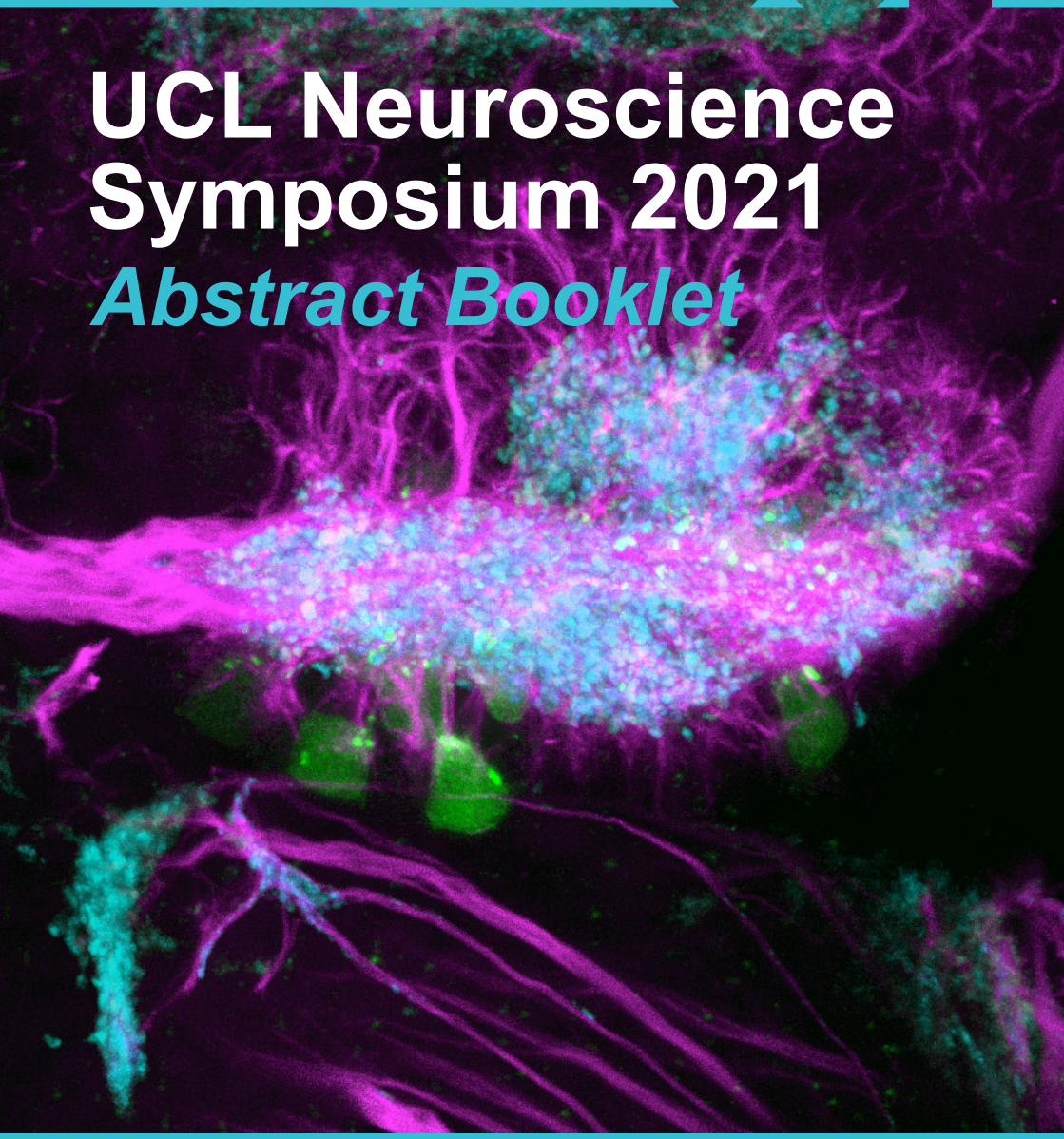
UCL NEUROSCIENCE DOMAIN

UCL Neuroscience Symposium 2021

Abstract Booklet



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2021 Rapid Poster Presentation Prize

The 10 posters shortlisted for the 2021 Rapid Poster Presentation Prize are highlighted in blue

Cognition and Behaviour

1. Ilinca Angelescu - Max Planck UCL Centre for Computational Psychiatry and Ageing Research

POSTER TITLE
Measuring mood bias on reward with a brief smartphone task

AUTHORS
Angelescu I, Mason L, Rutledge R

ABSTRACT
Mood is an important determinant of well-being, affecting many areas of daily functioning. Research using reinforcement learning tasks has shown that the interaction between mood and behaviour is bidirectional: experiences affect mood (Kuppens, Oravecz, & Tuerlinckx, 2010) while mood affects the appraisal of experiences (Tamir & Robinson, 2007). Under laboratory conditions, it has been shown that positive moods can increase the subjective value of reward outcomes, while negative moods have the opposite effect (Eldar & Niv, 2015). Depression is characterised by strong negative moods, but it is controversial whether depressive symptoms reduce sensitivity to rewards (Xie et al., 2021; Rutledge et al., 2017). In a large sample (N=3099), we evaluated a brief smartphone-based reinforcement learning task to quantify an individual mood bias on the perception of reward. In depressed and non-depressed individuals, we found that negative mood induction had a stronger effect on mood despite being worth an equivalent number of points. Mood change was modulated parametrically with the wheel of fortune across ten outcomes ranging from large losses to large gains. Participants in the clinical range for depressive symptoms reported ratings of momentary happiness throughout the task that were consistently lower, but there was no difference in mood change between participants with and without mood symptoms. Furthermore, we found that the extent of the impact of negative mood inductions was predictive of preference for stimuli learned about before vs after the mood induction. Thus, the task has promise as a brief cognitive probe for measuring a bias of mood on learning.

2. Roberta Bianco - UCL Ear Institute (Presenting on the day, Room 2- Cognition & cognitive dysfunction)

POSTER TITLE
Long-term implicit memory for sequential auditory patterns in humans

AUTHORS
Bianco R, Chait M.

ABSTRACT
Memory is critical to discover regularities in our environment and in communication signals such as music and language. Despite growing empirical accounts of our sensitivity to structures in sounds, longstanding questions pertain to how memory supports such sensitivity. We combined behavioural manipulation and modelling to investigate the dynamics of auditory memory formation and its long-term effects. Participants listened to rapid sequences of 20 random tones interspersed with repeated patterns. They were asked to press a button as soon as they detected a repeating pattern. Most of the patterns were new but some reoccurred every three minutes unbeknownst to the listeners. We found that listeners became progressively faster in response to the patterns to which they were exposed sparsely and only a few times. Remarkably, the memory for these patterns was implicit and lasts for months after initial exposure. The listeners' behaviour was reproduced by a statistical learning model integrating parameters associated with sensory memory buffer, short- and long-term memory decay. These findings offer a new venue to understand what sound features are committed to memory and how failure of mnemonic operations, such as encoding or retrieval, may hamper humans' ability to capture fine structures within temporally evolving sounds.

3. Sylvia Blackmore - Queen Square Institute of Neurology (Presenting on the day, Room 2 - Cognition & cognitive dysfunction)

POSTER TITLE
Predictive coding and spectral asymmetry in PFC

AUTHORS
Blackmore S, Veselic S, Kennerley S.

ABSTRACT
Predictive coding is a neural process theory with specific hypotheses as to how predictions and prediction errors are coupled in the brain. Previous work in the sensory domain has shown predictions and prediction errors are encoded at different frequencies in local field potential activity, indicating a spectral asymmetry between predictions and prediction errors. Tests of these prediction in higher order cognition, and the prefrontal cortex in particular, have been less frequent. However, regions of the prefrontal cortex have been shown to perform such computations in single neuron recordings encoding value and reward prediction error. Here, we tested predictions of predictive processing in four subregions of the PFC. We recorded LFP activity from monkeys while they performed a value-guided decision-making task, and found all four subregions of PFC encoded either probability or magnitude of reward using the same frequency band (theta). Reward prediction errors were encoded at higher frequency bands. Our findings show evidence in support of a spectral asymmetry between the encoding of predictions and prediction errors in PFC.

4. Edmund Chong - Sainsbury Wellcome Centre

POSTER TITLE
A novel behavioral paradigm for parametric spatial working memory in rats

AUTHORS
Chong E, Calcaterra L, Akrami A

ABSTRACT
Spatial working memory (SWM) is the short-term maintenance and update of spatial information. SWM is important for a broad range of cognitive tasks that involve reasoning about physical objects and spatially-organized information, even in abstract non-spatial contexts. What are the neural computations underlying SWM?

We trained rats to perform a novel, parametric SWM task (PSWM), where 2D visual stimuli are projected onto the floor of a large behavioral arena, and animals learn to maintain stimulus locations in their working memory over a delay period. Our projection arena exploits the previously-reported tendency of rodents to attend to stimuli close to the ground, and their rapid acquisition of visual tasks involving such stimuli. Our paradigm additionally overcomes several key limitations of existing rodent SWM tasks: target location is continuous as opposed to discrete, and can be systematically controlled. It also spans a large space within animals' field of view, and mimics rodent naturalistic behavior. Animals were successfully trained to perform the task over several weeks, and we obtained a precise behavioral readout of the spatial precision of working memory in continuous spatial coordinates. Future experiments will involve the use of multiple tools to monitor and perturb brain activity during task performance, allowing the detailed investigation of the neural computations underlying PSWM behavior.

5. Louis Dannatt - UCL Queen Square Institute of Neurology

POSTER TITLE
Unsupervised clustering on task-related representations in the prefrontal cortex

AUTHORS
Dannatt L, Butler JL, Kennerley S.

ABSTRACT
Neuronal representations in the prefrontal cortex (PFC) are complex and highly heterogeneous. The classical view suggest that neurons are selective to decision and task variables with single neuron activity, similar to receptive fields in the visual cortex. More recently, however, it has been proposed that neurons are selective to random mixtures of task variables and can only be understood at the population level. There is evidence of both in the PFC which leads to believe that the area represents decision variables through a combination of single neuron activity and random mixed selectivity. To the best of our knowledge, we apply for the first time a clustering algorithm on non-human primate neuronal representations in the PFC. This method is a non-biased approach and can simultaneously find single neuron and random mixed selective populations. We find evidence of both types of selectivity and differences of selectivity in areas of the PFC.

