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2018 Research Poster Prize – Sponsored by Cerevance

The 10 posters shortlisted for the 2018 Research Poster Prize are highlighted in blue and will all be displayed in the Jeffery Hall.

Laboratory Posters | Jeffery Hall

L1. Neil Burgess - UCL Institute of Cognitive Neuroscience

POSTER TITLE
Spatial cell activity during virtual navigation of open arenas by head-restrained mice

AUTHORS
Chen A, King JA, Lu Y, Hayman R, Cacucci F, Burgess N

ABSTRACT
We present a mouse virtual reality (VR) system which restrains head-movements to horizontal rotations, potentially compatible with multi-photon imaging. We show that this system allows expression of the spatial navigational behaviour and neuronal firing patterns characteristic of real open arenas (R). Place and grid, but not head-direction, cell firing had broader spatial tuning in VR than R. Theta frequency increased less with running speed in VR than in R, while firing rates increased similarly in both. Place, but not grid, cell firing was more directional in VR than R. These results suggest that the scale of grid and place cell firing patterns, and the frequency of theta, reflect translational motion inferred from both virtual (visual and proprioceptive) cues and uncontrolled static (vestibular translation and extra-maze) cues, while firing rates predominantly reflect visual and proprioceptive motion. They also suggest that omni-directional place cell firing in R reflects local-cues unavailable in VR. Finally, changing the 'gain' of movement of point of view compared to physical movement indicates a differential influence of (virtual) visual cues on place fields and of physical motion on grids, suggesting that the two representations are not necessarily coherent.

L2. AJ Copp – UCL GOS Institute of Child Health

Dianne Gerrelli

POSTER TITLE
Understanding congenital disease through investigations of human embryonic and fetal development

AUTHORS
Gerrelli D, Crespo Lopez B, Moreno N Lisgo S, Lindsay S, Copp AJ

ABSTRACT
The Human Developmental Biology Resource (HDBR www.HDBR.org) is a unique resource funded by the MRC and Wellcome Trust. It provides human embryonic and foetal tissue for gene expression studies related to congenital disease, including both birth defects and

inherited metabolic disorders. Use of the material should particularly illuminate developmental gene expression underlying aspects of functioning that characterise humans as opposed to lower animals (e.g. higher brain function, language). This research is essential if we are to introduce new methods for prevention of congenital defects and develop an improved understanding of “what makes us human”. The HDBR has ethics approval for the collection, storage and distribution of material between 4 and 20 weeks post conception. The material can be used to generate cell lines, stem cells, protein, RNA and DNA. In addition, paraffin wax and frozen sections of embryos and early foetuses are available for in situ hybridisation and immunohistochemistry. For users who do not have experience in gene expression analysis the HDBR offers an in-house gene expression service using in situ hybridisation and/or immunohistochemistry. We will highlight data from recent projects that have used our resource to study gene expression in the human embryonic and foetal brain and spinal cord.

L3. Frances Edwards – UCL Department of Neuroscience, Physiology & Pharmacology

Damian Cummings

POSTER TITLE
Alzheimer’s disease: Developing mouse models to seek novel drug targets and treatments

AUTHORS
Edwards, FA

ABSTRACT
We concentrate on APP, TAU and TREM2 knock-in mouse models to understand the earliest changes in Alzheimer’s disease. By combining these knock-in models with other risk-factors, we hope to produce improved models in which we can study interactions of microglia and synaptic transmission before and during plaque deposition. Furthermore, we hope to identify factors that may result in rising amyloid beta leading to the development of neurofibrillary tangles and neurodegeneration. As well as seeking new drug targets, we are investigating the possibility of using drugs already approved for other conditions in slowing disease progression.Techniques:• In vitro electrophysiology; patch clamp and field recording• Acute brain slices• Cultures (organotypic, neurones, astrocytes, microglia)• Molecular biology• Immunohistochemistry• Confocal microscopyCollaborations:• Genomics, John Hardy• Neuroinflammation, Ken Smith• Mass-spectrometry, Kaj Blennow, Henrik Zetterberg, Jörg Hanrieder, Sweden• Mouse models: Saito & Saido; JAX labs; DRI (Bart DeStrooper)• Pharmaceuticals: UCL Drug discovery institute, Paul Whiting & Jamie BislandLab members:• Senior Research Fellows: Dr Dervis Salih; Dr Damian Cummings• Postdoctoral RA: Dr Wenfei Liu• Research Assistants: Rui Wang; Katie Stringer• PhD Students: Jonathan Brenton, Diana Benitez Jimenez, Katie Stringer• MSc students: Philippa Rosewell, Orjona Taso• MSci students: Natalie Wong, Victoria SmithFunding: ARUK; MRC; DRI; Cure Alzheimer’s

L4. Patrizia Ferretti - UCL GOS Institute of Child Health

Citlali Helenes Gonzalez

POSTER TITLE
Improving in vitro models of human neural cell development in health and disease

AUTHORS
Ferretti P.

ABSTRACT
In vitro human neural cell cultures provide a useful model to mimic the effects of central nervous system (CNS) injury or disease. However, traditional 2-dimensional (2D) in vitro models are limited as they fail to take into account the impact of tissue dimensionality on cellular phenotype and behaviour. In the Ferretti laboratory, we aim to: 1) establish novel 3-dimensional (3D) models using different matrices to build scaffolds to support human neural stem cells (hNSCs) and their differentiated progeny, 2) to explore differences in cellular behaviour of neural cells in 2D vs 3D hydrogel cultures and 3) to investigate the use of our culture systems to study neural pathologies including Duchenne's Muscular dystrophy (DMD), Down syndrome (Trisomy 21; T21), and hypoxic-ischaemic (HI) injury. We have established conditions for the preparation of a brain-derived matrix to generate a scaffold to be used in 3D-systems. Further, we show here that dystrophin expression, implicated in DMD, is upregulated in hNSCs and astrocytes when grown in 3D vs 2D. Finally, neural cells cultured in 3D hydrogels show a reduced susceptibility to cell death induced by oxygen-glucose deprivation when compared to 2D. These findings emphasise the importance of considering dimensionality when modelling human CNS in vitro.

L5. Gabriele Lignani - UCL Institute of Neurology

POSTER TITLE
Novel genetic technologies for overcoming in vivo gene therapy limitations

AUTHORS
Lignani G.

ABSTRACT
Gene therapy holds promise as a potential treatment for neurological diseases. However, limitations are still present, including: limited packaging capacity of viral vectors, difficulties in developing approaches to treat dominant negative mutations, and, in the case of epilepsy, difficulties distinguishing neurons actively involved in seizure generation from those that support normal brain functions. In the lab we are developing alternative techniques to overcome these limitations:i.Two CRISPRa approaches to increase endogenous gene expression; one to rescue Dravet Syndrome (Scn1a haploinsufficiency) and the other to treat intractable acquired focal epilepsy (KCNA1 upregulation). ii.In vivo CRISPR-based approaches to correct dominant negative mutations associated with different pathologies such as ataxia (KCNA1), Dravet Syndrome (GABRG2) and progressive myoclonic epilepsy (KCNC1). iii.We are repurposing activity-dependent promoters, recently used to target specific neuronal populations during behavioural tasks, to drive gene therapy tools (KCNA1 or CRISPRa) in order to selectively target only neurons involved in seizure generation and spare the healthy ones. Our aim is to develop new gene therapy approaches with rapid potential for translation. We use techniques ranging from molecular biology to in vivo electrophysiology, and models spanning from cell lines to animal models and iPSC-derived neurons from patients.

L6. Sara Mole - MRC Laboratory for Molecular Cell Biology

POSTER TITLE
Batten disease

AUTHORS
Mole S

ABSTRACT
The Mole Laboratory is mainly interested in the neuronal ceroid lipofuscinoses (NCL, Batten disease). These are monogenic inherited neurodegenerative diseases characterised by the accumulation of autofluorescent lipofuscin-like (age pigment) material in lysosomes, and neuronal loss. Those affected suffer seizures, visual failure, declining mental and motor skills, and die prematurely. The age of onset ranges from birth to late in adulthood, mostly affecting children, and is characteristic for the underlying genetic defect. Thirteen genes have been identified, and over 400 mutations. We curate the international NCL mutation database.We have 4 main research interests: (1) Genetics, classification and diagnosis; (2) The molecular and cellular basis; (3) Identification of new therapeutic targets and drugs; (4) Developing gene therapy to treat the brain and the eye. We work closely with UCL colleagues towards all aims, coordinate an EU H2020 consortium, BATCure, to achieve aims (2-4), and make extensive use of systems approaches and the genetic tractability of fission yeast Schizosaccharomyces pombe to speed aims (2,3).

L7. Richard Poole – UCL Department of Cell and Developmental Biology

Thomas Mullan

POSTER TITLE
Many ways to make a neuron? Investigating early embyronic neuronal specification and post-embyronic glia-to-neuron cell fate switches

AUTHORS
Poole R

ABSTRACT
In the Poole lab we are interested in the cellular and molecular mechanisms that regulate neuronal specification. With a small nervous system arising from an invariant developmental cell lineage and an abundant genetic toolkit, the nematode Caenorhabditis elegans represents a model in which we can investigate these mechanisms with single-cell resolution. C. elegans neurons arise non-clonally from many branches of the embryonic lineage, this suggests that multiple mechanisms of neuronal specification may be employed concurrently in the worm. We have two main projects in the lab, which we investigate using unbiased forward genetic approaches and modern genetic techniques. Firstly, in the embryo we are interested in the early segregation of neuronal potential into specific lineage branches. Taking advantage of the invariant cell lineage we use 4D-lineaging approaches to identify upstream regulators of the proneural gene hlh-14/ASCL1 in one side of an otherwise bilaterally symmetric lineage. Secondly, we investigate sexually dimorphic glia-to-neuron cell fate switches during post-embryonic development, we expect this will shed light on the fundamental mechanisms of plasticity and transdifferentiation. Together, these projects will identify conserved principles of neuronal specification, which could be key drivers of novel therapies and brain repair strategies.

L8. **Ede Rancz - The Francis Crick Institute**

Sarah Aldous

POSTER TITLE
Predictive coding in the mouse visual cortex - towards a new model system

AUTHORS
Rancz E

ABSTRACT
Recently there has been a shift away from purely feedforward models of the brain toward models that emphasize feedback connections and implement hierarchical generative frameworks and predictive coding strategies. We are interested in the structural and functional underpinnings of how internally generated top-down information and bottom-up sensory information interact in the cerebral cortex to guide behaviour. Our goal is to establish a model system, using layer 5 pyramidal neurons (L5PNs) in the mouse visual cortex, to study the biological basis of predictive coding.Using trans-synaptic tracing we show that L5PNs, which project to several behaviourally relevant targets, receive long-range inputs from both sensory areas and higher-order regions associated with internal models. By studying their morphological and biophysical diversity and the distribution of inputs along their dendrites through molecular anatomy and in vitro whole cell recordings, we are investigating how these signals are integrated in single neurons.To understand how L5PN activity relates to both sensory stimuli and behaviour we carry out extracellular recordings, 2-photon calcium imaging, and behavioural experiments in a novel multi-sensory virtual reality system, which enables independent and precise control over several sensory modalities.

L9. **Antonella Riccio - MRC Laboratory for Molecular Cell Biology**

H Crerar

POSTER TITLE
Regulation of gene expression in neurons

AUTHORS
Riccio A

ABSTRACT
The goal of the Riccio lab is to understand how gene expression is regulated in neurons attranscriptional and translational levels. The lab employs a wide array of cell and molecularbiology techniques to manipulate gene expression in vivo and in vitro. There are four mainlines of research in the lab: (1) Nitric oxide-dependent regulation of gene expression indeveloping neurons. We discovered that epigenetic factors become nitrosylated in responseto physiological stimulation and we have performed a proteomic analysis to identify nuclearproteins nitrosylated in cortical neurons. (2) Identification of the epigenetic mechanisms thatregulate cortical development in vivo. A genome wide analysis of genes regulated byHDAC2 has revealed that chromatin remodelling factors represent novel targets of HDAC2that are necessary for the proper development of the cortex. (3) Understanding how nucleararchitecture and chromatin structure contribute to gene expression in response to synapticactivation. We identified a novel class of regulatory elements that coordinate the expressionof activity-dependent genes in cortical neurons. (4)

Transport and translation of mRNAs inaxons of sympathetic neurons. We discovered novel elements located within the 3'UTRs thatare necessary for axonal transport and translation of transcripts in response to neurotrophinstimulation

L10. Paul Whiting - ARUK UCL Drug Discovery Institute

POSTER TITLE
Finding new therapeutic approaches for dementias

AUTHORS
Whiting P

ABSTRACT
The Alzheimer's Research UK Drug Discovery Institute (ARUK DDI) at UCL was initiated in October 2015. Part of the Institute of Neurology, its goal is to find new therapies for the dementias, including Alzheimer's, Vascular, Parkinson's, Fronto-temporal, etc. We now have a staff of over 25 scientists, including undergraduate, M.Sc. and Ph.D. students. Our disciplines span from neurobiology, high throughput screening & pharmacology, through to medicinal chemistry. As such our expertise, together with fully equipped lab, enables us to progress projects from "target validation" through to drug screening and the development of novel small molecules that modulate that drug target. We cannot do this alone: our success depends upon a close partnership with other labs at UCL (and beyond), and indeed 6 of our projects are collaborations with UCL PI's. Similarly, a number of our projects benefit from partnership with pharma (AstraZeneca, Janssen, Lilly). Our main areas of focus are currently (i) lowering toxic protein species (including beta amyloid, huntingtin, c9orf72), enhancing the heat shock protein response, modulating microglial function, maintaining synaptic health. The poster will give examples of our projects, and invite opportunities for further collaborations to find new treatments for these devastating diseases.

Developmental Neuroscience | Elvin Hall

1. Rebecca Bolton - UCL Institute of Ophthalmology

POSTER TITLE
The NRP1 adhesion domain is required for cardiovascular development

AUTHORS
Bolton R, Raimondi C, Ruhrberg R

ABSTRACT
Mice lacking neuropilin 1 (NRP1) have severe cardiovascular and neuronal defects. NRP1 promotes vascular endothelial growth factor (VEGF) and extracellular matrix signalling to support blood vessel growth and semaphorin class 3 (SEMA3) signalling for vascular remodelling. Additionally, NRP1 promotes cell-cell adhesion in vitro through a heterophilic interaction of 18 amino acid sequences in the b1 and b2 domains with unknown proteins. We tested the physiological importance of this interaction in vivo by introducing a germline mutation into the adhesion domain of mouse NRP1, termed Nrp1YSNN. Homozygous Nrp1YSNN/YSNN mutant embryos had impaired interventricular heart septation. Nrp1YSNN/YSNN pups were not observed after birth. To overcome lethality, we combined

the Nrp1YSNN with a floxed Nrp1-null allele and a tamoxifen-inducible, endothelial Cre transgene. Activating the null mutation on a Nrp1YSNN background impaired vascular branching in the postnatal retina. In vitro analysis confirmed that the cell adhesion properties of NRP1 were lost in the mutated protein. Moreover, expression of wild type NRP1, but not NRP1YSNN, effectively rescued the migratory defect of NRP1-deficient endothelial cells (ECs). Together, these findings support the idea that NRP1 has an adhesion domain important for cardiovascular development.

2. Alessia Caramello - The Francis Crick Institute

POSTER TITLE
Region-specific roles of SOX9 during forebrain neuroepithelial progenitor differentiation

AUTHORS
Caramello A, Rizzoti K, Galichet C and Lovell-Badge R

ABSTRACT
During central nervous system (CNS) development, the transcription factor SOX9 is expressed in neuroepithelial progenitors (NEPs) from E11.5. SOX9 is required for NEPs induction and maintenance, and also for their switch from neurogenesis to gliogenesis. To further characterise its role, we have deleted Sox9 exclusively in the CNS, before onset of its expression, using Sox1Cre.NEP differentiation potential is altered in Sox1Cre;Sox9fl/fl mutants. In particular, PDGFRa+ oligodendrocyte precursors are missing in mutant embryos, but recover post-natally. We show that this is due to functional compensation by SOX8, a SOXE member closely related to SOX9, as Sox1Cre;Sox9fl/fl;Sox8-/- embryos completely lack oligodendrocytes. We are currently investigating the mechanisms underlining oligodendrocyte recovery in Sox9 mutants. In Sox1Cre;Sox9fl/fl embryos, we also observe a defective development of the archicortex; ALDH1L1+ gliogenic progenitors and GFAP+ astrocytes are reduced, while dentate gyrus Prox1+ neurons are mislocalised. During spinal cord development, SOX9 controls gliogenesis via induction of NF1A. Within the developing forebrain, NF1A is co-expressed with SOX9 exclusively in the archicortex. However, its expression is not altered Sox1Cre;Sox9fl/fl embryos, suggesting that the molecular networks controlling gliogenesis are region-specific.In conclusion, dissection of SOX9 function highlights its region-specific roles, and reveal further complexity for gliogenic molecular networks.

3. Camille Charoy - UCL Institute of Ophthalmology

POSTER TITLE
Dual role of Neuropilins in VEGF- and Semaphorin- mediated assembly and maintenance of Boundary Caps in the nervous system

AUTHORS
Charoy C, Schwarz G, Mackenzie F, Denti L, Ruhrberg C

ABSTRACT
During embryogenesis, neural crest-derived boundary cap (BC) cells are located at the border of the central and peripheral nervous system, where they organise axon entry and exit and maintain CNS/PNS separation. During late embryogenesis, BC cells transdifferentiate into neurons and glia, but when removed from their normal tissue context,

they behave like neural stem cells, raising the possibility that they may be exploited for nervous system repair. Prior work in chick suggested that guidance cues of the semaphorin family contribute to BC organization. However, little is known about the role of neuropilins in regulating BC formation, neuroglia differentiation or the switch from the maintenance to differenciation phase.We have begun to analyse a collection of mice with complementary mutations in the genes of the class 3 semaphorins SEMA3A and SEMA3F and their receptors neuropilins NRP1 and NRP2 as well as the alternative NRP1 ligand VEGF-A. In situ hybridisation with a BC marker showed that NRP1 and NRP2 act as receptors for SEMA3A and SEMA3F, respectively, to differentially regulate dorsal versus ventral BC organisation. In addition, we found that NRP1 acts as a VEGF-A receptor to regulate BC formation in vivo and BC stem cell maintenance in vitro.Our data suggest that the neuropilins have a dual role in BC organisation and maintenance as receptors for both semaphorins and VEGF.

4. Ziqi Chen - UCL Ear Institute

POSTER TITLE
Cellular mechanisms of sensory organ segregation in the embryonic inner ear

AUTHORS
Chen Z, Daudet N

ABSTRACT
The inner ear contains multiple sensory organs separated by non-sensory epithelial domains. The mechanisms of development of these organs remain unclear. Here, we studied the expression of the prosensory marker Sox2 during the formation of two sensory organs, the anterior and the lateral cristae, in developing chick otocysts. We found that the cristae arise at the edge of a larger Sox2-expressing pan-sensory domain, the bulk of which gives rise to another organ, the utricle. Over time, the distance between the cristae and the presumptive utricle increase, suggesting a segregation process. This is accompanied by striking changes in cell morphology at the interface of segregating sensory organs: cells enlarge, become elongated and progressively align along the lateral border of the cristae. Multicellular rosettes and phosphorylated myosin regulatory light chain (pMLC) staining are present throughout the sensory and non-sensory domains of the otocyst, suggesting that acto-myosin contractility is involved in cristae segregation. We are now using pharmacological and genetic approaches to test this hypothesis.

5. Rosalyn Flower - UCL Department of Cell and Developmental Biology

POSTER TITLE
Investigating the sex-linked mechanisms of Hirschsprung disease using mouse models

AUTHORS
Flower R, Lovell-Badge R

ABSTRACT
Hirschsprung disease (HSCR) is a complex developmental disorder characterised by the lack of enteric neurons in distal portions of the gut. Importantly, HSCR presents a strong sex bias with four times more males affected than females for reasons that are unknown. To identify sex-specific differences in gene expression in the developing enteric nervous system

that may be important in HSCR, we performed RNAseq analyses on normal neural crest cell derivatives and mesenchymal cells isolated from Wnt1-cre;R26YFP mouse embryonic guts. To identify a sex-biased mouse model, we screened several mouse models with mutations of Ret, Sox10 and Ednrb for a sex bias in the frequency of HSCR-like phenotypes, phenotype severity and observed numbers of male and female mutants born. Surprisingly, we found that female mutants in a Ret mutant model were underrepresented at postnatal stage 0, resulting in a male:female sex bias of 3:1. Further investigation identified that female-specific lethality occurred between E18.5 and P0, likely due to cannibalisation by the mother after birth. Through ex utero examination of E18.5 embryos we identified breathing difficulties, irregular respiration rhythms and cyanosis specifically in female mutants. We are currently investigating the development and organisation of neural networks controlling respiratory function in the brainstem.

6. Olivia Gillham – UCL GOS Institute of Child Health

POSTER TITLE
Modelling human CNS developmental pathologies using 3D hydrogel scaffolds

AUTHORS
Gillham O, and Ferretti P

ABSTRACT
The study of human central nervous system (CNS) development and function is hindered by the limited possibility of in vivo experimental manipulation. Monolayer cultures of human neural stem cells (hNSCs), neurons and glia have therefore conventionally provided means to investigate human CNS physiology and pathology, at both cellular and molecular levels. However, evidence is mounting that dimensionality impacts upon cellular phenotype and behaviour. We therefore aim to establish 3-dimensional (3D) cultures using foetal brain- and induced pluripotent stem cell (iPSC)-derived NSCs, in order to model human CNS development, injury and congenital disorders. Using this model, we first sought to assess the effect of mimicking hypoxic-ischaemic (HI) damage on developing and mature neural cells. Secondly, we sought to study Down syndrome (Trisomy 21; T21) neural cell differentiation, and a postulated increased susceptibility of T21 neural cells to damage.Foetal brain-derived hNSCs were used to establish a 3D system using collagen-I/Matrigel hydrogel scaffolds. Differentiation of hNSCs towards neuronal and glial lineages was characterised at different time-points, and methods of reproducible injury established. To model neural damage, cells were exposed to either oxygen-glucose deprivation (OGD), or chemically-induced Ca2+ dependent cell death. Significantly, hNSCs and neurons cultured in 3D hydrogel scaffolds were found to display a reduced susceptibility to Ca2+ and OGD-induced cell death compared to 2D culture. These findings emphasise the importance of considering dimensionality when modelling human CNS tissue in vitro. In order to provide a source of T21-NSCs, neurons and glia, T21 foetal skin fibroblasts were reprogrammed to produce iPSCs. Pluripotency of reprogrammed T21 iPSCs and euploid control iPSCs was characterised, and both control and T21-NSCs were demonstrated to be able to differentiate into both neurons and astrocytes. Analysis of the responses of T21-derived neural cells to HI injury and Ca2+ level alterations is currently underway.

