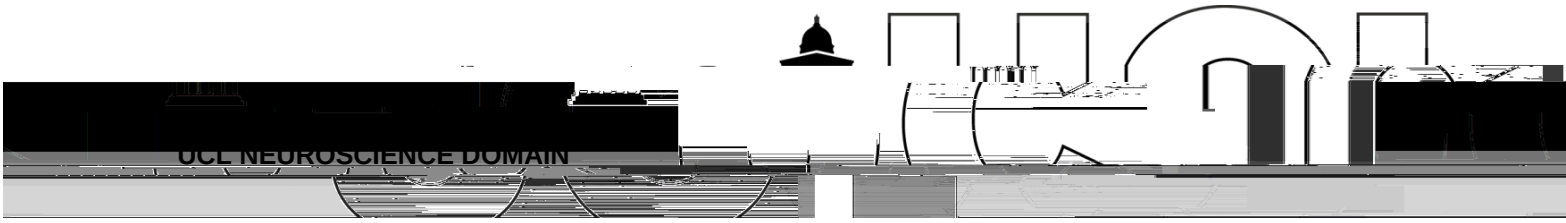
UCL Neuroscience Symposium 2022



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Cognition and Behaviour | Elvin Hall

1. **Emma Clark**

Emma

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

Sequence and Inference Probe accuracy were indistinguishable. A hybrid model captured

Inference Probe accuracies. Our results suggest that humans factorize state spaces underlying their experience, allowing for compositional reuse of knowledge.

12.

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-
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-

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

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

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

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

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

POSTER TITLE

Understanding c9orf72 hexanucleotide repeat linked to mitochondrial dysfunction

AUTHORS

Sharon Tooley, Teresa Niccoli

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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.

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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

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

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
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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

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

ABSTRACT

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

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

ABSTRACT

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

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

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

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.

These results and those from future experiments will help elucidate the mechanistic role of PrPC in AD and how its inter

47. Hemanth Ramesh Nelvagal -

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

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
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

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
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 no or mild clinical encephalopathy also had lower EEG power relative to

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 ase 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- -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

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

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 tration, 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

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

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,

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

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AUTHORS
Sheng K, Bicknell B, Häusser M

ABSTRACT

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

Progranulin (PGRN) is a lysosomal glycoprotein important for neuronal survival. Several

2. Neuromodulation using flexible arrays of graphene stimulating electrodes as DBS devices

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

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-

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-
(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-

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

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