UCL NEUROSCIENCE DOMAIN

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UCL Neuroscience Symposium 2019

Abstract Booklet

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The 10 posters shortlisted for the 2019 Research Poster Prize are highlighted in blue and will all be displayed in the Jeffery Hall.

Cognition and Behaviour | Elvin Hall

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

POSTER TITLE
Functional and behavioural investigation of amygdala to hippocampus connectivity

AUTHORS
AlSubaie, R, 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.

2. Ana Campos Espinoza - UCL Psychology and Language Sciences

POSTER TITLE
Brain responses and speech perception in children with typical and atypical language development: Study pre-registration plan

AUTHORS
Campos Espinoza A, Tuomainen O, Rosen S, Halliday L.

ABSTRACT
Despite important changes in language skills occurring in early childhood, it is unknown whether neural responses supporting speech perception change during this period and if they are influenced by typical/atypical language development (Skeide & Friederici, 2016). We aim to investigate differences in brain responses to speech in two groups of Spanish-speaking children (4.0-4.11 year old) according to their language status: a typically-developing (TD) and a Developmental Language Disorder (DLD) group. EEG will be recorded using an Optimal Paradigm (Niemitalo-Haapola et al., 2013) during passive

auditory perception of phonemic changes resulting in different linguistic conditions. Participants will be also tested in their language and speech perception skills.
We hypothesise that language developmental status will be associated with neural responses to speech, with language skills affecting the perception of acoustic differences involving higher-level linguistic representations. We expect significant between-group differences in cortical discrimination indices: larger Mismatch Negativity (MMN) amplitudes and greater increases in theta phase locking values (PLV) for the TD than the DLD group. We predict a “Group x Condition” interaction, with larger effects in the TD group for i) native than non-native phonemic contrasts, ii) words than non-words iii) content than function words. Finally, we expect correlation between brain responses and behavioural measures.

3. Federico Claudi - Sainsbury Wellcome Centre

POSTER TITLE
Decision-making strategies in natural behaviours

AUTHORS
Claudi F, Campagner D, Shamash P, Branco T.

ABSTRACT
Algorithms for making decisions do not perform optimally under all conditions, and evolution has endowed the brain with multiple decision-making systems, such as model-free and model-based reinforcement learning (Dayan and Daw 2008). While much is known about the neural bases of these systems, little is known about how the brain arbitrates between them. Determining the mechanisms underpinning the choice of decision strategies is a key step for understanding how behaviour emerges from multiple decision-making systems as well as the causes of aberrant decision-making behaviour, and it has the potential to improve the development of flexible machine-learning algorithms.

Innate behaviours, such as escape from threat, provide a powerful platform for investigating the neural mechanisms of decision-making (Evans et al. 2019). Here we have developed an innate behavioural assay to study decision strategies in a spatially dynamic environment, where mice escape from threats (Evans et al. 2018) and navigate through a spatial maze to reach a shelter. Analysis of choice behaviour in response to changes in the maze configuration shows that mice engage in both model-free and model-based strategies. We are currently combining this behavioural paradigm with chemogenetic manipulations and recordings of neuronal activity, to investigate the neural basis of choosing different decision-making strategies.

4. Jasmine Harju-Seppanen - UCL Research Department of Clinical, Educational and Health Psychology

POSTER TITLE
Network analysis of psychosis

AUTHORS
Harju-Seppanen J, Bell V.

ABSTRACT
Whilst psychotic disorders rarely occur in childhood, psychotic-like experiences (PLEs) are relatively common. Although PLEs are associated with an increased risk, the majority of children with these experiences do not develop a psychotic disorder. Nevertheless, there is evidence that this developmental experience of psychosis may become abnormally persistent. Network theory has increasingly been applied in the study of psychopathology, proposing that symptoms are constitutive of mental disorders- not the outcome of a latent variable. The present study used data from the Adolescent Brain Cognitive Development (ABCD) study and performed an exploratory analysis to investigate the relationship between psychotic and affective symptoms, cognition (vocabulary, working memory and fluid intelligence), hormonal measures (DHEA and testosterone) and neuroimaging measures (cortical thickness of frontal, temporal and parietal lobe) (N=1420). Sub communities within the networks were identified and it was found that the neuroimaging, hormone, cognitive and volumetric variables formed separate communities, whilst the psychotic and affective symptoms formed one network. Anxiety was the most central node, suggesting it may be an important in sustaining in the network. Network analysis provides a novel way to understand psychosis, and how symptom associations are influenced by variables at different levels of explanation. However, further research is required.

5. Alice Milne - UCL Ear Institute

POSTER TITLE
Tonic pupil response to predictable auditory sequences

AUTHORS
Milne AE, Tampakaki C, Zhao S, Chait M.

ABSTRACT
Pupillometry can be used across populations (e.g. infants and adults) and species (e.g. human and non-human primates); therefore, offering a potential technique to implicitly study sequence processing and statistical learning across different subject groups. However, it remains unclear exactly how sequence processing will be reflected in the pupil response. Abrupt changes to the sequential structure of auditory sounds are found to elicit a phasic pupil dilation response that is thought to reflect an arousal-based spike in norepinephrine. However, slower changes to pupil dilation (tonic response) are also observed. These tonic changes have been linked to the release of acetylcholine and hypothesized to be associated with learning processes. Here we aimed to assess if the predictability of a rapid stream of auditory tone pips would modulate tonic pupil diameter. We presented either deterministic or random sequences of tones and systematically varied the number of different tone frequencies in each sequence. We tracked pupil diameter while subjects completed an auditory task unrelated to the sequence structure. We found that predictability modulated tonic pupil dilation in some conditions but not others and demonstrate both the potential and limitations of this technique for studying structure sequence processing.

6. Karyna Mishchanchuk - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Parallel hippocampal projections in decision making under uncertainty

AUTHORS
Mishchanchuk K, MacAskill A.

ABSTRACT
Recent evidence reinforces the idea that the hippocampus is important for integrating past experience to predict the likely outcome of upcoming actions. Among the different projection populations from the ventral hippocampus (vH), the prefrontal cortex (PFC) and nucleus accumbens (NAc) projections in particular are likely to have important yet distinct roles in decision making process.

To explore the role of these projection populations in decision making we use two-armed bandit task with different probabilities of reward associated with each arm. Using probabilistic reversal learning paradigm we are able assess learning and behavioural strategies used by mice during decision making under uncertainty in a highly controlled manner. We show that bilateral optogenetic inhibition of PFC-projecting vH neurons affects the way mice use their past experience to inform their future choices. Ongoing experiments aim to carry out inactivation of NAc-projection, which will enable us to compare contributions of these different populations and gain better understanding of the overall role of vH in decision making. Future directions also include in vivo calcium imaging in freely behaving animals during the bandit task using GCaMP sensors to further investigate decision making strategies and contributions of different vH projection populations to different aspects of this process.

7. Tara O'Driscoll - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
The development of temporal coding in the rat hippocampus

AUTHORS
Varsavsky I, O'Driscoll T, Muessig L, Cacucci F, Wills T.

ABSTRACT
The hippocampus is a major brain area involved in episodic memory and spatial cognition. During exploration, the hippocampus of rodents shows a prominent 5-10 Hz oscillation in its field potential (theta), as well as spatially-modulated activity of its principal cells (place cells). Place cells encode location, and preferentially fire in unique locations within an environment (place fields). This occurs through two distinct mechanisms: a rate code where firing rates change as a function of the animals' location, and a temporal code where action potentials fire at a certain phase of the theta rhythm within a place field (phase code). Phase coding mechanisms are thought to contribute to sequence generation during experience. Two such phase codes are theta sequences and phase precession. While it is well understood how the hippocampal rate code emerges in postnatal development, it is unclear how the phase code emerges in individual place cells. To investigate this, we recorded place cell ensembles as rats ran on a 1D linear track across a number of developmental ages (2-5 weeks). This may provide insight into how phase codes emerge in the hippocampus during early development, and how this relates to the emergence of hippocampus-dependent spatial memory.

8. Marcus Richards - UCL Division of Population Health

POSTER TITLE
Identifying the lifetime cognitive and socioeconomic antecedents of cognitive state: seven decades of follow-up in a British birth cohort study

AUTHORS
Richards M, James S-N, Sizer A, Sharma N, Rawle M, Davis D, Kuh D.

ABSTRACT
Objectives: The life course determinants of cognitive function have been studied using longitudinal population-based cohort data, but less is known about whether the pattern of these pathways is similar or distinct for clinically-relevant cognitive state. We investigated this for the Addenbrooke's Cognitive Examination (ACE-III).
Participants: 1762 community-dwelling men and women of European heritage, enrolled since birth in the MRC National Survey of Health and Development (the British 1946 birth cohort).

Results: Path modelling estimated direct and indirect associations between APOE status, father's social class, childhood cognition, education, midlife occupational complexity, midlife verbal ability (National Adult Reading Test; NART), and the total ACE-III score. Controlling for sex, there was a direct negative association between APOE ε4 and the ACE-III score, but not between APOE ε4 and childhood cognition or the NART, p=0.97). The strongest influences on the ACE-III were from childhood cognition and the NART; educational attainment and occupational complexity were modestly and independently associated with the ACE-III.

Conclusions: The ACE-III in the general population shows a pattern of life course antecedents that is similar to neuropsychological measures of cognitive function, and may be utilised to represent normal cognitive ageing as well as a screen for cognitive impairment and dementia.

9. Ioannis Sarigiannidis - UCL Institute of Cognitive Neuroscience

POSTER TITLE
The neural basis of temporal cognition under induced anxiety

AUTHORS
Sarigiannidis I, Roiser J, Robinson O.

ABSTRACT
Anxiety alters how we perceive the world and also aspects of cognitive performance. Prominent theories of anxiety suggest that one explanation for the effect of anxiety on cognition is that anxious thoughts "overload" limited cognitive resources, competing with other processes, in a dual-task fashion. Having found evidence of this in previous behavioural studies, we expect that performing a task under anxiety would activate neural networks associated with dual-task processing, including the prefrontal and the anterior cingulate cortex. To test this, we combined a widely-used translational anxiety manipulation (threat of shock) with a simple time perception task, which we have previously found to be affected by anxiety. During this task, participants had to watch a picture which flashed briefly on the screen and then decide whether its duration was more similar to short or long

exemplars presented earlier. Thirteen healthy participants performed this task during functional magnetic resonance imaging under threat and safe conditions.
Threat increased activation in the anterior cingulate cortex relative to safe blocks, consistent with previous studies. In addition, the interaction between threat and stimulus duration produced clusters in frontopolar areas. Post-hoc analysis of the interaction showed that there was stronger pre-frontal activation for the shorter durations in the safe condition which was abolished under threat. However, the effect of threat on time perception was not significant ($t(12)=-1.36$, $p=0.196$, Cohen's $d=0.37$), but on the same direction as in our previous studies.

These results are consistent with the hypothesis that anxiety affects cognition by overloading cognitive resources, since it leads to activations of key neural networks that are strongly associated with dual-task processing. However our results should be interpreted with caution until independently replicated given the relatively small sample size and lack of effect of the anxiety manipulation on behaviour.

10. Shana Silverstein - UCL Psychology and Language Sciences

POSTER TITLE
Observational fear learning: a behaviorally translational approach from mouse to man

AUTHORS
Silverstein SE, Yoshida T, Valton V, Roiser J, Viding E, Holmes A.

ABSTRACT
Learning from others' experiences is a highly evolutionarily conserved mechanism providing necessary information about threat and safety. This behavior is observed across species, including humans. Various behavioral tasks have been established to assay socially acquired fear, but the literature on observational fear learning (OFL) remains scarce. We first established a paradigm in mice using a modified version of cued-Pavlovian fear conditioning. Employing complementary behavioral, anatomical, and in vivo optogenetics, we defined a novel mechanism subserving observational fear that has not previously been identified. We demonstrated a critical contribution of the dorsomedial prefrontal cortex (dmPFC) to OFL and showed that ventral hippocampal (vHPC) inputs to the dmPFC negatively gate OFL. Second, we developed an OFL paradigm for human participants and applied detailed computational modelling of trial-by-trial variation of behavior to examine learning rates and variability during OFL. The Baysian model comparison revealed participants' choices were best characterized combining learning rates and variability parameters. Moreover, we observed a negative correlation between learning rate and trait anxiety level. Together, our findings reveal a novel translational model of OFL in both mice and humans with therapeutic implications for conditions associated with atypical fear learning, including generalized anxiety and post-traumatic stress disorders.

11. Hande Tunbak - UCL Division of Medicine

POSTER TITLE
Social isolation alters social Behaviour and Brain Activity in the Juvenile Zebrafish

AUTHORS
Tunbak H, Vazquez-Prada M, 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 with deep two-photon imaging, we have identified the main brain areas that are involved in processing visual social stimuli. In addition, we have revealed that social deprivation alters social preference and results in an abnormal brain activity pattern in juvenile zebrafish, thus highlighting the importance of visual experience for social preference.

12. Ryan Wee - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Hippocampal circuits for the state-dependent control of feeding behaviour

AUTHORS
Wee R, MacAskill A.

ABSTRACT
The hippocampus is classically thought to represent the spatial environment, but increasing evidence suggests that hippocampal representations encompass both spatial and nonspatial states. One example of a dynamically changing state is hunger, and animals need to anticipate changes in hunger to guide adaptive feeding behaviour. It remains unclear whether the hippocampus represents the hunger state during behaviour, which circuits are involved, and how hunger is encoded in the synaptic properties of hippocampal neurons.

To understand how ventral hippocampus (vH) encodes hunger, we employed Ca2+-based fibre photometry of vH population activity – specifically the CA1/subiculum region – during food presentation. We found that vH specifically encodes the anticipatory period prior to food consumption, and that changes in hunger altered vH activity during this anticipatory period. Using rabies tracing, we found that non-overlapping CA1/subiculum neurons targeting the nucleus accumbens (NAc-projectors) and ventromedial hypothalamus (VMH-projectors) receive distinct afferent input. Lastly, we used slice electrophysiology and projection-specific in vivo fibre photometry to show that NAc-projectors were uniquely sensitive to ghrelin.

These findings indicate that the vH encodes the anticipation of food consumption and that anticipatory-related activity is modulated by hunger state changes, an effect that is likely mediated through the NAc-projectors.

Developmental Neuroscience | Elvin Hall

13. Zeinab Asgarian - Wolfson Institute of Biomedical Research at UCL

POSTER TITLE
Myeloid Translocation genes in cortical interneuron development
AUTHORS
Asgarian Z, Stryjewska A, Oliveira M, Magno L, Kessaris N.

ABSTRACT
Normal cortical function is dependent on a fine balance of excitation from glutamatergic neurons and inhibition from GABAergic local interneurons (INs). The two populations of neurons are generated from spatially distinct progenitors in the developing telencephalon. The Medial and Caudal Ganglionic Eminences (MGE and CGE, respectively) are the two main sources of cortical INs, producing 60% and 30-40% of cortical INs, respectively. The identification of factors that define the identity of INs that arise from these two embryonic sources is essential for understanding normal cortical development and disorders caused by genetic defects. Using transcriptional profiling of developing cortical interneurons we identified a pair of related transcriptional co-factors, namely, Mtg8 (for Myeloid Translocation Gene 8) and Mtg16, as being enriched in developing MGE- vs. CGE-derived INs. MTG proteins are non-DNA-binding proteins that associate with numerous histone deacetylases (HDACs), transcription factors (TFs) and transcriptional co-repressors to regulate gene expression in tissues during development and in adult. Known DNA binding partners of the MTG proteins include NEUROG2 and ASCL1 in the nervous system and TAL1/SCL1 in erythroid progenitors. MTG proteins can form homo- and hetero-oligomers, an essential aspect of their mechanism of action. The brain is one of the main sites of expression of Mtg8 and Mtg16 and human mutations in these genes have been associated with neurological defects.