7. Karolin Kramer - UCL GOS Institute of Child Health

POSTER TITLE
Generation of a patient-derived dopaminergic cell model of aromatic L-amino acid decarboxylase (AADC) deficiency

AUTHORS
Kramer K, Barral S, Ng J, Pope S, Heales SJ, Kurian MA

ABSTRACT
Background: Aromatic L-Amino Acid Decarboxylase (AADC) deficiency is a severe pharmacoresistant neurological disorder due to inherited autosomal recessive loss-of-function mutations in the DDC gene. The resultant impairment of AADC enzyme activity severely impacts on monoamine synthesis, leading to reduced levels of dopamine and serotonin. Affected patients present with marked neurodevelopmental delay, hypotonia, oculogyric crises and autonomic dysfunction. Currently, there are few truly disease-modifying therapies.Aims: To generate AADC patient-derived induced pluripotent stem cells (iPSC) for subsequent differentiation into midbrain dopaminergic neurons, and to utilise this model to better define disease mechanisms and test novel therapeutic strategies.Methods: Patient and age-matched control fibroblasts were reprogrammed into iPSC using Sendai virus methods. A modified dual SMAD inhibition protocol was then utilised for differentiation of all iPSC lines to day 70 of maturation. The generated neuronal model was then analysed for mature mDA neuronal identity and AADC disease-specific features.Results: We have generated iPSC lines from skin fibroblasts derived from two patients with AADC deficiency and one age-matched control subject. One patient harboured a homozygous missense mutation (p.R347G) and the other was a compound heterozygote for a nonsense variant (c.C102T) and missense mutation (p.L408I) in DDC. Generated iPSC lines were confirmed as being truly pluripotent, then successfully differentiated into midbrain dopaminergic (mDA) neurons, with characteristic neuronal morphology, expressing tyrosine hydroxylase (TH) and microtubule-associated protein 2 (MAP2). Using high performance liquid chromatography (HPLC), we detected significantly marked reduction of AADC enzyme activity in patient mDA when compared to the age-matched control (P=0.0071). Conclusion: our iPSC-derived mDA neuronal model represents an ideal platform to further elucidate disease mechanisms, as well as to screen novel pharmacological agents to treat AADC deficiency.

8. Jenny Lange - UCL GOS Institute of Child Health

POSTER TITLE
Human dystrophin expression in neural stem cells and in the developing brain

AUTHORS
Lange J, Muntoni F, Tedesco FS, and Ferretti P

ABSTRACT
Dystrophin is an actin binding protein connecting the cytoskeleton to the extracellular matrix and is a crucial component of the dystrophin-glycoprotein complex. Mutations in the dystrophin gene can result in Duchenne muscular dystrophy (DMD), which is characterised by progressive muscular atrophy leading ultimately to the death of the affected individual by the second or third decade of life. 1 in 3 patients also experience neural deficits, however cognitive impairment is not progressive, suggesting a neurodevelopmental origin of the

neural defects. Little is known about expression and regulation of dystrophin in the developing human brain. We are investigating the expression of dystrophin in embryonic and foetal human brains, as well as in cultured human neural stem cells (hNSCs), astrocytes and neurons. Analysis of proteins from developing brains and cultured cells revealed differential expression of dystrophin isoforms, as well subtle changes during embryonic development. Immunofluorescence staining was used to examine dystrophin expression in hNSCs grown in 2 dimensional (2D) cultures as well as in 3D hydrogels that mimic tissue cytoarchitecture. Finally, neural cells obtained from DMD patient-derived induced pluripotent stem cells were differentiated into neural progenitors and astrocytes and are being used to study the impact of dystrophin mutations on cell behaviour.

9. Paromita Majumder - UCL Institute of Ophthalmology

POSTER TITLE
Autophagy in the organ of Corti of young, adult and aged mice

AUTHORS
Majumder P, Forge A, Taylor RR

ABSTRACT
Autophagy plays a housekeeping role in removing misfolded or aggregated proteins, clearing damaged organelles, such as endoplasmic reticulum, peroxisomes and mitochondria.In cells of the organ of Corti (auditory sensory epithelium of the inner-ear), after extrinsic insults the dysfunctional mitochondria not only produce energy and buffer Ca2+ less efficiently, but also release harmful reactive-oxygen-species.Dysfunctional autophagy has been observed in ageing tissues and with several age-associated diseases. Here we assess distribution of LC3II, a protein converted from LC3-I to initiate formation and lengthening of the autophagosome in the different cells in the organ of Corti of young, adult and aged mice.We investigated LC3II distribution in C57BL6-LC3-GFP mice using confocal live imaging in the cochlear apical coil in auditory bulla preparations (post-natal-day (P)4, young adult-P40, 6 months and 1 year old).The images stacks were recorded every 5µm using a Zeiss-510 NLO-META.Our data show outer-hair-cells had a drastic reduction of LC3II-GFP after hearing onset but in inner hair cells, the effect observed was the opposite. We identified LC3II in supporting cells such as Deiters'-cells and outer-pillar-cells.Our data suggest a modulation of differential autophagy during the onset of mouse hearing and the importance for inner hair cell survival during ageing

10. Marco Ortiz - UCL Department of Cell and Developmental Biology

POSTER TITLE
Regulation of the proliferation of neural stem cells in the adult hippocampus by Shh signalling

AUTHORS
Ortiz MA, Urban N, Vaga S, Guillemot F

ABSTRACT
Shh signalling has been proposed to control proliferation of neural stem cells (NSCs) in the adult hippocampus, but the stage in this adult neurogenic lineage that is regulated by Shh has not been defined. We use both mouse genetics and tissue culture experiments to

address this question. We find that hippocampal NSCs are heterogeneous in their response to Shh signaling, with a quarter of them expressing the Shh signaling reporter Gli1-LacZ. This Shh responding NSC population is enriched in the anterior hippocampus. Conditional deletion of the Shh co-receptor Smoothened reduces the number of proliferating NSCs. We are currently performing experiments to determine whether Shh is capable of activating quiescent NSCs or whether it extends the proliferation of already cycling NSCs. We also examine the transcriptional programme induced by Shh using a cell culture model of proliferating and quiescent adult hippocampal NSCs. With this project, we hope to shed light on the poorly understood mechanisms that activate quiescent stem cells in the adult hippocampus.

11. Titinun Suannun - UCL Eastman Dental Institute

POSTER TITLE
Development of engineered neural tissue containing elongated neurons supported by aligned glia for peripheral nerve regeneration

AUTHORS
Suannun T, Knowles JC, Phillips JB

ABSTRACT
Much peripheral neural tissue engineering research focuses on developing biomaterial scaffolds that mimic the autograft and promote host neurite regeneration from proximal to distal stump, whereas here we aim to improve long gap repair by populating constructs with functional neurons. With a ready-to-implant construct populated with neurons exhibiting long neurite extensions supported by glial cells, the gap between proximal stump and muscle could potentially be reconnected promptly. Immediate muscle innervation would help reduce atrophy as regeneration progresses.To test the concept, a method was developed for neurite extension in vitro using engineered neural tissue (EngNT) formed from simultaneous self-alignment of Schwann cells and collagen fibrils in a tethered gel resulting in an anisotropic tissue-like structure. The results showed that neurites of NG108-15 cell line co-cultured with EngNT aligned parallel to Schwann cells, and neurite growth from neurons in EngNT was longer than neurite growth in control cultures without Schwann cells. These results indicate that EngNT may be an appropriate substrate for generating long neurites in vitro with a view to generating therapeutic constructs containing long functional neurons. Combining EngNT with techniques such as 3D-printed mould design and mechanical tension could further improve the potential of EngNT to support neurite elongation.

12. Weixin Wang - UCL Institute of Ophthalmology

POSTER TITLE
Müller glia isolated from human iPSC/ESC derived retinal organoids produce neuroprotective antioxidants against oxidative stress

AUTHORS
Wang WX, Eastlake K, Murray-Dunning C, Coffey P, Limb GA

ABSTRACT
Summary of research: Intravitreal transplantation of Müller cells into animal models of retina degeneration has shown that these cells partially restore visual function without integration

into the neural retina. This effect has been ascribed to the neuroprotective effects and metabolic support of Müller glia to retinal neurons. They produce antioxidant molecules to protect neurons against oxidative stress and glutamate toxicity. Because of the need to produce Müller cell populations that can be used therapeutically, we have isolated Müller glia from retinal organoids formed by human iPSC/ESC, examined the antioxidant properties of these cells and compared them with the human Müller cell line MIO-M1. The results showed that purified populations of Müller glia could be obtained from human iPSC/ESC derived retina organoids and these cells expressed a variety of Müller markers. They consistently expressed mRNA encoding the antioxidants PRD6, FOHL1, CQ10A, GST, GSR, LIAS, HO1 and SOD2. Our findings demonstrate that retinal organoid derived Müller glia display potent antioxidant ability as judged by the gene expression of antioxidants and the release of antioxidants into culture supernatant. These cells hold promising potential for in vivo transplantation to repair the neural retina due to the neuroprotective antioxidants that they produce.

13. Magdalena Zak - UCL Ear Institute

POSTER TITLE
Elucidating the molecular signals guiding the formation of inner ear sensory organs

AUTHORS
Zak M, Pagnol V, Daudet N

ABSTRACT
The inner ear comprises distinct sensory organs responsible for sound detection and the perception of balance and head movements. The mechanisms controlling their formation remain unclear. Our recent work has shown that several of the sensory organs arise by progressive segregation from a common prosensory domain. During this process, Notch signalling uses lateral induction to propagate and maintain sensory identity among interacting cells. To further characterise the molecular signals regulating the specification and segregation of sensory organs, we performed a transcriptome profiling of chicken inner ears after gain- and loss-of Notch function. Our results identified a number of candidate Notch targets. Among these, we found a significant enrichment of key elements of Wnt signalling pathway. Our functional studies confirm that the Wnt signalling is critical for the normal morphogenesis of sensory organs, suggesting that it could mediate at least in part the prosensory effects of Notch signalling in the ear.

Disorders of the Nervous System | Elvin Hall

14. Filipa Almeida - UCL Institute of Neurology

POSTER TITLE
Translational repression of tau by antisense long non-coding rna mapt-as1 as a potential therapeutic approach

AUTHORS
Almeida F, Zareba-Paslawska J, Karda R, Waddington SN, Svenningsson P, Simone R, de Silva R.

ABSTRACT
The microtubule-associated protein tau (MAPT) is responsible for the stabilization of the axonal network. The formation of hyperphosphorylated tau inclusions is a common hallmark of tauopathies, a group of neurodegenerative disorders that includes Alzheimer's disease (AD). Several studies in mouse models of AD and tauopathies have shown that the reduction of tau is beneficial. Previously, we demonstrated that MAPT-AS1, an antisense long non-coding RNA (lncRNA) gene that overlaps with the 5'-untranslated region of MAPT, significantly inhibits tau translation. Subsequently, we aimed to investigate the therapeutic potential of this lncRNA in in vivo models by using an AAV9 vector with a CMV promoter. Two groups of 7-10 month-old hTau mice expressing the human full-length tau on a Mapt-/- background, were intra-cranially injected in the right hippocampus with either the full-length MAPT-AS1 transcript tNAT1 (FL), or inactive tNAT1 (ΔM). Mice injected with FL showed robust decrease in the protein levels of tau 8 weeks post-injection when compared to ΔM-injected mice. Furthermore, qRT-PCR analysis indicated that tau protein levels were inversely correlated with tNAT1-FL lncRNA levels, which was not the case with the ΔM construct. Overall, our findings suggest that AAV9-mediated delivery of MAPT-AS1 transcripts is a promising gene therapy approach for tauopathies.

15. Serena Barral – UCL GOS Institute of Child Health

POSTER TITLE
An iPSC-derived dopaminergic model of genetic parkinsonism reveals key mediators of neurodegeneration and precision therapies

AUTHORS
Barral S, Fatma A, Erdem FA, Wallings R, De La Fuente Barrigon C, Lignani G, Privolizzi R, Haya Alrashidi H, Heasman S, Ngoh A, Ng J, Meyer E, Counsell JR, Waddington SN, Schorge S, Vowles J, Cowley SA, Sucic S, Freissmuth M, Heales SJR, Wade-Martins R

ABSTRACT
Dopamine Transporter Deficiency Syndrome (DTDS) is a severe early onset progressive neurological disorder presenting with infantile parkinsonism-dystonia and leading to early death. DTDS is due to loss-of-function mutations in SLC6A3, encoding the dopamine transporter (DAT). DAT is expressed in dopaminergic neurons and plays a crucial role in regulating amplitude and duration of dopamine (DA) signaling. Dysfunctional DA homeostasis has been implicated in a wide number of neurological and neuropsychiatric conditions, including Parkinson's disease. We generated a midbrain dopaminergic model of DTDS using human induced pluripotent stem cells (iPSCs). Our model recapitulates key hallmarks of disease, with significantly reduced dopamine transporter activity and accumulation of dopamine metabolites, compared to age matched and isogenic controls. Moreover, in patient-derived midbrain neurons we observed dysregulation of DA metabolism with significantly reduced expression of the DA degradation enzymes monoamine oxidase A and B. Patient showed neurodegeneration, with apoptotic neuronal loss associated with TNFα-mediated inflammation and dopamine toxicity. Loss of transporter function was successfully rescued by the pharmacochaperone Pifithrin-μ, and a lentiviral gene therapy approach. Our iPSC-derived model of DTDS has enabled detailed dissection of the molecular and cellular mechanisms of disease, as well as development of targeted precision therapies for this currently pharmacoresistant disorder.

16. Jenna Carpenter - UCL Institute of Neurology

POSTER TITLE
Investigating the pathogenic mechanisms of progressive myoclonic epilepsy with ataxia

AUTHORS
Carpenter J, Heneine J, Sampedro Castaneda M, Praschberger R, Mannikko R, Jepson J, Lignani G, Schorge S

ABSTRACT
The progressive myoclonic epilepsies (PMEs) are a highly heterogeneous group of rare disorders characterised by muscle jerks (myoclonus) and epileptic seizures that worsen over time. Loss of function mutations in the Golgi SNARE receptor complex member 2 (GOSR2) gene and a recurrent c.959G.A (p.Arg320His) de novo mutation in KCNC1 (Kv3.1) have been identified as important causes of PME with ataxia. GOSR2 is an essential protein involved in ER-Golgi trafficking and Kv3.1 is a voltage-gated potassium channel that contributes to rapid action potential repolarisation and high frequency firing. Here we use a combination of genetic strategies, viral vectors and electrophysiology to show that patho-mechanisms underlying PME with ataxia may converge on dendritic dysfunction. Using primary cortical cultures from mice, we show that lentiviral-mediated overexpression of GOSR2 mutants results in a reduction of miniature excitatory post-synaptic currents. For KCNC1-PME, we find that overexpression of the Arg320His mutant in interneurons results in dendritic collapse and neurotoxicity and have excluded a proton leak current through the voltage-sensor domain of the channel as a potential mechanism of toxicity. We are now developing an in vitro CRISPR/Cas9 knock-in model of KCNC1-PME and alternative in vivo strategies in order to further elucidate the mechanisms of GOSR2/KCNC1-PMEs.

17. Bimali Hapuarachchi - UCL Institute of Neurology

POSTER TITLE
A cell model for the study of the association of EIF2AK3/PERK with PSP

AUTHORS
Hapuarachchi B, Hamilton J, Ehteramyan M, Willumsen N, Warner T, de Silva R

ABSTRACT
The EIF2AK3 gene encoding the endoplasmic reticulum unfolded protein response (UPR) sensor, PERK, is a risk factor for the tauopathy, progressive supranuclear palsy (PSP). Activated PERK and UPR markers are associated with tau inclusions in PSP and Alzheimer's disease brains. The associated SNP, rs7571971, is in linkage disequilibrium with coding SNPs, rs867529(Ser136Cys), rs13045(Gln166Arg) and rs1805165(Ala704Ser), forming the coding haplotypes of three highly conserved residues; HapA (conserved): S136-R166-S704 and HapB (divergent): C136-Q166-A704. A previous study showed that the divergent risk Haplotype B (HapB) has increased PERK activity suggesting that this forms the basis of the genetic risk. To investigate functional implications, we generated isogenic HEK293 cell lines for tet-inducible expression of PERK coding haplotypes with a C-terminal myc-tag to discern from endogenous PERK. With Western blot analyses, we demonstrated robust, inducible expression of myc-tagged PERK. Interestingly, with subsequent passages, the HapB PERK variants alone undergo C-terminal cleavage as evidenced by loss of the myc-tag which results not only in increased PERK protein but also reduced activated p-

PERK. This suggests that the increased risk of PSP from the divergent HapB is due to the C-terminal cleavage and reduced PERK activation leading to impaired UPR that could contribute to accumulation of pathological tau.

18. Saul Herranz-Martin - UCL School of Pharmacy

POSTER TITLE
Gene therapy for CLN7-Batten disease

AUTHORS
Herranz-Martin S, Kleine Holthaus SM, Mole SE, Rahim AA

ABSTRACT
Gene therapy approaches are emerging as a powerful tool for the treatment of neurodegenerative disorders. In this work we have generated AAV9 virus carrying the wild-type version of the human CLN7 gene, which is mutated in a subset of patients with Batten disease or nuclear ceroid lipofuscinose disease. This is a lysosomal storage disorder whose main symptoms are visual impairment and blindness, seizures, deterioration of motor skills and memory loss. There is still no cure and patients die within the first or second decade of life.For the proof of the concept of our study we have injected AAV9 virus codifying for CLN7 in a knock-out mice model for this gene. Untreated animals have a show a deterioration in their motor skills, coordination and anxiety from 6 months onwards with a survival average of nine months. Our gene therapy approach delays the onset of the disease, since animals performing better different behavioural tasks and increasing their lifespan. Taking together these results, we think our gene therapy approach might be a suitable approach for the treatment of this disorder.

19. Davor Ivankovic - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Defective axonal autophagosome maturation in AP-4 deficiency syndrome

AUTHORS
Ivankovic D, Lopez-Domenech G, Drew J, Tooze SA and Kittler JT

ABSTRACT
Adaptor protein (AP) complexes mediate key sorting decisions in the cell through selective incorporation of transmembrane proteins into vesicles. Little is known of the roles of AP-4, despite its loss of function leading to a severe early onset neurological disorder, AP-4 deficiency syndrome. Here we demonstrate an AP-4 epsilon subunit knockout mouse model that recapitulates the characteristic neuroanatomical phenotypes of AP-4 deficiency patients. We show that Atg9a, critical for autophagosome biogenesis, is an AP-4 cargo, which is retained within the trans-golgi (TGN) network were AP-4 function is lost. TGN retention in-vivo and in-vitro results in depletion of axonal Atg9a, leading to defective autophagosome generation and aberrant expansion of the distal axonal compartment. This specific reduction in the capacity to generate axonal autophagosomes leads to defective axonal extension and transient distal accumulation of ER within axonal swellings, underlying the impaired axonal integrity and white matter loss in AP-4 deficiency syndrome.

20. Sarah Jolly - UCL Institute of Neurology

POSTER TITLE
Characterisation of the CNS expression and function of Notum, a negative regulator of Wnt signalling pathway

AUTHORS
Jolly S, Schuhmacher L, Lines G, Mahy W, Willis N, Bictash M, Jones EY, Fish P, Jaie Bilsland J, Vincent JP, Whiting P, Salinas P

ABSTRACT
The Wnt signalling pathway regulates several aspects of brain development and function, including synapse formation, synaptic transmission and maintenance in the adult, as well as blood brain barrier formation and maintenance. There is some evidence suggesting that the Wnt signalling pathway is downregulated in Alzheimer's disease (AD) and that this could contribute to AD pathogenesis.Signal transduction by Wnt proteins is tightly regulated. For example, Wnt signalling is downregulated by Notum, a secreted carboxylesterase that removes the palmitoleoylate moiety normally appended on Wnts in the secretory pathway to ensure binding to Frizzled receptors and signal transduction. The contribution of Notum in the mammalian central nervous system has yet to be explored.Here we describe the expression of Notum in the mouse brain. We show that Notum is expressed in specific cell types throughout the brain and spinal cord and is specifically enriched in some thalamic nuclei. The expression of Notum in human brain was also examined. Additionally, mouse models of AD as well as biopsies of human frontal cortex from AD patients were used to determine whether Notum expression is affected during the progression of the disease. To investigate the roles of Notum, we developed several mouse models including a conditional knock-out and a reporter line. Together with small molecule inhibitors these genetic tools will enable the assessment of Notum function in the mammalian brain.

21. Aikaterini Kalargyrou - UCL Institute of Ophthalmology

POSTER TITLE
Investigating the mechanisms of molecular exchange in between retinal neurons

AUTHORS
Kalargyrou A, Ali R, Pearson R

ABSTRACT
Retinal degeneration due to the loss of photoreceptors (PRs) is the leading cause of untreatable blindness. Repair by transplantation of healthy PRs is a promising therapeutic tool. Previous studies have shown that transplantation of PR precursors can rescue visual function in some models of retinae dystrophy. This, was thought to arise from donor PRs integrating within the host retina. However, we have recently shown that, many reporter-labelled cells previously interpreted as integrated donor cells, were actually host PRs that acquired the label through a novel mechanism of molecular exchange that permits acquisition by the host cell of many proteins expressed by the donor. Molecular information is able to transfer either through direct cellular contact or by packaging the information and spread in extracellular-vesicles (EVs). Our study provides evidence that PRs release a variety of EVs in a developmentally-dependent manner. PR-EVs bear proteins typical of PR and of endocytic origin. Moreover, molecular exchange may occur in the absence of cell

contact, though the spreading mechanism maybe also driven through assembling-disassembling of nanoscaled protrusions. This yet unknown phenomenon of material transfer may broaden our understanding of retinae development and enable the design of more efficient therapeutic approaches.