6. Constance Destais - UCL Institute of Cognitive Neuroscience

POSTER TITLE
Investigating accuracy maximisation as a possible cause for negative affective bias

AUTHORS
Destais CA, Ibrahim LF, Locke SM, Robinson OJ

ABSTRACT
Negative affective bias is the tendency to prioritise emotionally negative or unfavourable information or outcomes, and is exacerbated in mood disorders. However, little is known about what underlies this bias. We test whether a need for accuracy, rather than reward, drives negative affective bias. We modulate priors and payoffs in a perceptual-discrimination-task to create a trade-off between accuracy- and reward-maximisation. Using signal detection theory, we obtain participants' decision criteria and compute a benchmark decision-threshold for optimal accuracy-maximisation. The difference between participants' decision criteria and this benchmark measures their accuracy-maximisation. Bias is measured on a previously-validated cognitive task. We predicted that participants showing more negative bias would show greater accuracy-maximisation. In a small pilot sample (n=13), counter to predictions, there was a trend for a negative correlation (r=-0.15,p=0.63) between participants' negative bias and accuracy-maximisation. This suggests that accuracy maximisation does not drive negative bias, however, the small sample size prevents us from drawing strong conclusions. Future work will replicate this in a larger sample (n>100), in which we also test whether negative bias correlates with self-reported preference for accuracy, and whether accuracy-maximisation correlates with self-reported psychiatric symptoms.

7. Samuel Failor - UCL Queen Square Institute of Neurology

POSTER TITLE
Learning orthogonalizes visual cortical population codes

AUTHORS
Failor SW, Caranidni M, Harris KD

ABSTRACT
The response of a neuronal population to a stimulus can be summarized by a “rate vector” in a high-dimensional space. Learning theory suggests that the brain should be most able to produce distinct behavioral responses to two stimuli when the rate vectors they evoke are close to orthogonal. To investigate how learning modifies population codes, we measured the orientation tuning of 4,000-neuron populations in visual cortex before and after training on a visual discrimination task. Learning suppressed responses to the task-informative stimuli, most strongly amongst weakly-tuned neurons. This suppression reflected a simple change at the population level: sparsening of population responses to relevant stimuli, resulting in orthogonalization of their rate vectors. A model of F-I curve modulation, requiring no synaptic plasticity, explained the learning effect.

8. Wanying Gan - UCL Queen Square Institute of Neurology

POSTER TITLE
To investigate the relationship between music preference and perceptual speed in a music-in-noise task.

AUTHORS
Wanying G

ABSTRACT
Musical preference drives individual musical tastes and sensitivity of specific acoustic characteristics. Several neuroimaging studies have shown regions that respond more actively in perceiving liked music versus disliked music. An ERP study reported that acoustic characteristics such as rhythm, timbre and melody were perceived at different levels when listening different music genres. Based on previous findings, however, little known in how these musical characteristics represent in the cortex, and the neural representation of musical preference remains unclear.

By referring to speech-in-noise test and Coffey et al.(2019)'s music-in-noise task, this study created a music-in-noise detection task that make participants detect music clips with background noise of environmental sounds, at specific signal-to-noise levels. In this online behavioural experiment we focused on peoples' reaction speed when listening out for three genres of music: Jazz, Country and Rock, and try to find out the relationship between reaction speed and preferred music genre. The reaction time was recorded during the experiment. The result showed that the average reaction time when listening the preferred music genre was shorter than listening other music genres. But for later music genre recognition task, the result was affected by participants' familiarity of music. The next step can analyse frequency spectrum at the point of reporting hearing music, on acoustic level.

9. Alexandra Gilbert - UCL Department of Cell and Developmental Biology (Presenting on the day, Room 5 - Neural circuits and behaviour)

POSTER TITLE
Modulating sleep homeostasis using long and short days in zebrafish

AUTHORS
Gilbert A, Rihel J

ABSTRACT
A pervasive mystery in neuroscience and medicine is how we build up sleep pressure while we're awake and release it during sleep. By modulating sleep pressure through changes in waking time, we can study the homeostatic response to sleep deprivation and identify the molecular targets regulating sleep homeostasis. Traditionally, harsh drugs and harmful physical sleep deprivation assays are used to induce sleep homeostasis in the larval zebrafish in order to discover these critical targets. Here, we present a simple method for studying sleep homeostasis by changing the day length of larval zebrafish. Following longer days (extended light phase), zebrafish exhibit increased sleep pressure as measured by three metrics: 1) they fall asleep quicker (shorter sleep latency), 2) they have more total sleep, and 3) they have more consolidated sleep (increased sleep bout lengths). Following shorter days (shortened light phase), larvae show lowered sleep pressure. Our results demonstrate that using long and short days is an effective, mild and high-throughput method to study the neural and molecular mechanisms driving sleep homeostasis in zebrafish. We use sleep-regulating drugs such as caffeine and melatonin as well as sleep mutants to show that our method is consistent with traditional methods of sleep pressure modulation.

10. Elena Gutierrez - UCL Queen Square Institute of Neurology

POSTER TITLE
OFC encodes novelty during a novel associative learning task in rhesus macaques

AUTHORS
Gutierrez E, Veselic S, Kennerley S

ABSTRACT
Every day we choose between options never encountered before. However, the pervasiveness of novelty in naturalistic decision-making has so far been poorly reflected in non-human primates studies investigating neural responses to decision variables. Here, we analysed neuronal activity during a task involving choices between well-learned ("overtrained") or novel stimuli to address the question of how novelty is encoded at the neuronal level in the anterior cingulate cortex (ACC) and orbitofrontal cortex (OFC), prefrontal regions underlying value-based computations. Although both regions encoded all decision parameters, a greater proportion of OFC neurons encoded a pure novelty signal. Value coding in OFC was also particularly tuned to whether a stimulus was novel: the encoding of value in novel and overtrained trials was more positively correlated in ACC than in OFC, and the former region presented a greater proportion of neurons encoding value on both trial types. Finally, novelty-related OFC activity declined as stimuli became more familiar. Altogether, these results posit OFC as a critical locus for the encoding of novelty as a decision variable.

11. Anna Hengstschlaeger - UCL Division of Psychiatry (Presenting on the day, Room 2 - Cognition & cognitive dysfunction)

POSTER TITLE
What are the neural correlates of impaired awareness of social cognition and function in dementia? A systematic review.

AUTHORS
Hengstschläger A, Sommerlad A, Huntley J.

ABSTRACT
Introduction: Deficits in social cognition and function are characteristic of dementia and are commonly accompanied by losing awareness of presence or extent of these deficits. This lack of awareness can impair social relationships, increase burden for patients and carers, and contribute to higher institutionalization rates. Despite clinical importance, neural correlates of awareness of social cognition and function in dementia remain unclear. Method: A systematic review of functional and structural neuroimaging studies was conducted to investigate neural correlates of impaired awareness of social cognition and function in any dementia type.

Results: Eight studies were included in the review. Deficits in awareness of impairments in social cognition and function were associated with structural or functional abnormalities in frontal pole, orbitofrontal cortex, temporal pole, middle temporal gyrus, inferior temporal gyrus, fusiform gyrus, amygdala, hippocampus, parahippocampal gyrus and insula. Conclusion: Several structures are associated with awareness of social cognition and function in dementia, many of which overlap with established neural correlates of social cognition. More research is needed to understand the complex phenomena of awareness of social cognition and function and its impairment in dementia, improving neuroscientific understanding, aiding identification of this symptom, and targeting interventions to reduce burden and improve care.

12. Marta Huelin - UCL Institute of Behavioural Neuroscience (Presenting on the day, Room 2 - Cognition & cognitive dysfunction)

POSTER TITLE
The role of experience in memory consolidation

AUTHORS
Huelin Gorriz M, Bendor D.

ABSTRACT
To date, most studies investigating memory consolidation focus on neural recordings obtained during tasks the subjects have been previously overexposed to. While this strategy guarantees a higher stability of the spatial map encoding for that experience, the reality of more naturalistic settings is that everyday animals can encounter multiple events of diverse duration and relevance. Yet, it remains unclear how the brain prioritizes and successfully stores multiple novel events.

To address this question, we exposed a group of rats to pairs of novel linear tracks across different days. Each day, rats were allowed to run in each track for a different fixed number of laps, and the experience was preceded and followed by a sleep session. We observed awake and sleep hippocampal replay of all tracks regardless of the stability of their spatial representations. However, when presented with similar experiences of different duration, the hippocampus prioritised the consolidation of the longer experience if the spatial representation of the shorter one was still unstable. Finally, we found that both awake hippocampal replay and theta sequences influenced the levels of subsequent sleep replay. These results aim to add further understanding of how experience shapes the encoding and consolidation of different spatial trajectories.

13. Alizee Kastler - Wolfson Institute for Biomedical Research

POSTER TITLE
Understanding how social interactions modulate pain

AUTHORS
Kastler A, Dreosti E.

ABSTRACT
We cope better when we are not alone. Supportive social environments, such as close social bonds, have a natural and strong analgesic effect and thus decrease our perception of pain. In humans, although functional and anatomical studies have identified overlapping areas of activity in the nociceptive and social circuits, the underlying circuitry as well as its molecular mechanisms are still not known. This is mainly due to the limited spatio-temporal resolution of fMRI studies.

To understand how pain and social circuits modulate one another, we took advantage of the highly social juvenile zebrafish, which allows whole brain imaging with a single cell resolution. Here, we show that zebrafish exposed to noxious temperatures increase their heat tolerance in the presence of a social cue. These data demonstrate that social context can modify noxious responses through a descending modulatory pathway, similarly to

humans. To dissect in more detail the mechanism and its circuitry, we are using targeted pharmacological treatments as well as whole brain imaging.

These data will provide invaluable insights on the mechanisms of pain modulation, and potentially identify new treatments for people suffering from chronic pain.

14. Hyunwoo Kim - UCL Division of Psychology and Language Sciences

POSTER TITLE
Machine versus human affect recognition of posed and spontaneous expressions

AUTHORS
Kim H, Girard K, Küster D, Krumhuber EG.