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

POSTER TITLE
Modelling childhood neural pathologies in 3-dimensions

AUTHORS
Gillham O, Lange J, Vagaska B, Tedesco F, Muntoni F, Ferretti P.

ABSTRACT
We developed 3D (3-dimensional) cultures and established human neural stem cells (NSCs), either from embryonic CNS or iPSCs (induced-pluripotent stem cells), for modelling human damage in normal CNS and in CNS affected by congenital diseases, such as Duchenne muscular dystrophy (DMD), to test the hypothesis they present increased susceptibility to neural damage. Response to damage was compared in 2D and 3D cultures following calcium homeostasis disruption, to mimic traumatic injury, or oxygen-glucose deprivation (OGD), that can affect the developing CNS in uterus or perinatally. NSCs and neurons cultured in 3D hydrogels displayed reduced susceptibility to Ca2+ and OGD-induced cell death compared to 2D culture. This was not due to limited drug permeability in 3D, as dead cells were found to be distributed throughout the gel. Together, these results indicate that 3D cultures provide a more favourable environment for the cells, allowing one to analyse cell behaviour and pharmacological responses in a more “tissue-like” situation.

Interestingly, differences in the dystrophin isoforms expressed in neural cells were observed in 2D versus 3D. Furthermore, astrocytes differentiated from DMD-iPSCs displayed increased vulnerability to damage. This is of great importance in the context of CNS comorbidities in DMD patients with different dystrophin mutations.

15. Alex Fudge - Wolfson Institute of Biomedical Research at UCL

POSTER TITLE
The specific expression of BMP4 in immature oligodendrocytes

AUTHORS
Fudge AD, Richardson WD, Li H.

ABSTRACT
Oligodendrocyte precursors (OPs) are a proliferating cell population that continue to generate oligodendrocytes in the central nervous system (CNS) into adulthood. OPs undergo differentiation and maturation to become mature oligodendrocytes that provide myelin sheaths for axons. From a transcriptome database, we identified a candidate marker, bone morphogenetic protein 4 (Bmp4), for the immature stage of oligodendrocytes, when the cells are newly differentiating from OPs. We have confirmed, by RNA in situ hybridisation followed by immunofluorescence, that Bmp4 is exclusively expressed in immature oligodendrocytes in adult mouse CNS. Since the number of new-born immature oligodendrocytes in a brain region reflects the differentiation ability of OPs, this new marker can be used to assess the efficacy of treatments designed to increase remyelination in animal models of demyelinating diseases. Furthermore we are investigating its function in adult oligodendrocyte generation. Given its well-known in vitro inhibitory effect on OP differentiation, we speculate that after being secreted from immature oligodendrocytes, BMP4 may act as a microenvironmental cue for neighbouring OPs to hold back from differentiation.

16. Flavie Lesept - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
The impact of AP-4 epsilon subunit loss on axonal autophagosome biogenesis and neuronal connectivity

AUTHORS
Lesept F, Szulc B, Ivankovic D, White I, López-Doménech G, 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 use a neuronal specific AP-4 epsilon subunit conditional knockout to investigate the impact of AP4ε loss of function on brain development and connectivity. We show that AP-4 loss of function leads to the somatic retention of ATG9A, a protein critical for the biogenesis of autophagosomes. We find this leads to a reduction in the capacity to generate axonal autophagosomes leading to axonal changes and de novo generation of distal axonal swellings. Additionally, we investigate the impact of axonal swellings on the integrity and function of excitatory synapses.

17. Modinat Liadi - UCL Queen Square Institute of Neurology

POSTER TITLE
Partial recovery of proprioception in rats with dorsal root injury following human olfactory bulb cell transplantation

AUTHORS
Lab Poster, Ying Li, Spinal Repair Unit.

ABSTRACT
There is still no effective treatment for the devastating injuries of the brain and the spinal cord. The irreversible disability after CNS injury is often the result of disconnection of nerve fibres responsible for carrying critical messages to and from the brain. The CNS has little or no innate regenerative powers that can re-establish the neuronal connections resulting in permanent and often devastating neurological disability. In the UK there are approximately 40,000 individuals living with disabilities of spinal cord injuries (SCI). SCI places tremendous financial burden on the families, communities and on the NHS.

Our group is carrying out studies of treatment of these injuries by transplanting the specialised cells known as olfactory ensheathing cells (OECs). OECs are located in the nose and the brain, and possess properties to promote nerve regeneration. Transplantation of OECs to the lesion site in experimental models aided recovery after spinal cord injury. The first clinical application by our collaborators showed encouraging outcome of axonal regeneration and functional recovery after transplantation of autologous human OECs (hOECs) to the site of injury with simultaneous bridging of the spinal cord gap with autologous peripheral nerve grafts. However, the clinical application did reveal a limitation of hOECs when treating injuries of large size and cavity. The yield of hOECs from the limited mass of biopsy tissue alone was not sufficient to bridge the severed connections.

To overcome this limitation we here present our latest work on the use of collagen as a substrate to fabricate 3D hOECs scaffolds to test it's function in a rat spinal root injury model. This preliminary study is the first to transplant human olfactory bulb cells into a rat model of dorsal root injury. We have found: (1) Human olfactory bulbs can be harvested and cultured using similar protocols to rat olfactory bulbs; (2) Half of hOEC transplanted rats recovered some degree of forelimb function compared with controls; (3) the study has shown that we can maximise the usage of limited cells by combining with a biomaterial; (3) the study has provided important information which is relevant for future clinical applications.

Disorders of the Nervous System | Elvin Hall

18. Emily Annuario - UCL Queen Square Institute of Neurology

POSTER TITLE
siRNA screen reveals new risk genes for Parkinson's disease

AUTHORS
Plun-Favreau H, Lab.

ABSTRACT
Genome-wide association studies constituted a breakthrough in the identification of genetic loci associated with multifactorial diseases, such as Parkinson's disease (PD). The research community is now facing two major challenges: identifying the causal gene(s) on these loci, and understanding their contribution to pathogenesis. In this study, an assay for mitophagy, a key pathway in PD, was implemented to screen for candidate genes. We identified two genes that directly interact, KAT8 and KANSL1, as important regulators of the mitophagy process, and consequently new PD risk genes, in all likelihood. KANSL1 is located on the MAPT locus, however, whether MAPT is the prime candidate on this locus remains controversial. Here, we provide biological and genetic evidence that the KANSL1 gene is another important gene on the MAPT locus. Overall, this study highlights the untapped potential of biological high content screening to exploit the genetic data and identify new causal genes for disease.

19. Isabelle Austin-Zimmerman - UCL Division of Psychiatry

POSTER TITLE
CYP2D6 genetic variation and antipsychotic-induced weight gain

AUTHORS
Austin-Zimmerman I, Wannasuphoprasit Y, Calafato MS, Irizar A, Thygesen J, Bramon E.

ABSTRACT
Antipsychotics are known to cause weight gain, disrupt glucose metabolism, increase serum cholesterol and triglyceride and increase risk of arterial hypertension. CYP2D6 constitutes a major metabolic pathway for many antipsychotics and there is a growing amount of evidence demonstrating a relationship between CYP2D6 genotypes and clinical outcomes to antipsychotic drugs. This study aims to investigate whether CYP2D6 metabolic status influences antipsychotic-induced weight gain and/or metabolic syndrome. We conducted a systematic review and meta-analysis of the current literature on CYP2D6 genetic variation and antipsychotic-induced weight gain. We analysed a sub-sample of the UK Biobank to investigate a relationship between CYP2D6 metabolic status and BMI/waist circumference. The meta-analysis showed significant difference in BMI between intermediate metabolisers and extensive metabolisers. No other comparisons of weight or BMI were significant, which may be due to small sizes in the poor metaboliser group. Our analysis of the UK Biobank did not show any evidence of increased BMI or waist circumference depending on CY2D6 metabolic status. These results do not suggest that CYP2D6 genetic variation influences antipsychotic-induced weight gain. However, additional studies with a larger sample sizes, enriched with extreme metabolisers, are needed to confirm these results.

20. Conceição Bettencourt - UCL Queen Square Institute of Neurology

POSTER TITLE
DNA methylation profiling across multiple brain regions of patients with multiple system atrophy

AUTHORS
Bettencourt C, Foti SC, Chatterjee A, Lashley T, Balazs R, Vire E, Holton JL.

ABSTRACT
Multiple system atrophy (MSA) is a fatal late onset neurodegenerative disease. MSA is mostly sporadic and its aetiology remains elusive. Clinically, it is characterized by a variable combination of parkinsonism, ataxia and autonomic failure. The presence of α-synuclein within oligodendrocytes in the form of glial cytoplasmic inclusions (GCIs) is the diagnostic hallmark of MSA. Pathologically, MSA can be categorised into striatonigral degeneration, olivopontocerebellar atrophy or mixed subtypes. To get insights into molecular mechanisms associated with MSA, we have analysed DNA methylation patterns in brain samples of MSA mixed cases and controls. We have studied three brain regions (cerebellum, and frontal and occipital cortices) and selected white matter to enrich for glial cells that are affected in MSA. We have investigated global DNA methylation changes by immunohistochemistry as well as changes at single nucleotide resolution by using Illumina MethylationEPIC arrays, evaluating over 850,000 methylation sites per sample. Global levels of DNA methylation did not differ significantly between cases and controls. Our preliminary results from the EPIC arrays, however, identified important loci with significantly altered DNA methylation levels between cases and controls, suggesting that DNA methylation changes at specific loci are associated with MSA.

21. Tom Dufor - UCL Department of Cell and Developmental Biology

POSTER TITLE
Mechanisms of synapse vulnerability and resilience in a Wnt signalling deficient model

AUTHORS
Dufor T, Rogdakis T, Palomer E, Brar K, Buechler J, Lopes D, Marzo A, Salinas P.

ABSTRACT
Synaptic degeneration is an early hallmark of neurodegenerative diseases and is highly correlated with cognitive decline in Alzheimer's disease (AD). However, the mechanisms triggering synapse vulnerability or resilience to synaptic injury remain poorly understood. Growing evidences suggest a link between a deficient Wnt signalling and AD. Dickkopf-1 (Dkk1), an endogenous secreted Wnt antagonist, is elevated in the brain of AD patients and is required for amyloid-β-mediated synapse loss. Our lab has developed an inducible transgenic mouse model allowing the expression of Dkk1 in the adult mouse brain. Two weeks of induction lead to the disassembly of 40% of excitatory synapses in the hippocampus, LTP deficit and memory loss. No neuronal death or inhibitory synapse loss were observed, resembling the early stage of AD. Nonetheless restoring Wnt signalling, by stopping the expression of Dkk1, rescues all the previous phenotypes. In follow up experiments we found that Dkk1 expression over longer period of time (2.5 months) do not induce further synaptic degeneration in the hippocampus, suggesting that a subset of synapses are resilient. We are trying to identify cell types, subcellular compartment (ie: dendritic spines), and molecules involved in the resilience and/or vulnerability of synapses to Dkk1.

22. Kirsten Ebanks - UCL Queen Square Institute of Neurology

POSTER TITLE
Neuropathological analysis of genes implicated in Parkinson's by genome wide association studies

AUTHORS
Ebanks K, Warner TT, Lewis PA, Bandopadhyay R.

ABSTRACT
Parkinson's Disease (PD) is an incurable movement disorder affecting 1% of the population over the age of 65. Despite extensive research, the aetiology of idiopathic PD remains unclear. Genetic studies have shown that heritability plays a strong role in disease risk. Recent genome wide association studies (GWAS) have revealed several genes associated with PD, many of which deal directly with mechanisms of vesicular transport including Cyclin- G associated kinase (GAK) and Rab7L1. Additionally, both GAK and RAb7L1 have been shown to interact with leucine rich repeat kinase (LRRK2). In this study, we have investigated whether GAK and RAB7L1 are altered in the PD brain. Using archival brain tissue from Queen Square Brain Bank, immunohistochemistry and immunoblots were performed on human brain tissue in control and PD cases representing early, mid-stage and late-stages of disease progression. We show that expression of GAK is region specific, with basal ganglia showing higher expression compared to that in cingulate gyrus. Rab7L1 expression levels were very low in cingulate cortex and immunohistochemical localization showed punctate expression in neurons of the cortex. Further work are in progress to determine the role of GAK and RAb7L1 in PD progression and its relationship with alpha-synuclein expression.

23. Sarah Jolly - UCL Queen Square Institute of Neurology

POSTER TITLE
Notum, a negative regulator of wnt signalling, as a therapeutic target for Alzheimer's disease? From target validation to the development of small molecule inhibitors

AUTHORS
Jolly S, Schuhmacher L, Palomer E, Frew S, Mahy W, Monaghan A, Jones E.Y, Bilsland J, Fish P, Vincent JP, Bictash M, Salinas P, Whiting 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 and human brains. We show that Notum is expressed in specific cell types throughout the brain and spinal cord and is specifically enriched in endothelial cells. Additionally, mouse models of AD as well as human brain biopsies from AD patients were used to determine whether Notum expression is affected during the progression of the disease. One of our key goals was to develop a 'fit for purpose' Notum inhibitor to determine the role of this enzyme in modulating Wnt signalling in the mammalian CNS, and its potential as a therapeutic for AD. We have developed highly potent (<10 nM) inhibitors of Notum with good ADME properties and CNS penetration in vivo. Their in vivo pharmacodynamics profiles is now being investigated.

24. Felix Jozsa - Imperial College Healthcare NHS Trust

POSTER TITLE
Searching for the missing link in Angelman syndrome

AUTHORS
Jozsa F, Giese KP.

ABSTRACT
Angelman syndrome (AS) is a rare genetic disorder caused by loss of function of the maternal UBe3A allele on chromosome 15, resulting in near total deficit of the CNS E3 ubiquitin ligase E6-AP (Sell, 2015). It is characterised clinically typically by seizures, microcephaly and developmental delay.

Calcium/calmodulin-dependent kinase II (CaMKII) is an abundant CNS kinase crucial to hippocampal long-term potentiation and memory. Key findings in hippocampal slices of the rodent AS model include hyperphosphorylated and dysfunctional CaMKII (Weeber, 2003). Experimental work showed rescue of LTP deficits in AS models possessing a further mutation blocking CaMKII hyperphosphorylation (van Woerden, 2007).

A substrate of E6-AP that regulates CaMKII phosphorylation is therefore a likely causative candidate for AS pathology. Adapting the previously posited UBe3A binding domain (UBD) (Greer, 2010), we show that the synaptic scaffolding protein Calcium/Cam associated serine kinase (CASK), known to regulate CaMKII phosphorylation, is a potential E6-AP substrate. This proposed intermediary between the E6-AP and CaMKII could serve as a future therapeutic target for this rare genetic disorder for which there is no current treatment.

25. Lorenza Magno - UCL Queen Square Institute of Neurology

POSTER TITLE
A platform to assess primary microglia function across different states in vitro: potential for drug-screening and target validation

AUTHORS
Magno L, Lau D, Costelloe K, Van Ingelgom A, Phadke L, Patel L, Bictash M, Whiting P.

ABSTRACT
Human genetic studies have indicated an essential role for microglia (MG) in neurodegeneration, in particular in Alzheimer's disease (AD). Therefore, modulating the function of MG may be a viable therapeutic approach for AD. To complement our ex vivo platform of target validation, in vitro MG model systems are required. While MG complexity in vitro is reduced, various culturing conditions and challenges can elicit different functional states of MG. These may be suitable for disease modelling and potentially, phenotypic screening. We obtained primary MG from rat brains and cultured in 96-well format, suitable for screening, in serum-free defined medium (Bohlen et al., 2017, Neuron) as well as various challenging conditions. MG cultured under serum-free defined-medium conditions exhibit a resting phenotype. Serum exposure promoted an amoeboid morphology and increased proliferation. We assessed MG morphology, survival, and expression. By using RNAScope, we confirmed detection of key MG genes including Tmem119, and disease-associated genes such as TREM2 and PLCG2. In conclusion, we have developed a platform to assess primary MG function in vitro in different states of activation suitable for screening with high

throughput techniques. We will further validate the platform with an array of pharmacological and genetic tools targeting various MG relevant pathways.

