUTHORS**
Dowsell R, Gold M.

**ABSTRACT**
Background: Adenylyl cyclases (AC) catalyse the biosynthesis of cAMP, a ubiquitous second messenger that mediates synaptic plasticity. The two catalytic domains of ACs are well characterised, however, the function of the 12 transmembrane helices, beyond subcellular anchoring, remains a mystery. We hypothesised these helices act as receptors to regulate catalytic activity in an isoform-specific manner. We aimed to develop a high-throughput screen for ligands of the neuronally enriched Ca2+-sensitive AC8.

Methods: Full-length AC8 and isolated catalytic domains were purified in HEK293-F and E. coli respectively. A FRET-based plate reader assay was developed to quantify cyclase activity comparing transmembrane vs. catalytic domain responses in real-time.
Results: The purified full-length AC8 and isolated catalytic domains were both activated by the known catalytic domain ligand forskolin, with EC50 of 3.30 µM and 3.76 µM respectively.
Conclusion: We have developed a rapid, easy to use ligand screen for the transmembrane regions of ACs. Our preliminary data allows us to pursue high-throughput screens of neuronal compounds to identify transmembrane- and isoform-specific modulators of ACs. These findings will help overcome the challenge of how cAMP is spatiotemporally regulated at the synapse.

**84.** **Yunan Gao - UCL Queen Square Institute of Neurology**

**POSTER TITLE**
Evaluating seizure susceptibility in vivo after focal knockout of astrocytic potassium channel Kir4.1

**AUTHORS**
Gao Y, Codadu NK, Bonaccini Calia A, Masvidal-Codina E, Guimera-Brunet A, Mazarakis ND, Wykes RC

**ABSTRACT**
Kir4.1 inwardly-rectifying potassium channels play a key role in maintaining physiological levels of extracellular potassium ions in the brain and are exclusively expressed in glial cells in CNS. Kir4.1 channel levels are reduced in temporal lobe epilepsy patients. Global knockout of Kir4.1 in mice were shown to be lethal with lifespan of only 3-4 post-natal weeks. This hampers our ability to understand the properties of an epileptic network lacking Kir4.1. To overcome the above problems, we have investigated targeted regional knockout in hippocampus of adult kcnj10-floxed (Kir4.1) mice. Continuous telemetry recordings indicate that these animals develop spontaneous seizures 7-14 days after injection of astrocyte-specific GFAP-cre viral constructs. To examine the Kir4.1 knockout effects on ultraslow potential shifts associated with seizures, we used an awake head-fixed setup, with graphene-transistors capable of wideband recordings. Optogenetic-activation of pyramidal neurons induced seizures in a stimulation frequency- and duration-dependent manner. Furthermore, almost all seizures induced were observed to be associated with large ultraslow potential shifts and their metrics were analysed. Here, we report a novel method to record spontaneous seizures and optogenetically induce seizures on-demand in a focal conditional Kir4.1 knockout mouse model.

**85.** **Sonia Garcia Ruiz - UCL Great Ormond Street Institute of Child Health**

**POSTER TITLE**
Splicing noise is detectable across human tissues and modelling its characteristics is likely to improve our understanding of age-related diseases

**AUTHORS**
García-Ruiz S, Zhang D, Reynolds RH, Gustavsson E, Guelfi S, Collado-Torres L, Botia JA, Ryten M

**ABSTRACT**

Alternative splicing is a characteristic of most multi-exonic human genes. However, RNA-sequencing data from human tissues suggests that this process can be inaccurate. We characterised splicing noise using RNA-sequencing data from 40 human tissues, provided by the Genotype-Tissue Expression Consortium. We focused on reads mapping with a gapped alignment to the genome that could be assigned to a transcript through sharing of known acceptor or donor splice sites but were absent from annotation.
This analysis demonstrated significantly higher levels of mis-splicing at acceptor versus donor splice sites across all samples and tissues studied. Using linear regression models to predict mis-splicing rates across human introns, we found that both local and more surprisingly, gene-level features were significantly associated with splicing noise. Although 3'/5' consensus sequence scores were key predictors, their importance varied across tissues suggesting that splicing noise might be affected by RNA-binding protein (RBP) expression. We found evidence to support this hypothesis through the analysis of RNA-sequencing data following siRNA knockdowns of spliceosomal RBPs, and by demonstrating significant changes in the distribution of splicing noise with age which correlated with RBP expression.