ABSTRACT
The field of automated facial expression analysis (AFEA) has progressed rapidly in recent years. Existing research suggests that machine classifiers perform reasonably well in recognising emotions from posed and prototypical expressions (Zeng, Pantic, Roisman & Huang, 2009). However, much less is known about the reliability of AFEA in the context of subtle and spontaneous expressions (Yitzhak et al., 2018). Furthermore, there is limited evidence as to whether peak intensity images extracted from dynamic expressions (e.g., Lewinsky et al., 2014) appropriately reflect the target emotion. The present study aims to fill this gap in the literature by investigating machine versus human affect recognition for peak intensity frames of posed and spontaneous expressions.

15. Carl Lindersson - UCL Institute of Cognitive Neuroscience

POSTER TITLE
Region-specific encoding of decision variables across prefrontal cortex

AUTHORS
Lindersson C, Butler JL, & Kennerley, S

ABSTRACT
In many brain areas, single neurons' firing rate have been correlated with specific variables, such as visual edges, objects, and locations. However, single neurons in the prefrontal cortex (PFC) have been suggested to encode a random mix of variables and that their function can only be understood at the neural population-level. In contrast, we show that neurons across the monkey PFC can be clustered into functional groups depending on their response profile. Using single-unit recording data, from a decision-making task based on sampling two sequential stimuli, we built neuron response profiles combining stimuli location, value magnitude, and value probability. Two unbiased clustering algorithms sorted these response profiles into clusters, which resembled decision variables. So far, we have found novel support for categorical encoding of positive and negative value in the orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), and ventromedial prefrontal cortex (VMPFC), while the lateral prefrontal cortex (LPFC) also encoded location. Further regression analyses will validate what variables are encoded and rule out mixed selectivity. This study will show how subregions of the PFC compare regarding categorical encoding of decision variables

and whether clustering algorithms can extract functional computations that could not be easily revealed with classical (non-clustering) analysis methods.

16. Lennart Luettgau - Max Planck UCL Centre for Computational Psychiatry & Ageing Research (Presenting on the day, Room 2 - Cognition & cognitive dysfunction)

POSTER TITLE
Reinstatement of cortical outcome representations during second-order conditioning

AUTHORS
Luettgau L, Porcu E, Tempelmann C, Jocham G

ABSTRACT
Naturalistic learning scenarios are characterized by infrequent experience of external feedback to guide behavior. Higher-order learning mechanisms like second-order conditioning (SOC) may allow stimuli that were never experienced together with reinforcement to acquire motivational value. Despite its explanatory potential for real-world learning, surprisingly little is known about the neural mechanism underlying such associative transfer of value in SOC. Here, we propose that during SOC, cortical patterns representing outcomes are reinstated by first-order conditioned stimuli (CS) to establish associative links between second-order CS and outcomes. During fMRI, we presented healthy human subjects with appetitive and aversive gustatory outcomes (orange juice and quinine solution). On a separate day, participants underwent first-order conditioning (outside fMRI), establishing associations between visual CS and gustatory outcomes, followed by SOC (during fMRI). Multivariate cross-session, cross-modality searchlight classification during SOC showed reinstatement of cortical patterns representing previously paired gustatory outcomes in the lateral orbitofrontal cortex (OFC) during presentation of (visual) CS. This OFC region showed increased functional covariation with amygdala, where neural pattern similarity between second-order CS and outcomes increased from early to late stages of SOC. Our data suggest a mechanism by which motivational value might be conferred to stimuli that were never paired with reinforcement.

17. Anushay Mazhar - UCL Institute of Cognitive Neuroscience

POSTER TITLE
Does an extended family improve mentalising in Autistic Children: a cross-cultural perspective from UK and Pakistan

AUTHORS
Mazhar A, White S

ABSTRACT
Behavioural difficulties in autism may arise from an inability to infer other people's mental states (mentalizing). This is a milestone which is missed by autistic children – at least in Western Cultures. Neurotypical Pakistani children develop this skill slower, whilst Western neurotypical children with more siblings develop mentalizing more quickly. There is currently no research on mentalizing in autism from countries with non-Western cultures, a group that is disadvantaged because of their condition and the design of mentalising tasks, therefore more sensitive to the enhancing effects of siblings/family members.

We will investigate how Pakistani and British autistic and neurotypical children (4-11 years) understand other people's minds. We hypothesize that British children will perform better than Pakistani, and neurotypical children will perform better than autistic children in both populations. We expect that the difference between the neurotypical and autistic groups will be less pronounced in the Pakistani children and children with extended family. We further hypothesize that having an extended family would be related to better performance on mentalising tasks for all groups, but this relationship will be strongest for autistic-Pakistani children.

This study will highlight the cross-cultural differences that exist in socio-cognitive processing in autism, cautioning against making generalisations from research conducted in the West.

18. Elena Menichini - Sainsbury Wellcome Centre

POSTER TITLE
Sensory priors, choice and outcome history in service of optimal behaviour in noisy environments

AUTHORS
Menichini E, Pedrosa V, Low R, Akrami A

ABSTRACT
While navigating the world, we constantly make decisions under uncertainty which can originate from ambiguous sensory inputs or unknown action outcomes. In face of noisy perceptions, we build and continuously update our priors and expectations about future events, in order to efficiently estimate sensory information. Via learned policies, agents then have to map the relevant sensory information onto appropriate behavioural responses in order to maximize reward. In a non-stationary environment where action values may change, the rules mapping stimuli to outcome may not be fixed and exploratory behaviour represents an optimal strategy to identify the most rewarded contingencies at any given context. How do animals integrate knowledge about the statistical context and action policy of the environment into an overall model of the world? In this work, we investigate how previous experience (sensory priors, choice and outcome history) can inform such models during decision-making in a perceptual categorization task. Combining behaviours in rats and humans with computational models, we show agents' sensitivity to history of sensory and action events as a mechanism to constantly update policies.

19. Jessica Passlack - UCL Department of Neuroscience, Physiology and Pharmacology

POSTER TITLE
Limitations imposed by neural circuits on successor representation models of decision making

AUTHORS
Passlack J, Burgess N, MacAskill A.

ABSTRACT
Successor representations (SRs) have gained popularity as a model for the hippocampus and its role in decision making. SRs create a predictive cognitive map by learning the future discounted occupancy of all states given the state you are in. Mapping an SR onto a neural circuit exposes two distinct problems that are not immediately evident from implementing SRs algorithmically. Firstly, in order to drive behaviour the SR must be used to evaluate the value of all possible actions given your current state. In a neural circuit, either the SR is encoded in a single set of neurons requiring each action to be individually cycled through, or there is an SR specific to each possible action allowing parallel evaluation of action-options. Neurophysiological evidence suggests the brain combines both solutions, trading off storage and time inefficiencies. The second issue concerns storing multiple reward expectations to drive different behaviours in the same environment depending on current context. The simplest solution, which is also supported by neurophysiological evidence, is to store a separate SR for each context allowing for learning of context-specific reward expectations. These thought experiments highlight the importance of considering how algorithms map onto neural circuits for the interpretation of neuronal activity.

20. Mariana R. Pereira - UCL Great Ormond Street Institute of Child Health

POSTER TITLE
The development of emotional face processing under a predictive processing framework: an online familiarization-novelty lookit study with infants

AUTHORS
Pereira MR, de Haan, M, Baldeweg T, Barbosa, F, Ferreira-Santos, F

ABSTRACT
Predictive Processing(PP) models define the brain as an active machine that generates predictions at each contact with the world, based on previous experiences, and proposes that mismatch between the prediction and the input produces prediction errors. A theoretical PP framework for emotional face processing proposed by our group highlights the role of variations in FEE valence(pleasantness) as the main generators of prediction errors until early childhood, and variations in arousal(activation) as the biggest source of mismatch later in development.

The current study uses a familiarization-novelty paradigm to assess this hypothesis. Infants between 2- and 24-months of age(n>100, ongoing) are first familiarized to a FEE of happiness with low arousal levels, followed by an experimental block in which the familiar face appears on the screen paired with one of four novel faces: happiness high arousal, neutral, anger low arousal, or playful. The infants' visual behaviour is recorded through webcam. Preliminary analyses show age is a significant predictor of arousal modulation, with FEEs with higher arousal eliciting more visual preference in older than younger infants. These preliminary results suggest that the arousal modulation might be present earlier in development than initially proposed, redefining what we know about emotional face processing in development.

21. Philip Shamash - Sainsbury Wellcome Centre

POSTER TITLE
Mice learn multi-step routes by memorizing subgoal locations

AUTHORS
Shamash, P, Olesen SF, Iordanidou P, Campagner D, Banerjee N, Branco T

ABSTRACT
The behavioral strategies that mammals use to learn multi-step routes in natural settings are unknown. Here we show that mice spontaneously adopt a subgoal memory strategy. We first investigated how mice navigate to shelter in response to threats when the direct path is blocked. Initially, they fled toward the shelter and negotiated obstacles using sensory cues. Within twenty minutes, they adopted a subgoal strategy, initiating escapes by running directly to the obstacle's edge. Mice continued to target this subgoal location after the obstacle was removed, indicating use of spatial memory. However, standard models of spatial learning – egocentric-movement repetition and internal-map building – did not explain how subgoal memories formed. Instead, mice used a hybrid approach: memorizing salient locations encountered during spontaneous 'practice runs'. This strategy was also used during geometrically identical reward-seeking behavior. These results suggest that subgoal memorization is a fundamental strategy by which rodents learn efficient multi-step routes in new environments.

22. Margot Tirole - UCL Institute of Behavioural Neuroscience

POSTER TITLE
How to deal with limited storage: the temporal dynamics of memory triage during sleep

AUTHORS
Tirole M, Bendor D.

ABSTRACT
A challenge that comes with experiencing multiple contexts each day is to continually accumulate and consolidate more information while retaining previous memories. Numerous human and rodent studies have shown that salient episodic memories are better remembered in the long term than neutral ones. As a matter of fact, highly rewarding, traumatic or novel experiences can lead to intrusive or extremely vivid recall recall years after the event (e.g. Post Traumatic Stress Disorder, Flashbulb memories).
In less extreme cases, daily memory triage is thought to ensure the storage of relevant memories at the detriment of less important ones, and has been shown to correlate with an overall increase in their reactivation frequency during sleep. However, the temporal dynamics of memory triage during sleep have not yet been investigated.
In this study we modulate two factors known to modulate memory triage: reward and recency. Recording from many hippocampal neurons simultaneously in the rat, we tracked the encoding and consolidation of salience-modulated representations. Comparing the relative proportions of replay events for each context during sleep we reveal the temporal dynamics of prioritised memory consolidation, as well as the interaction between these salience modulating factors.