26. Henry Martin - UCL Queen Square Institute of Neurology

POSTER TITLE
Ephaptic coupling in a model of Episodic Ataxia type 1
AUTHORS
Martin HGS, Kullmann DM.

ABSTRACT
Episodic Ataxia type 1 (EA1) is a dominantly inherited disorder where in individuals experience lifelong paroxysmal occurrences of ataxia. In a mouse model of EA1 mirroring a dominant negative mutation in the Kv1.1 A-type potassium channel, evidence has implicated changes in GABA release at the Cerebellar Basket to Purkinje cell synapse as important in the etiology of the disorder. EA1 associated mutataion results in a broadening of presynaptic action potentials and via increased in calcium influx leads to elevated GABA release. However in the mature cerebellum loss of Kv1 type potassium channel function is predicted to also impact non-synaptic ephaptic coupling between Basket and Purkinje neurons. Using precise measure of Basket cell and Purkinje cell firing, we looked for a deficit in ephaptic coupling in EA1 mice. Surprisingly ephaptic inhibition of the Purkinje cell appeared unimpaired, a finding we confirmed with pharmacological isolation of the ephaptic signal. These findings that suggest that while inhibitory drive onto Purkinje cells is increased in EA1 temporal precision is not sacrificed.

27. Sara Mole - MRC Laboratory for Molecular Cell Biology

POSTER TITLE
Batten disease

AUTHORS
Sara Mole – Mole laboratory.

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 450 mutations. We curate and host the international NCL mutation database. We have 4 main research interests: (1) Genotype-phenotype correlation, and diagnosis; (2) Molecular and cellular basis; (3) Identification of new therapeutic targets and drugs; (4) Developing gene therapy to treat the brain, eye and periphery. 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).

28. Amy Monaghan - UCL Queen Square Institute of Neurology

POSTER TITLE
Developing a High Content Screening Platform to Identify Genetic and Small Molecule Modulators of PINK1 Dependent Mitophagy in Neurodegenerative Diseases

AUTHORS
Monaghan AE, Melandri D, Annuario EA, Kempthorne L, Pan K, Ketteler R, Bictash M, Whiting P, Plun-Favreau H.

ABSTRACT
Mitophagy is a selective form of autophagy which removes damaged mitochondria. Defects in mitophagy are associated with a range of neurodegenerative diseases, including Parkinson's disease, Alzheimer's disease and frontotemporal dementia. The Plun-Favreau lab at the UCL ION and the Alzheimer's Research UK UCL Drug Discovery Institute have collaborated closely to develop a High Content Screening assay capable of identifying both genetic and small molecule modulators of oligomycin/antimycin induced mitophagy. The assay has been optimised and automated for screening, and been used to enable four High Content Screens across a range of small molecule and genetic libraries. This work has resulted in the biological validation of a novel genetic pathway, first identified in sporadic Parkinson's disease Genome Wide Association Studies, which is now under further investigation in the Plun-Favreau lab. This work highlights a key aim of the Alzheimer's Research UK UCL Drug Discovery Institute, which is to connect high quality academic neuroscience research with innovative drug discovery technologies, enabling the identification of new therapeutics and pathways in neurodegenerative diseases.

29. Paige Mumford - UCL Queen Square Institute of Neurology

POSTER TITLE
The Effect Of Three Copies Of 40 Hsa21 Orthologs On Amyloid Pathology In A Mouse Model

AUTHORS
Mumford P, Noy S, Luo D, Cleverley K, Tybulewicz V, Fisher EMC, Wiseman FK.

ABSTRACT
Down syndrome (DS) is caused by trisomy of chromosome 21 (Hsa21). People with DS develop the hallmarks of Alzheimer's disease (AD), amyloid plaques and neurofibrillary tangles, by age 40 and the majority develop dementia, in part due to having three copies of APP leading to raised Aβ. Other Hsa21 genes have been implicated in AD mechanisms and recent work found that three copies of ~240 Hsa21 genes, excluding APP, exacerbated amyloid pathology. This study investigates how three copies of 40 Hsa21 orthologs effects amyloid pathology. Using a cross between the AppNL-F knock-in mouse model of amyloid pathology and the Dp10Yey model with three copies of 40 Hsa21 orthologs, we conducted western blotting, immunohistochemistry, and ELISAs. Three copies of the 40 Hsa21 orthologs did not affect APP processing or Aβ isoform levels but reduced plaque deposition and elevated S100B protein. Triplication of one or more of these 40 Hsa21 genes reduces Aβ deposition and may be protective against AD pathology in people with DS. S100B, a gene found in three copies and elevated in the Dp10Yey, has been suggested to modify Aβ aggregation. Next we will determine if S100B is the causal gene for the changes in Aβ deposition observed.

30. Teresa Niccoli - UCL Department of Genetics, Evolution & Environment

POSTER TITLE
Using Drosophila melanogaster to model dementias

AUTHORS
Niccoli lab.

ABSTRACT
Our lab we uses Drosophila melanogaster models to study neurodegeneration associated with dementias. Drosophila melanogaster make excellent models to study neurodgeneration as they exhibit an elaborate range of behaviours, underpinned by a complex nervous system, composed of the same classes of neuron as seen in humans. Flies also have glia and a blood brain barrier separating the brain from the rest of the organism. As flies have a very short lifespan and are cheap to maintain, it is possible to study disease progression over an entire lifespan, important in late onset disorders. Finally, as flies carry homologues to 75% of human disease genes, our results are likely to translate to the human disease context. We mainly use two adult onset models of dementia: an Aß expressing fly to study Alzheimer's disease and a C9orf72 hexanucleotide repeat expansion model, to model Fronto Temporal Dementia. We use a number of assays to measure phenotypes associated with neurodegeneration: lifespan, climbing, circadian rhythm and eye morphology.

31. Zhen-Yi Andy Ou - UCL Queen Square Institute of Neurology

POSTER TITLE
Brain-derived neurotrophic factor in cerebrospinal fluid as a biomarker for Huntington's disease

AUTHORS
Ou Z. A, Byrne L, Rodrigues F, Wild E.

ABSTRACT
Huntington's disease (HD) is a progressive neurodegenerative disorder, caused by a genetic mutation in the HTT gene. Brain-derived neurotrophic factor (BDNF), a member of the neurotrophin family, is synthesized in the cortical neurons and transported to striatal neuron to promote neuronal survival. BDNF synthesis and transportation are regulated by huntingtin (HTT) protein. However, BDNF expression and function are reduced in HD, which may contribute to the death of striatal neurons. BDNF in blood has been implied as a potential biomarker for HD. However, BDNF has not been quantified in cerebrospinal fluid (CSF) in HD. Other CSF BDNF measurements in neurodegeneration have used insufficiently sensitive assays, resulting in potentially unreliable conclusions. We compared several BDNF immunoassays and chose a Simoa single-molecule platform to quantify BDNF in CSF and plasma in 20 pre-manifest and 40 manifest HD mutation carriers and 20 matched controls. BDNF concentration did not distinguish between the healthy controls and HD mutation carriers at any stage and did not correlate with clinical and imaging measures. These findings provide evidence that BDNF is not a reliable biomarker for disease progression in HD.

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

POSTER TITLE
Bi-directional modification of sleep and wake by amyloid beta oligomers

AUTHORS
Ozcan G, Lim S, Rihel J.

ABSTRACT
Sleep disruption is an early feature of Alzheimer's Disease (AD) and has been implicated in disease progression, as prolonged wakefulness exacerbates the production of toxic amyloid-beta (Aβ) species (Roh et al, 2012 Science). One proposed mechanism by which Aβ affects sleep is via AD-related cell death, including sleep/wake regulatory neurons (Lim et al, 2014). We tested an alternative hypothesis that Aβ oligomers may acutely signal to modulate sleep behaviour (Mander et al, 2015) by exposing the larval zebrafish brain to Aβ oligomers of various lengths. We found that short oligomeric Aβ species increased larval wakefulness while longer forms triggered an acute, temporary increase in sleep. Genetic disruption of putative Aβ binding targets revealed that Aβ's sleep and wake activity operates through distinct molecular pathways, as Aβ-induced wakefulness required functional Adrenergic receptor b2 (Adrb2) and Progesterone membrane receptor component 1 (Pgrmc1), while Aβ-driven sleep required Prion Proteins (PrP). Furthermore, pharmacological inhibition of either Aβ-PrP interactions or components of the Aβ-PrP signal-transduction cascade prevented longer Aβ oligomers from inducing sleep. Our data reveals that Aβ oligomers acutely modify sleep/wake behaviour without neuronal cell death and suggests that changes to the brain's balance of Aβ oligomeric species during AD progression (Lesne, 2014) may disrupt the stability of a bi-directional, Aβ-sensitive sleep/wake switch.

33. Ernest Palomer - UCL Department of Cell and Developmental Biology

POSTER TITLE
Coordinated downregulation of Wnt signalling in Alzheimer's Disease

AUTHORS
Palomer E, Vaher K, Podpolny M, Salinas P.

ABSTRACT
The Wnt antagonist Dickkopf-1 is elevated in the Alzheimer´s Disease (AD) brain and is required for amyloid-ß-mediated synapse loss. Nonetheless, the expression of other Wnt signalling components remain unexplored in AD. In this study, we have analysed the mRNA levels of 40 Wnt signalling components by qPCR in hippocampal samples of two AD models (APP/PS1 and hAPP-NL-G-F). Our analyses demonstrate that several Wnt antagonists are up-regulated while many Wnt ligands and receptors are down-regulated in the hippocampus of two AD models. These findings suggest a coordinated deregulation of Wnt signalling components, resulting in diminished Wnt signalling early in AD. Since differential epigenetic regulation could favour the coordinated deregulation observed, we analysed the levels of several active and repressive histone marks at Wnt components loci. The active mark H4K16Ac is equally abundant at the promoters of all Wnt components analysed in WT animals. However, in the hAPP-NL-G-F model H4K16Ac is reduced at Wnt ligands and receptors loci compared to control. Our results demonstrate that Wnt signalling is down-regulated early in AD, potentially through reduced H4K16Ac at Wnt loci. These results postulate Wnt signalling as a therapeutic target for synapse protection in early stages of AD.

34. Silvia Purro - UCL Institute of Prion Diseases

POSTER TITLE
Transmission of Amyloid-Beta protein pathology from cadaveric pituitary growth hormone

AUTHORS
Purro SA, Farrow M, Linehan J, Nazari T, Thomas DX, Chen Z, Mengel D, Saito T, Saido T, Rudge P, Brandner S, Walsh DM, Collinge J.

ABSTRACT
We previously reported the presence of Amyloid-Beta protein (AB) deposits in individuals with iatrogenic Creutzfeldt-Jakob disease (iCJD) who had been treated during childhood with human cadaveric pituitary-derived growth hormone (c-hGH) contaminated with prions1. Our findings led us to argue that implicated c-hGH batches may have been contaminated with AB seeds. Therefore, we proceeded to identify and analyse archived vials of c-hGH. Certain c-hGH batches to which patients with iCJD and AB pathology were exposed had significant levels of AB1-40, AB1-42 and tau, and this material seeded the formation of AB plaques and cerebral AB-amyloid angiopathy in intracerebrally inoculated AppNL-F/NL-F mice. These results confirm the presence of AB seeds in archived c-hGH vials and are consistent with the hypothesised iatrogenic human transmission of AB pathology. This experimental confirmation has implications both for the prevention and therapy of AD and should prompt a review of risk of iatrogenic transmission of AB seeds via medical and surgical procedures long recognised to pose a risk of accidental prion transmission.

This work was funded by the UK MRC, NIHR UCLH/UCL Biomedical Research Centre, LWENC and NIA.

Reference
1. Jaunmuktane,Z. et al. Nature 525, 247-250 (2015).

35. Yichen Qiu - UCL Queen Square Institute of Neurology

POSTER TITLE
GeneLoop: activity dependent gene therapy for epilepsy

AUTHORS
Qiu Y, Shekh-Ahmad T, Turner T, Carpenter J, Schorge S, Kullmann D, Lignani G.

ABSTRACT
Epilepsy is characterized by repetitive seizure episodes, it affects nearly 1% of population worldwide. Approximately 25-30% of them suffer from drug-resistant epilepsy which cannot be managed by medication. Recent developments in gene therapy hold promise to provide reversible and non-invasive alternatives. Current gene therapy strategies modify broad range of neurons with little discriminations between pathological and healthy cells. Over-suppression of healthy neurons may affect normal functions such as memory and learning. Our project aims to improve the precision of gene therapy for epilepsy by selectively targeting over-excitable neurons in an epileptic network and supressing epileptic events on-demand. Neurons respond to intense signals by activating different signalling pathways. Those mechanisms can be useful to activate desirable genes. Overexpressing specific ion channels can modulate the level of neuronal excitabilities and suppress firing. We design and create the constructs, followed by in vitro validation in cell cultures. We then apply it to

animal epilepsy models and evaluate how effective and robust the system is in vivo. So far we have analyzed neuronal network activity with patch clamp and in vitro multi-electro array recordings and showed sinificant decrease of overall neuronal excitability. Preliminary in vivo data are encouraging to suggest a potential new treatment for epilepsy.

36. Dervis Salih - UCL Queen Square Institute of Neurology

POSTER TITLE
Genetic variability in response to Abeta deposition influences Alzheimer's risk

AUTHORS
Salih DA, Bayram S, Lin P, Sokolova D, Guelfi S, Reynolds RH, Shoai M, Ryten M, Brenton J, Zhang D, Matarin M, Botia JA, Shah R, Brookes KJ, Guetta-Baranes T, Morgan K, Bellou E, Cummings DM, Edwards FA, Escott-Price V, Hardy J.

ABSTRACT
Genome-wide association studies (GWAS) of late-onset Alzheimer's disease (AD) risk have previously identified genes primarily expressed in microglia that form a transcriptional network. In transgenic mouse models of amyloid deposition we previously showed that the expression of many of the mouse orthologs of these risk genes are coordinately up-regulated by amyloid deposition. In this new study, we use statistical comparison of an improved RNA-seq-generated amyloid-responsive mouse network with previous human AD GWAS to predict five new genetic risk loci for the disease (OAS1, CXCL10, LAPTM5, ITGAM and LILRB4). This work suggests that genetic variability in the microglial response to amyloid deposition is a major determinant for Alzheimer's risk, and discovery of these genes may help to predict the risk of developing AD. These findings also provide further insights into the mechanisms underlying AD for potential drug discovery. Data available at: www.mouseac.org

37. Marco Sancandi - UCL School of Pharmacy

POSTER TITLE
Structural Changes Occurring in the Olfactory Pathway of a rat Model of Pre-Motor Parkinson's Disease Are Partially Prevented with Exendin-4 Treatment

AUTHORS
Sancandi M, Constanti A, Mercer A.

ABSTRACT
The symptomatology of Parkinson's disease consists of motor and non-motor symptoms (NMSs). The latter arise several years before the appearance of motor symptoms, and are not ameliorated by conventional dopaminergic agonist/replacement treatments. However, NMSs can be improved by using treatments other than the dopaminergic ones, such as the glucagon-like peptide-1 receptor agonist exendin-4 (EX-4). Recently, using injections of the neurotoxins N--N-ethyl-2-bromobenzylamine (DSP-4) and 6-hydroxydopamine (6-OHDA), a rat model of pre-motor PD, that displayed hyposmia in the absence of motor symptoms was developed. In this study, taking advantage of this model, the effect of partial noradrenergic and dopaminergic denervation in the primary olfactory cortex, the olfactory bulbs, and the prefrontal cortex was investigated. Surprisingly, the combined denervation led to a reduction in the expression of interneuronal calcium binding proteins and triggered neuroinflammation

in the olfactory cortex, whilst the number of dopaminergic interneurones in the olfactory bulbs was found to be increased. These structural changes were partially prevented following treatment with EX-4.