### 86. Gedion Girmahun - UCL School of Pharmacy

**POSTER TITLE**
Local drug delivery to modulate the immune response to Engineered Neural Tissue implants

**AUTHORS**
Girmahun G, Matar O, Phillips J, Roberton V.

**ABSTRACT**
Engineered Neural Tissue (EngNT) can support peripheral nerve regeneration by incorporating therapeutic cells to guide nerve growth after injury. Here we study how microparticles for the controlled local release, of the immunosuppressive agent tacrolimus, modulate the immune response to EngNT constructs containing allogeneic cells. In vitro analysis of the engineered constructs was performed and data on drug release, Schwann cell alignment, and the effects of microparticles on alignment was obtained. An in vivo experiment was performed in which EngNT constructs containing allogeneic cells were used to repair a 10mm sciatic nerve gap in Dark Aguoti rats. After 3 weeks constructs were harvested and analysed for T-Cell (markers: CD3, CD4 and CD8) and macrophage (marker: ED-1) infiltration, to assess the extent to which the immune response was modulated due to tacrolimus release. In conclusion, local immunosuppression is potentially a promising approach to facilitate the use of allogeneic cell transplantation in nerve tissue engineering. Future work will focus on optimising drug dosage and treatment duration and studying the long-term effects on regeneration, with the aim to improve development of drug loaded engineered neural tissue.

### 87. Saadia Hasan - UCL Queen Square Institute of Neurology

**POSTER TITLE**
Progranulin is Required for Lysosomal Function and Global Proteostasis in Neurons

**AUTHORS**
Hasan S, Fernandopulle MS, Humble SW, Frankenfield AM, Li H, Ward ME, Hao L

**ABSTRACT**

Progranulin (PGRN) is a lysosomal glycoprotein important for neuronal survival. Several studies implicate PGRN as a key modulator of lysosomal interactions and proteolysis. However, the exact mechanism remains unknown. Here we show PGRN loss decreases degradative properties of the lysosome. We developed proteomic strategies to generate an atlas of lysosomal surface proteins using proximity-based labeling via ascorbate peroxidase from human inducible pluripotent stem cell derived neurons (iNeurons). We isolated intact lysosomes using rapid immunopurification to compare lysosomal contents of PGRN-deficient iNeurons. Lastly, we monitored global proteostasis using dynamic stable isotope labeling using amino acids in cell culture (dSILAC) to generate a half-life profile for proteins detected. We observed increased v-ATPase subunits on the surface of PGRN-deficient lysosomes, indicating dysregulation in lysosome acidification. Lysosome isolation revealed increased catabolic enzymes in PGRN-lacking iNeurons. Since acidic pH is necessary for enzymatic activity, we tested global proteolytic capacity next. dSILAC results determined substantially altered protein half-lives. A number of these proteins, including VCP, TARDBP, and MAPT, are linked to neurodegenerative disease and are prone to misfolding/aggregation if not processed correctly. Together, these results implicate PGRN as a major regulator of lysosomal function, which in turn influences the proteostasis of many disease-relevant proteins.

**88. Dawn Lau - UCL Queen Square Institute of Neurology**

**POSTER TITLE**
An in vitro model system for microglia-targeted drug discovery

**AUTHORS**
Lau D, Navarron CM, Pendery M, Costelloe K, Jeganathan F, Van Ingelgom A, Phadke L, Patel L, Whiting P, Magno L

**ABSTRACT**
Introduction:
Microglia have been strongly implicated in the pathological process of neurodegenerative diseases. Crucially, human genetic studies have indicated an essential role for microglia in Alzheimer's disease; therefore, modulating the function of microglia may be a viable therapeutic approach. To facilitate this, in vitro microglia model systems are required. While microglia complexity in vitro is simplistic, modulating culturing conditions and challenges can elicit different functional states of microglia which could be suitable for disease modelling, phenotypic screening, and target validation.