22. Aleksandra Lasica - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
The effects of GSK3A and GSK3B on Tau phosphorylation and Bace1 expression in mouse N2a neuroblastoma cells

AUTHORS
Lasica AB, Salih DA, Edwards FA

ABSTRACT
Glycogen synthase kinase 3 (GSK3), existing as two paralogues: GSK3A and GSK3B, has been implicated in the pathogenesis of Alzheimer's disease (AD). This project seeks to differentiate between GSK3A- and GSK3B-specific processes, which may help to develop GSK3 paralogue-specific drugs as novel therapeutics for AD management. SiRNA-mediated reduction in GSK3A or GSK3B expression enabled the assessment of paralogue-specific effects on phosphorylated-Tau and expression of β-site APP cleaving enzyme 1 (Bace1) in mouse neuroblastoma (N2a) cells. GSK3B knock-down reduced phosphorylation of Tau at Ser-396/404 and expression of Bace1, whereas decreased GSK3A levels induced a non-significant tendency of lower Bace1 expression. Intriguingly, the effect of GSK3A knock-down on phospho-Tau levels was dependent upon siRNA species used, likely reflecting off-target effects. Collectively, these data suggest that GSK3 influences phosphorylation of Tau and expression of Bace1 via GSK3B paralogue but the role of GSK3A in these processes should be further investigated. Approaches used in this project will help to distinguish actions of GSK3A versus GSK3B in phenotypes associated with AD.

23. Marco Leite - UCL Institute of Neurology

POSTER TITLE
High density recording of local field potentials and spiking activity during seizures

AUTHORS
Leite M, Magloire V, Kullmann DM

ABSTRACT
The ability to record over 386 electrophysiological channels at high temporal resolution with Neuropixels probes allows for the spike sorting of potentially hundreds of neurons alongside the recording of local field potentials (LFP) over multiple brain regions.Here, we show the first preliminary recordings of chemically-induced focal seizure recorded with Neuropixels probes. We optogenetically identify parvalbumin-positive interneurons and track their behaviour over the evolution from interictal to generalized seizure activity. Spike sorting over large amplitude stereotyped fast activity such as epileptiform LFPs provided its own challenges. We further analyse the spatiotemporal evolution of epileptiform LFP at an unprecedented spatial coverage and resolution.

24. Andreas Lieb - UCL Institute of Neurology

POSTER TITLE
Biochemical autoregulatory gene therapy for focal epilepsy

AUTHORS
Lieb A, Yichen Q, Dixon CL, Heller JP, Walker MC, Schorge S, and Kullmann DM

ABSTRACT
Around 70 Million people worldwide are affected by epilepsy, of whom 30% do not respond to commonly available drugs. The only effective treatment option for focal-onset refractory epilepsy to date is surgical resection, which is often restricted by the proximity to eloquent cortex. Here we propose a biochemical closed-loop method for detection and suppression of epileptic seizures.We created an enhanced glutamate-gated Cl- channel (eGluCl) and confirmed an EC50 around 10 □M. We then evaluated the effect of lentivector-mediated eGluCl expression in an acute chemoconvulsant induced model of epilepsy. It showed particular effectiveness in reducing 4–14Hz spike-wave complexes (associated with motor convulsions), as well as the absolute number of spikes and the cumulative ECoG coastline. eGluCl was also effective in reducing the frequency of spontaneous epileptic seizures in the chronic tetanus toxin induced model of focal refractory epilepsy. eGluCl did not affect performance in the rotarod and elevevated grid tests, indicating that eGluCl has a minimal impact on normal brain-function.In this work we propose a novel biochemical closed-loop gene therapeutic approach, which detects an important biomarker of seizures and inhibits seizure generation and generalization. This novel approach presents the first autoregulatory gene-therapeutic strategy targeting intractable focal epilepsy.

25. Ciara Mulhern - UCL GOS Institute of Child Health

POSTER TITLE
Identification of p.T647P mutation in TNFAIP3 leading to a novel interferonopathy

AUTHORS
Mulhern C, Hong Y, Omoyinmi E, Casimir M, Brogan P, Eleftheriou D

ABSTRACT
The interferons (IFN) are signalling proteins synthetized and released by immune host cells in response to the presence of several pathogens such as viruses, bacteria, parasites and tumour cells (1,2). The induction, transmission, and resolution of the IFN-mediated immune response is tightly regulated (3). The interferonopathies comprise of an expanding group of complex genetic disorders characterised by disturbance of the homeostatic control of these IFN mediated immune responses (2,3,4). Herein, we describe a patient with an enhanced interferonopathy, presenting with a severe neuroinflammatory phenotype, including optic neuritis and granulomatous inflammation of the brain. Through the use of whole exome sequencing, we have identified a p.T647P missense mutation in TNFAIP3, contained within the important fourth zinc finger domain of the protein. TNFAIP3 (A20), a ubiquitin modifying enzyme, functions to repress the NF-kB and interferon pathways (5,6). Through the use of functional experiments, we show that key cellular components of these immunoregulatory pathways are upregulated in patient cells, resulting in enhanced NF-kB and interferon stimulation, and culminating in an overactive neuroinflammatory process in this patient. We conclude that the substantive interferonopathy, observed in this patient is driven by the

p.T647P mutation in TNFAIP3. 1. Crow YJ. Type I interferonopathies: a novel set of inborn errors of immunity. Annals of the New York Academy of Sciences. 2011;1238(1):91-8. 2. Lee-Kirsch MA, Wolf C, Kretschmer S, Roers A, editors. Type I interferonopathies—an expanding disease spectrum of immunodysregulation. Seminars in immunopathology; 2015: Springer. 3. García-Sastre A, Biron CA. Type 1 interferons and the virus-host relationship: a lesson in detente. Science. 2006;312(5775):879-82. 4. Volpi S, Picco P, Caorsi R, Candotti F, Gattorno M. Type I interferonopathies in pediatric rheumatology. Pediatric Rheumatology. 2016;14(1):35. 5. Saitoh T, Yamamoto M, Miyagishi M, Taira K, Nakanishi M, Fujita T, Akira S, Yamamoto N, Yamaoka S. A20 is a negative regulator of interferon regulatory factor 3 signalling. Journal of Immunology. 2005 Feb 1;174(3):1507-126. Zhou Q, Wang H, Schwartz DM, Stoffels M, Park YH, Zhang Y, et al. Loss-of-function mutations in TNFAIP3 leading to A20 haploinsufficiency cause an early-onset autoinflammatory disease. Nature genetics. 2016;48(1):67-73.

26. Christina Murray - UCL Institute of Neurology

POSTER TITLE
Genetic and proteomic profiling of sporadic, familial and TREM2 variant Alzheimer's disease post-mortem brains

AUTHORS
Murray CE, Heywood WE, Mills K, Lashley T

ABSTRACT
TREM2 is a genetic risk factor for late onset Alzheimer's disease (AD). As TREM2 is expressed on microglia and involved in neuroinflammation, this indicated inflammatory involvement in AD. Here we explore the gene expression profiles of 286 inflammatory genes in post-mortem brains from the frontal cortex of sporadic AD (SAD, n=10), familial AD (FAD, n=7), TREM2 variant cases with AD (TREM2 SAD, n=3), TREM2 variant cases that had no AD pathology (TREM2 controls, n=2) and normal controls (n=6), comparing to the proteomic profile in the same cases. RNA was extracted from all cases and analysed using the Nanostring human inflammation panel. Proteins were extracted and analysed using label-free mass spectrometry. Data was analysed using IPA software. At the genetic level, TREM2 SAD cases had higher upregulation of genes involved in the neuroinflammatory pathway compared to SAD cases, whereas TREM2 controls had large levels of downregulation. At the protein level, TREM2 SAD cases showed upregulation of APP and MAPT but TREM2 controls show downregulation of these proteins. TREM2 variants have differing levels of neuroinflammation and proteins involved in the pathological hallmarks, suggesting that another factor independent of the TREM2 variant may be needed to determine whether these variants produce AD pathology.

27. Iqra Nazish - UCL Institute of Neurology

POSTER TITLE
Investigation of the role of LRRK2 in murine macrophage RAW264.7 cells

AUTHORS
Nazish I, Warner T, Hardy J, Lewis P, Pocock J, Bandopadhyay R

ABSTRACT
Introduction: Pathogenic mutations and polymorphisms in the leucine-rich-repeat-kinase 2 (LRRK2) gene are linked to familial Parkinson's disease (PD), idiopathic PD and to two inflammatory conditions, leprosy and Crohn's disease. In the brain, LRRK2 is expressed strongly in microglia and macrophages indicating its potential role in innate immunity. How LRRK2 dysfunction causes PD remains ambiguous. LRRK2 protein harbours two critical enzymatic activities, the kinase and the GTPase making it a highly druggable target for potential therapies for PD. Herein, we aimed to establish a link between LRRK2 dysfunction and signalling mechanisms in the murine macrophage cell line (RAW264.7) and the pathological processes in PD.Materials and Methods: Using WT, T1348N-LRRK2 (this mutation prevents GTP binding) and LRRK2-KO RAW264.7 cell lines, we tested LRRK2 phosphorylation dynamics and TNF-alpha release following treatment with lipopolysaccharide (LPS, a proinflammatory mediator) and after treatment with 4-specific LRRK2- kinase inhibitors. Standard immunoblot procedures were used to monitor LRRK2-phosphorylation at 4 specific phospho-sites and secreted TNF-alpha levels were measured using ELISA. Statistically significant differences were analysed using ANOVA and T-test using Graph-PAD prism.Results: We observed significant upregulation of LRRK2 phosphorylated at Ser935 and Ser955 residues with LPS (100ng/ml) treatment from 2h-24h in RAW264.7 cell line. Kinase inhibition was found to decrease baseline LRRK2 phosphorylation at 4h with LPS treatment reversing the effect. LPS treatment for 24h and 48h upregulated TNF-alpha secretion following LPS stimulation in both WT and the GTPase-deficient mutant RAW264.7 cells with no significant difference in the basal secretion between the cell lines.Conclusion: LPS most significantly stimulated phosphorylation of LRRK2 in WT cells and GTPase-deficient RAW264.7 at 4h. Specific LRRK2 kinase inhibitors acted to decrease LRRK2 phosphorylation at Ser935 residue which is a readout of LRRK2 kinase activity. Our preliminary data of TNF-alpha release with LPS treatment appeared to be independent of T1348N mutation.

28. Teresa Niccoli - UCL Institute of Neurology

POSTER TITLE
Screening for modifiers of C9orf72 hexanucleotide repeat expansion toxicity in Drosophila

AUTHORS
Niccoli T, Moens T, Thoeng A, Konrad M, Dias Pereira Atilano M, Partridge L and Isaacs AM

ABSTRACT
C9orf72 hexanucleotide (G4C2) repeat expansion is the most common genetic cause of ALS and FTD. It produces highly repetitive sense and antisense RNAs that form intracellular foci. These RNAs undergoes non-atg mediated translation (RAN translation) to generate 5 different dipeptide repeat proteins. We developed several Drosophila melanogaster models of this expansion, and showed that these repeats are toxic to neurons. To identify downstream pathways mediating toxicity, we have carried out an unbiased genetic screen for modifiers of the phenotype of flies expressing 36(G4C2) repeats.Expression of 36(G4C2) in adult neurons leads to a dramatic reduction in lifespan. To identify modifiers, we crossed flies carrying 36(G4C2) repeats to 2000 over-expression lines from the FlyORF library. We induced expression only in adult neurons to avoid any potential confounding developmental effects and scored their lifespan, lines significantly increasing or decreasing lifespan were scored as enhancers or suppressors. We identified approximately 150 genes acting as suppressors or enhancers. Secondary screening has confirmed a number of strong

suppressors, affecting different cellular processes. We are now in the process of characterizing these, checking whether they are affecting downstream toxicity or directly the levels of dipeptide repeat proteins generated from the repeats.

29. Alexandra Petrache - UCL School of Pharmacy

POSTER TITLE
Enhanced inhibitory function of resilient calretinin-expressing interneurons in an AppNL-F/NL-F mouse model of Alzheimer's disease

AUTHORS
Petrache AL, Saito T, Saido TC, Ali AB

ABSTRACT
Alzheimer's disease (AD) patients lose memory and cognitive functions. Evidence suggests a disruption of synaptic inhibitory-excitatory balance which correlates with the accumulation and spread of amyloid-β (Aβ) protein that plays a prime role in the pathogenesis of AD leading to neurodegeneration. We hypothesise that these processes are related to over-active calretinin-expressing (CR) interneurons - a sub-class of inhibitory cells specialised to govern only inhibition. To investigate this hypothesis, we performed whole-cell intracellular recordings combined with neuroanatomy in brain slices from the first Aβ precursor protein knock-in mouse model (AppNL-F/NL-F) and age matched wild-type mice.Our results suggest a preservation of CR cells co-localised with the enzyme for the inhibitory neurotransmitter GABA, GAD67 throughout the brain despite the presence of Aβ plaques and increased neuro-inflammatory markers; astrocytes and glial cells. The co-localisation of GAD67 in CR cells suggests a maintained inhibitory function of CR cells which was corroborated by electrophysiological recordings that showed an increased inhibitory activity within the network of CR cells in AppNL-F/NL-F mice. Our data suggest that CR-expressing interneurons are resilient in the AppNL-F/NL-F AD model. We propose manipulating this network to normalise synaptic imbalance in early AD could potentially serve as a novel therapeutic target for AD

30. Laura Poupon - UCL School of Pharmacy

POSTER TITLE
Exendin-4 provides neuroprotection and enhances therapeutic hypothermia in a model of hypoxic-ischemic encephalopathy

AUTHORS
Poupon L, Rocha-Ferreira E, Zelco A, Leverin A-L, Carlsson Y, Edwards DA, Thornton C, Hagberg H, 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. This can result in mortality for the infant or significant and lasting brain damage. HIE is a global problem with an incidence of 1.5 per 1000 live births: 15-20% of neonates dying during the postnatal period and 25% developing irreversible and lifelong mental and physical disabilities including cerebral palsy. Exendin-4 is a small peptide drug approved by the FDA in 2005 for the treatment of T2DM. It is a GLP1 receptor (GLP-1R) agonist that plays a role in regulating blood sugar levels by

enhancing insulin production. Exendin-4 has also demonstrated neuroprotective properties, and is currently being tested in clinical trials for Alzheimer's and Parkinson's diseases. Given the need to develop effective treatments for neonatal HIE, the encouraging studies supporting the neuroprotective properties of exendin-4 constitutes an attractive therapeutic option. In this study, we confirmed GLP-1R expression in the perinatal human and murine brains. We demonstrated significant neuroprotective and anti-inflammatory effects of exendin-4 treatment in context of HI injury. Furthermore, we demonstrate its ability to be used in synergistic combination with therapeutic hypothermia that enhances neuroprotection and ameliorates brain damage.

31. Dervis Salih - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Trem2 coordinates anti-inflammatory responses and phagocytosis in primary microglial cultures

AUTHORS
Liu W, Cummings DM, Garcia-Reitboeck P, Taso O, Pocock JM, Hardy J, Edwards FA, Salih DA

ABSTRACT
Introduction: SNPs in immune genes like TREM2, CD33 and PLCG2 have been identified as risk factors for Alzheimer's disease (AD) by human GWAS studies, confirming a critical role for microglia in AD pathogenesis. Accumulated evidence has suggested that TREM2 regulates the functions of microglia/macrophages by restricting inflammation and promoting phagocytosis. Here we generate TREM2 deficient primary microglia by in vitro acute Trem2 knockdown, and investigate mechanisms of TREM2 action in relation to microglial activation. Results: Trem2 siRNA knockdown resulted in loss of ~70% Trem2 expression in primary microglia leading to acute down-regulation of microglial genes such as Csf1r, Igf1 and Cd68 and greatly impaired phagocytosis. TREM2 deficiency led to significant attenuation of IL4-induced anti-inflammatory activation at both gene expression and protein levels. In contrast, Trem2 expression was substantially depressed by LPS treatment. We are also investigating how TREM2 alters IL-4 anti-inflammatory signaling, and novel secreted chemokines/cytokines regulated by TREM2.Conclusions: These results suggest that TREM2 pushes the microglia towards an anti-inflammatory phenotype. We will now go on to investigate whether risk factor mutations in TREM2, such as R47H, have similar effects to gene knockdown. If similar, this suggests that enhancement of TREM2 effects should be targeted for drug discovery.

32. Anqi Shi - UCL School of Pharmacy

POSTER TITLE
Alzheimer's disease hyperactive hippocampal cck-expressing interneurons lose memory neuropeptide cck, but preserve cannabinoid type-1 receptors

AUTHORS
Anqi S, Takashi S, Takaomi CS, Afia A

ABSTRACT

Cognitive decline is a major symptom in Alzheimer's disease (AD), which is closely associated with brain network hyper-excitability and inhibitory interneuron dysfunction. A major inhibitory interneuron in the brain that releases the neuropeptide cholecystokinin (CCK), thought to be important for memory functions also colocalises presynaptic cannabinoid type-1 (CB1) receptors. Using the AppNL-F/NL-F knock in mouse model of AD aged-matched to wild-type mice, we per-formed in vitro whole-cell recordings combined with immuno-histochemistry in the CA1 region of the hippocampus to investigate whether the synergetic synaptic modulatory mechanisms of CCK-cells and CB1 receptors were altered in AD. We discovered during pre-phenotypic symptoms of AD (2 months), CCK cells were hyper-excited in the AppNL-F/NL-F model in contrast to wild-type mice. Confocal microscopy analysis revealed exclusive colocalisation between CCK-expression and CB1 receptors in AppNL-F/NL-F mice consistent with wild-type mice during this period. However, in the presence of post-phenotypic symptoms of AD (12-16 months), including amyloid beta plaques, increased neu-ro-inflammation; astrocytosis and gliosis, there was a reduced expression of CCK, but pre-served CB1 receptor expression without CCK colocalisation in the AppNL-F/NL-F model. Our data suggests that CCK interneurons are vulnerable in AD, and this altered inhibitory function probably contributes to the process of neurodegeneration.

33. Yoshiteru Shimoda - UCL Institute of Neurology

POSTER TITLE

Glutamate/GABA transients during interictal spikes and focal neocortical seizures

AUTHORS

Shimoda Y, Magloire V, Leite M, Kullmann DM

ABSTRACT

Seizures emerge from a disturbance in the finely tuned excitation / inhibition balance present in the brain. However, how this balance evolves throughout epileptic activity remains to be established. Indeed, in vivo electrophysiological recordings of excitatory and inhibitory synaptic activity are technically very challenging, especially during seizure episodes. Here, we take advantage of electrography, two-photon imaging, and genetically-encoded glutamate and GABA sensors to directly observe glutamate and GABA release profiles during chemically-induced focal seizures. Specifically, AAV-hSyn-iGluSnFr or AAV-hSyn-iGABASnFr was injected into layer 2/3 of the visual cortex of C57BL/6 mice. 2-3 weeks later, head-plates and electrocorticogram (ECoG) electrodes were implanted and craniotomies were performed over the visual cortex. A chemoconvulsant (pilocarpine, 3.5M, 200-300nL) was then injected locally into layer 5 to induce focal seizures. Glutamate and GABA sensor imaging combined with ECoG recordings allowed us to precisely look at the relationship between the different phases of seizure activity, from inter-ictal events to the termination of ictal discharges. In this way, we observed that both glutamate and GABA release is time-locked to the beginning of interictal spikes, while a possible build-up of glutamate and GABA seems to occur before the onset of long-lasting seizures.

34. Roberto Simone - UCL Institute of Neurology

POSTER TITLE

Antisense long non-coding RNA MAPT-AS1 represses tau protein synthesis through an embedded MIR repeat

AUTHORS
Simone R, Javad F, Emmett W, Almeida F, Ehteramyan M, Zuccotti P, Modelska A, Zareba-Paslawska J, Siva K, Kay V, Hondhamuni G, Trabzuni D, Ryten M, Wray S, Preza E, Kia D, Pittman A, Lees A, Hardy J, Denti M, Quattrone A, Svenningsson P, Warner TT, Plagno

ABSTRACT
We investigated MAPT-AS1, an antisense long non-coding RNA (lncRNA) gene overlapping with the microtubule-associated protein tau (MAPT) and characterized how MAPT-AS1 affects tau gene expression.Using RNA-Seq and qRT-PCR, we assessed expression of MAPT-AS1 and MAPT in brain and hiPSC-derived neurons. In neuroblastoma cells, we silenced or stably expressed MAPT-AS1 splice variants and targeted deletions to identify its essential functional domains and characterized effects on tau by western blot, qRT-PCR, smFISH, polysome profiling and luciferase-assays. By hippocampal injection of adult htau mice with AAV9 vectors carrying MAPT-AS1 transcripts we investigated in vivo effects of MAPT-AS1 on tau levels.We demonstrated both in neuroblastoma cells and htau mouse CNS that MAPT-AS1 specifically represses MAPT translation. This repression requires both the overlapping 5' region of MAPT-AS1 complementary to the MAPT 5'-untranslated region and a 3' inverted mammalian-wide interspersed repeat (MIR) element. Furthermore, two 7-mer motifs within the MIR, complementary or identical to sequences within 18S rRNA, are essential for MAPT repression.Our data suggest that MAPT-AS1 represses tau translation by interfering with ribosome recruitment onto MAPT mRNA. We identified hundreds of additional human lncRNAs containing MIR elements that frequently overlap with genes linked to neurodegenerative diseases, with implications for proteostasis in neurodegeneration.