38. Yoshiteru Shimoda - UCL Queen Square Institute of Neurology

POSTER TITLE
Investigating inhibitory restraint in a chemoconvulsant model of epilepsy in awake mice

AUTHORS
Shimoda Y, Magloire V, Marvin JS, Cornford J, Mercier MS, Looger LL, Kullmann DM.

ABSTRACT
A failure of the inhibitory system underlies cortical seizure generation and propagation, and two alternative mechanisms, K+ accumulation hypothesis and inhibitory restraint hypothesis, have been proposed to play a crucial role in this breakdown. Here, we investigated whether inhibition promotes (K+ accumulation) or prevents (inhibitory restraint) hyperexcitable activity in a chemoconvulsant model of epilepsy in awake mice.

Two-photon calcium imaging of parvalbumin-positive (PV+) and neurogliaform interneurons indicates that these two interneuron populations are active during interictal activity and seizures. In addition, optogenetic depolarization of PV+ interneurons suppresses interictal activity while their hyperpolarization promotes it. Together, these findings are in favour of the inhibitory restraint hypothesis showing that inhibition is still functional during pathological discharges and could prevent hyperexcitable activity. Finally, combining two-photon imaging and a genetically-encoded glutamate and GABA sensors (iGluSnFR and iGABASnFR), we observe a differential distribution of glutamate and GABA, which is dependent on the distance from the focus. Thus, the extracellular glutamate transient is higher close to the focus while the extracellular GABA transient was the highest far from it, suggesting a breakdown of inhibition at the focus. We are currently investigating mechanisms that contribute to the breakdown of this inhibitory restraint and the transition to seizures.

39. Krista Sibley - UCL Queen Square Institute of Neurology

POSTER TITLE
Limbic thalamus volume loss in typical amnestic young onset Alzheimer's disease

AUTHORS
Schott J, Parker T, Sibley K.

ABSTRACT
Although typically associated with hippocampal atrophy, it has been suggested that the thalamus may also be a site of significant subcortical neuropathological change in Alzheimer's disease (AD), most notably in the anterior limbic nuclei (Braak and Braak, 1991). However, studies investigating individual thalamic nuclei in vivo have been limited.

We applied an automated thalamic nuclei segmentation tool (Iglesias, et al. 2018) to a cohort of 27 young onset AD patients with a typical amnestic presentation, and 24 healthy age-matched controls, with 3 Tesla volumetric T1-weighted MRI data. We aimed to investigate whether AD is associated with limbic thalamus volume (the sum of lateral dorsal, medial

dorsal and anterior thalamic nuclei). Following adjustment for age, sex and total intracranial volume we found evidence that left limbic thalamic volume was significantly lower in patients compared to controls (-8.04% decrease; p=0.012). Right limbic thalamic volume was not significantly associated with AD (-3.44% decrease; p=0.32).

Furthermore, in patients there was evidence of a positive association between the limbic thalamus and hippocampus in the left hemisphere (p=0.03), but not in the right (p=0.34). These data suggest that the limbic thalamus may undergo atrophy, potentially with a left sided predominance, in typical amnestic young onset AD.

40. Nathan Skene - UCL Queen Square Institute of Neurology

POSTER TITLE

Genetic Identification of Cell Types Underlying Brain Complex Traits Yields Novel Insights Into the Etiology of Parkinson's Disease

AUTHORS

Skene NG, Bryois J, Hansen TF, Kogelman LJA, Watson HJ, Eating Disorders Working Group of the Psychiatric Genomics Consortium, International Headache Genetics Consortium, The 23andMe Research Team, Brueggeman L, Breen G, Bulik CM, Arenas E, Hjerling-Leffler J, Sullivan PF.

ABSTRACT

Genome-wide association studies (GWAS) have discovered hundreds of loci associated with complex brain disorders, and provide the best current insights into the etiology of these idiopathic traits. However, it remains unclear in which cell types these variants may be active, which is essential to understand disease etiology and for disease modelling. Here we integrate GWAS results with single-cell transcriptomic data from the entire nervous system to systematically identify cell types underlying psychiatric disorders, neurological conditions, and other brain complex traits. We show that psychiatric disorders are predominantly associated with excitatory neurons from the cortex/hippocampus, medium spiny neurons from the striatum, diverse sets of midbrain neurons, and inhibitory neurons from the cortex/hippocampus. Cognitive traits were generally associated with similar cell types but their associations were driven by different genes. Neurological disorders were associated with different cell types, consistent with other lines of evidence. Notably, we found that Parkinson's disease is not only genetically associated with dopaminergic neurons but also with serotonergic neurons and cells from the oligodendrocyte lineage. Using post-mortem brain transcriptomic data, we confirmed alterations in these cells, even at the earliest stages of disease progression. Altogether, our study provides a solid framework for understanding the cellular basis of complex brain disorders and unravels a new unexpected role of oligodendrocytes in Parkinson's disease.

41. Himanshu Tyagi - UCL Queen Square Institute of Neurology

POSTER TITLE

Clinical and imaging evidence for dissociable effects in a randomised trial directly comparing ventral capsule and anteromedial subthalamic nucleus stimulation in Obsessive-Compulsive Disorder (OCD)

AUTHORS
Tyagi H, Zrinzo L, Akram H, Apergis-Schoute A, Drummond L, Fineberg N, Foltynie T, Jahanshahi M, Limousin P, Matthews K, Robbins T, Rothwell J, Ruge D, Sahakian B, Hariz M, Joyce E.

ABSTRACT
Obsessive compulsive disorder (OCD) has a lifetime prevalence of 1-2 %. Standard treatments are ineffective in up to 40% of cases. Even with the best treatments, there remains a subgroup with severe symptoms and significant disability. Studies of deep brain stimulation (DBS) for OCD have shown improvement in both symptoms and quality of life in severe OCD. Two targets in particular have shown promise: the anteromedial subthalamic nucleus (STN) and the ventral capsule/ventral striatum (VC/VS). We report a within subject comparison of the effect of DBS on OCD symptoms at STN and VC/VS sites both individually and together (ClinicalTrials.gov #NCT02655926). The aims of the study were to determine: a) the efficacy of DBS at each site; b) whether stimulation of both sites improves the response compared to either site alone; and c) the critical stimulation contacts at the VC/VS site. Methods: Six participants, with severe treatment refractory OCD, were recruited via the UK specialist OCD service and underwent implantation of bilateral electrodes at both the VC/VS and anteromedial STN sites. A Leksell frame-based MRI-guided and MRI-verified approach under general anaesthesia was used. The subthalamic nucleus was localised on axial T2-weighted stereotactic images and the VC/VS localised on coronal and axial proton density images (Siemens, 1.5T). Using a double blind cross-over design, 12-weeks stimulation at STN and VC/VS sites was compared, followed by stimulation at both sites for 12 weeks. The primary outcome measure was YBOCS with an improvement of greater than or equal to 35% as the predefined response. Results: Accurate stereotactic and anatomical lead location was confirmed on immediate postoperative stereotactic MR images in all patients. For the VC/VS target, the deepest DBS lead contact was within the nucleus accumbens, the one superior to that in the “shell” of the nucleus accumbens while the superior two contacts were within the inferior aspect of the anterior limb of the internal capsule. For the whole group, the mean reduction in YBOCS scores were: STN 16.3; VC/VS: 19.2; STN + VC/VS: 22.0 which represents a mean reduction of 42%, 53%, 62% from their own baseline scores and a reduction to predefined mild/subclinical symptoms of 0%, 50% 50% respectively. The top two DBS contacts of the quadripolar lead were found to be the most effective at the VC/VS target in all 6 patients.

42. Vinojini Vivekanandam - UCL Queen Square Institute of Neurology

POSTER TITLE
Defining the phenotype of Andersen-Tawil Syndrome: The largest reported series

AUTHORS
Vivekanandam V, Germain L, Skorupinska I, Seutterlin K, Fialho D, Kozyra D, Sud R, Holmes S, James N, M.G. Hanna, Matthews E.

ABSTRACT
Anderson Tawil Syndrome (ATS) is a rare channelopathy traditionally characterised by periodic paralysis, cardiac arrhythmias and dysmorphic features. Mutations in the KCJN2 gene have been associated with ATS. Accurate and early diagnosis is important in facilitating treatment of episodic paralysis and preventing potentially life-threatening cardiac events.

We aim to fully characterise the phenotype in a carefully stratified cohort including cognitive deficits and cardiac risk. 62 patients were identified with KCJN2 mutations. Comprehensive clinical information was collected for these patients. Cardiac symptoms were prominent. Two thirds had daily or very frequent palpitations. 12.9% reported syncope. Serious cardiac complications requiring Implantable Cardiac Defibrillator (ICD) occurred in 8.06% patients. 39% reported pain which has previously not been appreciated as part of ATS. Interestingly, 4 patients had fasciculations. 25% of patients had no decrement on Long Exercise Tests (LET) and 6.25% had less than <40% decrement despite having episodic weakness. Lower limb Muscle MRI was abnormal in 6 patients. Excess sleepiness was reported. While dysmorphic features exist, these can be subtle. Short stature is not ubiquitous. Heterogeneity within families was commonly seen. The phenotypic spectrum of ATS is broader than currently appreciated. This is important to recognise to allow accurate diagnosis and development of screening and treatment regimens.

43. Nathan Woodling - UCL Department of Genetics, Evolution & Environment

POSTER TITLE
Which age-related changes in astrocytes contribute to Alzheimer's disease?

AUTHORS
Woodling N, Rajasingam A, Aleyakpo B, Niccoli T, Partridge L.

ABSTRACT
Age is the greatest risk factor for Alzheimer's disease (AD); interventions that can slow age-related decline thus represent attractive strategies to prevent AD. Work from our group and others has begun to uncover which genes and cell types contribute most to the modulation of healthy lifespan, using the short lifespan and genetic tools available in the fruit fly Drosophila melanogaster. We have found that inhibition of insulin signalling, an established intervention that extends lifespan in model organisms, can extend healthy lifespan in Drosophila when this inhibition is restricted to glial cells, or even to the astrocyte subset of glial cells. These results suggest that astrocytes play a key role in brain ageing. We now plan to extend these studies to AD models in which amyloid-beta peptide is expressed in the Drosophila brain. In ongoing studies, we will test (1) which genes are differentially expressed in astrocytes with age, and (2) whether any of these gene expression changes are detrimental or protective against Amyloid-beta toxicity.

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44. Daniel Brierley - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
A lateral parabrachium-projecting subpopulation of preproglucagon neurons encodes meal termination

AUTHORS
Brierley DI, Selim I, Barburas P, Trapp S.

ABSTRACT
Preproglucagon (PPG) neurons in the nucleus tractus solitarii (NTS) produce GLP-1, and their chemogenetic activation induces a sustained anorectic effect. However, their inhibition or ablation does not affect ad libitum intake, but delays termination of abnormally large meals. This discrepancy may reflect a neuroarchitecture of discrete subpopulations of PPGs characterised by distinct projection targets, which are selectively recruited under specific physiological conditions. We hypothesised that PPGs projecting to the lateral parabrachial nucleus (lPBN) may represent a subpopulation mediating large-meal satiation. We investigated this putative PPGNTS→lPBN subpopulation using a triple-transgenic fluorescent reporter mouse to show that YFP+ PPG varicose axons terminate in the lPBN, in close apposition to tdRFP+ GLP-1R-expressing neurons. We then determined that PPGs projecting to the lPBN are indeed a discrete, functionally-relevant subpopulation by injecting a retrograde DREADD (rAAV2-retro-DIO-hM3D(Gq):mCherry) into the lPBN of Glu-Cre mice. This selectively transduced a minority (~35%) of PPGs, which were not collateralised to other brain regions. Chemogenetic activation of this subpopulation was sufficient to reduce chow intake in dark phase hour 1 (by 48%; p=0.030) predominantly by decreasing meal 1 size (by 63%; p=0.022). This PPGNTS→lPBN subpopulation may thus comprise part of a meal termination circuit independent of the wider brain GLP-1 system.

45. Alvaro Castano - The Francis Crick Institute

POSTER TITLE
Neuronal programming by microbiota enables environmental regulation of intestinal motility

AUTHORS
Castaño A, Obata Y, Boeing S, Bon-Frauches AC, Gomez de Agüero M, Boesmans W, Yilmaz B, Lopes R, Huseynova A, Rao Maradana M, Vanden Berghe P, Murray AJ, Stockinger B, Macpherson AJ, Pachnis V.

ABSTRACT
The enteric nervous system (ENS) plays fundamental roles in gastrointestinal (GI) physiology and gut homeostasis. Gut luminal factors, such as microbiota and diet, influence the organisation and functions of the ENS and have been implicated in the aetiology of GI diseases, including gut motility disorders. Here we have used a novel AAV-based strategy to identify neuron-specific transcriptional programmes that integrate ENS output with the divergent tissue and luminal microenvironment along the gut. We demonstrate that the environmental biosensor Aryl hydrocarbon receptor (AhR) is induced in colonic neurons by microbiota and regulates intestinal peristalsis in an AhR ligand-dependent manner. AAV-mediated neuron-specific deletion of AhR or degradation of cellular AhR ligands led to severe defects in colonic peristalsis and defective propulsion of intestinal contents. These observations suggest that local environmental cues act as neuromodulators of the ENS by regulating the AhR-dependent transcriptional profile of enteric neurons. Our work provides a novel insight into the molecular mechanisms that integrate neuron-intrinsic genetic programs and environmental factors leading to the formation of functional intestinal neural circuits.

46. Elise Chan - UCL Queen Square Institute of Neurology

Poster Title
Novel Fluid Biomarkers in Frontotemporal Dementia

AUTHORS
Brierley DI, Selim I, Barburas P, Trapp S.

ABSTRACT
Frontotemporal dementia is a common young onset form of dementia with both genetic and sporadic variants. Currently, there are no reliable biomarkers to differentiate the forms of FTD, however recent studies have shown a link between FTD and neuroinflammation. This project will aim to look at a new panel of markers to see if these differ between people with FTD and controls, and whether there is any association of these markers with clinical, cognitive and imaging measures. We will investigate whether plasma levels of three cytokines and complement proteins differ between FTD and controls. We will also assess relationships between cytokines and complement proteins with other clinical markers and age and disease duration. IL-6, IL-10 and TNFα levels will be measured using the Cytokine Panel A on the Simoa platform (Quanterix, Massachusetts) in a group of healthy controls and patients with FTD with different genetic mutations (progranulin, tau and C9orf72). Plasma levels will be compared between groups using a linear regression model on Stata v.14. We expect to see an increased in cytokine concentration in FTD compared to controls, particularly in the progranulin mutation cases, which have been shown to be associated with chronic immune dysfunction and microglia activation.

Neural Excitability, Synapses and Glia: Cellular Mechanisms | Elvin Hall

47. Isabel Christie - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Astrocytes as intracranial baroreceptors

AUTHORS
Christie IN, Marina N, Turovsky EA, Sheikhbahaei S, Korsak A, Gourine AV.