Materials & Methods:
Primary microglia cultured in serum-free defined medium were characterised for morphology, gene expression, and function. Phagocytosis assays were carried out with pHrodo-labelled apoptotic SH-SY5Y and measured on the IncuCyte S3. Cytokine secretion was measured via a mesoscale cytokine assay, while calcium flux was quantified with the FLIPR.

Results and conclusion:
We have developed a model system to assess primary microglia function in vitro with high throughput techniques and validated with pharmacological tools. Our protocol produces robust microglia that are homeostatic or activated, dependent on culturing conditions, with high purity and survival. We developed and validated functional assays for microglia such

as phagocytosis, cytokine production, and calcium flux, which can be used to identify and validate novel therapeutic targets for microglia dysfunction.

**89.** **Leela Phadke - UCL Queen Square Institute of Neurology**

**POSTER TITLE**
Development of a triculture model to explore glial contribution to neuronal activity

**AUTHORS**
Phadke L, Lau D, Ibarra S, Magno L, Whiting P, Jolly S

**ABSTRACT**
Neuroinflammation and hyperexcitability have been implicated in the pathogenesis of neurodegenerative disease, and new models are required to investigate the cellular crosstalk involved in these processes. We developed an approach to generate a quantitative and reproducible triculture system that is suitable for pharmacological studies. Primary rodent cells were grown in a triculture medium formulated to support neurons, astrocytes, and microglia, or a coculture medium formulated to support only neurons and astrocytes. Immunocytochemistry was used to confirm the intended cell types were present at 14 days in vitro. Multi-electrode array (MEA) recordings indicate that microglia in the triculture model suppress neuronal activity in a dose-dependent manner. MEA was also used to quantify the response of the two culture types to different stimuli; 4-aminopyridine (4-AP) and lipopolysaccharide (LPS). 4-AP modulated neuronal activity in both cocultures and tricultures, indicating that neurons in the triculture model remain functional and were not negatively impacted by the presence of the microglia. LPS-exposed tricultures displayed an increase in neuronal activity which was not observed in LPS-exposed cocultures. The triculture is a more relevant model than standard cocultures and may be used in the development of assays for drug discovery, using neuronal excitability as a functional endpoint.

**90.** **Mohammed Rupawala - Neuroscience, Physiology & Pharmacology**

**POSTER TITLE**
Single-channel event-related potentials versus cortical microstate analysis of nociceptive responses in human neonates

**AUTHORS**
Rupawala M, Laudiano-Dray MP, Whitehead K, Meek J, Fitzgerald M, Olhede S, Jones L, Fabrizi L.

**ABSTRACT**
Single channel vertex event-related potentials (ERPs) have been used extensively to study pain in neonates. However, considering the complexity of the pain experience and of the brain networks engaged in the processing of noxious input, this approach could be reductive and not allow to capture the multifaceted temporospatial dynamics of nociception. Here we recorded electroencephalography responses to two consecutive identical clinically-required heel lances in eleven term neonates and used global event-related field topography (microstates) to characterise changes in nociceptive dynamics between the two stimuli and compared it with traditional ERP analysis. ERP analysis identified two periods of significant amplitude differences whereas microstate analysis revealed modulation of an initial identical

sequence of states followed by distinct microstate activity to first and second lance. This difference results from a shift in peak response from the vertex to other electrodes as different underlying networks are engaged. This suggests that neonatal nociceptive processing of repeated identical stimuli does not only result in the modulation of the activation of the same network, but also in the engagement of additional distinct processes. A microstate approach overcomes constraints related to discrete single-channel peak identification and allows for the characterization of a complex continuous dynamic nociceptive processing stream.

### 91. Andrew Vaughan - MRC Laboratory for Molecular Cell Biology

**POSTER TITLE**
Super-resolution imaging in neurons

**AUTHORS**
Vaughan A, Hng K

**ABSTRACT**
Neurons are specialised cells whose gross morphology is indicative of their role in information processing. However, to carry out their function they must also maintain highly organised and dynamic protein structures at a nanoscopic level. Such structures have been difficult to study until the recent introduction of super-resolution imaging techniques that improve the resolution of light microscopy. The UCL Super-resolution Facility (SuRF) provides all UCL staff access to techniques such as Image Scanning Microscopy (ISM), structured illumination microscopy (SIM), stimulated emission depletion (STED) and single-molecule localization microscopy (SMLM). Here we show how a technique such as STED can be used to resolve the axonal membrane periodic skeleton (MPS), as well as structures within the synapses. We also demonstrate a single-molecule imaging approach to achieving high precision localization of proteins in axons.