35. Nathan Skene - UCL Institute of Neurology

POSTER TITLE
Genetic identification of brain cell types underlying schizophrenia

AUTHORS
Skene NG, Bryois J, Bakken TE, Breen G, Crowley JJ, Gaspar HA, Giusti-Rodriguez P, Hodge RD, Miller JA, Muñoz-Manchado A, O'Donovan MC, Owen MJ, Pardiñas AF, Ryge J, James T

ABSTRACT
With few exceptions, the marked advances in knowledge about the genetic basis for schizophrenia have not converged on findings that can be confidently used for precise experimental modeling. Applying knowledge of the cellular taxonomy of the brain from single-cell RNA-sequencing, we evaluated whether the genomic loci implicated in schizophrenia map onto specific brain cell types. The common variant genomic results consistently mapped to pyramidal cells, medium spiny neurons, and certain interneurons but far less consistently to embryonic, progenitor, or glial cells. These enrichments were due to distinct sets of genes specifically expressed in each of these cell types. Many of the diverse gene sets associated with schizophrenia (including antipsychotic targets) implicate the same brain cell types. Our results provide a parsimonious explanation: the common-variant genetic results for schizophrenia point at a limited set of neurons, and the gene sets point to the same cells. While some of the genetic risk is associated with GABAergic interneurons, this risk largely does not overlap with that from projecting cells.

36. Victoria Smith - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Characterisation of APP knock-in mice: Electrophysiological and migroglial profiles

AUTHORS
Smith VC, Wong N, Peerboom C, Hall C, Benitez Jimenez D, Roberts M, Fernandes Freitas MM, Liu W, De Strooper B, Salih DA, Cummings DM, Edwards FA

ABSTRACT
In transgenic mice expressing human APP(Swedish)/PSEN1(M146V), loss of spontaneous action potentials and a concomitant increase in glutamate release probability occur prior to detectable plaques. APP knock-in mice offer potentially improved models, avoiding artefacts of transgenic overexpression. In brain slices prepared from APPKI(NLF) mice at 9 months (age of first detectable plaques), an increased probability of glutamate release was observed compared to wild-type but frequency of spontaneous action potential-driven events was unchanged. NLGF mice show earlier plaque deposition due to an additional Arctic mutation. Surprisingly, at 4 months-old (when first plaques are detected), there were no detectable synaptic changes. By 9 months (heavy plaque load), a change in release probability became evident in NLGF mice. At 9 months, both APP knock-in lines start to show increased Iba1 and a higher proportion of CD68-positive microglia, accompanied by altered microglial gene expression profiles. Thus the change in probability of glutamate release and microglial response is consistent across models but the absence of spontaneous action potentials observed in transgenic mice may be an artefact of APP overexpression. Furthermore, while the change in APP conformation caused by the Arctic mutation results in earlier plaque formation, sequestering Abeta into plaques may dampen effects on neuronal function.

Homeostatic and Neuroendocrine Systems | Elvin Hall

36. Dan Brierley - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Preproglucagon neurons are sufficient for physiological satiety in lean mice, but are only necessary under selective conditions

AUTHORS
Brierley DI, Reimann F, Gribble FM, Trapp S

ABSTRACT
GLP-1-producing preproglucagon (PPG) neuron activation reduces food intake, however it is unclear whether this represents potentiation of satiety or induction of nausea, and their necessity for physiological satiety is unknown. To address this, PPG-Cre mice were stereotaxically injected with Cre-dependent AAVs encoding either hM3Dq or hM4Di DREADDs. The effects of CNO-induced activation (PPG-Gq) or inhibition (PPG-Gi) on feeding behaviour were investigated using automated pellet dispensers and video coding of behavioural satiety sequences (BSS). In free-feeding PPG-Gq mice, CNO elicited a robust anorectic effect over 5hrs, with no compensatory refeeding within 48hrs. Intake was also supressed following an 18hr fast, when CNO advanced the onset of satiety from 15-20mins to ≤5mins in the BSS test, with the typical post-prandial behavioural sequence maintained. In

PPG-Gi mice, CNO did not elicit a hyperphagic response in free-feeding or fasted mice. However, following a 15min liquid diet preload, intake was increased during hour 1, driven by reduced latency to meal 1. With 1hr liquid diet access, liquid diet intake itself was increased by CNO, followed by a compensatory decrease in chow intake during the next hour. Thus, while PPG neurons are seemingly sufficient to induce physiological satiety, they may only be necessary following high-volume meals.

Neural Excitability, Synapses and Glia | Elvin Hall

38. Rawan Alsubaie - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Functional and behavioural investigation of amygdala to hippocampus connectivity

AUTHORS
AlSubaie R, Menichini E and MacAskill A

ABSTRACT
The Basomedial Amygdala (BMA) and ventral hippocampus (vHPC) are crucial for the appropriate behavioural response to affective cues. Classical studies have shown dense innervation of BMA axons in vHPC, but the functional properties of the circuit remain relatively unexplored. Through a series of anatomical, functional and behavioural experiments we describe a strong functional circuit between the BMA and vHPC. First, using anterograde and retrograde tracers, we confirmed reciprocal anatomical connectivity between the vHPC and BMA. Next, using ChR2-assisted circuit mapping we found strong excitatory and inhibitory synaptic input from BMA to vHPC, with interesting inhibitory circuit architecture. In order to begin to probe the behavioural role of this circuit we next manipulated the activity of BMA to vHPC axons in vivo during free behaviour, where we found this projection is sufficient to influence affective behaviour. Overall we show that BMA projection neurons anatomically and functionally connect to vHPC pyramidal neurons, and that this circuit may be involved in the control of appropriate affective behaviour.

39. Tim Church - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
The molecular mechanism underlying calcineurin-mediated long-term depression of synaptic strength via the anchoring protein AKAP79

AUTHORS
Church TW, Gold MG

ABSTRACT
Long-term depression (LTD) of synaptic strength is thought to constitute a fundamental mechanism for encoding memory. In the leading model for studying the molecular basis of LTD – calcium-dependent LTD at CA3-CA1 hippocampal synapses – LTD is brought about by the calcium-sensitive phosphatase calcineurin. We are investigating how anchoring of calcineurin in tandem with protein kinase A (PKA) by the anchoring protein AKAP79 enables this process to occur. We are pursuing a multidisciplinary approach to test a new hypothesis that posits that calcineurin may directly alter the activity of PKA in the context of the AKAP79

signalling complex to bring about LTD. In vitro, we are performing structural and enzymatic investigations with purified reconstituted signalling complexes. In silico, we are developing new quantitative models to understand interplay between the different components of the signalling complex. Importantly, we are also testing our novel hypothesis by introducing targeted mutations into regulatory subunits of PKA using a lentiviral-based knockdown-recovery approach in rat hippocampal slices. We anticipate that this strategy will reveal how the fundamental process of LTD is brought in mammalian synapses at the molecular level.

40. Jonathan Cornford - UCL Institute of Neurology

POSTER TITLE
Dendritic NMDA receptors in parvalbumin neurons enable strong and stable neuronal assemblies

AUTHORS
Cornford JH, Mercier MS, Leite M, Magloire V, Hausser M, Kullmann DM

ABSTRACT
Deletion of NMDA receptors from parvalbumin-positive (PV+) interneurons disrupts gamma oscillations and destabilizes hippocampal spatial representations. How do NMDA receptors contribute to synaptic integration by PV+ interneurons to support robust neuronal assemblies? We show, using two-photon glutamate uncaging, that NMDA receptors underlie supralinear summation of synaptic inputs in mouse hippocampal CA1 PV+ interneurons, but only in dendrites innervated by feedback connections from local pyramidal neurons. Incorporating NMDA receptors at feedback connections in an oscillating excitatory-inhibitory spiking neural network provided for cooperative interactions among clustered inputs, and increased the stability of cell assemblies in the face of distracting inputs. Disrupted cell assembly interactions may underlie cognitive and sensory gating deficits seen with impaired NMDA receptor signaling in PV+ interneurons.

41. Shehrazade Dahimene - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
The novel α2δ-like protein promotes N-type calcium channel trafficking and function

AUTHORS
Dahimene S, Page KM, Ho D, Kadurin I, Ferron L, Powell GT, Pratt WS, Wilson SW and Dolphin AC

ABSTRACT
N-type voltage-gated calcium channels (CaV2.2) play an important role in neurotransmitter release. The channel auxiliary α2δ-subunits modulate the trafficking and biophysical properties of the pore-forming α1 subunit. In this study we examined the interaction of CaV2.2 α1 with both α2δ-1 and a related α2δ-like protein, Cachd1, whose function is unknown. Recently, the cryo-EM structure of skeletal muscle CaV1.1 complex showed that Domain-I of the α1 subunit interacts with the α2δ-1 VWA-domain. Mutating the key residue Asp122 in CaV2.2 Domain-I abolished the effect of α2δ-1 on CaV2.2 channel trafficking and function. Surprisingly, Cachd1, which is predicted to have a disrupted VWA-domain which would disrupt such interactions, increased both WT CaV2.2 as well as Asp122Ala CaV2.2

currents to the same extent, although less than α2δ-1. In conclusion, we have validated the predicted site of interaction of the CaV2.2 α1-subunit with α2δ-1, and found that a key residue in the α1 Domain-I is essential for this interaction. Moreover, the effect of Cachd1, a related α2δ-like protein, on CaV2.2 remained in the presence of the Asp122 mutation in Domain-I, indicating that the interaction of Cachd1 with the α1 subunit is probably mediated by alternative domains.

42. Christine Dixon - UCL Institute of Neurology

POSTER TITLE
Glutamate receptor mutations in intellectual disability

AUTHORS
Dixon CL, Salpietro Damiano V, Hacke M, Houlden H and Kullmann DM

ABSTRACT
Ionotropic glutamate receptors mediate fast excitatory neurotransmission in the brain. Mutations in AMPA and NMDA receptor subunit genes have been associated with intellectual disability, underscoring the importance of these receptors in learning and memory. Here we investigate 11 point mutations in a related subunit, which were identified in patients with intellectual disability and other neurological symptoms.We expressed mutant channels in HEK cells and made whole-cell voltage clamp recordings to test steady-state responses to a maximal dose of agonist applied for 2 seconds. All subunits were tested from at least 3 separate transfections. Cells expressing wild-type receptors had currents of 440 □ 85 pA (mean □ SEM, n = 17 cells). In comparison, 5 of our mutations caused a clear reduction in agonist response (all $p < 0.05$, Kruskal Wallis test with Dunn's multiple comparisons test). However, receptors containing the other 6 mutations were indistinguishable from wild-type in this experiment. Based on our significant results, we conclude that intellectual disability can be caused by loss of function mutations in this glutamate receptor subunit. For the mutations that had normal responses to maximal agonist in our screen, we hypothesise that differences in channel kinetics may be leading to reduced channel function.

43. James Drew - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Investigating the role of the actin cytoskeleton in regulation of microglial shape and motility

AUTHORS
Drew J, Arancibia Carcamo L, Jolivet R, Lopez Domenech G, Attwell D, Kittler JT

ABSTRACT
Microglia have a highly complex and motile network of processes that contact neurons and synapses, sculpting neural connections in the developing and adult brain. Despite this, the mechanisms governing microglial shape and motility remain poorly understood. In the present study, we have investigated the role of the actin cytoskeleton in microglial motility. Through live imaging of acute hippocampal slices, we show that microglial motility is critically dependent on filamentous actin. Disruption of actin polymerisation leads to a complete loss of both surveillance and damage response of microglia. Further, we find that inhibition of the actin branching complex Arp2/3 leads to dramatic and reversible changes in microglial

morphology and motility. By genetically targeting a regulator of Arp2/3, we find that surveillance is reduced without affecting the ability of microglia to respond to damage, suggesting that microglia use specific actin regulators for different behaviours. This study highlights the critical role of the actin cytoskeleton for microglial motility and uncovers novel functions for actin regulators in modifying these behaviours.

44. Ivan Kadurin - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Optical-tracking of the activation of individual Voltage Sensing Domains in CaV1.2 reveals that proteolytic cleavage is required for the regulatory effect of α2δ subunits

AUTHORS
Kadurin I, Savalli N, Pantazis A, Olcese R and Dolphin A

ABSTRACT
Excitation-evoked Ca2+ influx depends on voltage-gated calcium channels (VGCC) complexes composed of a pore-forming α1 subunit containing four distinct voltage-sensing domains (VSD I-IV) and auxiliary β, and α2δ subunits modulating the channel properties. In humans, α2δ dysfunctions contribute to neuronal and cardiac diseases, but the underlying mechanisms of α2δ regulation remain elusive. α2δ proteins are post-translationally proteolysed into disulfide-linked α2 and δ polypeptides. We have previously generated α2δ mutants resistant to proteolysis between the α2 and δ to demonstrate that the cleavage is controlling N-type VGCC functionality. Now, we employed Voltage Clamp–Fluorometry (VCF) method to obtain quantitative measurements of the effect of α2δ cleavage on the activation of VSD of VGCC in live cells. VCF is based on site-directed fluorescent labelling of individual VSD, followed by simultaneous recording of ionic currents and fluorescence deflections caused by their activation. By VCF we demonstrate that in sharp contrast to wild-type α2δ, uncleavable α2δ mutants failed to induce facilitation of the activation of either VSD or ionic currents carried by L-type VGCC to hyperpolarized membrane potentials. Thus, the posttranslational cleavage of α2δ is required to enable their modulatory effect on the activation properties of individual VSDs and ionic currents of L-type VGCC.

45. Eleonora Lugara - UCL Institute of Neurology

POSTER TITLE
Acute reduction of the Extracellular Trans-Synaptic Protein LGI1 increases network excitability

AUTHORS
Lugara E, Leite M, Kaushik R, Chabrol E, Dityatev A, Lignani G and Walker M

ABSTRACT
LGI1 (Leucine Rich Glioma Inactivated 1) is a secreted trans-synaptic protein, which plays an important role in regulating neuronal communication. Mutations of LGI1 lead to temporal lobe epilepsy in humans and animal models. Autoantibodies against LGI1 have been detected in the serum of patients affected by limbic encephalitis and suffering from epileptic seizures. Deficits of LGI1 are therefore strongly implicated in the generation and spread of seizures in genetic and developmental forms of epilepsy, but the mechanisms by which LGI1 affects neuronal networks are still unclear. My aim is to understand how acute reduction of

LGI1 in the brain leads to epilepsy in rodent models. For this purpose, I chose and validated a silencing RNA against LGI1. Reducing LGI1 in cultured neurons led to increased excitability of neuronal circuits. Local field potential of ex vivo brain slices after injection of shRNA-LGI1 in the ventral hippocampus, revealed that upon stimulation of mossy fibres, neurotransmission in the CA3 area more readily facilitates. My results indicate that acute reduction in LGI1 is sufficient to increase neuronal network excitability. Further studies are planned to determine the mechanisms of this increased excitability and the impact that this has on epileptogenesis in in vivo animal models.

46. Vincent Magloire - UCL Institute of Neurology

POSTER TITLE
Harnessing neurogliaform interneurons to treat focal epilepsy

AUTHORS
Magloire V, Mercier MS, Shimoda Y, Muller M, Kullmann DM

ABSTRACT
Understanding how inhibition fails during seizures, and how to rescue it, remains largely unresolved. 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. Circumstantial evidence argues that neurogliaform (NGF) cells, if appropriately recruited, should be much more effective in preventing seizures. Using a newly developed mouse line (Ndnf-Cre) that enables selective targeting of NGF cells, we aim to investigate their role in seizure initiation and propagation. We are using a combination of calcium imaging, electrocorticography and closed-loop optogenetic stimulation, together with local chemoconvulsant application (pilocarpine). Patch-clamp whole-cell recordings from Ndnf+ neurons revealed late-spiking behaviour, and immunostaining confirmed the presence of neuropeptide Y and reelin, which are characteristic features of NGF cells. In addition, NGF cell photostimulation as frequently as every 20 seconds evoked steadily increasing inhibition on pyramidal neurons, and bursts of high-frequency photostimulation could, after an initial depression, induce a steady hyperpolarisation for the duration of the burst. In vivo calcium imaging during seizures revealed that NGF cells are recruited late, after the onset of ictal discharges. Using closed-loop optogenetic stimulation, we are now examining whether recruiting NGF neurons early during seizures can curtail them.

47. Philipe Mendonca - UCL Institute of Neurology

POSTER TITLE
Imaging of synchronous and asynchronous glutamate release in small central synapses using iGluSnFR glutamate fluorescent probe

AUTHORS
Mendonca P, Tagliatti E, and Volynski K

ABSTRACT
Traditionally, electrophysiological assays have been preferably employed to unravel the dynamics of synaptic vesicle release and synaptic plasticity. However, most electrophysiological approaches are based on indirect measurements (e.g. postsynaptic recordings) form large population of synapses. This substantially impedes the understanding

of the mechanisms that regulate transmitter release at the level of single presynaptic boutons. Using both electrophysiology and imaging methods we report how the recently developed fast fluorescent glutamate sensor iGluSnFR can be successfully used to overcome these issues. This approach reveals how presynaptic boutons respond to individual action potentials, with high temporal and spatial resolution. Briefly, we transfect primary cortical cultures with iGluSnFR cDNA, establish whole-cell patch-clamp recording from a presynaptic pyramidal neuron and simultaneously monitor action potential-evoked fluorescence responses in tens of presynaptic boutons with ~5 ms time resolution using an EM-CCD camera. This allows accurate quantification of both synchronous and asynchronous release components at different stimulation frequencies in individual presynaptic boutons. We are currently using this approach to investigate the role of Synaptotagmin-1 in controlling synchronous and asynchronous components of transmitter release in small central synapses.

48. Marion Mercier - UCL Institute of Neurology

POSTER TITLE
Long-term plasticity in hippocampal neurogliaform interneurons

AUTHORS
Mercier MS, Magloire V, Kullmann DM

ABSTRACT
Long-term potentiation (LTP) of excitatory transmission onto hippocampal principal cells plays an important role in memory encoding. Within stratum radiatum, LTP at Schaffer collateral-CA1 pyramidal cell synapses is balanced by a complementary increase in the recruitment of feed-forward inhibitory interneurons (Lamsa et al., 2005). CA1 pyramidal cells also exhibit LTP at their distal synapses located in stratum lacunosum moleculare (SLM), which receive excitatory input from entorhinal cortex layer III (ECIII). Whilst this pathway recruits strong feed-forward inhibition, mediated largely by neurogliaform interneurons, it is not known whether ECIII synapses onto SLM interneurons can also be potentiated.Using whole-cell recordings from SLM interneurons in acute mouse hippocampal slices, we find that a low-frequency pairing protocol induces pathway-specific, NMDA receptor-dependent LTP in these cells. A spike-timing-dependent-plasticity (STDP) protocol, however, induces LTP that is neither pathway-specific nor NMDA receptor-dependent, but is blocked by the calcium chelator BAPTA. Furthermore, LTP can be induced by selective optogenetic stimulation of EC fibers, but not of fibers from the nucleus reuniens of the thalamus, which also sends excitatory projections onto SLM interneurons. Finally, using a recently developed mouse line (Ndnf-cre) to selectively target neurogliaform cells, we show that LTP is expressed in this subset of SLM interneurons.

49. Gareth Morris - UCL Institute of Neurology

POSTER TITLE
Investigating the anti-seizure mechanism of antagomirs against microRNAs upregulated in epilepsy

AUTHORS
Morris G, Schorge S, The EpimiRNA consortium

ABSTRACT
The EpimiRNA consortium has identified antagomirs targeting microRNAs as promising novel therapeutics for epilepsy. These oligonucleotides exhibit potent anti-epileptic effects in multiple disease models, but their mechanism of action is unclear. We used ex vivo brain slices to explore the effects of candidate antagomirs on hippocampal circuitry.Antagomirs were administered to adult male Sprague Dawley rats via intracerebroventricular injection. Rats completed a novel object location (NOL) test the following day and acute hippocampal slices were prepared 2-4 days post injection. Single cell properties were measured with patch clamp recording. Network excitability was probed using electrical stimulation and, separately, by acute seizure challenge with 4-aminopyridine. Synaptic plasticity was tested with paired-pulse facilitation and LTP protocols. One slice from each animal was stained for PSD-95 and VGLUT1.Slices from all antagomir treated groups showed reduced excitability in response to electrical stimulation, whilst plasticity was largely unaffected. We did not observe obvious effects on pyramidal cell biophysics, response to seizure challenge or NOL test performance. One candidate appeared to be associated with reduced post-synaptic spine size.All antagomirs reduced hippocampal excitability, which can explain their anti-seizure effect. It is likely that this general change is mediated by different specific mechanisms for each antagomir.

50. Elizabeth Nicholson - UCL Institute of Neurology

POSTER TITLE
Neurophysiological characterisation of S218L Cacna1a mouse mutant knock in model of familial hemiplegic migraine type 1

AUTHORS
Nicholson E, Tiurikova O, Kullmann D, Rusakov D, Volynski K

ABSTRACT
Understanding of rare familial hemiplegic migraine (FHM) can provide key insights into the pathophysiology of more general forms of migraine. Here we focus on S218L FHM1 mutation in CACNA1a gene, which encodes the pore forming subunit of CaV2.1 (P/Q-type Ca2+ channel). S218L mutation shifts channel activation to hyperpolarised potentials and increases open channel probability. Paradoxically, this does not always translate into an increase in action potential (AP)-evoked synaptic transmitter release as S218L mutation was found to cause gain or loss of function in different neuronal preparations. We hypothesise that complex effects of S218L mutation may be explained by age-dependent homeostatic compensation. To test this we measure evoked and spontaneous EPSCs, short-term plasticity and presynaptic Ca2+ dynamics in layer 2/3 visual cortical neurons in both young and aged S218L mutant mice. We find that in young mice S218L mutation leads to a decreased AP-evoked presynaptic Ca2+ influx and increased short-term facilitation, indicating a loss of function phenotype. This is likely caused by a reduced duration of APs in the S218L mice. In contrast, in aged mice we observe a gain of function effect of the S218L mutation, arguing for the involvement of an age-dependent mechanism in the pathophysiology of migraine.

51. Guliz Ozcan - UCL Department of Cell and Developmental Biology

POSTER TITLE
Physiological, behaviorally relevant targets of amyloid beta sleep regulation in vivo

AUTHORS
Gurel GO, Rihel J

ABSTRACT
Recent studies have highlighted links between Alzheimer's disease (AD) and sleep. In particular, sleep is disrupted in AD patients, often years before cognitive deficits. Furthermore, amyloid beta (Aβ) is most strongly secreted during waking, which leads to a daily rhythm of extra-neuronal Aβ. Therefore, worsening sleep may exacerbate Aβ plaque formation and AD progression. While most studies have concentrated on sleep's contribution to disease pathology, another hypothesis is that one of Aβ's physiological functions may be to regulate sleep. We have designed a novel assay in zebrafish to test this idea. Our experiments indicate that physiological and temporary upregulation of Aβ can promote both zebrafish wakefulness and sleep depending on its oligomeric structure, through activation of discrete subpopulations of neurons. We propose that one physiological function of Aβ is to modulate sleep via the direct regulation of neuronal activity by binding to specific receptors. Basic knowledge of the mechanistic link between Aβ and sleep may help identify novel early biomarkers of AD progression, and the zebrafish model is especially well suited to future drug discovery efforts.