ABSTRACT
Astrocytes provide neurons with metabolic and structural support, modulate neuronal circuit activity and function as versatile surveyors of brain metabolic milieu, tuned to sense metabolic insufficiency. Here we demonstrate that astrocytes are highly sensitive to small physiologically-relevant changes in cerebral perfusion pressure. Two-photon imaging studies conducted in anaesthetised and artificially ventilated rats show that acute decreases in cerebral perfusion pressure trigger robust intracellular calcium responses in cortical astrocytes. In vitro we demonstrate that the mechanosensitivity of brainstem astrocytes is mediated by the interactions of TRPV4 channels and connexin 43 hemichannels. This leads to ATP release, which propagates astroglial Ca2+ excitation via P2Y1 receptor activation and causes excitation of sympathetic neuronal circuits. This study expands our understanding of the role of astrocytes as physiological sensors of brain blood flow. The advance in understanding is demonstrating experimentally that these ubiquitous brain cells directly sense decreases in cerebral perfusion pressure. We present evidence that astrocytes in the brainstem control the activities of sympathetic circuits to increase arterial blood pressure and heart rate in order to maintain brain blood flow and preserve brain oxygen delivery. This research suggests a relationship between cerebral hypoperfusion and systemic hypertension, in which astrocytes are the essential brain baroreceptors.

48. Alessandro Galloni - National Institute for Medical Research

POSTER TITLE
Synaptic integration in L5 pyramidal neurons of secondary visual cortex

AUTHORS
Galloni A, Laffere A, Rancz E.

ABSTRACT
Sensory processing in the cerebral cortex involves integration of feedforward sensory information and multimodal feedback signals. Thick-tufted layer 5 (ttL5) pyramidal neurons are well-placed for integrating these diverse inputs due to their large dendritic tree and dendritic nonlinearities, which endow them with unique computational properties.
Here, we explore the mechanisms of multimodal integration by describing a genetically targeted population of ttL5 neurons in the mouse medial secondary visual cortex (V2m). We map the precise dendritic targets of their main inputs using subcellular channelrhodopsin-assisted circuit mapping (sCRACM). Surprisingly, in this population the feedforward inputs from primary visual cortex target mainly apical and tuft dendrites in V2m, whereas inputs from retrosplenial cortex, considered as feedback, target mainly basal dendrites.
To determine how these inputs functionally interact, we measure the postsynaptic effects of electrically stimulating these pathways. Unlike previously described ttL5 neurons, we find that ttL5 neurons in V2m generally do not display Ca2+-based supralinearities or bursting. We explore the conditions required for linear and non-linear summation further in a biophysical model. These results argue against the classical notion that sensory inputs target the basal compartment and top-down inputs target the apical tuft, and demonstrate that ttL5 properties differ depending on brain region.

49. Anna Hands - UCL Queen Square Institute of Neurology

POSTER TITLE
Examining the effect of V3 interneurons and astrocytes on ESC-derived motoneuron maturation in vitro

AUTHORS
Hands A, Bryson JB, Brownstone R, Greensmith L.

ABSTRACT
Current methods for restoring function to paralysed muscles rely mainly on stimulation of host nerves. However, this is only effective with intact motoneurons and neuromuscular junctions (NMJs). When transplanted into a peripheral nerve, embryoid bodies (EBs) containing embryonic stem cell (ESC)-derived motoneurons can form functional NMJs, enabling control of muscle contraction by stimulation of the graft. However, if purified motoneuron aggregates are used, functional NMJs do not form. Therefore, other cells within EBs seem to contribute to the ability of ESC-derived motoneurons to mature and functionally innervate host muscle. We hypothesised that spontaneous activity arising from intra-graft microcircuits is necessary for motoneuron maturation. To investigate this, we generated culture pure populations of ESC-derived motoneurons, astrocytes and V3 interneurons in vitro.

Results:
•Co-culture of motoneurons with astrocytes accelerated morphological and

electrophysiological motoneuronal development, the formation of glutamatergic and cholinergic synapses, and the development of glutamate-dependent, motoneuronal spontaneous activity which was modulated by cholinergic signalling.
•When V3 interneurons were added to the motoneuron/astrocyte co-cultures, development and maturation of motoneuronal spontaneous activity was accelerated and the number of glutamatergic and cholinergic synapses on motoneurons were increased and decreased, respectively.

These results provide insight into the role of other cell types in motoneuron maturation.

50. Patrick Hosford - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Mechanisms of CO2-induced inhibition of cortical neuronal activity

AUTHORS
Hosford PS, Hadjihambi A, Millar J, Gourine AV.

ABSTRACT
Suppression of neuronal activity by CO2 has been well documented but a precise mechanism remains unknown. We investigated the effect of hypercapnia and acidosis on cortical neuronal activity evoked by somatosensory stimulation.

Parenchymal pH and evoked neuronal activity in the somatosensory cortex were monitored using carbon fiber microelectrodes in vivo. Connexin hemichannnel activity was assessed by carboxyfluorescein (CBxF) dye loading.

Evoked potentials reduced to 59±6% and 49±5% of control response in conditions of 5 and 10% inspired CO2, respectively. Decreases in pH were recorded: -0.12±0.05 with 5% and -0.17±0.09 pH units with 10% CO2. A similar decrease in parenchymal pH induced by systemic administration of acetazolamide had no effect on the evoked potentials (n=8). Isocapnic acidosis had no effect on the evoked activity.

DPCPX (A1 antagonist; 1mg kg-1) had no effect on the inhibitory effect of 10% CO2. However, P2Y1 receptor antagonist MRS-2500 (5M), prevented the inhibitory effect of CO2 on cortical neuronal activity. Hypercapnia caused an increase in CBxF dye loading, indicative of connexin opening.

Inhibition of cortical neuronal activity caused by CO2 is independent of pH changes and likely to be mediated by connexin hemichannel mediated ATP release and its actions on P2Y1 receptors expressed by inhibitory interneurons.

51. Megan Jones - UCL Department of Cell and Developmental Biology

POSTER TITLE
Contribution of a genetic variant of the Wnt receptor LRP6 to synaptic impairment in the ageing hippocampus

AUTHORS
Büchler J, Jones M, Dufor T, Metzakopian E, Bradley A, Gibb A, Salinas PC.

ABSTRACT
Alzheimer's disease (AD) affects around 40 million people worldwide. Synapse loss is the strongest correlate to cognitive decline. Substantial evidence exists for the role of Wnt signalling in synaptic stability in the mature brain. Importantly, deficient Wnt signalling has been linked to synapse loss in AD. A variant of LRP6 (LRP6-Val) has been linked to late onset AD and reduced Wnt signalling. However, the effect of LRP6-Val on synapses is currently not understood.To examine the effect of LRP6-Val on synapses in vivo, we have generated a novel knock-in mouse model. We have explored the structural and functional phenotype of synapses in the CA1 stratum radiatum using electrophysiology, imaging and cell biology.

Our results demonstrate that LRP6-Val is present at both pre- and postsynaptic sites. LRP6-Val reduces Wnt signalling leading to synaptic defects in an age dependent manner. Smaller presynaptic sites, fewer vesicles and dendritic spine defects are accompanied by reduced release probability.

This study reveals a synaptic phenotype of LRP6-Val with age and highlights importance of Wnt signalling in the ageing brain. Further work is required to elucidate the mechanism behind the synaptic defects. We predict that this variant will exacerbate the synapse loss and plaque load in AD.

52. Jasmina Jovanovic - UCL School of Pharmacy

POSTER TITLE
Investigating the structural role of GABAA receptors in inhibitory synapse formation and circuitry of the basal ganglia

AUTHORS
Arama JE, Tyagarajan SK, Panzanelli P, Fritschy JM, Jovanovic JN.

ABSTRACT
The molecular mechanisms involved in the assembly and functional maturation of GABAergic synapses during ontogeny remain largely unknown. Recently we have demonstrated that GABAARs, the main postsynaptic components of inhibitory synapses, can initiate the formation of functional synapses in heterologous co-culture model systems. To investigate these synaptogenic effects of GABAARs in vivo, we have carried out quantitative immunohistochemical analysis of GABAergic synapses in the nuclei of the basal ganglia of the alpha1- or alpha2–GABAAR knockout mice using antibodies specific for the main pre- and postsynaptic markers. We have characterized the number and size of the postsynaptic alpha1/2/3 or 5 or gamma2-containing GABAAR clusters, the number of co-localized VGAT or GAD65 positive GABAergic terminals, the number and size of synaptic gephyrin and neuroligin-2 clusters, and the density of TH-positive dopaminergic terminals. Our study demonstrates an overall reduction in the number of inhibitory synapses and profound structural changes in the remaining synapses in the striatum of the alpha2 subunit knockout mice, indicating that the alpha subunits may play an important role in inhibitory synapse formation and maintenance in vivo.

53. Carmen Kivisild - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Regulation of tonic and phasic inhibition by phosphorylation of α5-GABAA Receptors

AUTHORS
Kivisild C, Bright DP, Smart TG.

ABSTRACT
In the brain, the main role for γ-aminobutyric acid receptors (GABAARs) is to control neural excitability by using a combination of phasic (transient) and tonic (persistent) inhibition. Phasic inhibition is mediated by receptors located synaptically, while extrasynaptic receptors give rise to tonic inhibition. These two forms of inhibition are known to have distinct functional characteristics that differentially impact upon their control of neuronal excitation. GABAARs containing α5 subunit (α5-GABAARs) exhibit properties that associate with both forms of inhibition. However, it is unclear how the ratio between phasic and tonic inhibition via α5-GABAARs is regulated. Using electrophysiology and super-resolution imaging we show that phosphorylation of the intracellular domain of α5 subunit can alter the subcellular location of the receptors and thus regulate the form of inhibition mediated by α5-GABAARs. These receptors are important in the hippocampus for learning and memory and have been shown to be involved in many neurological disorders linked to cognitive deficits like Alzheimer disease, as well cognitive decline in normal ageing. A greater understanding of the molecular mechanisms that regulate the functional properties of these receptors may enable the development of treatments to improve cognition.

54. Helen Langley - UCL Queen Square Institute of Neurology

POSTER TITLE
Regulation of synaptic vesicle endocytosis by Synaptotagmin-1 ring-like oligomers

AUTHORS
Langley H, Tagliatti E, Volynski KE.

ABSTRACT
Fast, synchronous neurotransmitter release at the active zone depends on a complex and dynamically-regulated machinery, in which the synaptic vesicle (SV) protein Synaptotagmin-1 (Syt1) plays a crucial role as both Ca2+-sensor and release trigger. Yet while much attention has been focused on Syt1 function in SV exocytosis, its complementary role in presynaptic endocytosis is less well understood. Recently, it has been discovered that Syt1 molecules self-oligomerise into ring-like structures in vitro and that these rings may serve as regulatory structures in both SV exocytosis and endocytosis. We have thus investigated the functional effects of disrupting Syt1 oligomerisation in cultured hippocampal neurons. A point mutation, Syt1 F349A, abolishes oligomerisation but does not disrupt any other known function of Syt1. Using this construct, we have established that Syt1 oligomerisation is a major factor in the presynaptic distribution and recycling of both Syt1 itself and of SVs. In the absence of oligomers, Syt1 molecules are more diffusely distributed between axons and synapses, while optical investigation of vesicle release with the pH-sensitive GFP variant pHluorin reveals that Syt1 F349A accelerates the endocytosis of SVs, particularly via clathrin-dependent mechanisms. We thereby suggest that Syt1 ring-like oligomers play multiple important roles in the SV cycle.

55. Oscar Marcelo Lazo - UCL Queen Square Institute of Neurology

POSTER TITLE
Rab10 as a novel regulator of the sorting of TrkB to retrograde axonal transport.

AUTHORS
Lazo OM, Schiavo G.

ABSTRACT
Neurotrophic signalling from the axon terminal is propagated retrogradely by organelles called signalling endosomes. At arrival to the soma, these organelles have diverse destinations and regulate several neuronal functions, including gene expression, synaptic maturation and dendritic branching. The diversity of molecular signatures that control their transport and specific targeting is, nevertheless, only partially understood. A main determinant of the fate of these organelles and their transport is the association with different GTPases of the Rab family, including Rab5 and Rab7. By using microfluidic chambers, we have found that knockdown of Rab10 decrease the ability of hippocampal neurons to retrogradely transport TrkB from axon terminals to the cell bodies. In addition, we discovered that endogenous Rab7 and Rab10 localise at different domains in axons. Internalised TrkB is not accumulated in Rab10 domains in time, but appears to transit through this axonal compartment. After studying internalisation and recycling of TrkB in axons of neurons expressing constitutively-active and dominant-negative mutants of Rab10, we have hypothesised that this Rab protein defines a transition compartment regulating the sorting of TrkB receptors to the retrograde axonal transport pathway. Further characterisation of the impact of Rab10 activity on the maturation from early to late endosomes will be crucial to understand the physiological relevance of this mechanism regulating retrograde propagation of neurotrophic signalling.

56. Eleonora Lugara - UCL Queen Square Institute of Neurology

POSTER TITLE
Impact of LGI1 autoantibodies on neuronal networks

AUTHORS
Lugarà E, Colclough L, Ramberger M, Irani S, Walker MC.

ABSTRACT
Leucine-rich glioma-inactivated 1 (LGI1) is a brain secreted protein predominantly found in the neurons of the temporal lobe. LGI1 interacts presynaptically with ADAM23 and with Kv1.1 potassium channels, indirectly controlling their density and activity. Postsynaptically, LGI1 binds to ADAM22, and to AMPA receptors, affecting AMPA receptor excitability and concentration at the synapse. Mutations in the gene encoding LGI1 lead to temporal lobe epilepsy in humans and animal models. Autoantibodies against LGI1 have been detected in the serum of adult patients with limbic encephalitis, affected by seizures and cognitive impairments. It is not clear if the seizures are generated by inflammation due to the antibodies or through a direct effect of the antibodies on LGI1. We used immunofluorescence technique and multielectrode arrays (MEA) to investigate their binding pattern in primary cultures from rat hippocampal preparations and their effect on network excitability. We found that IgGs-LGI1 are able to bind rat neuronal cultures but did not have a significant network effect when measured by multielectrode arrays after 30 minutes, 1hr, 24hr and 48hr of application. Work in progress aims to test different IgG concentrations and

time-points to investigate acute, sub-acute and chronic application of LGI1 autoantibodies in neuronal cultures.

57. Marion Mercier - UCL Queen Square Institute of Neurology

POSTER TITLE
Long-term plasticity in hippocampal neurogliaform interneurons

AUTHORS
Mercier MS, Magloire V, Cornford JH, 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.

58. Tuamoru Odii - UCL Queen Square Institute of Neurology

POSTER TITLE
Probing the activity-dependent dynamics of astrocytic interaction in tripartite synapses using super-resolution microscopy

AUTHORS
Odii T, Reynolds JP, Heller JPD, Rusakov DA.

ABSTRACT
Astrocytes play active roles in shaping and maintaining neuronal circuits through secretion and clearance of neurotransmitters as well as extracellular potassium buffering. Whilst the molecular signal exchange between astroglia and synapses occurs in a highly heterogeneous microenvironment on the nanoscale, the spatial subcellular distribution of the underlying molecular machineries remains poorly understood. Previously we successfully imaged and analysed the nanoscale relationship between astrocytic processes and glutamatergic synapses. Here, we extended our study to investigate the plastic relationship between astrocytic processes and GABAergic synapses as there is very little known about astrocyte engagement of inhibitory synapses. We employed immunohistochemistry of hippocampal sections followed by super-resolution single molecule localisation microscopy

(SMLM) which can circumvent the optical diffraction limit and offers ease of use and flexibility not seen in electron microscopy. To achieve different conditions compatible with long-term synaptic potentiation or depression, we incubated acute hippocampal brain slices with inducing reagents for LTP and LTD of excitatory and inhibitory systems. Through multi-colour imaging, we were able to localise clusters of receptors and transporters in astrocytic and neuronal membranes in fixed brain slices. We analysed the altered positional relationship between synapses and astroglial receptors and transporters in potentiated or depressed synapses.