23. Hande Tunbak - Wolfson Institute for Biomedical Research

POSTER TITLE
Lonely or Loner?

AUTHORS
Tunbak H, Dreosti, E

ABSTRACT
Loneliness and social isolation are linked to severe health conditions and affect millions of people around the world. With more people than ever experiencing social isolation during the covid pandemic, it is crucial that we fully understand the consequences of social deprivation to successfully predict and overcome the difficulties we face returning to our normal social lives post-covid.

A large area of my research focuses on using the zebrafish animal model to assess the impact of social isolation on behaviour and brain function. As in humans and other social species, early social deprivation reduces social preference in juvenile zebrafish. Results thus far reveal that whole-brain functional maps of anti-social isolated (lonely) fish are distinct from anti-social (loner) fish found in the normal population. These isolation-induced activity changes indicate profound disruption of neural activity in brain areas linked to social behaviour, social cue processing, and anxiety/stress. Furthermore, several affected regions are modulated by serotonin, and treatment with anxiolytics rescues social preference in isolated fish.

Most of us will be anxious about returning to social normality. Still, with the proper support, we can overcome these challenges critical for the structure and stability of the networks and relationships that define our societies.

24. **Ivan Voitov - Sainsbury Wellcome Centre (Presenting on the day, Room 1 - Computational Neuroscience and AI)**

POSTER TITLE
Working memory is distributed, high-dimensional, and maintained by cortical feedback loops

AUTHORS
Voitov I, Mrsic-Flogel T

ABSTRACT
Visual working memory is often used to study latent representations of the sensory world, but the associated neural activity patterns, their maintenance, and their distribution across the brain, remain contentious. We identified the neural representations of visual working memory in mice alternating between a delayed (non)match-to-sample task and a discrimination task not requiring working memory but with identical stimulus, movement, and reward statistics. Transient optogenetic silencing of different cortical areas revealed a distributed role of the neocortex for working memory maintenance. Population activity during the inter-stimulus delay period in higher visual area AM and premotor area M2 was dominated by orderly low-dimensional dynamics, which we found to be completely independent of working memory engagement. In contrast, neural representations of visual working memory were embedded in a high-dimensional population code, which was (1) present in both cortical areas, (2) persisted throughout the inter-stimulus delay period, and (3) predicted correct responses to the subsequent stimulus during the working memory task.

To test the hypothesis that distributed latent representations are instantaneously interdependent ('bound') by cortical feedback loops, we silenced one cortical area while recording the feedback it received from the other. Transiently breaking the feedback loop at the onset of the working memory delay had little impact on the average activity it carried, but selectively disrupted representations of visual working memory. Our findings therefore identify reciprocal cortical feedback loops as key circuit motifs underlying the maintenance of distributed and high-dimensional representations of working memory.

25. Baihan Wang - UCL Division of Psychiatry (Presenting on the day, Room 2 - Cognition & cognitive dysfunction)

POSTER TITLE
Genome-wide association analysis of adolescent verbal memory as a psychosis endophenotype

AUTHORS
Wang B, Kuchenbaecker K, McQuillin A, Austin-Zimmerman I, Giannakopoulou O, Zartaloudi E, Bhat A, Harju-Seppanen J, Lam CL, Lumer E, Bramon E.

ABSTRACT
Verbal memory impairment is one of the most evident cognitive deficits in psychosis, which often manifests during adolescence before psychosis onset. It has also been found in unaffected relatives of patients with psychosis, making it an endophenotype for psychosis. We conducted a mixed-model genome-wide association study (GWAS) to investigate the genetic basis of verbal memory in an ancestrally diverse sample of children and young people, and examined its genetic correlations with various psychosis phenotypes. 10,571 participants aged 8.5 to 12.8 years recruited in the Adolescent Brain Cognitive Development Study were analysed. Verbal memory was assessed by the Rey Auditory Verbal Learning Test, which included three measures of immediate recall, short-delay recall, and long-delay recall. GWAS revealed that short-delay recall was significantly associated with rs73984566 ($p = 1.70 \times 10^{-8}$; nearest genes: NABP1 and MYO1B), and long-delay recall was significantly associated with rs9896243 ($p = 1.85 \times 10^{-8}$; located in the NSF gene). We also found negative genetic correlations between all three verbal memory measures and schizophrenia or bipolar disorder. Our results suggest vesicular transport and membrane fusion as mechanisms underlying verbal memory deficits in psychosis. Future studies with larger samples are needed to replicate our findings.

26. Elliott Wimmer - UCL Queen Square Institute of Neurology

POSTER TITLE
Replay is separately associated with planning and memory maintenance

AUTHORS
Wimmer GE, Liu Y, McNamee D, Dolan R

ABSTRACT
Prominent theories of neural replay propose that it supports evaluation and planning of future actions, as well as memory maintenance. Here, within the same experimental setting, we test these hypotheses in a model-based reward learning task where participants engaged with two separate, randomly alternating, environments. Using

magnetoencephalography (MEG) and multivariate analysis, we found evidence for compressed forward replay during planning and backward replay following outcome receipt. During planning, forward replay strength predicted choice selection for exploratory decisions. Replay strength for the current, but not distal, environment reflected demands for model-based planning and positively correlated with potential reward value. Following reward receipt, backward replay for the distal environment increased as a function of decreasing recent experience in that environment, consistent with replay supporting a memory maintenance function. Our results indicate that computational and on-going task demands modulate the degree to which awake replay contributes to planning and memory maintenance.

27. **Laura Zaikauskaite - UCL Division of Psychology and Language Sciences**

POSTER TITLE
Temporal dynamics of interactions between moral emotions and moral cognition in General Public vs. Extinction Rebellion activists. Evidence from event-related potentials.

AUTHORS
Zaikauskaite L., Hodge, J., Tuomainen J., Devlin J.T.

ABSTRACT
Is pro-environmental behaviour driven by a system of moral values? Growing evidence suggests that the human moral judgement system fails to motivate environmental actions in the way it motivates other moral behaviours because climate change issues lack features of an intentional moral transgression (Jamieson, 2010; Markowitz & Shariff, 2012). Studies suggest that unintentionally caused harms are judged less harshly than intentional ones because they do not provoke powerful emotional reactions, including automatically generated intuitions of what's a wrong or a right thing to do (Cushman, 2008; Young et al., 2007). To date, the neural correlates implicated in shaping moral perception of environmental behaviours are not well understood. Therefore, this EEG study aims to find out whether morality of eco-(un)friendly behaviours is primarily driven by emotional (N1, N2, P2) or rational (P300, slow wave) processes. Alternatively, null results could suggest the case of neutralisation. According to this, moral aspects of socially unacceptable behaviours are being removed before commencing the act and thus consistency between moral attitudes and morally questionable behaviours remains intact (Sykes & Matza, 1957). We will present the results from the pilot 2-person (non-activist, activist) x 2-eco-unfriendly images (low-, high-arousal) reaction times study with 4 participants.

Computational Neuroscience

28. **Freddie Bickford Smith - UCL Department of Experimental Psychology Centre**

(Presenting on the day, Room 1 Computational Neuroscience and AI)

POSTER TITLE
Understanding top-down attention using task-oriented ablation design

AUTHORS
Bickford Smith F, Roads BD, Luo X, Love BC

ABSTRACT
Top-down attention allows neural networks, both artificial and biological, to focus on the information most relevant for a given task. This is known to enhance performance in visual perception. But it remains unclear exactly how attention brings about this perceptual boost, especially when it comes to naturalistic settings like recognising an object in an everyday scene. What aspects of a visual task does attention help to deal with? We aim to answer this with a computational experiment based on a general framework that we call task-oriented ablation design. First we define a broad range of visual tasks and identify six factors that underlie task variability. Then on each task we compare the performance of two neural networks, one with top-down attention and one without. These comparisons allow us to characterise the task-dependence of attention's perceptual boost, giving a clearer idea of the role attention plays in naturalistic settings. A counterintuitive finding is that visual clutter, often cited as a key reason why attention is necessary, is only weakly linked to the influence of attention in our model. We argue that this and our other findings have implications for both computational neuroscience and machine learning.

29. Tom George - Sainsbury Wellcome Centre (Presenting on the day, Room 1 - Computational Neuroscience and AI)

POSTER TITLE
Reservoir networks can learn temporal regularities by selectively suppressing chaos

AUTHORS
George TM, Onih A, Clopath C, Akrami A

ABSTRACT
Recent work has shown that reservoir networks (random connected recurrent neural networks) can perform 'chunking' of temporal inputs - a fundamental requirement for efficient time series compression. These models are appealing due to their architectural parallels to the brain and low-cost unsupervised training procedure. The internal mechanism they exploit and the full extent of their capabilities beyond chunking remain unclear. Here we uncover the mechanism by projecting the network dynamics to a low dimensional subspace. The network learns temporal structure by separating and classifying input-driven feedback-stabilised dynamic trajectories. In this network, internal chaos is selectively suppressed during periods where the input is structured allowing for reliable classification of trajectories. The network learns the temporal community structure within the input stream, and its representations show high similarity to previous neuroimaging results in humans. We conclude that simple RNNs can provide testable mechanistic explanations of temporal structure learning in the brain and are a promising starting point for studying more complex types of structure learning.

30. Grace Lindsay - Gatsby Computational Neuroscience Unit

POSTER TITLE
Task-trained neural networks learn different recurrent visual processing strategies than bio-inspired ones do

AUTHORS
Lindsay G, Mrsic-Flogel T, Sahani M.

ABSTRACT
Recurrent processing in the visual system has been found to be important for processing noisy or degraded stimuli. Convolutional neural networks (CNN) are models of the visual system that typically only capture the feedforward pass. Here, we compare four different types of recurrence added to a feed forward CNN: task-trained lateral connections, task-trained feedback, bio-inspired lateral connections (surround suppression), and bio-inspired feedback (predictive coding). All four types increase the ability of the network to classify digit images with several styles of noise added. However, through further analysis of classification patterns and neural activity we show that training is more important than the anatomy of the recurrence: both lateral and feedback task-trained networks impact activity in similar ways, which are distinct from how bio-inspired recurrence works. By analyzing the task-trained networks further, we show that recurrence at the first layer does not denoise the representation of images there, but does lead to denoising at later layers. This work has implications for the use of CNNs as models of recurrent processing and the application of common analyses also serves as a test of the tools of systems neuroscience.