### 92. Rob Wykes - UCL Queen Square Institute of Neurology

**POSTER TITLE**
Development of nanotechnologies to detect and treat pathological brain activity

**AUTHORS**
Wykes RC

**ABSTRACT**
The Wykes labs are located at the UCL Queen Square Institute of Neurology and within the Nanomedicine Lab at the University of Manchester. We are a vibrant, dynamic group consisting of 1 PI (Dr Wykes), 6 post-doctoral researchers, 1 PhD student and 2 MSc students.

Our research focuses on technology development to understand, detect and treat CNS disorders; and can be broadly broken down into 4 research categories:
1. Development and concurrent application of imaging and electrophysiological approaches to characterise seizure activity and spreading depolarisations in preclinical models of epilepsy, migraine, glioblastoma and stroke. A recent focus is application of implantable Graphene-based transistor arrays to map wide bandwidth pathological brain activity.

2. Neuromodulation using flexible arrays of graphene stimulating electrodes as DBS devices in preclinical models of Parkinson's and epilepsy
3. Gene therapy and Nanoparticle approaches to treat drug-refractory forms of epilepsy and glioblastoma.
4. Clinical translation of graphene micro-transistor arrays for epilepsy pre-surgical detection of the seizure onset zone.
Examples of our work in these four areas will be displayed in our lab poster presentation.

### 93. Yichao Yu - UCL Division of Medicine

**POSTER TITLE**
Remote and selective control of astrocytes by magnetomechanical stimulation

**AUTHORS**
Yu Y, Payne C, Marina N, Korsak A, Southern P, García-Prieto A, Christie IN, Baker RR, Fisher EMC, Wells JA, Kalber TL, Pankhurst QA, Gourine AV, and Lythgoe MF

**ABSTRACT**
Astrocytes play crucial and diverse roles in brain health and disease. The ability to selectively control astrocytes provides a valuable tool for understanding their function and has the therapeutic potential to correct dysfunction. Existing technologies such as optogenetics and chemogenetics require the introduction of foreign proteins, which adds a layer of complication and hinders their clinical translation. We have developed a novel technique, magnetomechanical stimulation (MMS), that enables remote and selective control of astrocytes without genetic modification. MMS exploits the mechanosensitivity of astrocytes and triggers mechano-gated calcium and adenosine triphosphate (ATP) signalling by applying a magnetic field to antibody-functionalised magnetic particles that are targeted to astrocytes. Using purpose-built magnetic devices, we determined the mechanosensory threshold of astrocytes, identified a sub-micrometre particle for effective MMS, established the in vivo fate of the particles, and induced cardiovascular responses in rats after delivering particles to specific brainstem astrocytes. By eliminating the need for device implantation and genetic modification, MMS is a method for controlling astroglial activity with an improved prospect for clinical application than existing technologies.

### 94. Asaph Zylbertal - Neuroscience, Physiology & Pharmacology

**POSTER TITLE**
SimFish: an end-to-end, ecologically-optimised larval zebrafish model

**AUTHORS**
Pink S, Zylbertal A, Bianco IH

**ABSTRACT**
In vivo studies have yielded insights into sensorimotor behaviour and its neural basis, yet these studies often leave questions about the ecological milieu that shaped these properties, and the extent to which they represent optimal, or even universal, solutions. Deep reinforcement learning (DRL) agents optimised by ecological simulation represent a promising approach to address such questions, capably replicating both behavioural and implementational features of target systems in a deliberately composed neural substrate. The resulting models are fully observable and modifiable, allowing their properties to be

directly linked to an associated environmental basis. Using ecological, anatomical, and ethological data, we designed a detailed simulation that replicates the sensory constraints and environmental pressures assumed to be responsible for shaping zebrafish behaviour and its underlying neural substrate. DRL agents trained in this simulation reproduced both low- and high-level features of observed behaviours, as well as neural tuning properties previously documented in the zebrafish brain. These similarities show that in silico ecologically-optimised models are a promising tool to study systems in an end-to-end fashion, test the importance of particular ecological pressures, and to locate universal behavioural and algorithmic solutions in sensorimotor systems.