52. Krishma Ramgoolam - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Visualization of endogenous CaV2.2 Channel

AUTHORS
Ramgoolam K, Nieto-Rostro M, Pratt W and Dolphin A

ABSTRACT
CaV2.2 constitutes the pore subunit of N-type calcium channels, which are important for neurotransmitter release in the central and peripheral nervous system. Immunohistochemical detection of native CaV2.2 has not been possible until now due to the low expression of these channels and lack of suitable antibodies. We have now developed a constitutive knock-in (KI) transgenic mouse, expressing CaV2.2 with an epitope tag (2xHA) inserted in the extracellular loop between S3 and S4 of Domain II (CaV2.2_HA KI). The tag did not affect the function of the channel when expressed in vitro (Cassidy et al., 2014). In the peripheral sensory nervous system, our data show CaV2.2_HA to be expressed on the cell surface of dorsal root ganglion neurons (DRGs). In the spinal cord, CaV2.2_HA is predominantly in the superficial laminae LI and LII of the dorsal horn, mainly in the primary afferent terminals, since HA staining is reduced following rhizotomy. These mice will be instrumental in the future to understand the presynaptic role of N-type calcium channels in physiological and pathological states and will also be of use to examine the trafficking and recycling of the channels in several neural cell types.

53. Candela Sanchez Bellot - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Investigating projections from ventral subiculum to prefrontal cortex and nucleus accumbens

AUTHORS
Sanchez-Bellot C, MacAskill AF

ABSTRACT
The subiculum is the main output region of the hippocampus. Despite targeting multiple downstream regions, its efferents are thought to be organised as parallel projections, with any one neuron targetting only one downstream region. This raises the possibility that different projections have specific contributions to behaviour. Here, we focus on projections from the ventral subiculum (vS) to the prefrontal cortex (PFC) and nucleus accumbens (NAc), involved in mediating affective behaviour. Through anatomical, electrophysiological and morphological investigation of these projections from vS, we describe specific properties of NAc and PFC projecting neurons, and interestingly, a marked distinction within the PFC-projecting population itself, along the radial axis of the hippocampus. Ongoing experiments involve an intersectional strategy to specifically target different PFC-projecting cells in ventral subiculum and characterisation of a depression model to study the involvement of these projections in bringing about depressive-like behaviours. Acknowledging distinctions within projection populations will greatly aid in future local circuitry and behavioural investigations into the role of ventral subiculum projections in affective behaviour and disorders.

54. Craig Sexton - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Probing spontaneous gating of the GABAa receptor

AUTHORS
Sexton CA, Smart TG

ABSTRACT
Tonic inhibition largely results from the activation of extrasynaptic GABAa receptors, causing a persistent inhibitory membrane ‘leak’ conductance. This near constant inhibitory tone affects neuronal signalling through shunting inhibition and modulates the input-output relationships of most neurons. Tonic inhibition is thought to result from low concentrations of extracellular GABA, but there is also evidence for a spontaneous gating component contributing to the tonic current. We demonstrate that the subunit composition of receptors is a crucial factor in determining spontaneous receptor activity, particularly the identity of the β subunit, with β3-containing receptors showing high levels of spontaneous activity, whilst receptors containing β2 show almost none. We have identified the large extracellular amino-terminal domain of the β3 subunit to be the main determinant of spontaneous activity, and have also identified two adjacent residues in the large intracellular loop which can be phosphorylated to modulate the level of spontaneous activity. We reveal that neurosteroids, endogenous allosteric modulators of GABAa receptors, can affect the level of spontaneous current. Our results indicate that spontaneous activity of GABAa receptors is highly malleable and is likely to contribute to neuronal plasticity to control levels of excitability in neuronal circuits.

55. Sergey Sitnikov - UCL School of Pharmacy

POSTER TITLE
An investigation of the intracellular mechanism underlying cholinergic-induced action potential threshold plasticity in hippocampal neurons

AUTHORS
Sitnikov S, Pigott BM, Brown DA, Shah MM

ABSTRACT
Cholinergic innervation of the hippocampal Dentate Gyrus (DG) plays an important role in hippocampus-depending learning. We have shown that axonal muscarinic receptor stimulation leads to a persistent reduction in the action potential (AP) threshold in DG granule cells (GCs) (1). This effect depends on enhanced T-type Ca2+ channel function. The intracellular mechanism coupling muscarinic receptors to T-type Ca2+ channels remains unknown. Here, we investigated whether this coupling involves Ca2+ calmodulin-dependent kinase (CaMKII). To test this, we made electrophysiological recordings from mature GCs in acute brain slices. Post-hoc morphological analysis was performed to determine if recorded neurons had an axon longer than 30 □m (so-called 'long-axon (LA)' neurons).Bath application of 1µM Oxotremorine-M (Oxo-M) onto LA neurons but not short-axon (SA) neurons caused a long-lasting reduction in the AP threshold. Consequently, AP firing was persistently enhanced in LA neurons. Moreover, Oxo-M application onto both LA and SA neurons transiently depolarised the resting membrane potential (RMP) and induced an afterdepolarisation (ADP) following the action potentials. LA-neuron pre-treatment with CaMKII inhibitors selectively prevented the AP threshold plasticity and increase in AP firing. Our results, therefore, suggest that axonal muscarinic receptor-induced AP threshold plasticity involves CaMKII. (1) Martinello et al., (2015) Neuron, 85, 346-63.

56. Erica Tagliatti - UCL Institute of Neurology

POSTER TITLE
Regulation of synaptic neurotransmitter release by synaptotagmin 1 oligomerisation

AUTHORS
Tagliatti E, Nicholson E, Bello O, Mendonca P,Krishnakumar SS, Rothman JE, Volynski KE

ABSTRACT
Synaptic transmission forms the basis of neuronal communication in the brain. Vesicular release of neurotransmitter involves highly specialised machinery optimised for speed and coupled to the action potential-evoked presynaptic Ca2+ influx. It is generally thought that fast synchronous release is triggered by the vesicular Ca2+-release sensor Synaptotagmin 1 (Syt1). Recently, it has been demonstrated that Syt1 readily forms ring-like oligomers on lipid surfaces (Wang et al. PNAS 2014). Importantly, Syt1 oligomers assemble and disassemble in a Ca2+-dependent manner. This prompts a hypothesis that formation of such Syt1 oligomers at the interface between synaptic vesicles and the plasma membrane may act as a clamp to prevent spontaneous vesicular fusion. Upon action potential arrival and presynaptic Ca2+ influx Syt1 oligomers would disassemble allowing fast vesicle fusion. To test this hypothesis we investigated the effect of a dominant Syt1 mutant (F349A) that disrupts formation of Syt1 oligomers in vitro on spontaneous and evoked release in small central synapses in culture. We find that Syt1F349A overexpression increases spontaneous

release and de-synchronizes evoked synaptic vesicle fusion. These results argue that Syt1 oligomerization plays a major role in synchronization of synaptic transmitter release and vesicle recycling.

57. Yajing Xu - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
The role of microglia in the postnatal maturation of spinal sensory circuitry

AUTHORS
Xu Y, Moulding D, Zavery F, Fitzgerald M, Beggs S

ABSTRACT
Maturation of sensory systems is an activity-dependent process and requires modality specific sensory input in early postnatal life. Spinal somatosensory circuitry is functional at birth, but extensive neuronal reorganization occurs postnatally, as A-fibres shift their projection targets and local inhibitory circuits mature. It is now known that microglia refine neuronal circuitry through synaptic and neuronal remodelling as part of normal CNS development. However, the role of microglia in the postnatal maturation of spinal somatosensory circuitry is not known. Here we describe postnatal changes in microglial number and phenotype in the spinal dorsal horn in rats and their influence on excitatory and inhibitory circuitry.Using immunohistochemistry we quantified the phenotype and density of microglia, neurons, apoptotic nuclei, and excitatory/inhibitory synapses in rat spinal cord between postnatal day (P)3 - P17.During normal postnatal development, the ratio of microglia per neuron increased with age. Phagocytic activity was highest during the first postnatal week and decreasing after P7. Apoptotic cell number decreased with age, with nearly all of them in apposition to microglial processes and phagocytic cups from P7 onwards.Here we identify a potential regulatory role for microglia in the sensory spinal cord in controlling the development of somatosensory network connectivity.

Novel Methods, Resources and Technology Development | Elvin Hall

58. Liam Collins-Jones - UCL Department of Medical Physics and Bioengineering

POSTER TITLE
A 4D infant head atlas for use in optical image reconstruction of brain function over the first two years of life as part of the BRain Imaging in Global HealTh (BRIGHT) project

AUTHORS
Collins-Jones L, Cooper R, Hebden J, Elwell C

ABSTRACT
The BRIGHT project is a longitudinal study of UK and Gambian infants from birth to 24 months seeking to investigate the effect of malnutrition and early adversity on infant brain development. As part of BRIGHT, functional near-infrared spectroscopy (fNIRS) (a non-invasive optical imaging technique) is used to measure localised haemoglobin concentration changes across the cortex in response to a range of cognitive stimuli. Three-dimensional

images of the haemodynamic response, a marker of functional activation, can be reconstructed if a model of photon propagation is used as part of the fNIRS data analysis. This requires prior anatomical knowledge.Using an MRI atlas as prior anatomical knowledge reconstructs accurately localised cortical activation in adults. Image reconstruction using subject-specific anatomy has been demonstrated in infants; to date, an atlas-guided approach has not.Using averaged structural MR data, we have produced an atlas of head models with realistic spatial mapping of brain and extracerebral tissue for use in optical image reconstruction at ages 1, 6, 9, 12, 18 and 24 months.We aim to use this atlas to reconstruct images of haemoglobin concentration changes across this age range, and hence use fNIRS BRIGHT project data to establish function-for-age curves for charting brain development.

59. Matt Earnshaw - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Visualizing, editing and simulating neuronal models with Open Source Brain

AUTHORS
Gleeson P, Earnshaw M, Cantarelli M, Sadeh S, Cayco-Gajic NA, Silver R

ABSTRACT
Ensuring reproducibility, accessibility, standardization, and provenance tracking of models is essential for improving the scientific value of simulations. In computational neuroscience, making models available in open and accessible formats is important for improving transparency and reusability. The Open Source Brain (OSB) initiative (online at http://www.opensourcebrain.org) is an online platform which facilitates model accessibility, sharing and collaborative development. It provides a location for neuronal and network models from different brain regions and species, and offers tools for visualization, analysis and simulation. While OSB can host models in any format, the use of machine readable standardised model descriptions, such as the NeuroML 2/LEMS framework is core to OSB, because it allows automated access to the internal structure of models. This enables the 3D morphology, the network connectivity, the biophysical properties and the functional dynamics of the models to be automatically exposed in an accessible form.

60. Katarzyna Kozdon - UCL Department of Computer Science

POSTER TITLE
The evolution of training parameters for spiking neural networks with hebbian learning

AUTHORS
Kozdon K, Bentley P

ABSTRACT
Spiking neural networks are a promising tool for unsupervised processing of spatio-temporal data. However, they do not perform as well as the traditional machine learning approaches and their applications are still limited. Various supervised and reinforcement learning methods for optimising spiking neural networks have been proposed, but more recently the evolutionary approach regained attention as a tool for optimising neural networks. Here, we describe a simple evolutionary algorithm for developing hyperparameters for fully unsupervised spike-timing-dependent learning for pattern clustering using spiking neural

networks. Our results show that combining evolution and unsupervised learning leads to faster convergence on the optimal solutions, better stability of fit solutions and higher fitness of the whole population than using each approach separately.

61. Barbara Kramarz - UCL Institute of Cardiovascular Science

POSTER TITLE
Neurological Gene Ontology development and protein annotation facilitate more informative data analysis and interpretation

AUTHORS
Kramarz B, Roncaglia P, Bandopadhyay R, Brough D, Martin MJ, Hooper NM, Parkinson H, Lovering RC

ABSTRACT
The analysis and interpretation of high-throughput (HTP) datasets from '-omics' and GWAS studies relies on access to high-quality bioinformatics resources, such as Gene Ontology (GO, geneontology.org). The aim of this Alzheimer's Research UK-funded project is to enhance the GO resource by developing new neurological GO terms and using GO for annotation of proteins associated with dementia. Annotation priorities include interactors of amyloid-beta and tau, and neuroinflammation-relevant processes. At the time of abstract submission, eighty new GO terms have been contributed to the database as a result of this project [AmiGO2 Statistics; http://amigo.geneontology.org; accessed 20 Apr 2018], including e.g. 'regulation of neuron projection arborization', 'regulation of spontaneous synaptic transmission', or 'regulation of astrocyte activation'. To date 3,459 GO annotations to 537 gene products have been submitted to the GO Consortium database; among these, 2494 annotations to 306 human gene products [QuickGO Statistics; https://www.ebi.ac.uk/QuickGO/; accessed 19 Apr 2018]. Our ongoing contribution to the GO resource, focused on development of neurological GO terms and a detailed manual GO annotation of gene products, will improve analysis and interpretation of biomedical data and help to delineate the bases of dementia, potentially leading to identifying new treatment targets and/or novel diagnostic biomarkers.

62. Modinat Liadi - UCL Institute of Neurology

POSTER TITLE
Morphological and population effects of storing olfactory bulb tissue before cell culturing

AUTHORS
Liadi M, Li D and Li Y

ABSTRACT
Olfactory ensheathing cells (OECs) are a unique type of glial cells shown to aid recovery after spinal cord injury. Transplantation of these OECs, in particular from the olfactory bulb (OB), is considered a new therapy method for central nervous system (CNS) repair. Nevertheless, such intervention still presents logistical issues particularly the allograft method of intervention resulting in need of the harvested tissue been stored. In this study, we focus on this delay and its effects by investigating storage conditions and time. On the assumption that for clinical application the OB will not be immediately cultured upon removal we observed the effects of different storage conditions (DMEM, DMEMF, and HBBS) and

time-points (24hours and 48hours) on cellular properties and speculated what this could mean for functionality. Immunohistochemistry analysis reveals that storing the OB for periods up to 24hours negatively impacts total cell number and subsequently the OECs population. We observed that the storage conditions did not significantly contribute to the changes in the cell culture properties.

63. Edoardo Scarpa - UCL Chemistry

POSTER TITLE
Controlling cellular trafficking by nanoparticle avidity: from endocytosis to transcytosis

AUTHORS
Nyberg S, Scarpa E, Tian X, Rizzello L, Vuyyuru M, Kirschneck L, Šarić A, Battaglia G

ABSTRACT
Therapeutic intervention in the central nervous system (CNS) is limited by the presence of the blood brain barrier (BBB) that controls the movement of molecules across the BBB. However, transcytosis mechanism can be hijacked to transport therapeutics to the CNS. Polymersomes, synthetic nanoscopic vesicles, represent a promising drug delivery system. They can accommodate a variety of drugs at high concentration and their outer surface can be decorated Angiopep2 peptide (AP2), which enables transcytosis. We hypothesised that the intracellular trafficking of polymersomes decorated with AP2 is dependent on the density of ligands on the nanoparticle surface. To test this hypothesis, we produced pH sensitive polymersomes conjugated with different densities of AP2, and assessed transcytosis using a 3D transwell model. We show that the rate of transwell crossing by polymersomes varies according to the densities of AP2 conjugated on the surface. At high AP2 density (60 AP2/polymersome) polymersomes are compartmentalised in endocytic organelles positive for Rab5, 7 and 11. Contrarily, a medium AP2 density (25 AP2/polymersome) favours transcytosis through tubular structures. Real time live cell imaging studies and molecular dynamic modelling revealed that the avidity of system determines the intracellular trafficking of polymersomes. These results underline how ligand density contributes to the intracellular trafficking of nanoparticles and provide new insight into the mechanism of transcytosis through the BBB.

64. Ruth Wood - Sainsbury Wellcome Centre for Neural Circuits and Behaviour

POSTER TITLE
The Honeycomb Maze: a new behavioural apparatus for testing spatial navigation

AUTHORS
Wood R, Bauza M, Krupic J, Burton S, Delekate A, Chan D and O'Keefe J

ABSTRACT
The Honeycomb Maze is a novel behavioural paradigm for studying spatial navigation. It consists of 37 tessellated hexagonal platforms, each individually raised or lowered to control choices as the animal moves from start to goal. It offers several advantages over current mazes; experimenter control over platform configurations allows scaling of task difficulty, the maze permits concomitant spatial cell recording, and it produces a parametric behavioural output. The place navigation task requires an animal to navigate to an unmarked goal platform from one of several start platforms. Each trial consists of a series of sequential

choices in which the animal is confined to a raised platform and given a choice between two adjacent platforms. The correct choice is the platform with the smallest angle to the goal heading-direction. Rats learn rapidly and their behaviour is influenced by three maze factors: the angle separating the two choice platforms, the distance from the goal, and the angle between the correct choice platform and the goal heading-direction. Performance is significantly impaired in rats with hippocampal lesions and the three maze factors have a greater effect on performance in these rats compared to controls, suggesting the hippocampus plays a key role in processing vector space.

Cognition and Behaviour | Drama Studio

65. Mohammed Alsaif - UCL Institute of Epidemiology and Health Care

POSTER TITLE

The impact of total tooth loss on memory and executive function among older adults in England

AUTHORS
Alsaif M, Tsakos G, Cadar D, Watt R

ABSTRACT
The association between edentulism (total tooth loss) and cognitive functioning is poorly understood. We aimed to examine the prospective association between edentulism and cognitive performance on memory and executive function among 4,240 older adults (50+) from the English Longitudinal Study of Ageing.Memory was assessed with 10 words immediate and delayed recall, while executive function with a task of verbal fluency (animal naming). Linear regression was used with edentulism (dentate vs. edentate) at wave 3 and cognitive functioning 8-years later at wave 7.Our results showed that participants who were edentate at baseline recalled fewer words □=0.33 (95% Confidence Interval (CI): 0.01 - 0.64) than those who were dentate, while controlling for age, sex, marital status, education and wealth; but this association was explained by further adjustment for smoking and alcohol. Moreover, edentate participants named fewer animals □=0.79 (95% CI: 0.13 - 1.45) than dentate participants independent of all covariates.In a representative English population sample, we showed a strong association between edentulism and subsequent executive function, while the link with memory seems to be explained by lifestyle behaviours. Further investigations of the mediating factors and potential pathways are necessary to elucidate the link between edentulism and subsequent cognitive functioning.

66. Naheem Bashir - UCL Division of Psychology and Language Sciences

POSTER TITLE
Using tDCS to enhance speech production in fluent speakers and people who stutter

AUTHORS
Bashir N, Bernard R, Sinnott E, Turnbull C, Chard I, Zhang X and Howell P

ABSTRACT
Aims:Studies one and two investigated whether tDCS to the LIFG affected speech production in healthy individuals. Study three investigated whether applying tDCS to the LIFG during fluency-shaping therapy would enhance fluency in people who stutter (PWS). Methodology:In study one, 27 fluent participants received anodal or sham tDCS over the LIFG, during a picture naming task containing congruent and incongruent primes. In study two, 24 participants completed a tongue twister repetition task 1 hour before, during, and after receiving tDCS over the LIFG. In study three, speech therapy was delivered with concurrent online tDCS over the LIFG during 5 one-hour therapy sessions over 14 days. Results:Study one showed anodal (vs. sham) tDCS led to significantly quicker reaction times for incongruent trials. Study two showed that anodal tDCS (vs. sham) led to significantly quicker repetition times during and post-stimulation. Study three showed that participants who received anodal-tDCS, displayed substantial reduction in their SSI-3 scores. Conclusions:Findings demonstrate tDCS is a feasible method for improvement of speech production in fluent speakers, and potentially in PWS (work is ongoing). Results also reveal the importance of considering individual differences in response to treatment and tDCS in intervention protocols.

67. Hassan Bassam - UCL Institute of Neurology

POSTER TITLE
Are you sure about that? On origins of confidence in conceptual knowledge

AUTHORS
Stojić H, Eldar E, Bassam H, Dolan RP

ABSTRACT
Keeping track of uncertainty about our knowledge has a key role in guiding behaviour. It can help us to avoid coming dangerously close to irreparable harm or speed up identifying the most rewarding course of actions. Recent work in perceptual and motor processing has shown that people often behave close to prescriptions of Bayesian ideal observers, incorporating the uncertainty of the percepts or action execution in their perceptual decision or movements. When learning about abstract concepts, a large part of uncertainty is internal, over models relating observed variables to an unobserved variable we wish to predict. This study systematically examines whether and how people track uncertainty in the conceptual domain. Participants completed a function learning task where they learned to predict a continuous variable based on four observable features, providing predictions and confidence about their predictions. Participants' confidence reports indicate that they indeed have insight into the uncertainty about their own conceptual knowledge. We modelled human function learning with Gaussian processes; allowing us to predict confidence judgements of the participants. These models performed well at matching participants' predictions and reasonably well at matching confidence reports. Finally, we have examined several methods for eliciting confidence reports in an incentive compatible way.

68. Rachel Bedder - UCL Institute of Neurology

POSTER TITLE
A computational model of mood and future prospects

AUTHORS
Bedder R, Blain B, Lowther E, Rutledge R

ABSTRACT
Our mood is affected not only by what is currently happening, but also what we believe is likely to happen in the future. However, the cognitive mechanisms that underlie how future prospects impact our mood in response to current decision outcomes is unknown. Fluctuations in mood in response to probabilistic outcomes were assessed in healthy participants (N=43) using a gambling paradigm with frequent experience sampling on mood. Participants made decisions between safer and riskier gambles in Gain blocks, where they could win points, and Loss blocks where they could lose points. Importantly, participants were shown whether the next two blocks of trials were Gain or Loss blocks to assess the effects the future prospects on both mood and behaviour. We adapted an established computational model that explains mood fluctuations based on recent rewards and prediction errors (Rutledge, et al., 2014) to include parameters which modulated mood based on future prospects. We evaluated the models using BIC values fit for each subject. The model where future prospects adjusted baseline mood (r2 = 0.55+0.2) was preferred according to Bayesian model comparison. In this model, future Gain blocks increased happiness when making decisions in Gain trials, but decreased happiness when making decisions in Loss blocks.