31. **Anahita Talwar - UCL Institute of Cognitive Neuroscience (Presenting on the day, Room 1 - Computational Neuroscience and AI)**

POSTER TITLE
Stick or switch: modelling attentional set-shifting with CANTAB IED

AUTHORS
Talwar A, Cormack F, Huys Q, Roiser JP.

ABSTRACT
Background: The CANTAB Intra-Extra Dimensional Set Shift task probes reversal learning and attentional set shifting. Individuals with psychiatric diagnoses score more errors than controls on the extra-dimensional set shift stage of the task. We present a computational model of the task, which elucidates how attention and learning mechanisms interact to produce variations in set-shifting ability.

Methods: Healthy participants (N=753) completed the CANTAB IED task, and questionnaires assessing symptoms of mental health disorders. Reinforcement learning models were fit to trial-by-trial data and participants' model parameters were estimated. Model fit was assessed qualitatively and quantitatively.
Results: The best-fitting model uses reinforcement learning to learn values of stimulus features, and incorporates attention to bias learning. Participants who failed the set-shift stage had lower learning rates, and showed higher attentional bias to a specific stimulus dimension at early stages. These parameters were significantly associated with symptoms of compulsivity.

Conclusions: Our findings indicate that participants who fail the extra-dimensional shift stage of the IED are initially highly biased towards a specific stimulus dimension, and their learning rate is too low to shift this attention to another dimension. This provides a possible mechanism by which patients with psychiatric disorders exhibit difficulties in attentional set shifting.

32. **Alessandra Nicoletta Cruz Yu - UCL Institute of Cognitive Neuroscience**

POSTER TITLE
Emotion inference and learning

AUTHORS
Yu ANC, Smith R, Bilek E, Garfinkel SN, Friston KJ.

ABSTRACT
Under the process theory of active inference, emotion arises as latent states of an internal generative model in the brain, inferred through an approximate Bayesian process of minimizing free energy to best explain incoming multimodal sensory information. Smith et al. (2019) previously presented a simple formal Markov decision process model of emotion conceptualization and learning as proof of principle that such emotional processes can be modelled using active inference. They further employ the model in simulations of emotional awareness, learning, and disorder. In the present work, we expand Smith et al.'s Markov Decision process model to incorporate a more diverse set of emotions and multimodal sensory information, including interoception, action tendencies, and cognitive appraisals, in order to provide proof of principle that active inference can accommodate—and integrate—constructionist and appraisal theories of emotion. Furthermore, we simulate learning and aberration in interoceptive awareness through in silico experiments, namely, to identify a sample computational mechanism that may go awry in alexithymia. This work not only provides a first principles account bridging active inference and existing theories of emotion, but a promising foundation for modelling emotional belief states in both health and disorder in computational psychiatry.

33. Yibo Zhao - UCL School of Pharmacy (Presenting on the day, Room 3 - Disorders of the nervous system: molecular and genetics)

POSTER TITLE
LRRK2 Protein-protein Interaction Interactome and brain region specificity

AUTHORS
Yibo Z, Claudia M

ABSTRACT

Background: Mutations in LRRK2 are the most common genetic cause of familial Parkinson's disease (PD). However, due to the complexity in its structure, function, and expression pattern, the physiological/pathological roles of LRRK2 are still not fully understood.

Aim: This project aims at collating the many data generated in 15 years of LRRK2 research and integrating them in a homogeneous, computational model to describe and simulate LRRK2's activity in physiological/pathological pathways.

Methodology: The LRRK2 model is built in consecutive steps: 1) protein-protein interactions are derived to define the general interactome around LRRK2; 2) the general interactome is merged with co-expression data in human brain to define multiple brain region-specific LRRK2 interactomes, 3) each specific-interactome is functionally annotated. Machine

learning is performed to contrast and compare the specific-interactome across different brain regions based on the composition and functions.

Results: We identified brain region-specific LRRK2 interactomes and a core LRRK2 interactome, which is conserved across all the brain regions. Brain region-specific LRRK2 interactomes were grouped based on their functional similarity into 3 clusters. Regions that are prevalently involved in PD neurodegeneration were allocated in the same cluster. Additionally, we found that LRRK2 interactome in substantial nigra is highly associated with apoptosis and inflammation.

34. **Liang Zhou - Gatsby Computational Neuroscience Unit**

POSTER TITLE
Learning sensory representations for flexible computation with recurrent circuits

AUTHORS
Zhou L, Menendez J, Latham P.

ABSTRACT
Neural circuits are optimized over a lifetime of experience to solve a wide range of ethologically relevant tasks. This seems to be the case in motor cortical circuits, which are able to recycle existing activity patterns in the pursuit of new goals. A popular approach to modeling time-dependent tasks is to optimise recurrent neural networks (RNNs), but it is often computationally expensive and difficult to train them to perform multiple tasks. Here, we propose a model in which a general-purpose RNN is exploited for solving new tasks without needing to continuously re-optimize the recurrent connectivity. Instead, learning a new task boils down to learning an appropriate low-dimensional representation of the task-relevant stimuli that will drive the RNN to produce the correct responses. Doing so can drastically reduce the number of parameters that need to be learned, leading to much faster optimisation. This setting in principle lends itself well to biologically plausible learning algorithms. We empirically show that such an architecture can be utilised to accurately model behavioural performance on a variety of tasks, with performance comparable to that of fully-trained RNNs.

Developmental Neuroscience

35. **Joanna Aloor - UCL Department of Cell and Developmental Biology**

POSTER TITLE
An automated image processing pipeline to quantify brain-wide neurochemical expression in the larval zebrafish

AUTHORS
Aloor J, Trivedi C, Wilson S

ABSTRACT
A comprehensive view of brain-wide neurochemical profiles is essential to our understanding of neuronal control of behavioural and physiological responses. Investigating neurochemical identity in the zebrafish has thus far been explored in a region- or molecule-specific manner,

lacking a brain-wide understanding of the neurochemical repertoire. Here, we combined in situ hybridisation, immunohistochemistry, light-sheet microscopy, and diffeomorphic registration methods to develop standardized whole-brain neurochemical expression maps in larval zebrafish. Coupled with activity response profiles, our brain-wide approach to neurochemical analysis will help uncover the molecular mechanisms underlying information processing in the zebrafish brain. Using thresholding and segmentation techniques, we calculated the proportion of voxels positive for any neurochemical in each of 170 neuroanatomical regions, enabling us to identify regions of distinct neurochemical identity. We performed comparative analysis between the expression of different neurochemicals, revealing populations of colocalized expression. Voxel-wise permutation testing between two neurochemical groups identified clusters of neurons that exhibit differential expression patterns. We used our analysis pipeline to investigate the effect of a novel mutation on brain-wide neurochemical expression, revealing a link between anatomy, function, and neurochemical identity of distinct populations.

36. Emily Brookes - MRC Laboratory for Molecular Cell Biology at UCL

POSTER TITLE
Regulation of the Bdnf gene by genome topology and a novel enhancer during neuronal development

AUTHORS
Brookes E, Varsally W, Au HYA, Barrington C, Hadjur S, Riccio A

ABSTRACT
Bdnf encodes a neurotrophin with critical roles in brain development and function; Bdnf exerts positive effects on neuronal survival and differentiation, and on synaptic plasticity. Aberrant Bdnf expression is implicated in a variety of neurological disorders, while enhanced Bdnf expression is linked to the neuroprotective effects of exercise, enriched environment and anti-depressants. Here we show that developmental activation of the mouse Bdnf gene is accompanied by movement of the gene away from the nuclear periphery. Elucidating Bdnf chromatin looping led us to identify a putative enhancer which displays chromatin accessibility, histone modifications and transcription factor binding characteristic of enhancers, and is transcribed in postmitotic neurons. Inhibition of the enhancer using CRISPi prevents appropriate Bdnf upregulation during neuronal development, alters neuronal clustering, and abrogates Bdnf-mediated dendritic growth. Understanding the many-faceted regulation of Bdnf is important for understanding and treating neurological disease, and this study shows that 3D location, genome topology, and a novel enhancer are central to this.

37. Philippa Harding - UCL Institute of Ophthalmology (Presenting on the day, Room 4 - Disorders of the nervous system: cellular mechanisms)

POSTER TITLE
Molecular disruption in early cellular optic vesicle models derived from patients with microphthalmia and aniridia associated PAX6 variants

AUTHORS
Harding P, Lima Cunha D, Owen N, Eintract J, Moosajee M

ABSTRACT
PAX6 is an essential transcription factor regulating eye development. Heterozygous pathogenic mutations result in a range of ocular disorders, including aniridia, cataracts and Peter's anomaly. Missense variants are typically associated with milder phenotypes, although certain variants, such as c.372C>A, p.Asn124Lys, give rise to more severe ocular features including microphthalmia, a congenital, structural disorder reported in 11% of blind children. The disease-causing pathways affected downstream in these patients remain unclear.

To study PAX6 regulation of ocular development, we generated iPSC-derived 3D optic vesicles from a patient exhibiting severe microphthalmia, aniridia and cataracts with heterozygous hypomorphic variant c.372C>A. We molecularly characterised the models at 20- and 35-days differentiation through qRT-PCR and immunostaining.
RNAseq transcriptome-wide profiling was performed to characterise global gene expression changes compared to unaffected controls and models from a classic aniridia patient with nonsense variant c.781C>T, p.Arg261*.
Microphthalmic vesicles show significantly reduced RNA expression of early eye differentiation transcription factors PAX6, RAX, OTX2 and SOX2, alongside protein loss of neural retina marker VSX2. Ongoing total RNAseq analysis aims to reveal novel pathway disruption.

This work creates a valuable resource for exploring PAX6 regulation of early human eye development, providing insight into the variant-specific pathways underlying microphthalmia pathogenesis.

38. Polyxeni Katsouli - UCL Division of Medicine

POSTER TITLE
Identifying and characterizing the phenotype of Schwann cell precursors for use in peripheral nerve tissue engineering.

AUTHORS
Katsouli P.