## Sensory and Motor Systems | Drama Studio

### 95. Marta Andres Miguel - UCL Ear Institute

**POSTER TITLE**
Targeting hearing and swarming behaviour for malaria mosquito control

**AUTHORS**
Ellis D, Tytheridge S, Terrazas-Duque D, Bagi J, Freeman E, Andrés M

**ABSTRACT**
Malaria is a mosquito-borne disease that poses a huge public health burden in many low-income countries, particularly in Sub-Saharan Africa. One of the most successful strategies to fight malaria- transmission is to control the mosquitoes that transmit the parasite. In the lab, we are studying the neurobiology of the malaria mosquito vector with the aim of identifying novel pathways that can be targeted either pharmacologically or genetically to control mosquito populations. In particular, we are interested in uncovering the molecular pathways that mediate mosquito hearing and swarming behaviour, as they are essential for mosquito mating. Every sunset, male and female mosquitoes gather in swarms where they detect the mating partner by the sound produced by their wing-beats. Our approach consists on using transcriptomic, metabolomics and immunostainings to identify pathways involved in these processes, to then disrupt these mechanisms using genetic or pharmacological tools. Resulting phenotypes are analysed using different physiological and behavioural methods that allow us to study auditory, locomotive, mating and swarming behaviour defects. Our ultimate goal is to apply our findings to improve current mosquito control strategies by selecting molecules with insecticide potential that can be used to block these pathways to disrupt mosquito reproduction.

### 96. Paride Antinucci - Neuroscience, Physiology & Pharmacology

**POSTER TITLE**
Combined space-rate codes in tectum-pretectum control calibrated steering of hunting manoeuvres

**AUTHORS**
Antinucci P, Colinas-Fischer S, Bianco IH.

**ABSTRACT**

The vertebrate optic tectum and pretectum are required for hunting, yet their relative contribution to prey localisation and steering of predatory manoeuvres is unknown. We show that tethered larval zebrafish hunting in a virtual reality environment finely calibrate their tail and eye movements according to prey location. Two-photon calcium imaging in tectum-pretectum revealed that neurons tuned to prey-like visual features are heterogeneously distributed across the tectal-pretectal space map. Neurons tuned to convergent saccades - a behavioural hallmark of hunting initiation - formed a motor map in which steering was encoded by a pretectal rate code and a tectal space code distributed across the anterior-posterior axis. Consistent with a rate code, increasing pretectal activation level via spatially patterned optogenetic stimulations induced progressively larger contraversive steering. Tectal activations instead supported a space code such that stimulating increasingly posterior regions shifted movements ipsilaterally. Analyses of projection patterns and laser axotomies indicated that pretectal neurons mediate orienting tuns via a contralateral pretectobulbar pathway. Finally, optogenetic stimulations guided by the physiological activity pattern in tectum-pretectum supported a model in which combined tectal-pretectal activity additively modulate steering of tail movements. We conclude that a pretectal rate code combined with a tectal space code control orienting manoeuvres during hunting.

### **97.** Celian Bimbard - UCL Institute of Ophthalmology

**POSTER TITLE**
Behavioral origin of sound-evoked activity in mouse visual cortex

**AUTHORS**
Bimbard C, Sit T, Lebedeva A, Reddy, CB, Harris, KD, Carandini M

**ABSTRACT**
Many studies suggest that all cortical sensory areas, including primary ones, are multisensory. For instance, mouse primary visual cortex (V1) appears to be influenced by auditory signals. These effects may be due to auditory projections to the visual cortex. However, sounds also change internal state and elicit uninstructed body movements, and both effects have brainwide correlates. It is thus possible that sounds affect visual cortex and other brain regions mainly through changes in state or behavior rather than through direct auditory projections.