69. Franziska Broker - Gatsby Computational Neuroscience Unit at UCL

POSTER TITLE
Forget-me-some: general versus special purpose models in a hierarchical probabilistic task

AUTHORS
Bröker F, Marshall L, Bestmann S, Dayan P

ABSTRACT
Humans build models of their environments and act according to what they have learnt. In simple experimental environments, such model-based behaviour is often well accounted for as if subjects are ideal Bayesian observers. However, more complex probabilistic tasks require more sophisticated forms of inference that are sufficiently computationally taxing as to demand approximation. Here, we study two approximation schemes applied to a probabilistic serial reaction time task. One, pre-existing, scheme was a generically powerful variational method for hierarchical inference which has recently become a popular formalisation of a wide swathe of probabilistic learning tasks. A second, novel, scheme was more specifically tailored to the task at hand. We show that the latter model fit significantly better than the former, suggesting that subjects were sensitive to many of the particular constraints of the complex behavioural task. Further, the tailored model provided a different perspective on the effects of cholinergic manipulations in the task. Neither model fit the behaviour on more complex contingencies that competently. These results illustrate the benefits and challenges of general and special purpose modelling approaches, and raise important questions of how either type advances our understanding of learning mechanisms in the brain.

70. Merit Bruckmaier - UCL Institute of Cognitive Neuroscience

POSTER TITLE
Cerebral metabolism in the visual cortex: the effects of attention

AUTHORS
Bruckmaier M, Phan P, Tachtsidis I, Lavie N

ABSTRACT
It is well established that the level of perceptual load in attended processing affects visual cortex responses to unattended stimuli in support of a limited capacity load model of attention (e.g. Lavie, 2005). Here we propose that differences in cerebral energy consumption directly underlie the load induced modulations of the visual cortex response. We thus hypothesised that task conditions of high perceptual load will lead to an increase in metabolic demand for task-relevant processing, and result in reduced neural responses to task-irrelevant stimuli. Broadband functional near-infrared spectroscopy (fNIRS) was used to measure redox state changes in the mitochondrial enzyme cytochrome c oxidase (oxCCO) which are indicative of cellular oxygen metabolism. Participants responded to either colour targets (low load) or colour-orientation conjunction targets (high load) in a rapid stream of stimuli, while ignoring a peripheral, flickering checkerboard present on half of the trials. The oxCCO signal related to the presence of the checkerboard was significantly reduced under high load conditions in the right medial occipital gyrus and the medial occipital lobe. Load-dependent attentional modulations are therefore shown to have a direct impact on the cellular metabolism required for visual cortex responses to task-irrelevant stimuli.

71. Giulio Casali - UCL Department of Cell and Developmental Biology

POSTER TITLE
Entorhinal neurons exhibit cue locking in rodent VR

AUTHORS
Casali G, Dowell C, Shipley S, Hayman R, Barry C

ABSTRACT
The spatially regular firing pattern of rodent medial entorhinal (mEC) grid cells is hypothesized to function as a spatial metric relevant for navigation. The development of virtual reality (VR) for head-fixed mice confers a number of experimental advantages and has becoming increasingly popular as a method for investigating spatially-selective cells. Recent experiments conducted in 1D virtual linear tracks report that neurons in mEC fire at regular intervals in virtual space, analogous to grid cells activity on real linear tracks.We recorded from mEC as mice traversed virtual tracks, identifying a population of neurons with firing fields in phase with regularly repeating visual cues - thus resembling regular grid cell firing patterns. However, in the open field these cells lacked the six-fold periodicity typical of grid cells and in VR the frequency of their firing-pattern precisely matched to visual features in the VR. Indicating that their apparently grid-like activity was likely an artefact induced by the robust modulation of a subset of mEC neurons by visual cues.In light of these results we highlight the importance of controlling the periodicity of the visual cues in VR and the necessity of open field recordings for the accurate characterisation of mEC cells.

72. Sean Cavanagh - UCL Institute of Neurology

POSTER TITLE
Reconciling persistent and dynamic hypotheses of working memory coding in prefrontal cortex

AUTHORS
Cavanagh SE, Towers JP, Wallis JD, Hunt LT, Kennerley SW

ABSTRACT
Competing accounts propose that working memory (WM) is subserved either by persistent activity in single neurons or by dynamic (time-varying) activity across a neural population. Here we compare these hypotheses across four regions of prefrontal cortex (PFC) in a spatial WM task, where an intervening distractor indicated the reward available for a correct saccade. WM representations were strongest in ventrolateral PFC (VLPFC) neurons with higher intrinsic temporal stability (time-constant). At the population-level, although a stable mnemonic state was reached during the delay, this tuning geometry was reversed relative to cue-period selectivity, and was disrupted by the distractor. Single-neuron analysis revealed many neurons switched to coding reward, rather than maintaining task-relevant spatial selectivity until saccade. These results imply WM is fulfilled by dynamic, population-level activity within high time-constant neurons. Rather than persistent activity supporting stable mnemonic representations that bridge distraction, PFC neurons may stabilise a dynamic population-level process that supports WM.

73. Benjamin Chew - UCL Institute of Neurology

POSTER TITLE
Endogenous fluctuations in the dopaminergic midbrain modulate Choice Behavior

AUTHORS
Chew B, Hauser TU, Papoutsi M, Dolan R, Rutledge RR

ABSTRACT
Deficits in the dopaminergic reward pathways have been associated with gambling addiction as well as other psychiatric disorders where patients often co-present with problem gambling, such as Attention Deficit Hyperactivity Disorder (ADHD). While pharmacologically boosting dopamine increases risk-taking behavior, little is understood about whether endogenous fluctuations in dopaminergic brain areas can lead to momentary impulses that similarly influence choice behavior.In the present study, we explore the effect of intrinsic fluctuations in the substantia nigra and ventral tegmental area (SN/VTA) complex on risk-taking behavior. We used real-time functional Magnetic Resonance Imaging (rtfMRI), combined with an individually calibrated probabilistic gambling task, to probe whether changes in baseline levels of BOLD (Blood Oxygenation Level-Dependent) activity in the SN/VTA predict subsequent risk-taking behavior. When SN/VTA activity was low, participants exhibited greater risk-taking behavior, and were also slower to make a decision. Computational modelling revealed that the difference in risk-taking between conditions was driven by an increased bias to gamble for any option presented, as opposed to a change in individual utility functions. Our results suggest that endogenous fluctuations in SN/VTA BOLD activity modulate choice behavior, consistent with the possibility that low intrinsic dopamine may underlie impulsive behaviors in related psychiatric disorders.

74. Soraya Dunn - UCL Ear Institute

POSTER TITLE
Do ethological differences between species shape neural mechanisms in the hippocampus?

AUTHORS
Dunn SLS, Town SM, Bizley JK, Bendor D

ABSTRACT
The hippocampus is a brain region with important roles in memory and spatial navigation. Theta oscillations are a hallmark of the hippocampal local field potential (LFP) and play a critical role in many models of hippocampal function. However, these models are based almost exclusively on rodent studies. To investigate whether the specific ethological constraints of the rodent shape neural mechanisms in the hippocampus, we have recorded hippocampal LFP in the rat and the ferret (Mustela putorius). Ferrets are predatory carnivores that rely predominantly on distal senses, in contrast to the proximal sensing strategies of whisking and sniffing in rats. We have identified theta oscillations in the ferret hippocampus which occur at a 3.5-7.5 Hz, a lower frequency band than commonly observed in the rat (5-12 Hz). Ferret hippocampal theta showed a positive correlation with the animals' speed, however the gradient of this relationship was roughly half that found in the rat over the same speed range. Rats and ferrets were trained on comparable auditory/visual localisation tasks designed to manipulate sensory attention. Ferret theta oscillations were found to be continuous while the ferrets performed the behavioural task, even during immobility. This immobility-related activity was abolished by administration of atropine.

75. Irene Echeverria Altuna - UCL Institute of Neurology

POSTER TITLE
The role of rapid eye-movement sleep in memory consolidation

AUTHORS
Echeverria-Altuna I, Kukovska L, Bendor D

ABSTRACT
Evolution has made sleep a biological requirement, however, its exact role remains debated. One major hypothesis is that sleep underlies systems-level memory consolidation; the transferal and stabilization of new, hippocampal-dependent memories to cortical areas for long-term storage. This is thought to be a two-step process. First, during non-REM sleep, memories are transferred from the hippocampus to cortical areas (24-48h). Subsequently, REM sleep allows for associations between the recently stabilized memories and older ones to happen (a month in rodents, years in humans). Our study explores the role of REM sleep in the long-term consolidation of "neutral, positive and negative" memories. Three configurations of a maze are used to train mice in three hippocampal-dependent behavioral tasks – neutral, aversive and appetitive. As a result, mice are expected to form neutral, negative and positive memories. These memories are tested at two time points: at day 0 and day 30, when REM-dependent consolidation has most likely happened. In parallel, neural activity is recorded in microdrive-implanted mice and is used to analyse the correlation between the pattern of single-unit activation during the task and during REM sleep. Finally, further REM-related parameters are compared at both time points and across the three tasks.

76. **Sam Ereira - UCL Institute of Neurology**

POSTER TITLE
A neurocomputational account of self-other distinction

AUTHORS
Ereira S, Dolan RJ, Kurth-Nelson Z

ABSTRACT
Humans have a remarkable ability to simulate each other's minds but it is not known how the brain distinguishes between mental states attributed to self and mental states attributed to other, an ability impaired in many psychopathologies. We investigated how fundamental neural learning signals are selectively attributed to different agents. Subjects continuously learned two models of the same environment, where one was selectively attributed to self and the other was selectively attributed to another person. Combining computational modeling with magnetoencephalography (MEG), we tracked neural representations of prediction errors (PEs) attributed to self, and of simulated PEs attributed to the other agent. We found that the representational pattern of a PE reliably predicted the identity of the agent to whom the signal was attributed, consistent with a neural self-other distinction implemented via agent-specific learning signals. Strikingly, subjects with a smaller neural self-other distinction also had a reduced behavioural capacity for self-other distinction and had stronger psychopathological traits. Thus, we show that self-other distinction is realised through an encoding of agent identity intrinsic to fundamental learning signals. In a second experiment, we pre-trained subjects and found that the natural variation in self-other distinction can be partially explained by prior social experiences.

77. **Anushka Fernando - UCL Department of Neuroscience, Physiology & Pharmacology**

POSTER TITLE
Learning from ambiguous cues; assessing the role of projection populations within the ventral hippocampus

AUTHORS
Fernando ABP, MacAskill AF

ABSTRACT
The hippocampus is sensitive to novel events that are by definition unpredictable. Furthermore, evidence of reward-related signals in the hippocampus during learning have been reported which may vary along its dorso-ventral axis. Sensitivity to both novelty and reward are essential to learning from ambiguous cues to promote advantageous behaviour. This project assesses the role of the ventral hippocampus in resolving ambiguous cues to promote learning and behaviour during two complementary auditory discrimination tasks. Using an intersectional viral strategy in combination with in vivo fibre photometry, I recorded calcium activity-dependent changes in specific projection populations of the hippocampus in freely-behaving mice. Results show task-dependent changes in the activity of specific projection populations from the ventral hippocampus, suggesting a complex role of the ventral hippocampus in encoding reward learning under uncertainty.

78. Andrea Gajardo Vidal - UCL Institute of Neurology

POSTER TITLE
How distributed processing produces false negatives in voxel-based lesion-deficit analyses

AUTHORS
Gajardo-Vidal A, Lorca-Puls DL, Crinion JT, White J, Seghier ML, Leff AP, Hope TMH, Ludersdorfer P, Green DW, Bowman H, Price CJ

ABSTRACT
In this study, we hypothesized that if the same deficit can be caused by damage to one or another part of a distributed neural system, then voxel-based analyses might miss critical lesion sites because preservation of each site will not be consistently associated with preserved function. We used voxel-based multiple regression analyses of data from 359 stroke survivors to identify brain regions where lesion load is associated with picture naming abilities. Highly significant effects were detected in left temporal and frontal areas. Post-hoc analyses showed that damage to either of these sites caused the deficit of interest in less than half the affected patients. After excluding all patients with damage to one or both of the identified regions, our second analysis revealed a new region (i.e. left anterior putamen) which had not been previously detected. Our results illustrate how (1) false negatives arise when the same deficit can be caused by different lesion sites; (2) some of the missed effects can be unveiled by adopting an iterative approach, (3) statistically significant voxel-based lesion-deficit mappings can be driven by a subset of patients; and, finally, (4) univariate voxel-based analyses cannot, in isolation, be used to predict outcome in other patients.

79. Eva Gutierrez-Sigut – UCL Deafness, Cognition and Language Research Centre

POSTER TITLE
Investigating brain lateralization during speechreading and reading in deaf adults using functional transcranial Doppler sonography (fTCD)

AUTHORS
Gutierrez-Sigut E, Mousley V, Monroy-Camarena L, MacSweeney M

ABSTRACT
Phonological processing is strongly linked to reading ability in hearing people. It has been proposed that as reading development progresses, visual word recognition becomes increasingly left lateralized due to mapping of orthographic forms onto the already left lateralized phonological forms (Maurer and McCandliss, 2008). In this line, greater phonological awareness has been linked with stronger left lateralization for visual word processing (Sacchi & Laszlo, 2016). This process might be challenging for deaf readers, whose phonological representations, constructed upon speechreading (lipreading) and articulatory feedback, might be underspecified.Here we investigate lateralization in profoundly deaf adults during language tasks using functional Transcranial Doppler sonography (fTCD). We measured laterality indices (LIs) during language generation (semantic fluency), rhyme judgement tasks, reading and speechreading of short stories. Results for language generation (the gold standard task to establish hemispheric lateralization) showed that participants were predominantly left lateralized. The strength of lateralization for the rhyme judgment task was lower but not significantly different from the generation task. Significantly lower LIs were found for both the reading and speechreading

tasks than for the generation task. We discuss the gradation of lateralization for this battery of tasks in terms of their language demands (see Bradshaw et al., 2017).

80. Leanne Hockey - UCL Institute of Neurology

POSTER TITLE
Attention and Inhibition in Tourette's Syndrome

AUTHORS
Hockey LN, Haggard P, Rothwell J & Joyce E

ABSTRACT
Tourettes syndrome (TS) is characterised by involuntary movements and vocalisations known as tics. Tics arise in childhood and overtime, severity often decreases. However, in a significant proportion, tics persist into adulthood and are socially disabling.Tics are thought to arise from a neurophysiological imbalance in the sensorimotor system. They are preceded by an 'urge' to tic and at this stage, some can actively suppress the tic from developing. Current psychological therapy uses this phenomenon to help people control their tics based on the hypothesis there is a problem with motor inhibition. However, this is often not successful in adults.Tics often automatically reduce when distracted or concentrating on something. This suggests that there may also be an additional problem with attention. Rather than focusing on urges to help prevent tics, learning distraction techniques may be a promising alternative therapy.We propose to investigate the extent to which adult TS is associated with problems in attention and inhibition. To do this we will: a) assess attention and inhibition on a range of cognitive tasks (CANTAB); b) assess neurophysiological imbalance using transcranial magnetic stimulation; and c) assess the relevance of comorbid symptoms to indices of impairment. Results may provide the basis for the development of new therapies.

81. Emma Holmes - UCL Institute of Neurology

POSTER TITLE
How are familiar voices represented in auditory cortex?

AUTHORS
Holmes E, Johnsrude IS

ABSTRACT
The ability to understand speech in the presence of competing talkers is fundamental to successful verbal communication. When two talkers speak simultaneously, intelligibility is 10–20% better when target speech is spoken by a familiar talker (e.g., friend or spouse), than by someone unfamiliar (Johnsrude et al., 2013). How cortical representations of familiar voices facilitate improved intelligibility is currently unknown.We recruited pairs of friends and couples. We used functional MRI to measure brain activity while participants heard target sentences spoken by their familiar partner and by two unfamiliar talkers, who were the partners of other participants in the experiment. On each trial, participants reported words from the target sentence, which was either presented alone or simultaneously with another sentence spoken by a different talker (which was always unfamiliar).We used Representational Similarity Analysis (RSA) to compare patterns of activity evoked by familiar and unfamiliar target talkers. We show that the pattern of brain activity evoked by a familiar

talker is more robust to a competing talker than the pattern evoked by unfamiliar talkers. Further, the RSA difference between familiar and unfamiliar talkers is larger for participants who gain a larger speech intelligibility benefit from their partner's voice.

82. Melanie Koelbel - UCL GOS Institute of Child Health

POSTER TITLE
Does auto-adjusting positive airway pressure (APAP) aid memory and learning in children with sickle cell diseaseand sleep disordered-breathing?

AUTHORS
Kölbel, M, Stotesbury, H, Kawadler J, Howard J, Inusa B, Rees D, Chakravorty S, Pelidis M, Thein SL, Kirkham F and Slee A

ABSTRACT
Background:Sleep disordered breathing (SDB), common in children with sickle cell disease, disrupts sleep at night and seems to impair executive function and processing speed, which often find support in memory processes and impaired lead to difficulties in academic attainment.Methods:Randomised trial of auto-adjusting positive airway pressure (APAP) with 30 Patients (mean age 12.6) were randomised for a 6 month at home treatment of either APAP and standard care (n=15;) or standard care alone (n=15). Sleepiness was measured with the Epworth Sleepiness Scale (ESS)). Neuropsychological assessment was administered before and after treatment period.Results: Patient receiving the APAP treatment felt less sleepy (ESS: mean -2; 95% confidence intervals (CI) -3.13; -0.87) compared to controls (ESS: mean 0.15; 95%CI -1.03; 1.32).Raw scores for spatial memory performance improved after APAP treatment for (1) (Dot Location Total: mean 3.26; 95%CI 1.65; 4.87) vs. controls (mean -0.14; 95%CI -1.89; 1.61), p=0.012 and (Dot Learning: mean 2.50; 95%CI 1.29; 3.70) vs. controls (mean 0.20; 95%CI -1.11; 1.50), p= 0.21. There was no statistically significant difference for Dot Delay. Discussion:Improving daytime sleepiness aids concentration thought the day, hence, improves academic attainment. Improving spatial memory, important for planed and guided behaviour could support and improve other cognitive domains.

83. Junfei Liu - UCL Institute of Cognitive Neuroscience

POSTER TITLE
Examining the plasticity of the reading network: insights from deaf readers of Chinese

AUTHORS
Liu JF, Twomey T, Wu MK, Yang YM, MacSweeney M

ABSTRACT
Chinese orthography generally maps more closely to meaning than to sound. Previous behavioural studies have shown a greater reliance on semantic than phonological information during reading Chinese characters in both deaf and hearing participants. The only published fMRI study of deaf readers of Chinese showed greater activation in several regions in the right hemisphere during both rhyming and semantic tasks in deaf than hearing controls. But this study did not assess participants' reading levels. Therefore, the effect of deafness on the reading network cannot be dissociated from reading levels.Using functional magnetic resonance imaging method (fMRI), the present study aimed to examine the brain

network supporting reading Chinese characters in deaf and hearing participants who were matched on reading levels. Fifteen deaf and 15 hearing participants were asked to make rhyming and semantic judgements on two simultaneously presented Chinese Characters. Whole brain analyses showed no significant difference between the two groups regardless of task. This study suggests that Chinese deaf and hearing adults may develop similar reading strategies such as using semantic cues of Chinese characters during learning to read. Therefore, the effect of deafness on the Chinese reading network might be limited.

84. Diego Lorca-Puls - UCL Institute of Neurology

POSTER TITLE
The impact of sample size on the reproducibility of voxel-based lesion-deficit mappings

AUTHORS
Lorca-Puls DL, Gajardo-Vidal A, White J, Seghier ML, Leff AP, Green DW, Crinion JT, Ludersdorfer P, Hope TMH, Bowman H, Price CJ

ABSTRACT
This study investigated how sample size affects the reproducibility of voxel-based lesion-deficit mappings. Our effect of interest was the strength of the association between brain damage and speech articulation difficulties, as measured in terms of the proportion of variance explained. First, we identified a region of interest (ROI) by searching on a voxel-by-voxel basis for brain areas where greater lesion load was associated with poorer speech articulation using a large sample of 360 stroke survivors. We then randomly drew thousands of bootstrap samples from this data set that included either 30, 60, 90, 120, 180, or 360 patients. For each resample, we recorded effect size estimates and p values after conducting exactly the same lesion-deficit analysis within the previously identified ROI and holding all procedures constant. The results show (i) how often small effect sizes in a heterogeneous population fail to be detected; (ii) how effect size and its statistical significance varies with sample size; (iii) how low-powered studies (due to small sample sizes) can greatly over-estimate as well as under-estimate effect sizes; and (iv) how large sample sizes ($N \geq 120$) can yield highly significant p values even when effect sizes are so small that they become trivial in practical terms.

85. Yi Lu - UCL Institute of Cognitive Neuroscience

POSTER TITLE
Absence of visual input affects spatial cell activity

AUTHORS
Lu Y, Chen G, Burgess N, Wills T, Cacucci F

ABSTRACT
It is known that visual cues can exert control over the spatial firing fields of place and grid cells. However, it is still an open question whether vision affects grid and place fields independently or not. Previous studies have shown that, in mice, grid cells lose their hexagonal firing regularity in familiar environments when the lights are turned off (Pérez-Escobar et al., 2016; Chen et al., 2016). To further explore the relationship between grid cell and place cell firing, it is interesting to know how place cell firing in mice responds to darkness. We recorded place and grid cells concurrently while mice performed random

foraging in the dark. Our results demonstrate that the spatial selectivity of place cell firing is much preserved while the spatial regularity of grid cell firing patterns is more severely disrupted. Secondly, within simultaneously recorded place cell populations some place cells display stable fields that correspond to those in the light sessions, while others remap (change their firing location with respect to the light session or stop firing). These results indicate that visual inputs differentially and independently affect place and grid cell firing.