ABSTRACT
Introduction: Engineered Neural Tissues (EngNTs) are cellularized scaffolds investigated for the treatment of peripheral nerve injuries. Schwann cell precursors (SCPs), have been hypothesized to be good candidates for EngNT seeding. This poster aims to appraise the peripheral nerve regenerative potential of SCPs based on an in vitro investigation.
Methods: Initially, a literature review was conducted to determine which genes are important for the Schwann cell repair phenotype. Such markers were measured using RT qRCP, as iPSCs differentiated towards SCPs. To evaluate whether relative gene expression changes in the membrane protein NCAD would correspond to differential protein abundance, immunofluorescent staining was used. Second, the regenerative ability of the SCP secretome was examined using a Dorsal Root Ganglia (DRG) neurite outgrowth assay.
Results: Transcriptional increases in NCAD did correspond to slight increases in protein abundance at the specific time point examined. There are indications that the SCP secretome induced slight increases in neurite growth in the particular conditions of this investigation.

Conclusions: SCPs display regenerative promise in vitro and hint they would be good candidates for EngNT seeding. Nevertheless, the aforementioned experiments should be repeated with a larger sample size to establish statistical significance, measuring several time points, ensuring researcher blinding and perhaps simulating wound environment stimuli such as hypoxia.

39. Neelum Mistry - UCL Division of Biosciences (Presenting on the day, Room 6 - Sensory motor systems and dysfunction)

POSTER TITLE
Naturally occurring tactile stimulation can augment cortical activity in neonatal infants with acquired brain injury

AUTHORS
Mistry N, Meek J, Fabrizi L, Whitehead K

ABSTRACT
Introduction
Neonatal animal studies show that cortical activity is necessary for typical development, suggesting that the suppression of activity following a brain injury in human infants could mediate their adverse outcomes. In healthy infants, cortical activity can be augmented by tactile stimulation. Here, we evaluated whether this augmentation is possible in infants with brain injury.

Methods
We analysed 5 EEG recordings from 4 pre-term infants with a unilateral intra-parenchymal lesion (IPL) associated with intra-ventricular haemorrhage (24-30 weeks gestational age; 7-69 postnatal days at EEG). We evaluated whether naturally occurring tactile stimulation of the hand contralateral to the IPL, e.g. caregiver touch, increased EEG power, using synchronised video-EEG.

Results
Time-frequency analysis showed that stimulation evoked a broadband increase in power in 3 of 5 recordings. This included a pronounced widespread delta energy increase, maximal in the contralateral temporal region (up to 10 dB).

Conclusion
These preliminary results show that naturally occurring tactile stimulation can augment cortical activity in infants with IPL; this could potentially support healthy development. However, this finding was not present in all recordings. Future work will examine whether this heterogeneity relates to factors such as sleep state or lesion location, and explore responses in the comparative healthy hemisphere.

40. Patricia Pascual Vargas - UCL Department of Cell and Developmental Biology

POSTER TITLE
A post translational modification regulates the trafficking and synaptogenic activity of the Wnt receptor Fz5

AUTHORS
Bossio A*, Stamatakou E*, Pascual-Vargas P, Schuhmacher LN, and Salinas PC

ABSTRACT
The dynamic localisation of receptors for synaptic organizing factors is a crucial process during the formation of neuronal connections. However, the mechanisms that control receptor localization and retention at the plasma membrane remain poorly understood. The surface localization of Frizzled-5 (Fz5), a receptor for the synaptic organizer Wnt7a, is highly enriched at synaptic sites and is regulated by neuronal activity (Sahores et al, 2010; McLeod et al, 2018). However, the mechanisms by which this Wnt receptor localises to synapses are unknown. Here we report a previously unidentified post-translation modification (PTM) of Fz receptors. We show that this PTM is increased both by high-frequency stimulation and by environmental enrichment. In addition, our data show that this PTM regulates the surface localization of Fz5. Further, we generated a mutant receptor which cannot be post-translationally modified and demonstrate that this mutant fails to induce presynaptic assembly. We also show that the lack of this PTM decreases the interaction of Fz5 with Dishevelled-1, a scaffold protein and key component of the Wnt signalosome. Lastly, we found that all Fz receptors can be modified by this PTM. Our findings are the first demonstration of this PTM in Fz receptors and identify a novel mechanism for controlling the localization of Fz5 during synapse assembly.

41. Rachele Rossi - Developmental Neuroscience, UCL Great Ormond Street Institute of Child Health

POSTER TITLE
Evaluation of DMD transcripts after golodirsen treatment of MyoD-converted fibroblasts from 4053-101 clinical trial patients

AUTHORS
Rossi R, Moore M, Torelli S, Ala P, Catapano F, Phadke R, Morgan J,Malhotra J, Muntoni F

ABSTRACT
Duchenne muscular dystrophy is an X-linked, neuromuscular disease caused by dystrophin gene (DMD) mutations which result in a substantial reduction or absence of the dystrophin protein. Deletions are the most commonly occurring mutation type, disrupting the transcriptional reading frame, and causing dystrophin loss. Antisense oligonucleotide-induced exon skipping can restore the mRNA reading frame and produce an internally deleted, yet functional dystrophin protein, as Exondys 51TM does in patients with confirmed DMD gene mutations amenable to exon 51 skipping.

Golodirsen (formerly SRP-4053) is a phosphorodiamidate morpholino oligomer (PMO) developed by Sarepta Therapeutics, Inc., to target exon 53 of the DMD gene. In Study 4053-101, we demonstrated exon skipping and dystrophin restoration in all patients. Some variability of protein restoration was observed in different patients, likely due to the not well-understood mechanism of delivery of PMOs and other factors. Here, we aim to assess the exon 53 PMO-induced skipping in primary cell cultures from these patients.
Fibroblasts, from patients enrolled in Study 4053-101, underwent Myo-D induced differentiation and were treated with golodirsen. After screening for exon skipping efficiency in treated patients' cells and in healthy controls, we evaluated the transcript 5'-3' imbalance

in treated vs non-treated patient cells by custom FluiDMD cards. To better understand the intracellular RNA dynamics of the deleted and skipped products, we investigated the transcript subcellular localization by BaseScope assay. Our data will be correlated with the previously obtained in-vivo data, to provide a more comprehensive assessment of the response to golodirsen in eligible patients.

42. Daisy Thompson-Lake - Developmental Neurosciences, UCL Great Ormond Street Institute of Child Health (Presenting on the day, Room 6 - Sensory motor systems and dysfunction)

POSTER TITLE
Disrupted cortico-basal ganglia-thalamocortical network in large family with inherited stuttering

AUTHORS
DaisyThompson-Lake DGY, Block S, Turner SJ, Reilly S, Kefalianos E, Bonthrone AF, Bahlo M, Scheffer IE, Liegeois FJ, Morgan AT*

ABSTRACT
Developmental stuttering affects around 1% of the population, with potential detrimental effects on mental health and long-term employment. Evidence suggests a strong genetic contribution to stuttering, yet gene-brain associations remain poorly understood due to a lack of brain MRI studies in affected families. We studied a four-generation family with autosomal dominant inheritance of persistent stuttering. We measured cortical morphology, subcortical volumes, and white matter integrity in seven family members (9-63 years). In affected family members, Broca's area failed to follow the typical age-related trajectory of cortical thinning observed in controls. Surface area analysis revealed the middle frontal gyrus region was reduced bilaterally in the family (all cortical morphometry significance levels set at a vertex-wise threshold of $p<.01$ corrected for multiple comparisons). Both the left and right globus pallidus were larger in the family than in the control group, and a larger right globus pallidus was associated with more severe stuttering. These findings denote disruption within the cortico-basal ganglia-thalamocortical network. The lack of typical development of these structures reflects the anatomical basis of the abnormal inhibitory control network between Broca's area and the striatum underpinning stuttering in these individuals.

Disorders of the Nervous System

43. Isabelle Austin-Zimmerman - UCL Division of Psychiatry (Presenting on the day, Room 3 - Disorders of the nervous system: molecular and genetics)

POSTER TITLE
Genome-wide association study investigating genetic loci for self-reported sleep duration: a meta-analysis with data from UK Biobank and the Million Veteran Program

AUTHORS
Austin-Zimmerman I, Levey DF, Giannakopoulou O, Zhou H, Irizar H, Kuchenbaecker K, McQuillin A, Polimanti R, Stein M, Bramon E, Gelernter J

ABSTRACT
Disordered sleeping has been linked to a wide range of negative health outcomes, including depression and psychosis. We conducted genome-wide association studies and trans-ancestry meta-analyses of long and short sleep – both compared to normal duration – using samples from UK Biobank and the Million Veteran Program. We estimated SNP-based heritability and calculated the genetic correlation (rg) between the two sleep traits and with other cognitive and neuropsychiatric traits. We also performed Mendelian randomisation analyses to consider the potentially causal direction of the observed correlations.
A trans-ancestry meta-analysis of short (<6 hours; n=60,092) versus normal (7-8 hours; n=404,860) sleep duration reveals 28 independent genome-wide significant loci. The strongest associations were near genes MADL1, SLC39A8, and TCF4. A trans-ancestry meta-analysis long (>9 hours; n=17,483) versus normal sleep duration reveals one genome-wide significant locus near PTPLB. The genetic correlation between long and short sleep was 0.2±0.05, P=1x10-5. Both long and short sleep were positively correlated to depression and Mendelian randomisation analysis suggests these are potentially causal associations.
In summary, we identify multiple novel risk loci for sleep duration. The low genetic correlation between long and short sleep suggests distinct underlying genetic architecture. Mendelian randomisation reveals a causal link between sleep disturbance and depression.

44. Iryna Benilova - MRC Prion Unit at UCL (Presenting on the day, Room 4 - Disorders of the nervous system: cellular mechanisms)

POSTER TITLE
Highly infectious prions are not directly neurotoxic

AUTHORS
Benilova I, Marinho A, Risse E, Jat P, Collinge J

ABSTRACT
Prion diseases are fatal transmissible neurodegenerative conditions caused by misfolded forms of the cellular prion protein with different partial resistance to proteinase K digestion. Studies in mice showed that prion infectivity and neurotoxicity are uncoupled and support the idea that onset of neuropathology is driven by a toxic species distinct from the infectious species.