59. Sylvain Rama - UCL Queen Square Institute of Neurology

POSTER TITLE
Glutamate imaging reveals multiple sites of stochastic release in the CA3 giant mossy fiber boutons

AUTHORS
Rama S, Jensen T, Rusakov D.

ABSTRACT
One of the most studied central synapses which have provided fundamental insights into cellular mechanisms of neural connectivity is the 'giant' excitatory connection between hippocampal mossy fibers (MFs) and CA3 pyramidal cells. Its large presynaptic bouton features multiple release sites and is densely packed with thousands of synaptic vesicles, to sustain a highly facilitating 'detonator' transmission. However, whether glutamate release sites at this synapse act independently, in a stochastic manner, or rather synchronously, remains poorly understood. This knowledge is critical for a better understanding of mechanisms underpinning presynaptic plasticity and postsynaptic signal integration rules. Here, we use the optical glutamate sensor SF-iGluSnFR and the intracellular Ca2+ indicator Cal-590 to monitor spike-evoked glutamate release and presynaptic calcium entry in MF boutons. Multiplexed imaging reveals that distinct sites in individual MF giant boutons release glutamate in a probabilistic fashion, also showing use-dependent short-term facilitation. The present approach indicates a qualitative step in our quest to understand basic mechanisms of neurotransmitter release at excitatory synapses.

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

POSTER TITLE
Push-pull regulation of prefrontal cortex by two opposing hippocampal pathways

AUTHORS
Sánchez Bellot C, MacAskill AF.

ABSTRACT
Hippocampal input tightly regulates prefrontal cortex (PFC) activity, and its disruption results in pronounced deficits in flexible behavior and disease. We found that the hippocampus-PFC projection is composed of two distinct populations of neurons that have opposing effects on downstream PFC. One promotes inhibition via preferential recruitment of feedforward

inhibition, while the other promotes excitation. This push-pull circuit provides a mechanism for the previously unexplained bidirectional hippocampal control of PFC.

61. Brittany Sincox - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Investigating the assembly of AMPA Receptors containing Type I and Type II TARPs

AUTHORS
Sincox B, Studniarczyk D, Bats C, Farrant M, Cull-Candy S.

ABSTRACT
AMPA receptors (AMPARs) are responsible for fast excitatory synaptic transmission in the brain. In addition, their regulation is central to synaptogenesis and plasticity – processes that are essential in learning and memory. Transmembrane AMPA receptor regulatory proteins (TARPs) are key contributors to the regulation of AMPARs, and since their discovery as auxiliary AMPAR subunits in 2005, there has been a strong focus in determining how TARPs interact with and modify AMPARs and synaptic transmission.

Cerebellar granule cells (CGCs) are simple neurons containing two types of AMPAR subunit (GluA2 and -4) and two TARPs (the Type I TARP -2 or stargazin and the Type II TARP -7). As such they offer an excellent model system to investigate the co-assembly of of AMPARs containing TARPs from each class. Our previous studies using mutant and knockout mice to examine the function of these two TARP classes provided evidence that, in neurons, -7 favours delivery of GluA2-lacking calcium-permeable (CP-) AMPARs. We are currently examining hetrologously expressed recombinant AMPARs to identify the rules that define how -2 and -7 interact with the pore-forming subunits of CP- and calcium-impermeable AMPARs to determine their assembly and trafficking.

62. Blanka Szulc - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Correct CYFIP1 dosage is essential for synaptic inhibition and the excitatory / inhibitory balance in the hippocampus

AUTHORS
Szulc BR, Davenport EC, Drew J, Taylor J, Morgan T, Higgs NF, Lopez-Domenech G, Kittler JT.

ABSTRACT
Altered excitatory/inhibitory balance is implicated in neuropsychiatric disorders but the genetic aetiology of this is still poorly understood. Copy number variations in CYFIP1 are associated with autism, schizophrenia and intellectual disability but the role of CYFIP1 in regulating synaptic inhibition or excitatory/inhibitory balance remains unclear. We show, CYFIP1, and its paralogue CYFIP2, are enriched at inhibitory postsynaptic sites. While upregulation of CYFIP1 or CYFIP2 increased excitatory synapse number and the frequency of miniature excitatory postsynaptic currents (mEPSCs), it had the opposite effect at inhibitory synapses, decreasing their size and the amplitude of miniature inhibitory postsynaptic currents (mIPSCs). Contrary to CYFIP1 upregulation, its loss in vivo, upon conditional knockout in neocortical principal cells, increased expression of postsynaptic

GABAA receptor b2/3-subunits and neuroligin 3 and enhanced the amplitude of mIPSCs in CA1 pyramidal neurons. Thus, CYFIP1 dosage can bi-directionally impact inhibitory synaptic structure and function, potentially leading to altered excitatory/inhibitory balance and circuit dysfunction in CYFIP1-associated neurodevelopmental disorders.

63. Erica Tagliatti - UCL Queen Square Institute of Neurology

POSTER TITLE
Synaptotagmin 1 oligomers clamp and regulate different modes of neurotransmitter release

AUTHORS
Tagliatti E, Oscar D, Bello, R. F. Mendonça P, Kotzadimitriou D, Nicholson E, Coleman J, Timofeeva Y, Rothman J, Krishnakumar S, Volynski K.

ABSTRACT
Tightly regulated synaptic release of neurotransmitters forms the basis of neuronal communication in the brain. Synaptotagmin1 (Syt1) plays a key role in this process, both as the major Ca2+ sensor for fast synchronous action potential-evoked transmitter release and as an inhibitor of both spontaneous and asynchronous release. This dual function of Syt1 allows precise synchronisation of transmitter release. Whilst the Syt1 Ca2+-activation has been well characterised, the molecular mechanism of Syt1 clamp remains enigmatic. Here we show that C2B domain-dependent oligomerisation forms the molecular basis for the Syt1 clamping function. This follows from the investigation of a structurally derived mutation (F349A), which selectively destabilises Syt1 oligomerisation without affecting the other molecular properties. Using a combination of fluorescence imaging and patch-clamp electrophysiology we tested the effect of this mutation on different modes of glutamate release in neocortical synapses. We find that Syt1 F349A is more efficient than Syt1 WT in rescuing synchronous release, but fails to restore the clamp on asynchronous and spontaneous release in Syt1 knock-out neurons. Furthermore, overexpression of Syt1 F349A in WT neurons potentiates synchronous, asynchronous and spontaneous release. Thus we conclude that Ca2+-sensitive Syt1 oligomerisation is critical for maintaining the balance between different modes of neurotransmitter release.

64. Fatma Taha - UCL School of Pharmacy

POSTER TITLE
Diazepam-induced loss of inhibitory synapses mediated by PLCδ/ Ca2+/Calcineurin signalling downstream of GABAA receptors

AUTHORS
Nicholson MW, Taha F, Ali AB, Duchen M, Haider S, Jovanovic JN.

ABSTRACT
Benzodiazepines facilitate the inhibitory actions of GABA by binding to GABAA receptors (GABAARs), ligand-gated chloride/bicarbonate channels, which are the key mediators of transmission at GABAergic synapses in the brain. Here we report that prolonged exposure to diazepam, the most widely used benzodiazepine in clinic, leads to a gradual disruption of GABAergic synapses. The loss of synapses and the preceding, time- and dose-dependent decrease in surface levels of GABAARs, mediated by dynamin-dependent internalisation, were blocked by Ro 15-1788, a competitive benzodiazepine antagonist, and bicuculline, a

competitive GABA antagonist, indicating that prolonged enhancement of GABAAR activity by diazepam is integral to the underlying molecular mechanism. Characterisation of this mechanism has revealed a metabotropic-type signalling downstream of GABAARs, involving mobilisation of intracellular Ca2+ and activation of the Ca2+/calmodulin-dependent phosphatase calcineurin, which promotes their endocytosis leading to disassembly of inhibitory synapses. Functional coupling between GABAARs and Ca2+ stores was sensitive to phospholipase C (PLC) inhibition, and regulated by PLCδ, a PLC isoform found in direct association with GABAARs. Thus, a PLCδ/Ca2+/calcineurin signalling converts the initial enhancement of GABAARs by benzodiazepines to a long-term downregulation of GABAergic synapses, this potentially underpinning the development of pharmacological and behavioural tolerance to these widely prescribed drugs.

65. Weixin Wang - UCL Institute of Ophthalmology

POSTER TITLE
TNFα-induced transcriptomic changes of neuroprotection in human Müller glia

AUTHORS
Wang W, Owen N, Eastlake K, Limb GA.

ABSTRACT
Purpose: Tumour necrosis factor alpha (TNF-α) is known to be responsible for inflammatory responses during retinal degeneration. Müller glia are known to produce neuroprotective molecules such as antioxidants that protect retinal neurons against oxidative stress and glutamate induced toxicity associated with degeneration. Many studies have suggested that TNF-α could induce either degeneration or neuroprotection, however its downstream effect on the change of antioxidants released by Müller glia has not been explored. This study investigated the transcriptomic changes of antioxidants induced by TNF-α in the human Müller glial stem cell line MIO-M1 by transcriptome sequencing.

Methods: MIO-M1 cells were cultured with TNF-α at 50ng/mL for 24 hours. Total RNA was extracted, and a cDNA library was prepared using the NEB Next mRNA Ultra II kit, followed by 75 bp pair-end sequencing on an Illumina NextSeq 500 platform with 26 million reads per sample. Sequencing data was analysed using the established bioinformatics pipeline. The transcriptional and translational expression of the antioxidants SOD2 and PRDX6, and the main gliotic marker intermediate filament glial fibrillary acidic protein (GFAP) were examined by both RT-PCR and Western blotting, respectively.

Results: The analysis identified 1708 upregulated genes and 1527 downregulated genes in the transcriptomics of MIO-M1 cells. Gene enrichment analysis revealed that five antioxidation enzymes including glutathione S-transferase omega-1, peroxiredoxin 6 (PRDX6), superoxide dismutatse 2 (SOD2), glutathione peroxidase 1 (GPX1) and peroxidasin homolog (PXDN) were significantly upregulated. RT-PCR and Western blotting analysis confirmed the increased expression of PRDX6 and SOD2. Interestingly, the results showed that TNF-α also induced downregulation of the gliosis associated marker GFAP.

Conclusions: This study reports the anti-oxidant transcriptomic analysis of the MIO-M1 cells in response to TNF-α treatment. Müller glia could respond to TNF-α signalling pathway by elevating antioxidant release and reducing the expression of gliosis associated proteins such as GFAP. These findings suggest that TNF-α may possibly promote Müller glia-dependent neuroprotection and this merits further investigations.

Novel Methods, Resources and Technology Development| Drama Studio

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

POSTER TITLE
Benchmarking transgenic zebrafish lines for optogenetic control of neural activity and behaviour

AUTHORS
Antinucci P, Dumitrescu A, Morley H, Leung K, Hagley T, Wyart C, Bianco IH.

ABSTRACT
Optogenetics allows control of activity with high spatiotemporal resolution in genetically defined neuronal populations. Following Channelrhodopsin-2, opsins with different ion selectivities, spectral tuning, photocurrents and kinetics have been developed. Currently, it is unclear whether opsins with improved properties are also superior in controlling behaviour. Moreover, most opsins were tested only in few organisms or experimental paradigms, making generalisation across species problematic. Here, we compared a range of opsins [Channelrhodopsin-2(H134R), CheRiff, ChrimsonR, Chronos, CoChR, eArch3.0, eNpHR3.0, GtACR1 and GtACR2] in zebrafish. First, we generated transgenic lines for targeted opsin expression via the Gal4/UAS system. We then assessed their ability to elicit/block spiking in vivo using electrophysiological and behavioural readouts. In assays testing excitation, CoChR outperformed Channelrhodopsin-2(H134R) in both photocurrent amplitude and ability to induce high-frequency (40-50 Hz) spiking. Additionally, CoChR was the most effective opsin in inducing tail bouts when stimulating trigeminal or motor neurons. In assays examining inhibition, GtACR1 and GtACR2 showed the largest inhibitory photocurrents and were the most effective in suppressing spontaneous swimming behaviour. In conclusion, we provide an expanded optogenetic toolbox for improved manipulation of neural activity in zebrafish. Our comparative analyses will guide opsin selection for interrogation of neural circuit function and precise control of behaviour.

67. Silvia Dragoni - UCL Institute of Ophthalmology

POSTER TITLE
AMPK as a regulator of leakage in the ex vivo retinal microvasculature

AUTHORS
Dragoni S, Caridi D, Turowski P.

ABSTRACT
Vascular leakage can be the cause or a significant co-morbidity for neuro- and retinopathies. VEGF is a major leakage inducer, but anti-VEGF therapies only work on 50% of the patients. It is necessary to clarify VEGF pathway but also to study other leakage inducers such as Bradykinin (BK). To measure acute permeability in real time we used the ex-vivo retina model and we established the method in mice for the first time. Our results showed that VEGF and BK induced permeability in the ex vivo retina. This coincided with vascular activation of p38, hsp27 and eNOS. Using small molecule inhibitors we demonstrated the involvement of p38, Ca2+ and eNOS in both VEGFA- and BK-induced leakage responses.

Surprisingly we also detected the activation of AMPK, which has never been associate with permeability in the neuro-vasculature before. The knock down of AMPK in the retina made VEGF and Bradykinin unable to induce any permeability or signalling, which were induced instead by adding AMPK activators A769662 and AICAR to the control retina. Finally we proved that AMPK is upstream of eNOS and VE-cad. The ex-vivo retina proved to be a reliable method and uncovered the role of AMPK in VEGF/BK-induced permeability.

68. Chloe Hall - UCL Mechanical Engineering

POSTER TITLE
Effects of amyloidosis on regional mechanical properties of mouse brain

AUTHORS
Hall C, Sheridan GS, Moeendarbary E.

ABSTRACT
The role of cellular and tissue mechanics in Alzheimer's disease has been largely overlooked, particularly regarding the mechanical properties and mechanosensation of neurons and glia.

Using atomic force microscopy (AFM) indentation we create high-resolution stiffness maps of the hippocampus and amyloid plaques in ex vivo brain slices from a mouse model of Alzheimer's disease. We have shown mechanical heterogeneity of neuronal cell body and dendritic layers of the hippocampus, consistent with previous studies. Additionally, our preliminary results show that hippocampal regions in close proximity to amyloid plaques exhibit a significantly stiffer mechanical nature compared to surrounding plaque-free areas.

In contrast, AFM measurements on primary glial cells which internalise amyloid-beta-42 show a reduced apparent elastic modulus. It's interesting that the soluble form of amyloid-beta exerts the opposite effect on the mechanical properties of individual cells when compared to neural tissue expressing aggregated plaques. These contrasting effects in our mechanical data may be linked to evidence that oligomeric amyloid-beta-42 is the most toxic species and that its aggregation into plaques reduces neurodegeneration.

We therefore hypothesise that insoluble amyloid plaques and soluble amyloid-beta oligomers will cause aberrant mechanical signalling in the brain, potentially contributing to the altered synaptic transmission seen in Alzheimer's disease.

69. Katarzyna Kozdon - UCL Computer Science

POSTER TITLE
Evolving AI: functional and structural plasticity in learning and homeostasis

AUTHORS
Kozdon K, Bentley P.

ABSTRACT
Despite artificial intelligence being hailed as brain-inspired, the link between AI and information processing in the brain is very questionable. Spiking neural networks, the third generation of artificial neural networks, aspire to mimic the activity of biological neurons

more closely than traditional AI, and to take advantage of the information contained in the temporal encoding of signals. Unlike traditional AI, spiking networks are characterised by action potential-like activation function, and use unsupervised learning method inspired by the Hebbian learning rules. Spiking networks are a promising tool for unsupervised processing of spatio-temporal data. However, despite their potential, spiking neural networks remain a niche area of research, they do not perform as well as the traditional AI approaches, and their real-world applications are limited. Here, we describe artificial neural networks with functional and structural plasticity; our networks were developed and optimised using evolutionary algorithms. We explored the role of selected plasticity mechanism in learning, and in maintaining the balance between learning and homeostasis. Networks' ability to recognise movement direction and shape was tested using simple videos. Our model allows implementation of brain-inspired unsupervised learning mechanisms in the third generation of AI networks, and testing their potential using applied tasks.