We used Neuropixels probes to record the responses of hundreds of neurons in V1 and hippocampus of awake mice to audiovisual stimuli, while filming the mouse. To explore the role of direct projections from auditory to visual cortex, in 3 mice we cut auditory fibers to visual cortex and recorded sound-evoked responses on the cut and uncut sides of the brain. V1 encoded a low-dimensional representation of sounds. The same representation was also present in hippocampus, which barely receives any auditory input. The sound-evoked activity of neurons in V1 and hippocampus were highly correlated with the temporal patterns of sound-evoked movements, which were stereotyped across trials and across mice. They were were unaffected by cutting direct projections from auditory cortex.
These results indicate that a large fraction of the multisensory activity that has been widely observed across the brain may have a simpler, behavioral origin.

### **98.** Charlie Dowell - Neuroscience, Physiology & Pharmacology

**POSTER TITLE**

Circuits controlling saccadic eye movements in larval zebrafish

**AUTHORS**
Dowell CK, Bianco IH

**ABSTRACT**
How are separate but kinematically related actions executed by motor circuits?
We investigated the circuitry controlling two ethologically distinct saccadic eye movements in larval zebrafish: the hunting specific convergent saccade and the exploratory conjugate saccade. By using functional Ca2+ imaging, neurite tracing, selective ablations and optogenetics, we characterised premotor and motorneurons controlling saccadic nasal eye movements. In oculomotor nucleus and rhombomere 6 we found neurons with activity selective for oculomotor features and convergent saccades. These two regions were connected by abducens inter-nuclear neurons, which were largely feature encoders. Our results indicate that premotor and motorneurons can generate distinct movements through a combination of action specific and feature based activity, that varies along the motor circuit.

**99. Roxana Florea - Cell and Developmental Biology**

**POSTER TITLE**
Stress increases the spread of widespread pain in two mouse models of joint pain as seen in patients with arthritis

**AUTHORS**
Florea R, Hestehave SK, Morgan OB, Géranton SM

**ABSTRACT**
Chronic joint pain is an escalating public health problem for which effective therapy is still needed. While its aetiology remains complex and inadequately understood, it is increasingly recognized that stressful life experiences are key contributors that predispose individuals with joint diseases to develop long-term widespread pain, even in healthy joints. The aim of this study was to characterise the effect of stress on the spread of pain in various models of persistent joint pain.

Male and female C57/BL6 mice were first exposed to stress by restraint for 1h/day for three consecutive days, followed by intra-articular injection of either Complete Freund's Adjuvant (CFA) or mono-iodoacetate (MIA).

Restraint stress induced a transient increase in mechanical hypersensitivity that lasted two weeks on all limbs. Upon recovery from the hypersensitive state, subsequent challenge with injection of either CFA or MIA in the ankle or knee joint, respectively, induced persistent hypersensitivity not only in the inflamed hindlimb but also in the non-injured hindlimb. These observations suggest that stress exposure can promote the spread of long-lasting hypersensitivity in persistent joint pain models, as seen in patients with joint pain.

**100. Sara Hestehave - Cell and Developmental Biology**

**POSTER TITLE**
Chronic pain and emotional comorbidities in joint pain, - targeting the chronic pain- and stress-regulator FKBP51 to combat it all

**AUTHORS**
Hestehave S, Géranton SM

**ABSTRACT**
Joint-diseases are not only accompanied by significant pain but also by secondary symptoms like low mood and memory dysfunction. Such comorbidities strongly impact patients' well-being, but receive little attention in preclinical studies. We hypothesised that inhibiting the stress regulator FKBP51 would reduce the pain that accompanies joint diseases and improve emotional comorbidities.

We used a mouse model to characterize the development of sensory, cognitive-, anxiety- and depressive-like changes in in mice with joint-pain and, explored the efficacy of the FKBP51 antagonist, SAFit2, in reversing both sensory and 'emotional' comorbidities. While sensory changes were apparent on the first day after induction of joint inflammation, emotional comorbidities required at least a month to develop. Treatment with SAFit2 from 8-12 weeks reduced the sensory changes and prevented/delayed the development of depressive-like behaviour, but had no effect on anxiety- or cognitive-outcomes. Sensory changes reappeared as soon as the treatment was interrupted. However, when given acutely during the induction-phase of the inflammation, sensory outcomes were reduced for more than 4 months, and the development of anxiety- and depressive-like behavior was completely prevented.