To test this hypothesis, we developed a multiparametric imaging-based assay and probed neurotoxicity of purified prions and crude infected brain homogenates (BH) prepared from mice infected with the RML strain of scrapie. This assay consists of time course studies followed by end-point analyses of neuronal morphology (Benilova, Reilly et al, PNAS 2020). Purified prions at titres exceeding the titre of RML BH eliciting maximal neurodegeneration were not acutely neurotoxic, whether dissolved in cell culture medium, Prnp0/0 or Prnp+/+

BH. As a prerequisite for undertaking fractionation of the toxic species from RML BH, we also looked for a detergent compatible with toxicity. Pretreatment of RML BH with sarkosyl abolished toxicity without diminishing the infectious titre.

The lack of detectable direct toxicity of highly infectious prions or sarkosyl-treated infectious BH is consistent with models of prion neurotoxicity being mediated by toxic species distinct from infectious prion assemblies.

45. Rohan Bhome - UCL Queen Square Institute of Neurology (Presenting on the day, Room 3 - Disorders of the nervous system: molecular and genetics)

POSTER TITLE
Brain DNA methylation ageing: observations from frontotemporal dementia, Alzheimer's disease and different brain cell types

AUTHORS
Bhome R, Lashley T, Bettencourt C

ABSTRACT
DNA Methylation (DNAm) changes are important in neurodegenerative disorders. Epigenetic clocks enable DNAm age, a possible surrogate for biological age, to be calculated. We used the DNAmClockcortical, specifically designed for cortical tissue, to evaluate DNAm ageing in Frontotemporal dementia (FTD), Alzheimer's disease (AD) and specific brain cell types from control samples.

Genome-wide DNAm profiles from cortical post-mortem brain tissue/nuclei were generated using Illumina methylation arrays (450K/EPIC). The DNAmClockcortical was used to calculate DNAm predicted ages. DNAm age acceleration was calculated as residuals and differences between predicted and chronological age. We compared age acceleration in FTD and AD vs healthy controls and in fluorescence-activated sorted glial nuclei vs neuronal nuclei.

There was no difference in DNAm age acceleration between FTD and controls but there was increased age acceleration in AD. In nuclei isolated from healthy brain tissue, neuronal DNAm age exceeded glial DNAm age until mid-life, after which this reversed.
We utilised a robust epigenetic clock specifically designed for cortical tissue, which outperforms previous clocks in this type of tissue. Our findings support an association between brain DNAm age acceleration and AD. The relationship between neuronal and glial DNAm ageing, especially a potential switch in mid-life, warrants further investigation.

46. Jackie Casey - UCL Queen Square Institute of Neurology (Presenting on the day, Room 3 - Disorders of the nervous system: molecular and genetics)

POSTER TITLE
Haploinsufficiency of progranulin causes impairments in mitophagy

AUTHORS

Casey J, Melandri D, Arber C, Soutar M, Holler C, O' Callaghan B, Kukar T, Rohrer J, Isaacs A, Plun-Favreau H, Wray S.

ABSTRACT
Background: GRN mutations, resulting in haploinsufficiency of progranulin, cause frontotemporal dementia (FTD) with TDP-43 pathology. Impairments in mitophagy, the selective autophagy of damaged mitochondria, have been identified in several neurodegenerative diseases, and multiple neurodegenerative disease genes, including PINK1, Parkin, VCP and TBK1, are known to play a role in this pathway. A role for progranulin in the regulation of neuronal mitophagy has not been explored, however progranulin deficient mice exhibit reduced xenophagy (selective clearance of bacteria). We therefore hypothesised that loss of progranulin would lead to defective mitophagy.
Methods: We examined mitophagy in an astroglioma cell line (H4 cells) and a neuroblastoma cell line (Parkin overexpressing SHSY5Y cells (PoE-SHSY5Y)) +/- siRNA against GRN. We also examined induced pluripotent stem cell (iPSC) derived cortical neurons from controls and three patients with GRN mutations (R493X and C31fs). PINK1/Parkin mitophagy was induced using Antimycin A (respiratory complex III inhibitor) and oligomycin (ATP synthase inhibitor). Mitophagy was then assessed using immunofluorescence and western blotting to examine levels of S65 phosphorylated ubiquitin and PINK1 accumulation. Downstream mitophagy was assessed by examining Mitofusin-2 ubiquitination and degradation, and TIM23 degradation by western blot.

Results: Reduced phospho-Ubiquitin accumulation was detected by immunofluorescence in patient iPSC-derived neurons and GRN siRNA treated PoE-SHSY5Ys. However, no significant difference in mitophagy was detected with western blotting. Reducing progranulin had a stronger effect in the astrocytic-like H4 cell line, with significantly reduced PINK1 and phospho-Ubiquitin. Preliminary work in iPSC-derived astrocytes also suggests that progranulin plays a role in mitophagy in astrocytes.

Conclusions: These results suggest that progranulin plays a role in mitophagy by regulating the stability and/or activity of PINK1. Ongoing work aims to understand the mechanisms by which progranulin and/or individual granulins contribute to this process and to dissect cell-type specific contributions of progranulin to mitophagy in iPSC- derived neurons, astrocytes and microglia.

47. Elisa Colato - UCL Queen Square Institute of Neurology (Presenting on the day, Room 2 - Cognition & cognitive dysfunction)

POSTER TITLE
Predicting disability progression and cognitive worsening in multiple sclerosis using patterns of grey matter volumes

AUTHORS
Colato E, Stutters J, Tur C, Narayanan S, Arnold LD, Gandini Wheeler-Kingshott CAM, Barkhof F, Ciccarelli O, Chard TD, Eshaghi A

ABSTRACT
Objective. There is a growing interest in network-based measures as promising prognostic markers in MS. We aimed to determine the ability of data-driven patterns of covarying

regional grey matter (GM) volumes to predict disability progression in secondary progressive MS (SPMS).

Methods. We analyzed cross-sectional structural MRI, and baseline and longitudinal data of Expanded Disability Status Scale (EDSS), Nine-Hole Peg Test (9HPT), and Symbol Digit Modalities Test (SDMT), from 988 people with SPMS from the ASCEND trial. We processed T1-weighted scans to obtain GM probability maps, applied spatial independent component analysis (ICA), and used survival models to determine whether baseline patterns of covarying GM volume measures predict cognitive and motor worsening.
Results. Compared with whole-brain GM, deep GM, and lesion volumes, ICA components correlated more closely with clinical outcomes. A mainly basal ganglia network had the highest correlations at baseline with the SDMT and was associated with cognitive worsening (HR=1.29, 95% CI 1.09 to 1.52, p<0.005). Two ICA networks were associated with 9HPT worsening (HR=1.30, 95% CI 1.06 to 1.60, p<0.01 and HR=1.21, 95% CI 1.01 to 1.45, p<0.05). ICA measures better predicted SDMT and 9HPT worsening (C-index=0.69–0.71) compared with models including only whole and regional MRI measures (C-index=0.65–0.69, p-value for all comparison <0.05).

Conclusions. GM network-based measures predicted disability progression better than single regional or whole-brain, or lesion, volume measures. We show that ICA can be applied to clinical trial data, and may play a role in stratifying participants who have the most potential to show a treatment effect.

48. **Cara Croft - UK Dementia Research Institute at UCL**

POSTER TITLE
Determining alpha-synuclein protein aggregate turnover and production dynamics

AUTHORS
Croft CL, Paterno G, Vause AR, Goodwin MS, Ryu DH, Moran C, Cruz PE, Giasson BI, Golde TE

ABSTRACT
Lewy bodies comprised of α-synuclein aggregates are found in neurodegenerative diseases including Parkinson’s disease and Lewy Body Dementia. There is still limited understanding of how α-synuclein and Lewy bodies are associated with cellular dysfunction and degeneration in these diseases.
We recently developed ex vivo models of intrinsic α-synuclein inclusion pathology in murine brain slice cultures (BSCs), transduced with recombinant adeno-associated viruses (rAAVs) to express human wild-type and mutant α-synuclein. These models develop inclusions which are highly recapitulative of Lewy bodies. We now extend these findings using photoswitchable versions of these rAAVs with long-term live imaging to understand the protein clearance and production dynamics of α-synuclein.

Using optical pulse-chase methodology we can follow individual cells expressing α-synuclein and track new and old populations of protein in these cells over long-term culture periods. Surprisingly, we find both soluble wild-type and mutant human α-synuclein, and insoluble aggregated forms show similar rates of production and turnover, suggesting aggregation nor mutations affect the dynamics of α-synuclein in this system.

This system facilitates the exploration of α-synuclein dynamics over long-term culture periods. This platform can further be used to provide mechanistic insight on how therapeutics, other genes and different mutations may affect α-synuclein protein dynamics.

49. Tom Dufor - UCL Department of Cell and Developmental Biology (Presenting on the day, Room 4 - Disorders of the nervous system: cellular mechanisms)

POSTER TITLE
Understanding the mechanisms of synapse vulnerability and resilience in a Wnt signalling deficient mouse model.

AUTHORS
Tom Dufor, Thanasis Rogdakis, Johanna Buechler, Karinder Brar, Douglas Lopes, Ernest Palomer, Ka Wan Li, Guus Smit, Patricia Salinas

ABSTRACT
Synaptic degeneration is an early hallmark of neurodegenerative diseases and is highly correlated with cognitive decline in Alzheimer's disease (AD). Studies show that some synapses are more vulnerable than others to amyloid-β toxicity. However, the underlying mechanisms remain poorly understood. Growing evidence suggests a link between deficient Wnt signalling and AD. Dickkopf-1 (Dkk1), an endogenous secreted Wnt antagonist, is elevated in the brain of AD patients and is required for amyloid-β-mediated synapse loss. Using an inducible transgenic mouse model that expresses Dkk1 (iDkk1) in the adult brain demonstrates that two weeks of Dkk1 induction led to a 40% reduction in excitatory synapses in the hippocampus, LTP deficit and memory loss without neuronal death, resembling early stages of AD. Importantly, we found that synapse degeneration in iDkk1 mice is not progressive suggesting that after a period of synapse degeneration, this process is stalled. At the peak of synaptic degeneration (two weeks induction), proteomic analyses of hippocampal synaptosomes from iDkk1 mice revealed an upregulation of astrocytic markers. We found that adding astrocytes to hippocampal neurons is protective against Dkk1-induced synapse loss, suggesting that these cells halt synaptic degeneration. This astrocyte protective effect is through secreted factors, which we are currently studying.