86. Laura Molina-Garcia - UCL Department of Cell and Developmental Biology

POSTER TITLE
Sexy learning in C. elegans: Integration of conflicting experiences

AUTHORS
Molina-Garcia L, Benavides-Laconcha S, Barrios A

ABSTRACT
To understand how the brain integrates conflicting (rewarding and aversive) memories during learning, we are dissecting a circuit for sexual conditioning in C. elegans. Sexual conditioning is a form of male-specific associative learning by which a rewarding experience with mates overrides an aversive association with starvation, thus switching the males' behaviour to a stimulus from repulsion to attraction (Sakai et al., 2013). Here it is shown that males can be sexually conditioned to many different chemosensory stimuli and this requires the male-specific MCM interneurons and the neuropeptide PDF. Two models have been proposed for how conflicting memories may be integrated during learning but conclusive mechanistic evidence for either one is lacking (Aso & Rubin, 2016). In one model, each memory is processed in parallel with different decay rates. In the alternative model, memories are integrated through reciprocal inhibition. In principle, the connectivity of the MCMs to the circuit for chemotaxis learning could support either form of integration (Sammut et al., 2015). Experiments testing each of these models will be presented. If integration occurs through reciprocal inhibition of reward and aversion, the prediction is that sexual conditioning will prevent the molecular changes that drive aversive learning (Cho et al.2016) from occurring.

87. Jake Ormond - Sainsbury Wellcome Centre for Neural Circuits and Behaviour

POSTER TITLE
Episodic memory encoding by a place cell sub-population

AUTHORS
Ormond J and Johansen JP

ABSTRACT
Study of the hippocampal place cell system has greatly enhanced our understanding of memory encoding for distinct places, but how episodic memories for distinct experiences occurring within familiar environments are encoded is not clear. Using an aversive spatial decision making task which induced partial remapping in CA1, we examined whether episodic experiences engaged a unique population of hippocampal neurons. We found that remapping cells exhibited distinct features not present in non-remapping cells. During memory encoding, they showed shifted theta phase preferences, suppression by aversive stimuli and their remapping closely tracked behavioral learning. Following learning,

remapping cells were more heavily involved in awake replay events, their degree of involvement correlated with their subsequent post-learning stabilization and they developed correlated firing patterns in aversive regions of the environment. Our data demonstrate a sequence of events occurring within a plastic subpopulation of CA1 place cells leading to the rapid incorporation of behaviorally relevant contextual information into a stable spatial representation.

88. Amalia Papanikolaou - UCL Division of Psychology and Language Sciences

POSTER TITLE
Interaction of adaptation states in the mouse primary visual cortex

AUTHORS
Papanikolaou A, De Franceschi G, Solomon SG

ABSTRACT
Sensory pathways in the brain adapt to the current environment by adjusting neuronal responses to the recent history of stimulation. How the adaptation state induced by one environment interacts with that induced by subsequent environments is unclear. We obtained extracellular recordings (n = 150) from the primary visual cortex of four awake mice in response to a vertical bar that randomly varied in horizontal location. The ensemble of bar locations was either uniform, or biased to one location. After initial exposure to a uniform ensemble, we presented a biased ensemble for 5-minutes before returning to the uniform ensemble. Biasing the ensemble decreased the gain of neurons with receptive fields near the adaptor, and repulsed receptive fields away from the adaptor. Return to a uniform ensemble increased gain and attracted receptive field profiles toward the previously adapted location, relative to pre-adaptation measurements. In a second experiment, 5-minutes exposure to one location bias was followed by 1-minute exposure to a new location bias. The second bias decreased the gain and repulsed the receptive fields of neurons around the newly adapted location. Neurons near the location of the original bias showed increase in gain, but no change in receptive field profile, suggesting dissociation of changes in gain and receptive fields. A mixture of both adaptation states was maintained during subsequent exposure to uniform ensembles. Our observations show that changes in environmental statistics lead to both rapid recalibration of neuronal responses, and a long-lasting aftereffect that is superimposed on subsequent adaptation states.

89. Heather Payne - UCL Institute of Cognitive Neuroscience

POSTER TITLE
Children born profoundly deaf show typical hemispheric asymmetries in cerebral blood flow during language production

AUTHORS
Payne H, Gutierrez-Sigut E, Woll B, MacSweeney M

ABSTRACT
Background: Most adults show left lateralisation for speech production (Price, 2012). The role of experience in the development of lateralisation is unclear. Children born deaf experience a drastically different spoken language input to hearing children, even if they use amplification. Measuring neural activity in this population has been difficult to date due to

incompatibility between imaging techniques and cochlear implants (CI).Aims: To test the effect of reduced auditory experience on language lateralisation, we measured lateralisation in children born deaf, using a child-friendly and CI-safe technique: functional transcranial Doppler sonography (fTCD).Methods: Using fTCD, we measured changes in cerebral blood flow velocity in the middle cerebral arteries of 21 children born deaf (>60dB loss in better ear) while they described an animation in spoken English or British Sign Language. A comparison group of hearing children were also tested.Results: We found left lateralisation during language production (mean lateralisation index=2.2 , sd=3.3; t(20)=3.06, p=.006), with no significant difference between deaf and hearing children (p>.1). The distribution of children with left (78%), right (16%), and low (6%) lateralisation was comparable with that of hearing children.Conclusion: Left lateralisation during language production is not dependent on auditory experience of spoken language.

90. Jacqueline Pitchforth – UCL GOS Institute of Child Health

POSTER TITLE
Prevalence of corticosteroid use and learning difficulties, behavioural or autism in patients with Duchenne Muscular Dystrophy

AUTHORS
Pitchforth JM, Quinlivan R, Manzur A, Munot P, Muntoni F

ABSTRACT
Corticosteroid use is a gold standard of care in (DMD). Adverse behaviour can be a major side-effect, especially for children with learning difficulties (LD), behavioural difficulties (BD), and/or autism. Our objective was to compare the prevalence of steroid use in a paediatric DMD population with and without these comorbidities.A cross-sectional audit of 150 DMD patients aged 5-21years was undertaken. The cohort was divided into 3 groups based on treatment with steroids. Data was collected on comorbidities. The prevalence of LD was 23% in GroupA (currently on steroids), 44% in GroupB (trialled and stopped steroids) and 31% in GroupC (steroid naïve having never taken any corticosteroids). BD prevalence was 24% in GroupA, 50% in GroupB and 19% in GroupC. Autism prevalence was 17% in GroupA, 22% in GroupB and 19% in GroupC. Of those with LD, BD and autism: 68%, 70% and 74% were on steroids compared to: 81%, 80% and 78% without LD, BD and autism.Prevalence of steroid use in DMD was lower in those with comorbidities. In view of the positive effect of steroids on DMD progression, this data could impact on long-term prognosis, with DMD boys that have LD, BD or autism having a poorer outcome.

91. Sonia Ponzo - UCL Division of Psychology and Language Sciences

POSTER TITLE
Balancing body ownership: visual capture of proprioception and affectivity during vestibular stimulation

AUTHORS
Ponzo S, Kirsch LP, Fotopoulou A, Jenkinson PM

ABSTRACT
The experience of our body as our own involves integrating different sensory signals (such as visual, proprioceptive, vestibular and interoceptive ones) according to their contextual

relevance. Both vestibular and interoceptive manipulations, separately, have been showed to modulate body ownership. However, the role of the vestibular system in balancing sensory modalities has not been clearly defined yet, with studies showing different weighting in favour of either vision or proprioception in multisensory integration tasks and no study investigating the combined effect of vestibular and interoceptive systems on embodiment. We used Galvanic Vestibular Stimulation (left, right and sham) in a Rubber Hand Illusion task with healthy participants (N=26) to investigate how vestibular stimulation of the right hemisphere (LGVS) affects proprioception and body ownership following mere visual exposure to a rubber hand and manipulations of synchronicity and affectivity of touch. Our results show that LGVS significantly increased proprioceptive drift towards the rubber hand during mere visual exposure to the rubber hand. Moreover, it also enhanced participants' embodiment of the rubber hand during synchronous affective touch. These findings suggest that the vestibular system influences body ownership by re-weighting the relationship between proprioception and vision, as well as the relationship between proprioception, vision and affective touch.

92. Vanessa Puetz - UCL Division of Psychology and Language Sciences

POSTER TITLE
Differential effects of abuse vs. neglect in childhood on neural threat processing

AUTHORS
Puetz VB, Viding E, Gerin MI, Pingault JB, Sethi A, Knodt A, Radtke SR, Brigidi BD, Harir AR & McCrory E

ABSTRACT
It has been shown that childhood maltreatment alters neural reactivity to threat, which may subsequently contribute to later psychopathology. However, it remains unclear whether the experience of abuse (i.e. physical, emotional and sexual abuse, characterized by active harm) or neglect (physical and emotional deprivation) differentially impact this neural reactivity (Sheridan and McLaughlin, 2014). Identifying such differential effects is important in developing interventions that more effectively mitigate the negative consequences associated with maltreatment broadly. Here we use data from a study of 1330 young adults to investigate, for the first time, differences in neural reactivity to facial cues signalling threat in individuals with childhood abuse experiences (n=70), childhood neglect experiences (n=87), or both childhood abuse and neglect experiences (n=50). These groups were compared with a group of non-maltreated participants (n=207) propensity score matched (PSM) on gender, age, IQ, psychopathology and SES, which allowed for critical isolation of differential effects associated with different maltreatment histories. Our analyses revealed that while childhood abuse was associated with heightened localised threat reactivity in ventral amygdala, experiences of neglect were associated with heightened reactivity in dorsal amygdala as well as in a distributed cortical fronto-parietal network supporting complex social and cognitive processing. Unexpectedly, combined experiences of abuse and neglect were associated with hypo-activation in several higher-order cortical regions as well as the amygdala. Our findings provide unique evidence that different forms of childhood maltreatment exert differential effects at the level of neural threat reactivity, which may in turn inform the diversity of associated psychopathological outcomes as well as efforts for more effective intervention.

93. Sabine Reichert - UCL Department of Cell and Developmental Biology

POSTER TITLE
The neuropeptide Galanin facilitates homeostatic rebound sleep in zebrafish

AUTHORS
Reichert S, Arocas OP, Rihel J

ABSTRACT
Sleep is controlled by a circadian timer and a homeostatic process that builds during wake and dissipates during sleep. The homeostatic process is widely considered a function of the duration of wakefulness but it is unclear how the intensity of brain activity in the preceding waking period influences subsequent sleep. Using a novel pharmacological paradigm, we find that zebrafish larvae experience sustained rebound sleep after an acute activation of widespread neuronal activity. By decoupling homeostatic sleep drive from waking time, we show that rebound sleep strongly correlates with total neuronal but not physical activity. During rebound sleep, expression of several neuropeptides, including the putative sleep regulator, galanin, is upregulated, and Galanin neurons in the preoptic area are highly active. Since galanin mutants have severely impaired homeostatic rebound sleep, we propose that Galanin neurons are sensitive to global neuronal activity and act as an output arm for the vertebrate sleep homeostat.

94. Marion Rouault - UCL Institute of Neurology

POSTER TITLE
Learning about self-performance in the absence of feedback

AUTHORS
Rouault M, Dayan P, Fleming SM

ABSTRACT
Metacognition, the ability to internally evaluate our own cognitive processes, is critical for adaptive behavioral control, particularly as most real-life decisions lack immediate feedback. Previous studies have focused on mechanisms supporting confidence estimates at the single-trial level, but little is known about the aggregation of confidence over longer time-scales, to form global beliefs about self-performance. For instance, when choosing a career, one may learn about self-competencies over multiple instances. Although learning from external feedback has been extensively studied, little is known about how humans use internal confidence signals to learn about self-performance over time in the absence of feedback. Here we developed a novel behavioral paradigm to adress this issue. In three studies, subjects played short tasks in parallel and eventually were asked to choose the task in which their performance was highest. Subjects' task choices were captured by a hierarchical model which updated global self-performance beliefs based on local confidence estimates. Strikingly, subjects show a pervasive underestimation of their performance in the absence of feedback, compared to a condition with full feedback, despite objective performance being unaffected. Our findings build a bridge between literatures on metacognition and learning, and support a functional role for confidence in higher-order behavioral control.

95. Philipp Schwartenbeck - UCL Institute of Neurology

POSTER TITLE
Neural computations underlying compositional judgements

AUTHORS
Schwartenbeck P, Kurth-Nelson Z, Mark S, Behrens T

ABSTRACT
Learning adequate representations of the environment is central to adaptive behaviour. This involves the formation of sparse and generalisable knowledge that forms a 'mental map'. Crucially, this map allows generalising knowledge to novel items, even in the absence of any previous experience. The neuronal and computational mechanisms underlying these processes are unclear. To interrogate these mechanisms, we developed a novel task in which subjects have to construct objects in a two-dimensional world. Importantly, this allows subjects to make judgements about a multitude of novel items built according to the relational structure of the task.I will present behavioural evidence that subjects successfully acquire and transfer such relational knowledge to novel stimuli. I will also present key predictions for the neural implementation of this knowledge, which we will test using functional neuroimaging. We predict that the relational knowledge underlying stimulus construction will be encoded in the entorhinal cortex (EC) and medial prefrontal cortex (PFC). Specifically, we predict that the EC encodes the underling dimensions (principal components) used for constructing novel items. We will contrast this global relational code with a stimulus specific and identity-based code, which we expect in the hippocampus and ventral PFC.

96. Chintan Trivedi - UCL Department of Cell and Developmental Biology

POSTER TITLE
Understanding innate behavioural states and underlying neural mechanisms in larval zebrafish

AUTHORS
Trivedi CA, Lekk I, Faro A, Mackay E, Martinho R and Wilson S

ABSTRACT
What are the signatures of internal state exhibited during spontaneous or innate behaviours? Such innate behaviours result from a complex interaction between internal factors such as stress or hunger and external factors such as global changes in the sensory environment. Not much is known about the interplay between internal and external factors in regulating behavioral states. Using the larval zebrafish as a model system, we developed assays and data analysis methods to reveal innate behavioural states during spontaneous exploration of a homogeneous environment. Furthermore, using mutants that disrupt a specific neuromodulatory circuit (the Habenula-Raphe pathway), we show that these zebrafish have a different basal behavioural state. We are now investigating the neural correlates of these differing innate behavioural states through population calcium imaging and whole-brain registration of neurotransmitter phenotypes at a single neuron level in wild-type and mutant zebrafish. These approaches collectively will help us identify functional circuits that drive innate behavioural states and potentially participate in modulation of these states.

97. Hande Tunbak - UCL Division of Medicine

POSTER TITLE
Development of social preference in the zebrafish brain

AUTHORS
Tunbak H, Dreosti E

ABSTRACT
Social interactions are a fundamental and adaptive aspect of animal and human everyday life. Despite the fact that several psychiatric and neurological diseases are characterised by prominent impairments of social functioning, little is still known about the development or detailed circuitry. A fundamental condition for social behaviour is social preference, the predisposition of animals to recognise and approach another counterpart. We have previously shown that juvenile zebrafish are one of the best models to study the formation of the social preference network: they show complex social behaviour and are still optically transparent. We have also shown that their social preference behaviour can be modified by environmental changes, such as drug exposure. By combining whole mount mRNA in-situ hybridization of relevant genes with deep two-photon imaging, we are now identifying in detail the main brain areas that are involved in processing visual social stimuli. In addition, we are exploring the impact of social deprivation on the development of the social brain circuitry and behaviour.

98. Tae Twomey - UCL Institute of Cognitive Neuroscience

POSTER TITLE
Examining the effect of language experience on plasticity in superior temporal cortices in deaf and hearing signers

AUTHORS
Twomey T, Waters D, Price C, MacSweeney M

ABSTRACT
It has been clearly demonstrated that parts of the superior temporal cortex (STC) are activated more in deaf than hearing people. Here we examined the impact of duration of sign language experience on the extent of plasticity in STC. We collected fMRI data as deaf and hearing signers (N=52) who learnt British Sign Language (BSL) either early or after the age of 15 years detected a semantic anomaly in BSL sentences; and a perceptual target in strings of nonsense gestures. A main effect of hearing status (deaf > hearing) was found in the STCs bilaterally, replicating previous findings. This effect was centred on Heschl's gyrus and included planum polare and planum temporale. Interestingly, when the nonsense gesture stimuli were used as a baseline, the group difference disappeared. The interaction between hearing status and sign language experience was not significant, irrespective of baseline. The current study demonstrates the importance of the baseline in testing for crossmodal plasticity: an obvious but often overlooked point. Our findings suggest that plasticity in the parts of STCs identified here is primarily driven by deafness and it not influenced, to any great extent, by sign language experience or linguistic status of the input.

99. Andrew Watson - UCL Institute of Neurology

POSTER TITLE
Cognitive subtypes in first-episode psychosis: An empirical longitudinal study of relationship to cognitive, symptom and functional outcomes

AUTHORS
Watson AJ, Deakin B, Suckling J, Dazzan P, Lawrie SM, Upthegrove R, Husain N, Chaudhry I, Dunn G, Jones PB, Lisiecka D, Lewis S, Barnes TRE, Williams S, Hopkins S, Knox E, Kelly B

ABSTRACT
Variable outcomes following a first-episode of psychosis are partly attributable to heterogeneity in cognitive functioning. Previous work in first episode psychosis has identified clinically meaningful cognitive subtypes based on pre-specified differences in estimated premorbid and current cognitive functioning. We used an empirical clustering technique to examine whether these cognitive profiles can be replicated with an unbiased method, their relationship with clinical, cognitive and global functioning at psychosis onset as well as their stability over time. K-means cluster analysis revealed three cognitive subgroups: 28% showing preserved premorbid and current IQ (PIQ); 29% displaying compromised premorbid and current IQ (CIQ). The preserved group performed significantly better than healthy controls on all IQ measures, with the exception of processing speed. Cognition remained relatively stable over 12-months following a first episode, and was largely independent of clinical symptoms. Findings show cognition to be a core symptom of schizophrenia, with relative stability over time.

Sensory and Motor Systems | Drama Studio

100. Paride Antinucci - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
A motor command centre linking vision to action in zebrafish hunting behaviour

AUTHORS
Antinucci P and Bianco IH

ABSTRACT
How do sensory representations trigger the selection and execution of appropriate motor programs? In this project, we aim to understand the activity patterns and circuit mechanisms of a key neural centre in the zebrafish pretectum capable of triggering hunting routines in response to prey-like visual stimuli. Using a wide range of techniques, including simultaneous behavioural monitoring and two-photon calcium imaging in partially tethered larvae, optogenetic stimulations of selectively labelled neurons, and targeted cell ablations, we are dissecting the structural and functional input-output connectivity patterns of this motor command centre as well as its necessity and sufficiency for hunting behaviour. To understand the circuit motif implemented by this command centre, we aim to reveal how it coordinates activity in downstream reticulospinal and oculomotor neurons controlling tail and

eye movements. This work will shed new light on how a hunting circuit in the vertebrate brain generates goal-directed actions from visual representations of prey-like visual stimuli.

101. Jonathan Ashmore - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Cochlear outer hair cell motors as transporters

AUTHORS
Ashmore J, Kulkovska L, Chui N, Delpoukas A

ABSTRACT
The inner ear of the mammalian contains an intrinsic power amplifier. It is built from the population of outer hair cells which are both mechanosensitive and simultaneously act as fast biological piezoelectric devices. The molecular basis of such actuators is a protein termed prestin, a member of the SLC26 anion-bicarbonate transport superfamily. Two unsolved problem are a) what is the structure of the protein and b) does the mammalian outer hair cell prestin transport anions?Although mammalian prestin forms a tetramer in the outer hair cell basolateral membrane, the structure has become clearer since the publication of the crystal structure of the bacterial homolog dgSLC26. The significance of the C-terminal STAS domain will be proposed. The transport properties of the mammalian prestin are more problematic since we find it to be a low efficiency antiporter. It can be shown to be a bicarbonate transporter by tagging the prestin with pHluorin, and to transport chloride by using the sensitivity of a YFP tag to anions. However the high expression levels of prestin also determines cell volume regulation; imaging experiments in the in situ mouse cochlea will be presented to show such changes.

102. Davide Bono - UCL Institute of Cognitive Neuroscience

POSTER TITLE
Where is my mouth? Rapid experience-dependent plasticity of perceived mouth position in humans

AUTHORS
Bono D, Haggard P

ABSTRACT
Moving the hand to the mouth is a basic and primitive motor action. However, this action presupposes an accurate representation of the position of the mouth in space. The mouth might thus be seen as a fixed reference point or ‘egocentre’ in personal space representation. Several studies using the ‘rubber hand illusion’ have suggested that the perceived position of hands, feet and other body parts can be adapted by multisensory experience. Yet, the notion that the mouth forms a reference point for bodily awareness might suggest that the representation of mouth position could not be adapted in the same way.The present study aims to investigate the spatial representation of mouth position using Chalk Teeth Illusion (CTI), a novel illusion based on the correlation of tactile and proprioceptive events. Participants’ fingers were passively stroked against the teeth of an invisible dental model, while the experimenter stroked the participant’s own teeth either synchronously or asynchronously. This tactile-proprioceptive stimulation lead to a drift in the perceived position of the participant’s teeth towards the dental model (expt 1), but only if the

stimulation was synchronous. Questionnaire responses confirmed an altered bodily awareness with respect to the mouth. Interestingly, the CTI was not strongly affected by body-representational, or 'top-down' factors that were previously shown to influence the rubber hand illusion. For example, altering the texture of the teeth on the dental model did not break the CTI. Removing one of the teeth from the dental model had a modest, trend-level effect on the CTI (Experiments 3 and 4). Our result suggests the representation of mouth position is not fixed or innate, but is surprisingly dependent on short-term multisensory experience.