These findings suggest FKBP51 inhibition as a future treatment for both pain and accompanying emotional comorbidities related to joint diseases.

**101.** **Chen Lu - UCL Ear Institute**

**POSTER TITLE**
Auditory evoked-potential abnormalities in a mouse model of 22q11.2 deletion syndrome correlate with inter-individual variability in hearing impairment

**AUTHORS**
Chen L, Jennifer L.

**ABSTRACT**
Auditory evoked-potential (AEP) abnormalities are common in people with genetic risk for schizophrenia, including carriers of the 22q11.2 deletion. We examined AEP abnormalities in the Df1/+ mouse model of human 22q11.2 deletion syndrome (22q11.2DS). Like 22q11.2DS patients, Df1/+ mice exhibit high inter-individual variability in peripheral hearing sensitivity. We measured both peripheral hearing sensitivity and cortical AEPs in 30 Df1/+ mice and 21 WT littermates. We then analysed the influence of genotype and hearing sensitivity on loudness-dependent AEP (LDAEP) and inter-tone interval time-dependent AEP (TDAEP) growth functions. Both LDAEP and TDAEP growth functions were abnormal in Df1/+ relative to WT mice. Moreover, the nature of the AEP abnormalities in Df1/+ mice correlated with inter-individual variability in peripheral hearing sensitivity. Results suggest that AEP abnormalities depend not only on genetic risk factors for schizophrenia but also on hearing impairment, which has been associated with schizophrenia in both cross-sectional and longitudinal studies.

**102.** **Oakley Morgan - Cell and Developmental Biology**

**POSTER TITLE**
Early life stress promotes vulnerability to chronic migraine in mice

**AUTHORS**
Morgan, O., Andreou. A., Geranton, S.

**ABSTRACT**
Early life adversity (ELA) is known to promote vulnerability to chronic pain, but the underlying mechanisms are not yet fully understood. In particular, the primary headache disorder, migraine, is greatly affected by childhood stress, with ELA identified as a major risk factor for the progression towards chronic migraine. FK 506 binding protein 51 (FKBP51) is a key player of the Hypothalamus-Pituitary-Adrenal (HPA) axis and regulates the stress response. Moreover, our lab has shown that FKBP51 is also a regulator of chronic pain states. Here, we hypothesised that FKBP51 plays a role in the interactions between ELA and migraine chronification.

We used animal models of ELA and migraine together with FKBP5 deficient mice, behavioural and molecular approaches to elucidate the role of FKBP5 in the ELA-induced exacerbation of migraine. Migraine was induced in adulthood.
Our results showed that ELA prolonged migraine hypersensitivity. Crucially, the exacerbation of migraine by ELA was not present in FKBP5 KO mice. Conversely, gene expression analysis of CNS tissue, taken in adulthood after ELA, revealed a down-regulation of FKBP5 mRNA following ELA, suggesting that ELA had led to complex long-term changes in the HPA axis. This study provides further understanding of the interactions between ELA and migraine.

**103.** **Marlies Oostland - Wolfson Institute of Biomedical Research at UCL**

**POSTER TITLE**
A machine learning-based classifier for identifying cell types in cerebellar Neuropixels recordings

**AUTHORS**
Oostland M*, Beau M*, Kostadinov D*, D'Agostino F, Chung Y, Maibach M, Martínez Lopera G, Lajko A, Zedler M, Cohen D, Häusser M

**ABSTRACT**
Neuropixels probes allow for high-quality recordings of dozens to hundreds of cells simultaneously and are increasingly adopted by labs across the world. However, as with all extracellular recordings, Neuropixels recordings do not allow for unambiguous cell type identification. To address this problem, we are developing a machine learning-based cell-type classifier for Neuropixels recordings from the cerebellum of mice. To acquire ground-truth data, we use mouse lines expressing ChR2 in specific cell types to optogenetically tag neuronal types. This approach allows us to identify the electrophysiological signatures of five major cell types in the cerebellar cortex: Purkinje cells, granule cells, Golgi cells, mossy fibre boutons, and molecular layer interneurons. We use the firing characteristics of extracellular units in conjunction with their waveform spatio-temporal profile to predict their cell type with a random forest classifier. At present, the classifier allows us to identify cerebellar neurons with high reliability (>90% for some cell types). We are currently increasing the dataset of optotagged neurons to further improve this performance. Our aim is to provide an open-

source tool for automated and reliable identification of cerebellar cell types, which can be extended to recordings from a wide range of species.