70. Francois Kroll - UCL Department of Cell and Developmental Biology

POSTER TITLE
Behavioural phenotyping of zebrafish F0 knockout

AUTHORS
Kroll F, Rihel J.

ABSTRACT
Genome-wide association studies are identifying hundreds of candidate genes associated with complex neurological diseases such as Alzheimer's, autism and schizophrenia. An important challenge now is translating these correlations to causality. Zebrafish is becoming a popular model for such reverse genetic screens: 76% of these genes have a clear orthologue in zebrafish and the behaviour of larvae can be quantified early in development. Nevertheless, generating knockout lines remains the main bottleneck. The process typically involves raising two generations of animals to adulthood, which drastically limits throughput in terms of time, cost and ethics. Recent developments of the CRISPR-Cas9 system have greatly improved knockout efficiency directly in the injected animals and have made screening in this F0 generation feasible. However, genetic mosaicism is still perceived as an obstacle to screening for behavioural phenotypes in the F0. Using sets of four guide RNAs, we could generate hundreds of F0 knockout animals in a few hours with low to no mosaicism, as assessed by known morphological phenotypes. Next, we could faithfully replicate a complex day/night behavioural phenotype when the swimming bouts were analysed on a frame-by-frame basis. We hope this work paves the way towards behavioural screening in F0 knockout zebrafish.

71. Alan Mejia Maza - UCL Queen Square Institute of Neurology

POSTER TITLE
A new semi-automatic method to quantify NMJ innervation

AUTHORS
Mejia Maza A, Sudre C, Devoy A, Sleigh J N, Fisher E M.C.

ABSTRACT
The neuromuscular junction (NMJ) is a tripartite, peripheral synapse composed of 1) peri-synaptic Schwann cells, 2) the pre-synaptic motor neuron terminal and 3) the post-synaptic muscle fibre [1,2]. Many neuromuscular diseases show degeneration of NMJs prior to loss of motor neuron cell bodies in the spinal cord [3]. Characterisation of the NMJ in mouse disease models provides a robust way to assess pathological progression. Mouse NMJ denervation is most often manually assessed by eye, which can be influenced by the examiner, so impacting cross-study comparisons. Moreover, with manual assessments, it is difficult to pair innervation status with other important NMJ parameters such as pre- and post-synaptic volume. To objectively study the mouse NMJ, we have developed a semi-automated method to assess a variety of its morphological features. Here, we test the validity of our method to characterise NMJ pathology in a mouse model of Charcot-Marie-Tooth disease type 2D (CMT2D) with known NMJ degeneration [4].

72. Dominic Scaglioni - UCL Great Ormond Street Institute of Child Health

POSTER TITLE
Optimisation of a high–throughput digital script for multiplexed immunofluorescent analysis of dystrophin, associated protein complex (DPC) and myofibre regeneration in entire transverse sections of muscle biopsies in Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD)

AUTHORS
Scaglioni D, Ellis M, Catapano F, Torelli S, Chambers D, Feng L, Morgan J, Muntoni F, Phadke R.

ABSTRACT
The primary molecular endpoint for many DMD clinical trials is the restoration of dystrophin protein. For accurate endpoint analysis, there is an urgent need to develop reliable, robust and objective quantification methodologies. We have developed an automated, high-throughput method for multiplexed immunofluorescent analysis of dystrophin, dystrophin associated proteins (DAPs) and regenerating myofibres in entire transverse sections of skeletal muscle biopsies. Whole section fluorescent slide scanning enabled assessment and quantification by image analysis of entire tissue sections from DMD, Becker muscular dystrophy (BMD) and control muscle biopsies. The script quantifies fluorescence intensity, percentage coverage and colocalisation data for dystrophin and DAPs at single myofibre as well as whole section level. Accurate identification of dystrophin positive sarcolemmal regions allows for the assessment of co-localised DAP fluorescence intensity. Selective assessment of DAP fluorescence intensity within regions of dystrophin positive sarcolemma compared to dystrophin negative regions enabled quantification of molecular functionality of restored dystrophin in assembly of the dystrophin associated protein complex. Overall, we present a novel digital dystrophin quantification script capable of multiparametric and unbiased analysis of dystrophin in relation to key DAPs and myofibre regeneration and its molecular functionality. Rigorous optimisation strategies are implemented to demonstrate ‘clinical trial readiness’ and regulatory compliance.

73. Marc Soutar - UCL Queen Square Institute of Neurology

POSTER TITLE
FBS/BSA media concentration determines CCCP's ability to depolarize mitochondria and activate PINK1-PRKN mitophagy

AUTHORS
Soutar M, Kempthorne L, Annuario E, Luft C, Wray S, Ketteler R, Ludtmann M H.R, Plun-Favreau H.

ABSTRACT
Mitochondrial quality control is essential for maintaining a healthy population of mitochondria. Two proteins associated with Parkinson's disease, the kinase PINK1 and the E3 ubiquitin ligase Parkin, play a central role in the selective degradation of heavily damaged mitochondria (mitophagy), thus avoiding their toxic accumulation.
Most of the knowledge on PINK1/Parkin mitophagy comes from in vitro experiments involving the treatment of mammalian cells with high concentrations of mitochondrial uncouplers, such as CCCP. A matter of controversy between mitochondrial physiologists and cell biologists is the discrepancy between concentrations of CCCP needed to activate mitophagy (usually >10μM), when compared to the much lower concentrations used to depolarize mitochondria (<1μM). Thus, there is an urgent need for optimizing the current methods to assess PINK1/Parkin mitophagy in vitro. In this study, we compare the methods commonly used by mitochondrial physiologists and biologists (live fluorescence microscopy and biochemistry respectively) to assess the ability of CCCP to depolarize SHSY5Y cells (Parkin overexpressing (POE)) and induce subsequent mitophagy.

74. David Zhang - UCL Queen Square Institute of Neurology

POSTER TITLE
Incomplete annotation of OMIM genes is likely to be limiting the diagnostic yield of genetic testing, particularly for neurogenetic disorders

AUTHORS
Zhang D, Guelfi S, Ruiz SG, Costa B, Reynolds RH, D'Sa K, Liu W, Courtin TP, Peterson A, Jaffe AE Hardy J, Botia J, Collado-Torres L, Ryten M.

ABSTRACT
There is growing evidence to suggest that gene annotation remains incomplete and that this may have a disproportionate impact on the human brain transcriptome. Here, we use RNA-sequencing data from GTEx to detect and validate transcription in an annotation-agnostic manner across 13 human brain regions and an additional 28 human tissues, and thereafter connect novel expressed regions to known genes. While we find novel transcription to be widespread, it is most abundant in human brain. We find that genes highly expressed in brain are significantly more likely to be renannotated, as are genes associated with Mendelian and complex neurodegenerative disorders. Overall, we improve the annotation of 63% of known OMIM-morbid genes and 65% of those with a neurological phenotype. Furthermore, we find that novel transcribed regions, particularly those identified in brain, tend to be poorly conserved across mammals but are significantly depleted for genetic variation within humans. Using the example of SNCA, we explore the implications of gene re-annotation for Mendelian and complex forms of Parkinson's disease. We validate, both in silico and experimentally a novel, brain-specific, potentially protein-coding exon of SNCA.

Finally, we release our findings as tissue-specific transcriptomes in a BED format and in an online platform vizER (http://rytenlab.com/browser/app/vizER). Together these resources will facilitate basic genomics research with the greatest impact on neurogenetics.

Sensory and Motor Systems | Drama Studio

75. Elena Amoruso - UCL Institute of Cognitive Neuroscience

POSTER TITLE
Investigating face perception distortions in controls and in one-handers: effects of sensorimotor cortical reorganisation on tactile localisation

AUTHORS
Amoruso E, Muret D, Longo M, Kirker S, Makin T.

ABSTRACT
Hand absence (congenital or acquired) is a key model for studying reorganisation in the human brain. While hand-face remapping in the sensorimotor cortex has been reported in one-handers, the perceptual consequences of this remapping remain unclear.
To investigate this , we compare how precisely and consistently congenital one-handers and acquired amputees localise touches on their face compared to matched controls.
Considering that a minimal amount of face remapping and a maintained hand representation has been reported in acquired amputees (Makin et al., 2015, Brain), we expect the mixed signals to lead to an increased variability in localisation in acquired amputees. Conversely, large-scale hand-face remapping has been observed in congenital one-handers (Hahamy et al., 2017, Current Biology). We thus hypothesise a decreased variability in localisation judgements in this group. Participants are randomly touched on one of 12 locations on their face. After each touch, they are asked to localise the felt location of the touch on a 3D face template displayed on a screen. Quantification of variable and constant error will allow us to infer participants' precision and potential biases for each target. Data collection is in progress and preliminary results will be presented at the symposium.

76. Ali Bangash - Wolfson Institute of Biomedical Research at UCL

POSTER TITLE
Axonal Protein Translation in Sensory Neuronal Pain Circuits

AUTHORS
Bangash MA, Millet Q, Gossage SJ, Santana-Varela S, Alles SRA, Zhao J, Cox JJ, Wood JN.

ABSTRACT
Pain is an essential physiological response to a variety of clinical injuries and its maintenance is linked to the expression of several specific genes in dorsal root ganglion (DRG) sensory neurons. Translational regulation of these mRNAs contributes to the adaptive response of the body to pain and mutations in key translation regulator genes like FMRP are linked to pain phenotypes in humans. While translational control of pain pathways has been demonstrated in the soma and peripheral terminals of DRGs, direct evidence of this occurring locally in central axonal projections in the spinal cord in vivo is missing

because of the heterogeneity of pre- and post-synaptic targets. We have utilized an axon-Translating Ribosome Affinity Purification (TRAP) method that allows specific high-throughput micro-array analysis of ribosome-bound actively translating mRNAs in central terminals of DRG neurons. Our strategy shows that adult DRG central terminals have a unique and complex translatome that potentially regulates neurotransmission, axon survival and growth enabling the formation and maintenance of neural circuits in vivo. These genes have strong links to clinical pain phenotypes and present targets for novel therapeutic strategies.

77. Maxime Beau - Wolfson Institute of Biomedical Research at UCL

POSTER TITLE
Probing the functional interactions between distinct distinct elements of the cerebellar cortex and deep nuclei circuitry in awake behaving mice

AUTHORS
Beau M, Chung Y, Kostadinov D, Paredes M, Hausser M.

ABSTRACT
The functional interactions between neurons in the cerebellar cortex and nuclei are crucial for understanding how the cerebellar output is computed, and yet are almost completely unexplored in behaving animals. This requires simultaneous recordings from neurons in the two brain areas, which is technically extremely challenging. To adress this problem, we have employed a new recording approach - Neuropixels silicon probes, which allow for sampling from 384 densely-spaced recording channels along a linear shank of approximately 4mm that is capable of spanning both cerebellar cortex and nuclei. We have used this approach to develop a workflow for characterizing correlation patterns within and between these regions while attributing them to optogenetically identified cerebellar cell types, recorded in awake head-fixed mice performing a sensorimotor integration behavioral task. Our results highlight the potential of employing new generations of silicon probes to address an unexplored direction in cerebellar research.

78. Bruna Caridi - UCL Institute of Ophthalmology

POSTER TITLE
Galectin-1 as a new therapeutic target in Diabetes-Induced Vascular Leakage

AUTHORS
Caridi B, Dragoni S, Turowski P.

ABSTRACT
The clinical benefit conferred by anti-vascular endothelial growth factor (VEGF) agents in retinal vascular diseases is unsteady. Galectin-1 (Gal1) activates a VEGF-like-compensatory pathway which plays a significant role in vascular permeability. Gal1 abluminally induced permeability in both ex vivo retina and rat brain Endothelial Cells. Based on small molecule inhibitors, our results indicated that VEGFR2 was involved in mediating Gal1-induced permeability. We confirmed that Gal1 is likely to bind Aflibercept (AFL), since its permeability inducing activity was completely suppressed by this agent. In addition, inhibition of Ca2+, eNOS, and p38 signalling pathways blocked the Gal1 response, indicating dependency on pathways also used by VEGF-A. Gal1 was found in the ganglion cell layer (GCL) and

choroid in mice, rats and humans. Staining appeared not to be associated with the vasculature in healthy tissue. However, staining increased in diseased retinae with accumulation around the vasculature. In human retinae, enhanced staining was not only found in samples from patients with Diabetic Retinopathy (DR) but also with diabetes without DR, suggesting that Gal-1 enrichment may occur generally in diabetes. Our results highlight the importance of marking Gal-1 interactions in VEGF-targeted therapies to increase the efficacy of those treatment.

79. Elisa Clemente - Wolfson Institute of Biomedical Research at UCL

POSTER TITLE
Trigeminal activity underlying thermal nociception in zebrafish

AUTHORS
Clemente EC, Browne LE, Dreosti E.

ABSTRACT
The ability to detect and respond to noxious stimuli plays a crucial protective role. It is essential for survival and shared across different species. However, it is still poorly understood how noxious stimuli are encoded by peripheral and central mechanisms. Rodents are commonly used as a model to study nociception, but the complexity and considerable inaccessibility of their nervous system can make it hard to answer certain questions. Zebrafish, conversely, are transparent (up to juvenile stages), amenable to multiple genetic techniques and comparably simpler, while still expressing conserved molecules known to be involved in nociception in rodents and humans. Here, we use the zebrafish as a model to understand how trigeminal neurons respond to thermal noxious stimuli. By using an infrared laser, we are measuring behaviour in response to innocuous warmth and noxious heat in restrained zebrafish. We will then use the same stimuli and genetically encoded calcium reporters to understand how trigeminal neurons respond to this range of thermal stimuli. Additionally, we are generating mutants for genes that have been shown to reduce or abolish pain in rodents and humans. Taken together, we aim to understand the role of these genes and trigeminal neurons in detecting thermal noxious stimuli.

80. Charlie Dowell - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Function and coordination of oculomotor and locomotor circuits

AUTHORS
Dowell CK, Bianco IH, Bianco Lab.

ABSTRACT
Vertebrates make rapid eye movements called saccades to fixate and scan their environment, often accompanied by other body movements to orient gaze. What circuits determine the degree of saccade-body coordination is not fully understood. In tethered larval zebrafish saccades are often followed by a turning tail beat at short latency. We found that these directional swims typically occur after saccades in a relatively narrow range of post-saccadic gaze angles, suggesting that a command of intended gaze might be decomposed into eye and body rotations. To investigate the neural basis of saccade generation and

coordination with tail movements, we functionally imaged the hindbrain since it is crucial for motor control, housing the oculomotor nuclei and all projection neurons from the brain to spinal central pattern generators. By clustering cells according to inferred spike rates and mutual information relative to different classes of eye and tail movement, we found anatomically discrete populations of cells that may drive specific oculomotor behaviours and associated locomotion. Photoconversion of fluorescent proteins in these regions has identified connections to pretectum and tectum - known areas of sensory integration upstream of premotor neurons. Combined, these results will help us identify circuits that elicit and coordinate oculomotor and locomotor behaviours .

81. Harsha Gurnani - UCL Department of Neuroscience, Physiology & Pharmacology

POSTER TITLE
Coordinated population activity of cerebellar Golgi cells

AUTHORS
Gurnani H, Silver RA.