103. Philip Coen - UCL Institute of Neurology

POSTER TITLE
Audiovisual spatial localization in head-fixed mice

AUTHORS
Coen P, Wells M, Liang L, Carandini M, Harris K

ABSTRACT
Many animals determine the location of objects in space by integrating auditory and visual cues. However, it has been suggested that mice integrate these cues differently from other mammals, allowing auditory cues to dominate when they conflict with visual cues. Moreover, it is not known whether mice use audiovisual integration to locate objects in space.To study audiovisual spatial integration, we modified a two-alternative forced-choice visual task in head-fixed mice (Burgess et al., Cell Reports). In our task, mice turn a wheel to indicate the position of a stimulus based on visual and/or auditory cues. The positions of auditory and visual cues varied independently, and could agree or disagree.Mice integrated auditory and visual cues without giving dominance to either modality. Indeed, a logistic model precisely predicted the responses to audiovisual stimuli based on summation of visual and auditory signals, with no cross-modal interactions. The model performed equally well whether the auditory and visual cues agreed or disagreed.Our results show that mice integrate audio and visual cues to localize objects, and the accuracy of our behavioural model indicates that the underlying computation is summation. We are now using scanning optogenetic inhibition to identify cortical regions involved in this process.

104. Quazi Fahm E Deen - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Investigating the role of Nav1. 8 in action potential propagation in nociceptors using the selective blocker PF-01247324

AUTHORS
Deen QFE, Koltzenburg M

ABSTRACT
Tetrodotoxin (TTX)-resistant Nav1.8 is preferentially expressed in peripheral nociceptors and generates the majority of the depolarizing inward current during an action potential (AP). Here, we used skin-saphenous nerve in vitro preparation/isolated sciatic-tibial nerve segments from C57Bl/6 mice to investigate whether acute pharmacological blockade of Nav1.8, using PF-01247324 (novel Nav1.8 blocker), has a demonstrable and selective effect

on AP propagation of peripheral putative nociceptors. In non-desheathed saphenous nerve, 10 µM PF-01247324 reduced the compound action potential (CAP) of A- and C-fibres by 15% and 19%. Application of 1µM TTX did change the amplitude of A- or C-fibre CAP so we hypothesised the perineurium to be the diffusion barrier. In desheathed sciatic-tibial nerves, 10µM PF-01247324 decreased the A-fibre CAP amplitude by 36% and that of C-fibres by 48%. Application of 100µM PF-01247324 decreased A-fibres by a further 2% and C-fibres by a further 7%. (p>0.1; 10 vs 100µM). Both 10 and 100µM PF-01247324 produced a small shift in AP onset latency when there was a reduction in CAP amplitude consistent with voltage-gated Na+ channel blockade. Our current results show that PF-01247324 does not abolish AP conduction completely. It raises concerns that blockade of Nav1. 8 has limited utility as an analgesic principle.

105. **Miranda Dyson - UCL Department of Genetics, Evolution & Environment**

POSTER TITLE
Characterising dopamine receptor- Dop1R1 expression in the Drosophila ellipsoid body

AUTHORS
Dyson M

ABSTRACT
A primary function of the basal ganglia in the mammalian brain is the initiation and maintenance of action through the relay of limbic, sensorimotor and associative information. The central complex in the insect brain is thought to share a deep homology with the basal ganglia.Similarities between the neural architecture of these two structures, their associations and communications, and their involvement in action indicates a potential parallel function. The following work centres around the characterisation of the D1 receptor; Dop1R1. Visualisation of its expression pattern through immunolabelling revealed targeted localisation to specific regions of the central complex. The D1 expression pattern was visible in defined rings of the ellipsoid body (EB), which are supplied by the ring neurons, via the lateral triangles. A dense D1 expression was seen to ramify the distal rings of the EB. Specific D1 innervation was also observed in the medial fan-shaped body layers as well as the anterior optic tubercle, revealing a novel visual pathway that associates with the EB. These results lend further support to a basal ganglia-central complex homology and suggest the presence of a D1/D2 action circuit comparable to that in mammals, modulating action in Drosophila.

106. **Oliver Gauld - Wolfson Institute of Biomedical Research at UCL**

POSTER TITLE
Two-photon all-optical interrogation of L2/3 mouse barrel cortex during a sensory discrimination task

AUTHORS
Gauld OM, Packer AM, Russell LE, Hausser M

ABSTRACT
To identify causal links between stimuli, neural activity and behaviour it is important to measure and manipulate neural activity in awake behaving animals with cellular resolution. Recently developed ‘all-optical’ methods for simultaneous two-photon calcium imaging and

holographic optogenetic photostimulation are advantageous for this goal as they allow targeting of optical interrogation based on the functional signature of the neurons. Here we apply an 'all-optical' approach (Packer et al, 2015) to interrogate layer 2/3 barrel cortex during a sensory discrimination task. Head-fixed mice were injected with a calcium indicator (GCaMP6s) and an opsin (C1V1), and an imaging window was installed over barrel cortex. Mice were trained to discriminate single-whisker deflections in a two-alternative forced choice task. Quantifying choice responses across stimulus conditions yielded high-quality psychometric curves. An electrically tuneable lens and a spatial light modulator enabled simultaneous volumetric two-photon calcium imaging and 3D holographic photostimulation during behaviour. During task performance, a sparse population of neurons showed stimulus and choice-modulated activity. Ongoing experiments are being performed to selectively manipulate these functionally relevant neurons during behaviour. These experiments will provide new insights into the mechanisms by which sensory information is encoded in cortical circuits, and how this information influences behaviour.

107. **Nathaniel Hafford Tear - UCL Institute of Ophthalmology**

POSTER TITLE
Antisense therapy for a common corneal dystrophy ameliorates TCF4 repeat expansion-mediated toxicity

AUTHORS
Hafford Tear NJ, Zarouchlioti C, Sanchez-Pintado B, Klein P, Liskova P, Dulla K, Semo M, Vugler AA, Muthusamy K, Dudakova L, Levis HJ, Skalicka P, Hysi P, Cheetham ME, Tuft SJ, Adamson P, Hardcastle AJ, Davidson AE

ABSTRACT
Fuchs endothelial corneal dystrophy (FECD) is a common disease for which corneal transplantation is the only treatment option in advanced stages, and alternative treatment strategies are urgently required. Expansion (≥50 copies) of a non-coding trinucleotide repeat in TCF4 confers >76-fold risk for FECD in our large cohort of affected individuals. An FECD subject-derived corneal endothelial cell (CEC) model was developed to probe disease mechanism and investigate therapeutic approaches. The CEC model demonstrated that the repeat expansion leads to nuclear RNA foci, with the sequestration of splicing factor proteins (MBNL1 and MBNL2) to the foci and altered mRNA processing. Antisense oligonucleotide (ASO) treatment led to a significant reduction in the incidence of nuclear foci, MBNL1 recruitment to the foci, and downstream aberrant splicing events, suggesting functional rescue. This proof-of-concept study highlights the potential of a targeted ASO therapy to treat the accessible and tractable corneal tissue affected by this repeat expansion-mediated disease.

108. **Steven Jerjian - UCL Institute of Neurology**

POSTER TITLE
Spinal modulation during action observation in the macaque monkey

AUTHORS
Jerjian SJ, Lemon RN, Kraskov A

ABSTRACT
Observation of grasp elicits activity in macaque motor areas, including pyramidal tract neurons (PTNs) projecting to the spinal cord. Some PTNs suppress firing during observation. The net effect of action observation on spinal circuits is poorly understood.One rhesus macaque was trained to perform or observe reach-to-grasp movements on two objects, affording precision grip and whole-hand grasp. On some observation trials, grasp visibility was altered, with a screen going opaque either after experimenter movement onset, or before information related to the upcoming observed grasp was available. Biphasic stimuli were delivered during task performance via electrodes implanted in the left medullary pyramid (300μA, 1.66Hz), and we recorded muscle activity through subcutaneous electrodes in right hand and arm muscles. Stimuli timings were binned relative to multiple task events, and average motor evoked potential (MEP) amplitudes within bins were compared across task epochs and conditions.During grasp observation, we found a specific facilitation of MEPs relative to baseline in the first dorsal interosseous (1DI) muscle for precision grip. This effect disappeared if grasp was obscured and the target object could not be predicted.Action observation can produce grasp-specific facilitation of spinal excitability, depending on whether the upcoming grasp can be observed or predicted.

109. Joanna Lau - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Supraspinal activity patterns controlling locomotion

AUTHORS
Lau JYN, Fitzgerald JE, Bianco IH

ABSTRACT
How does the brain control the execution of distinct locomotor behaviours? We are investigating this problem by examining population activity in the reticulospinal complex of larval zebrafish as they perform distinct classes of swims, and by building models describing the relationship between neuronal activity and low-level locomotor kinematics.Using transgenic animals expressing GCaMP6f throughout the supraspinal reticulospinal population, we combine two-photon calcium imaging of neural activity with high speed behavioural tracking during diverse visually-evoked swimming. We find that different swim types are associated with distinct, but partially overlapping, patterns of network activity. Using regression approaches we are building encoding models relating the activity of single cells to low-level motor kinematics. Whereas some neurons have activity related to kinematic features that are common to all swim types, we also find more specialised neurons that appear to be associated with particular motor kinematics that define very specific swim types. Precise laser ablation of such cells produces specific kinematic deficits, without affecting shared elements of locomotion.Our current data support a model in which sparse subsets of supraspinal neurons comprise distinct “kinematic modules”, which are differentially, and combinatorially recruited to generate the diversity of locomotor behaviours.

110. Pureza Laudiano-Dray - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Neural encoding of somatosensory input in very pre-term human infants

AUTHORS
Whitehead K, Laudiano-Dray P, Meek J, Fabrizi L

ABSTRACT
Neonatal animal models indicate that somatosensory-evoked neuronal bursting activity refines early sensory circuits, and that somatosensory maturation follows a rostral-caudal gradient. However, somatosensory development is poorly understood in human infants across the equivalent of the last trimester of gestation.To assess how somatosensory input is cortically encoded in the developing human brain, and whether this differs between body areas, we recorded EEG following mechanical stimulation of the upper and lower limbs in 40 healthy pre-term infants 28-35 weeks corrected age. Somatosensory stimulation evoked cortical bursting activity, especially in the delta and alpha-beta frequency bands. Somatosensory responses have a distinct developmental trajectory following hand and foot stimulation, with the former characterised by a prominent decrease in the delta component, while the latter was characterised by a prominent decrease in the alpha-beta component. This suggests that somatosensory circuits mature differently for hand and foot representations, as in animal models. Meanwhile, the somatosensory response evoked by stimulation of either limb became more topographically specific over the pre-term period, indicating refinement of cortical maps.

111. Andrew Peters - UCL Institute of Ophthalmology

POSTER TITLE
Corticostriatal interactions during visually-guided behavior

AUTHORS
Peters AJ, Steinmetz NA, Zatka-Haas P, Harris K, Carandini M

ABSTRACT
Animals can learn arbitrary stimulus-response associations. Although it is unknown how this process occurs, accumulating evidence has implied the importance of interplay between brain regions, with particular focus on the cortex and striatum. We are currently investigating how the cortex and striatum interact during decision making in mice by combining a visually-guided behavior with simultaneous widefield calcium imaging of the cortex and electrophysiology with Neuropixels probes in the striatum. These mesoscopic techniques allow us to characterize inter-areal relationships and activity propagation across many regions of the brain.Using this approach, we have been able to reveal correlations in activity between brain regions. Specifically, the cortex is topographically related to the striatum, where a posterior-to-anterior gradient of cortex corresponds to a medial-to-lateral gradient within striatum. This is consistent with and confirms the functional relevance of known anatomical connections. Activity during visually-guided decision making propagates along the same gradients, starting with visually-related posterior cortex and medial striatum and ending with motor-related frontal cortex and lateral striatum. We are currently examining which regions first carry decision-related information to ultimately provide evidence for what location or interaction of locations are involved in transforming sensation into action.

112. Joana RIbeiro - UCL Institute of Ophthalmology

POSTER TITLE
Transplantation of mouse end human ESC-derived photoreceptor precursors into Aipl1 -/- mouse model

AUTHORS
Ribeiro J, Kloc M, Naeem A, Sampson RD, Hoke JD, Smith AJ, Pearson RA, Gonzalez-Cordero A, Ali RR

ABSTRACT
Cell transplantation offers a treatment for advance retinal degeneration due to photoreceptor cell loss. This study aims to establish the optimal developmental stage of mouse embryonic stem cell (mESC) and human embryonic stem cell (hESC)-derived photoreceptors into the advanced degenerated AIPL1-/- retina.The Aipl1-/- model presents rapid retinal degeneration. Transplantation experiments mESC-derived photoreceptor precursors were isolated at different stages in vitro and transplanted into AIPL1-/- mice. Furthermore, dissociated photoreceptor cells or the entire retinal sheets derived from hESC were also transplanted into this model. Following transplantation visual function was assessed and eyes were analysed post-mortem.Following transplantation, despite maturation and the presence of pre-synaptic proteins in the donor mESC and hESC-derived photoreceptor cells no significant improvement in visual function was detected. This data shows mESC and hESC-derived photoreceptors survival and maturation following transplantation into a complete degenerated retina. Establishment of the optimal donor cell age for transplantation into the advance degenerated retina will aid the development of future clinical studies.

113. Hana Ros - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Heterogeneous mossy fiber activity patterns and their implications for sensorimotor encoding in the cerebellar cortex

AUTHORS
Roš H, Sadeh S, Cayco-Gajic NA and Silver RA

ABSTRACT
The brain gathers information about the body and the surrounding world, enabling it to build internal representations and to plan and execute movement. The cerebellum is thought to predict the sensory consequences of movements and coordinate movement by learning sensorimotor relationships. Cerebellar mossy fiber (MF) inputs convey a wide range of sensory and motor related information that is integrated by granule cells. But little is known about how populations of MFs encode sensory and motor signals locally within the input layer. To address this we used adeno-associated viruses to express the genetically encoded calcium indicator GCaMP6f in distinct precerebellar nuclei, implanted a chronic window over Crus I/II and vermis of the cerebellar cortex and performed two-photon (2P) imaging of MFs in awake behaving mice. Since MF synaptic rosettes are sparsely distributed, we used high speed 3D 2P Acousto-Optic Lens (AOL) microscopy to record their activity within a 250 x 250 x 250 µm imaging volume. We observed a wide range of activity patterns across MFs, with individual MFs exhibiting either an increase or a decrease in activity with locomotion. Surprisingly, positively and negatively modulated MFs were often observed within the same

local region (i.e. 10 - 100 µm), suggesting that individual GCs could be innervated by functionally opposed inputs that cancel out. To understand how such mixed local populations of bidirectionally modulated MFs affect population coding in this circuit, we analytically calculated the linear Fisher information in randomly connected feedforward MF-GC networks, either with bidirectionally or unidirectionally modulated inputs. We show that opposite signed MFs can counteract input noise correlations to enable better signal propagation in GCs. Our results suggest that MFs utilise a population code that conserves sensorimotor information by counteracting the deleterious effects of noise correlations.

114. Francisco Sacadura - Wolfson Institute of Biomedical Research at UCL

POSTER TITLE
"Thermal grill" model of human pain perception facilitates late but not early somatosensory evoked potentials

AUTHORS
Sacadura F, Brookes T, Beck B, Fardo F, Haggard P

ABSTRACT
The thermal grill illusion (TGI) involves a paradoxical burning heat sensation evoked by alternating non-noxious warm and cold temperatures. The TGI has been proposed as an experimental model of pain in humans. Reduced intracortical inhibition has been reported in chronic pain patients. We therefore combined TGI conditioning with double-digit electrical stimulation to investigate whether TGI affects intracortical inhibition, measured by the underadditivity of somatosensory-evoked potentials (SEPs) in double-digit stimulation. 32 participants received electrical stimulation to the right index, right middle or both fingers simultaneously, during four fingertip thermal stimulation conditions: warm index/cold middle (TGI), warm/neutral, neutral/cold or neutral/neutral. Importantly, thermal and electrical stimuli were adjusted according to individual pain and detection thresholds. To measure TGI, participants adjusted an additional thermal stimulus in the left hand to match the perceived temperature on the right middle finger. We found significant temperature overestimation of cold when paired with warm, confirming TGI. We found no thermal effects in early sensory SEP components (N20, P27, N33, P45, N80). However, TGI modulated later cognitive SEP components (P100, N140). Specifically, TGI conditioning increased N140 amplitude in single-digit, but not double-digit, stimulation. Our results suggest TGI conditioning increases the gain of later, "attentional" somatosensory processing and intracortical inhibition.

115. Ara Schorscher-Petcu - Wolfson Institute of Biomedical Research at UCL

POSTER TITLE
An optical platform for ultrafast and spatially precise evoked and quantified protective pain behaviour

AUTHORS
Schorscher-Petcu A, Browne L

ABSTRACT
Classically, nociceptive behaviour is studied using naturalistic stimuli that are usually limited to relatively low spatiotemporal precision. More recently, transdermal optogenetic approaches have been developed, allowing for precise light-driven activation of genetically

targeted nociceptor populations in freely-behaving mice. Here, we have developed a behavioural platform that provides vastly improved spatiotemporal precision and enables fully automated quantification. The system can target a laser pulse of defined duration (down to 100 microsec), diameter (down to 150 micrometer), and intensity to the plantar surface of a mouse paw. Withdrawal behaviours are concomitantly quantified at the millisecond timescale. We developed software to automate the analysis of high-speed recordings allowing for rapid objective detection and quantification of local withdrawal events, partial withdrawals (twitches), and whole body global repositioning. We validated the system in mice expressing ChR2 in a broad class of primary afferent nociceptors and investigated how varying a single optical stimulation affects the probability and magnitude of withdrawal events. This platform allows us to precisely probe the sensory-motor input-output relationship of genetically-defined cutaneous afferent subpopulations, to investigate the neural circuits driving these behaviours, and how those are transformed in disease.

116. Richard Somervail - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Spatially-defined modulation of the peri-personal space field for the defensive eye-blink

AUTHORS
Somervail R, Buffachi R, Iannetti GI

ABSTRACT
Sudden stimuli occurring within the defensive peripersonal space (DPPS), a protective area surrounding the body, elicit stronger defensive reactions. Recently our group has used electrical stimulation of the hand to induce a blink reflex (the hand-blink reflex; HBR) to characterise DPPS in humans: by changing the hand/stimulus position, the HBR magnitude is reliably modulated, allowing us to infer the spatial extension of the DPPS. Here we hypothesised that as DPPS has a protective function, fast-moving & threatening visual stimuli would expand the DPPS in the direction of their source. We put healthy human participants in immersive virtual reality environments and delivered electrical stimuli to the hand while fast-moving virtual arrows hit the participant from several directions. In other trials we delivered shocks without arrows. The HBR magnitudes of shocks delivered with arrows were not consistently different from those without arrows. However, shocks delivered while the participant was hit by arrows which were spatially congruent to the hand being stimulated produced larger HBR magnitudes than arrows which were incongruent to the hand. We therefore conclude that DPPS selectively expanded in the direction of the threat.

117. Matthew Topping - UCL Ear Institute

POSTER TITLE
Using mechanotoxic insecticides to probe sexually dimorphic auditory transduction and amplification in mosquitoes

AUTHORS
Topping MP, Albert JT

ABSTRACT
Hearing and acoustic communication play crucial roles in the mosquito life cycle. Mosquito auditory function is anatomically well understood; the flagellum acts as a sound receiver, with auditory cells being formed by Johnston's organ chordotonal neurons. Functionally however, mosquito hearing and auditory transduction are not well understood.Our experiments focus on auditory transduction and amplification in three mosquito species using Laser Doppler Vibrometry. We demonstrate that auditory transducers introduce characteristic signatures into sound receiver mechanics. We also find that auditory transduction and amplification are sexually dimorphic, with ultra-sensitive transducer populations occurring only in males. Spontaneous, self-sustained oscillations (SOs) of the flagellum are also male specific and result in substantial energy gain increases (up to 4 orders of magnitude greater than in a non-SO state). Exposing mosquitoes to toxins designed to sever efferent feedback loops results in significant increases in energy gain for all male mosquitoes tested.Transduction and amplification can be abolished by a mechanotoxic insecticide which has been shown to ablate the function of a Drosophila auditory TRP channel, suggesting that (i) molecular modules of transduction are conserved within Diptera and (ii) mechanotoxic compounds might be powerful tools to disturb mosquito reproductive behaviour.

118. Asaph Zylbertal - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Premotor assemblies in the optic tectum trigger innate visually guided behaviour

AUTHORS
Zylbertal A, Bianco IH

ABSTRACT
What neural signals initiate behavioural responses? Here we examine how activity in the zebrafish optic tectum, a key sensorimotor hub, is associated with execution of innate visually guided behaviours including prey-capture and loom-evoked escape. We are combining naturalistic behavioural assays in partially-tethered zebrafish larvae with high-speed volumetric calcium imaging using light-sheet microscopy. Our results indicate that spatially clustered groups of neurons in the optic tectum, termed neuronal assemblies, carry premotor signals that are likely to control hunting responses. Assemblies display bursts of activity with stereotyped spatiotemporal dynamics that are predictive of the occurrence, class and directionality of the behaviour. Tectal assemblies form a motor map that encodes the direction of motor responses and is aligned to the tectum's retinotopic map of visual space. This project unveils a critical stage in the transformation of sensory information into adaptive goal-directed behavioural responses, by building a detailed picture of the premotor function served by tectal activity.

Other | Drama Studio

119. Janet Clark - Other

POSTER TITLE
UCL-NIMH Joint Doctoral Training Program in Neuroscience

AUTHORS
Clark J, Roiser J

ABSTRACT
The University College London – National Institute of Mental Health (NIMH) Joint Doctoral Training Program in Neuroscience is an accelerated graduate program for exceptional students in neuroscience. The NIMH and UCL employ some of the most accomplished neuroscientists in the world and promise to offer an outstanding educational experience. This graduate training program brings together two powerhouses of neuroscience research and allows students to conduct collaborative research between two laboratories, one at UCL, the other at the NIH. Unlike many US graduate programs, students in the UCL-NIMH Joint Doctoral Training Program in Neuroscience choose their area of research, and their mentors, before completing their application. Students are registered in the UCL Doctoral School and receive a PhD from UCL in 4 years or less. Scholarships include students' fees and stipend, as well as a travel allowance. This joint training program is administered by the NIMH Intramural Research Program Office of Fellowship Training and Co-Directed by Dr. Janet Clark, Director, NIMH IRP Office of Fellowship Training and Dr. Jonathan Roiser, Professor of Neuroscience and Mental Health, Institute of Cognitive Neuroscience, Division of Psychology & Language Sciences at UCL.