### 104. Giulia Zuccarini - Neuroscience, Physiology & Pharmacology

**POSTER TITLE**
Brain-wide activity underlying hunting sequences in larval zebrafish

**AUTHORS**
Zuccarini G, Bianco IH

**ABSTRACT**
Animals typically accomplish goal-directed behaviours by generating sequential motor actions.

In larval zebrafish, hunting is an innate, visually-guided behaviour composed of a sequence of specialised swimming manoeuvres that are selected and tuned in response to a dynamic visual input. Previous work in the Bianco lab has identified a population of pretectal neurons that control hunting initiation, and neurons in the nucleus isthmi required for the maintenance of the prey-capture routine, but the neural mechanisms that drive the generation of the behavioural sequence are still unclear.

To investigate this, we are combining a virtual reality hunting assay with two-photon functional calcium imaging.

By presenting prey-like visual stimuli within a closed-loop environment, we successfully evoke naturalistic hunting sequences in tethered larvae. Preliminary functional imaging and circuit tracing data suggests that a network of brain regions interconnected with pretectum are recruited during hunting behaviour, including cerebellum, tegmentum, and intermediate hypothalamus.

In future work we will characterize the specific contributions of these various regions to shed light on the neural mechanisms of decision making, action selection and motor sequence generation.

# Other (History of Neuroscience, Public Awareness of Neuroscience, Resource Posters) | Drama Studio

**105.** Razna Ahmed - UCL Queen Square Institute of Neurology

**POSTER TITLE**
Evaluating the Role of High-Fidelity Neurosurgical Simulation in the Training of Aneurysm Clipping

**AUTHORS**
Ahmed R, Muirhead W, Marcus H

**ABSTRACT**
Intracranial aneurysm surgery is technically demanding and high risk. With the advent of the endovascular era there are an ever-smaller number of aneurysms being treated by open surgery and those that are treated, are often complex. Training neurosurgeons in open surgical aneurysm repair is consequently increasingly challenging within the operating theatre and there is a well-recognised need to develop these skills in simulation where possible prior to transferring them to the operating theatre.

Animal models, Virtual Reality and physical synthetic models often constructed using additive manufacturing have all been trialled, but all remain at best extremely partial simulations of the complex and dynamic operative environment of cerebral aneurysm clipping.

The widespread availability of additive manufacturing has led to the development and validation of models for aneurysm clipping from several established academic centres. To build on this experience we are validating a novel 3D printed model of middle cerebral artery aneurysm clipping incorporating the best elements of those that have been previously developed and adding innovative elements to overcome their limitations highlighted by their validation processes.

**106.** Barbara Dymerska - UCL Queen Square Institute of Neurology

**POSTER TITLE**
Using 7T MRI to probe the structure and function of the human brain at the microscale

**AUTHORS**
Dymerska B, Callaghan MF

**ABSTRACT**
7T MRI is a new neuroimaging capability within the Department of Imaging Neuroscience, Queen Square Institute of Neurology. It provides exquisite spatial resolution and enhanced functional contrast that can be used to more sensitively map neuronal responses of cortical regions, or pushed further to investigate small nuclei as well as discrete functional units of neuronal computation, such as cortical layers, columns and stripes. The step-change in our ability to probe the microscale organisation of the human brain, afforded by 7T, means that

we can now ask questions that dissociate activity from deep and superficial cortical layers so as to dynamically access feed forward and feedback message passing and how these go awry, e.g. in psychosis.

Using in vivo histology methods we can complement these functional investigations with microstructural characterisation on an unprecedented spatial scale and disentangle the biological basis for observed change to explore regionally-specific laminar patterns of degeneration. Such an approach could provide earlier and more specific prodromal markers of disease predictive of long-term clinical events before symptoms emerge; it could be used to track disease progression, discriminate between disease mimics or assess the efficacy of interventions. Collectively this would take us a big step towards personalised precision medicine.