ABSTRACT
Sensorimotor encoding by cerebellar granule cells (GCs) is important for downstream associative learning and motor control. Golgi cells (GoCs) provide both feedforward and feedback inhibition onto GCs and can regulate their excitability and spike timing, shaping their population response. Theoretical work predicts that parallel fibre (PF) and mossy fibre (MF) inputs on GoCs, and electrical synapses between GoCs, have a differential effect on GoC synchrony [Maex 1998, Vervaeke 2010]. However, it has not been possible to study GoC networks experimentally, due to their sparse distribution in the input layer.
We present the first GoC population recordings in awake animals. We performed calcium imaging of sparsely distributed, GCaMP6f-expressing GoCs in awake, head-fixed mice using high-speed acousto-optic lens 3D two-photon microscopy [Nadella 2016]. GoCs in Crus I/II region revealed strong, coherent activation across the recorded population (20-70 cells/region) during spontaneous whisking epochs. Despite a slow-timescale (hundreds of milliseconds) GoC network coherence, nearby GoCs were not synchronous and showed heterogeneous modulation on faster timescales within different behavioural epochs.
Thus, GoC populations show local modulation superimposed on network-wide signals, suggesting a mixed role of global and tuned inhibition on potentially different aspects of sensorimotor processing.

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

POSTER TITLE
Supraspinal population activity patterns controlling locomotion

AUTHORS
Lau JYN, Valera AM, Silver A, Fitzgerald JE, Bianco IH.

ABSTRACT
How does the brain control the execution of distinct locomotor behaviours? For our model system, we use the reticulospinal complex of larval zebrafish, as these cells provide the main source of descending motor control. We combine two-photon calcium imaging of

reticulospinal neurons with high-speed behavioural tracking during a diversity of visually-evoked swims, and build models characterising the relationship between neuronal activity and locomotor kinematics. Examination of reticulospinal recruitment across different swim types has revealed unique, but partially overlapping activity patterns. Regression-based encoding models which describe a cell's activity using low-level tail kinematics support this: some cells show activity related to kinematics shared across swim types, while others show activity related to kinematics unique to specific swims. Laser ablation of such cells produces specific kinematic deficits without affecting shared elements of locomotion. We are conducting high-speed population calcium imaging using AOL microscopy during behaviour to develop decoding models which predict motor output from neural activity. Combining encoding and decoding models will elucidate how locomotor outputs are represented across this supraspinal population. Our current data supports a framework where sparse groups of supraspinal neurons form distinct "kinematic modules", and these modules can be differentially combined to generate a diversity of locomotor behaviours.

83. Dollyane Muret - UCL Institute of Cognitive Neuroscience

POSTER TITLE
Investigating the information content of cortical sensorimotor reorganisation in one-handers

AUTHORS
Muret D, Amoruso E, Kirker S, Makin TR.

ABSTRACT
Hand absence (congenital or acquired) is a key model for studying reorganisation in the human brain. For example, increased bold activity was reported in the missing hand cortex of congenital one-handers during face and feet movements, suggesting remapping of multiple body-parts (Hahamy et al, 2017, 2018). However, it is not clear whether this dramatic brain remapping bears any relevance to individuals' behaviour. A first step towards understanding the functional consequences of brain remapping is investigating the information content underlying it. We scanned congenital and acquired one-handers and two-handed controls. All participants performed two different movements (i.e., squeezing or pushing an object) with each of 5 different body-parts involved in one-handers' compensatory behaviour. Using Representation Similarity Analysis, preliminary results in control participants reveal that dissimilarities between the two movements (i.e., functional content) is available for each body-part within their respective canonical brain area. These preliminary results validate our fMRI paradigm, allowing us to determine whether activity patterns in the missing hand cortex of one-handers actually store information relevant to motor control of the over-represented body-parts. With increased samples (currently being acquired), this study will thus provide a comprehensive understanding of the functional content of the cortical reorganisation observed in one-handers.

84. Andrew Peters - UCL Institute of Ophthalmology

POSTER TITLE
Cortex predicts striatal activity during behavior

AUTHORS
Peters AJ, Steinmetz NA, Harris KD, Carandini M.

ABSTRACT
The dorsal striatum is necessary for learning and executing stimulus-guided movements, but it is unclear how much of this functionality is derived from the cortex which serves as its major source of input. We aimed to characterize the relationship between activity in the cortex and striatum by recording population activity within both structures simultaneously in mice during a visually guided task. Dorsal striatal activity was recorded with Neuropixels probes along a diagonal mediolateral trajectory while cortical activity was recorded using widefield calcium imaging. Using regression to predict striatal activity from cortical activity, we found a topographical relationship between striatum and cortex similar with anatomical projections. This functional topography allowed us to define striatal domains within our recordings, which were active during our task in a sensorimotor gradient across the mediolateral axis. Surprisingly, a simple kernel within cortex was able to predict task-relevant responses within the striatum, indicating that striatal activity largely follows cortical activity invariantly across stimulus or movement contexts. Striatal activity only deviated from cortical predictions slightly for contralateral stimuli and movements in a manner not present in naïve mice, indicating that the corticostriatal relationship is largely consistent but shaped by learning.

85. L. Federico Rossi - UCL Institute of Ophthalmology

POSTER TITLE
Excitatory and inhibitory intracortical circuits for orientation and direction selectivity

AUTHORS
Rossi LF, Harris KD, Carandini M.

ABSTRACT
The computations performed by a neuron arise from the functional properties of the circuits providing its synaptic inputs. A prime example of these computations is the selectivity of primary visual cortex (V1) for orientation and motion direction. V1 neurons in layer 2/3 (L2/3) receive input mostly from intracortical circuits, which involve excitation and inhibition. To understand how an L2/3 neuron achieves its selectivity, therefore, one must characterize the functional organization of both its excitatory and inhibitory presynaptic ensembles. Here we establish this organization, and show how it predicts orientation selectivity and reveals a new cortical circuit for direction selectivity. We identified the presynaptic partners of pyramidal neurons in mouse V1 through rabies monosynaptic tracing, and imaged the functional properties of the postsynaptic neuron and of its presynaptic ensemble. Excitatory presynaptic neurons were predominantly tuned to the postsynaptic neuron's preferred orientation. Excitation and inhibition described an inverted Mexican hat, with inhibitory presynaptic neurons densest near the postsynaptic neuron and excitatory ones distributed more distally. Excitation and inhibition also differed in laminar origin: inhibitory presynaptic neurons concentrated in L2/3 while excitatory ones dominated in L4. The distribution of excitatory neurons in visual space was coaxial with the postsynaptic neuron's preferred orientation and lay upstream of the neuron's preferred direction. Inhibitory presynaptic neurons, instead, clustered more symmetrically around the postsynaptic neuron and favoured locations downstream of its preferred direction. These results demonstrate that L2/3 neurons obtain orientation selectivity from co-tuned neurons in L4 and beyond, and enhance it by contrasting an elongated excitatory input with a concentric inhibitory input. Moreover, L2/3 neurons can obtain direction selectivity through visually offset excitation and inhibition. These circuit motifs resemble those seen in the thalamocortical pathway and in direction selective cells in the retina, suggesting that they are canonical across brain regions.

86. **Maria Slobodina - UCL Department of Neuroscience, Physiology & Pharmacology**

POSTER TITLE
Cortical oscillatory dynamics in pre-term and full-term human infants

AUTHORS
Slobodina M, Whitehead K, Laudiano-Dray MP, Meek J, Fabrizi L.

ABSTRACT
Brain oscillations are important for the transfer and processing of information. These functions can be made more effective by coupling oscillations at different frequency bands. This coupling enhances the brain's capacity to transfer information along different spatial and temporal scales and facilitates carrying out multiple cognitive processes in parallel with slow frequency oscillations often acting as carrier for faster oscillations. In preterm electroencephalography (EEG), delta waves are frequently coupled with alpha-beta oscillations forming a complex known as delta brush, which is considered important for the development of sensory cortical networks. To test whether this coupling is developmentally regulated, we calculated the association between the phase of delta frequencies (1-2 Hz) and the amplitude of alpha-beta oscillations (8-20 Hz), using The Kullback-Liebler Modulation Index, at the scalp EEG sites overlying right and left somatosensory cortex during natural sleep in 102 pre-term and full-term neonates. These indices were then correlated with corrected gestational age (range 34 to 43 weeks). The coupling significantly decreased with age (by 3.5%), suggesting that the association between delta and alpha-beta oscillations is specific to the equivalent to the last trimester of gestation.

87. **Madeleine Verriotis - UCL Great Ormond Street Institute of Child Health**

POSTER TITLE
Structural brain changes in children with neuropathic pain: preliminary results

AUTHORS
Verriotis M, Sorger C, Peters J, Seunarine K. Walker SM, Clark C, Moayedi M.

ABSTRACT
Background:
Neuropathic pain (NP) in children can be difficult to diagnose and manage (1). Causes can differ from adults. To improve management, multimodal characterisation including neuroimaging is needed to indicate potential mechanisms, but there is limited neuroimaging research in children and young people (CYP).

Aim: To assess the feasibility & acceptability of neuroimaging in CYP with NP, and explore structural brain abnormalities.

Methods: Structural T1-weighted MRI scans (Prisma 3T scanner) from 18 CYP (F=9; mean age 14.2±2.1 years) attending the GOSH Pain Service who are clinically diagnosed with NP were compared with 47 healthy controls (F=40; mean age 13.9±1.9 years).

Results: 71% of CYP approached consented to MRI. After the scan, over two-thirds of families rated the acceptability of having an MRI as 10/10 (0=not at all acceptable; 10=very

much so; range 7-10/10). There was a strong negative relationship between age and bilateral amygdala volume in CYP with NP (n=18; r=0.55,p=0.019 and r=0.58,p=0.011 for L & R amygdala) but not controls (n=47; NS). These between-group differences were significant for the right amygdala (Fisher r-to-z 1-tailed test, z=1.71, p=0.043).

Conclusions: MRI was feasible and acceptable in a small cohort of CYP with NP. Preliminary analysis suggests structural abnormalities and age-related differences.

Acknowledgements: Additional members of the Developmental Imaging and Biophysics Section at the UCL GOS Institute of Child Health (Manuela Martinez-Barona Soye & Jamie M Kawadler; Section Head Professor Chris Clark) provided data from healthy control participants.

Funding: Great Ormond Street Hospital Children's Charity Grant W1071H & W1071I (to S.M.W); University College London – University of Toronto Joint Research and Exchange project grant (to S.M.W, M.M., M.V., & C.C.); Child Health Research Charitable Incorporated Organisation PhD grant 18/19-STU7 (to M.V., S.M.W., & C.S.).

References: 1. Howard RF, Wiener S, Walker SM. Neuropathic pain in children. Arch Dis Child. 2014 Jan;99(1):84–9.

88. Letizia Vestito - UCL Ear Institute

POSTER TITLE
Identifying genetic variants that underlie hereditary hearing loss within the 100,000 genomes project

AUTHORS
Vestito L, Ellingford J, Rosser E, Smedley D, Dawson S, Bitner-Glindzicz M.

ABSTRACT
Although mutations in over a hundred genes can cause hereditary hearing loss (HHL) in humans, less than 50% of HHL is explained by mutations in known genes. Moreover, their respective contributions to the frequency and type of inherited deafness are largely unknown. The opportunity to identify novel hearing genes by whole genome sequencing through the 100,000 Genomes Project has the potential to bridge this gap in our current knowledge. We have developed an analysis pipeline with the aim of identifying causal variants in probands with HHL utilising Exomiser and Genomiser to re-analyse sequences from individuals with no primary finding (NPF). A number of probands were recruited to the study with hearing or ear abnormality as a 'primary phenotype' and many more individuals had hearing or ear abnormality as a 'secondary phenotype'. We report the case of two sisters with hearing loss, microcephaly, intellectual disability, global developmental delay, delayed motor development and various other dysmorphic features. The two sisters were identified to have a likely pathogenic intronic mutation in TAF6 gene, a rare cause of Alazami-Yuan Syndrome.

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

POSTER TITLE
Experience shapes tectal activity and visually evoked behaviour

AUTHORS
Zylbertal A, Bianco IH.

ABSTRACT
What determines the behavioural response to a sensory stimulus? Here we examine how sensory-evoked neural activity and the associated visually guided behaviour are dynamically shaped by past experience. We combine a naturalistic behavioural assay in partially-tethered zebrafish larvae with high-speed volumetric calcium imaging using light-sheet microscopy. To account for observed variability in sensory-evoked activity, we modelled the responses of individual neurons to a set of prey-like visual stimuli, differing in spatial location, size and velocity. This analysis revealed that responses are strongly modulated by recent spontaneous and evoked activity within neuronal ensembles in the optic tectum, a key sensorimotor hub. In turn, the variable activity emerging from this modulation accurately predicts the release probability and latency of ensuing hunting behaviour. These dynamical processes enable integration of activity over a time scale of minutes, and result in potentiated responses to novel stimuli that are associated with fast and reliable behavioural outcomes. These findings suggest that stimulus history may affect behavioural outcomes by modulating early sensory processing. This unveils a key component of the neural substrate that govern variability in visually-guided behaviour.

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

90. Matteo Carandini - UCL Institute of Ophthalmology

POSTER TITLE
Charting the Structure of Neuroscience

AUTHORS
Carandini M.

ABSTRACT
What do neuroscientists study? To answer this question, I analyzed the itineraries created by attendees of the 2018 meeting of the Society for Neuroscience. I used co-occurrence in these itineraries to visualize and cluster the topics of the presentations they selected.The results reveal that some topics that might appear cognate are in fact distant. Other topics that were considered distinct are coalescing into regions of close interaction.

91. Yun Yung Cheng - UCL Queen Square Institute of Neurology

POSTER TITLE
A systematic review of DNA methylation in neurodegenerative diseases

AUTHORS
Cheng YY, Bettencourt C.

ABSTRACT
Neurodegenerative diseases (e.g. Alzheimer’s and Parkinson’s disease, frontotemporal dementia, amyotrophic lateral sclerosis, Huntington’s disease) are becoming increasingly

prevalent, in part because the elderly population has increased in recent years. Currently, there is no cure for any of these diseases. To elucidate the complex etiology of neurodegeneration a considerable amount of research has focused on identifying DNA sequence variation. However, discordance in disease development and onset in monozygotic twins has led to a rapidly expanding number of studies investigating epigenetic modifications. Epigenetics refers to changes in gene expression that do not entail a change in DNA sequence. Several studies, mostly focusing on DNA methylation and using both candidate-loci and genome-wide approaches, have provided valuable observations in different neurodegenerative diseases. This study aims to achieve a more comprehensive and updated understanding of the role of DNA methylation in neurodegeneration, by identifying and synthesizing all literature available in several electronic databases in a systematic way. We are using a rigorous protocol-driven approach and following PRISMA guidelines. In our search, DNA methylation and related terms are considered the exposure and neurodegenerative diseases the outcome. We will present the results from our systematic review and discuss major findings.

92. Janet Clark - UCL Department of Neuroscience, Physiology & Pharmacology

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.

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POSTER TITLE
Functional annotation of dementia-related miRNAs using the Gene Ontology

AUTHORS
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ABSTRACT
To understand the basis of disease it is crucial to know the functions of the genes involved and the pathways they act in. MicroRNA regulation of cellular processes is a relatively new field of study, but there is intense interest in this field, due to the potential use of microRNAs as therapeutic agents and biomarkers. The association of Gene Ontology (GO) terms with gene products has proven to be highly effective for large-scale analysis of biomedical datasets, but until recently there has been no substantial effort dedicated to applying GO terms to microRNAs. We have recognised this gap and have started an initiative to curate microRNAs. We will illustrate how our functional annotations can be used to visualise the roles of individual microRNAs in a dementia-relevant molecular interaction network, thereby demonstrating that this resource will be a valuable addition to the advancement of microRNA research and may be used to predict proteins with a role in dementia.