50. Clíona Farrell - UK Dementia Research institute at UCL

POSTER TITLE
Using organotypic hippocampal slice cultures from a mouse model of Down syndrome to assess microglia inflammasome activity in response to amyloid-β

AUTHORS
Farrell C, Mumford P, Salih D, Fisher E, Toomey C, Wiseman F.

ABSTRACT
Down syndrome (DS) is caused by trisomy of chromosome 21 (Hsa21) and is a leading genetic cause of Alzheimer's disease (AD). Neuroinflammation is altered in the post-mortem brain of people with DS, with altered microglial morphology and high levels of proinflammatory cytokines, including IL-1β. IL-1β is produced by inflammasome activity activating caspase-1 which cleaves and releases active IL-1β. We hypothesize that IL-1β levels are raised in the DS brain, via upregulation of inflammasome activity, and this persists when people with DS develop AD. We have shown raised IL-1β abundance in the

hippocampus of the Dp1Tyb mouse model which has an additional copy of 148 mouse orthologues for Hsa21 genes. I will prepare organotypic hippocampal slice cultures (OHSCs) from P9 pups from this model and WT controls. OHSCs will be stimulated with inflammasome inducing agents, LPS, Nigericin and oligomeric Aβ (or a combination of these) for 3, 6 and 12 hrs. Microglia/inflammasome activation state will be measured by quantifying ASC in IBA1+ microglia, using immunofluorescence. IL-1β and TNFα cytokine levels in conditioned culture media will be measured by ELISA and active caspase-1 levels will be measured by western blot. This experiment will give insight into how microglia with three copies of Hsa21 genes respond to inflammatory stimuli compared to euploid microglia.

51. Katherine Fodder - UCL Queen Square Institute of Neurology (Presenting on the day, Room 3 - Disorders of the nervous system: molecular and genetics)

POSTER TITLE
Brain co-methylation network analysis in progressive supranuclear palsy

AUTHORS
Katherine Fodder, Thomas T Warner, Conceição Bettencourt

ABSTRACT
Progressive supranuclear palsy (PSP), is a fatal, multifactorial, neurodegenerative disease. DNA methylation is an epigenetic modification that leads to changes in expression of target genes, and aberrant DNA methylation is implicated in many diseases. Weber et al. (2018) investigated brain DNA methylation profiles of PSP patients and found several DNA methylation alterations. We investigated this methylation dataset using a different DNA methylation analysis pipeline and carried out weighted correlation network analysis to identify co-methylation signatures associated with PSP.

Raw methylation data, derived from post-mortem frontal cortex tissue, was downloaded from the NCBI-Gene Expression Omnibus depository (GEO accession GSE75704). After quality control assessment and data normalisation, differential methylation analysis was performed. We then carried out weighted gene correlation network analysis (WGCNA) using those probes showing the highest variance of methylation levels, after adjustment for confounding factors (e.g. age).

From differential methylation analysis, similar to the results from Weber et al., we found DNA methylation changes associated with PSP, including several CpGs in DLX1 that are significantly hypermethylated in PSP cases compared to controls. From the network analysis, we found a signature of highly correlated CpGs associated with the disease status. Our results support a role for DNA methylation alterations in PSP.

52. Judy Zhexing Ge - UCL Queen Square Institute of Neurology and UK Dementia Research Institute at UCL (Presenting on the day, Room 4 - Disorders of the nervous system: cellular mechanisms)

POSTER TITLE

Osteopontin/SPP1-positive Perivascular Macrophages Mediate Synapse Loss in Pre-Plaque Alzheimer's Mouse Models

AUTHORS
Ge ZJ, De Schepper S, Rueda-Carrasco J, Childs T, Chiong IN, Crowley G, Sokolova, D, Shinohara M, and Hong S

ABSTRACT
Emerging literature suggests a heterogeneous population of tissue-resident macrophages in the brain that employ distinct pathways and mechanisms to execute diverse functions (De Schepper et al., Dev Neurobiol 2020). One major function recently proposed for microglia, the brain's primary macrophages, is to facilitate synaptic pruning in developing and diseased brains. In particular, we and others have shown that microglia mediate region-specific synaptic loss in Alzheimer's disease (AD) mouse models before the appearance of plaques (Hong et al Science 2016), yet we know little about the underlying mechanisms and potential subsets involved. Using single-molecule fluorescent in-situ hybridization and immunohistochemistry, we found a region-specific expression of a macrophage subcluster that highly upregulates Osteopontin/SPP1 in the hippocampus of pre-plaque AD mice as compared to age- and sex-matched wild-type controls. The SPP1 upregulation was specific to CD206+ LYVE1+ Ms4a7+ perivascular macrophages expressing low levels of Cx3CR1 and Tmem119. Further, our ongoing experiments in SPP1-KO mice suggest that SPP1 is necessary for microglia-mediated synaptic engulfment and loss in AD mouse models. Together, our data suggest a new role for Spp1+ perivascular macrophages in pre-plaque synapse pathology.

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

POSTER TITLE
Restoration of dystrophin expression in the brain to address neurobehavioural problems in Duchenne muscular dystrophy

AUTHORS
Gileadi TE, Siddle M, Fergus C, Kelly VP, Morgan JE, Montanaro F, Muntoni F

ABSTRACT
Duchenne muscular dystrophy (DMD) is a severe neuromuscular disease caused by mutations in the dystrophin gene, resulting in muscle degeneration and a dramatically shortened life expectancy. DMD patients have a higher prevalence of brain-related comorbidities including lower average IQ, anxiety disorders, attention deficit hyperactivity disorder, and autism spectrum disorder. Several antisense oligonucleotide (AON) therapies have recently been approved, and show promising improvements in DMD neuromuscular outcomes. AONs also have the potential of improving life quality by addressing the brain comorbidities of DMD patients, but pre-clinical studies are required to identify optimal treatment methodology, key target brain regions and cell types, and neurobehavioural outcomes. We aim to study these using an exon-skipping phosphorodiamidate morpholino (PMO) to restore dystrophin in a mouse model of DMD. PMO distribution around the brain was assessed following either intracerebroventricular (ICV) injection or the minimally-invasive intracisternal injection, with a wider distribution across brain regions observed following ICV administration. Assays quantifying exon skipping (quantitative PCR) and dystrophin protein (automated western blot system WES) have been developed to further assess treatment protocols. These assays are now used alongside immunohistochemical

and behavioural studies to investigate the therapeutic potential of the treatment and the physiological function of dystrophin in the brain.

54. **Cagla Kaya - UCL Department of Neuroscience, Physiology and Pharmacology**

POSTER TITLE
Investigating the consequences of trisomy 21 on mitochondrial pathways in induced pluripotent stem cell-derived cells

AUTHORS
Kaya C, Gillham O, Duchen M

ABSTRACT
Most people with Down syndrome (DS) develop dementia by the age of 60, which has many features in common with Alzheimer's disease (AD). The mechanism(s) that lead to AD-like dementia in DS subjects are not understood. Exploring the underlying pathology may reveal potential therapeutic targets and illuminate mechanisms of dementia in AD. There is a genome-wide dysregulation of genes in DS subjects due to trisomy 21, including the expression of proteins associated with AD, such as amyloid-beta (Aβ). Mounting evidence supports that dementia is associated with impaired metabolism and that Aβ may impair metabolism. Therefore, I explored mitochondrial function as a potential link between DS and AD. Initially, I analysed three published RNA sequencing datasets of induced pluripotent stem cell(iPSCs)-derived cells that were reprogrammed from fibroblasts obtained from DS and control subjects. My analysis identified significantly dysregulated mitochondrial pathways in several DS iPSC-derived cells. Then, I quantified the transcription of a select set of genes essential for removing reactive oxygen species produced from mitochondria in DS iPSC-astrocytes using quantitative PCR. I found that peroxiredoxin-6 (PRDX6) was significantly upregulated in DS iPSC-astrocytes, which was previously shown to be also upregulated in AD brains and protect against Aβ accumulation.

55. **Iris Kleerekooper - UCL Queen Square Institute of Neurology**

POSTER TITLE
Retinal dysfunction in acute optic neuritis: inflammation at the inner nuclear layer or retrograde axonal signaling?

AUTHORS
Kleerekooper I, Del Porto L, Dell'Arti L, Guajardo J, Leo S, Robson AG, Trip SA, Petzold A, Plant GT, Holder GE

ABSTRACT
Introduction
Here, we explore the structure-functional correlates of retinal dysfunction in acute optic neuritis (ON).

Methods
This cross-sectional study recruited acute ON patients (<14 days) and controls. Subjects underwent pattern electroretinography (PERG), pattern visual evoked potentials (PVEP), visual acuity testing and optical coherence tomography imaging.

Results
Twenty-six patients with acute ON (11 MS, 6 myelin oligodendrocyte glycoprotein associated ON [MOGON], 9 idiopathic ON) and six controls were recruited. P50 and N95 amplitudes were significantly reduced in ON affected eyes (median 2.3μV; range 0.8 – 5.0μV and 3.4μV; range 1.2 – 5.1μV, respectively) compared with controls (4.0μV; range 2.6 – 4.6μV and 5.6μV; range 4.6 – 6.8μV; p=0.003 and p<0.001, respectively), and in affected compared with fellow eyes (p<0.001). P50 peak times were significantly shortened in ON (p<0.001). P50 was positively correlated to inner nuclear layer (INL) thickness (rs=0.36; p=0.009) and there was a positive correlation between ganglion cell and inner plexiform layer (GCIPL) thickness and both P50 and N95 (rs=0.44, p=0.022 and rs=0.46, p=0.002, respectively).

Conclusion
These structure-function interactions suggest that early inflammatory processes in ON involve the macula. This could be due to: opening of the blood retina barrier; activation of glia; or acute retrograde effects of optic nerve damage, likely metabolic.

56. Serena Lu - UCL Great Ormond Street Institute of Child Health

POSTER TITLE
Impact of Ketogenic Diet Therapy on growth in children with epilepsy

AUTHORS
Lu S, Champion H, Mills N, Simpson Z, Whiteley VJ, Schoeler NE.

ABSTRACT
Ketogenic diet therapy consists of high-fat, low-carbohydrate, moderate-protein diets for the treatment of drug-resistant epilepsy. Research indicates potential growth-stunting in children on these diets, but evidence is inconsistent. Our aims were to determine whether weight and height were affected, alongside possible associated factors.
A retrospective review of medical records of children following treatment at 3 UK centres was conducted, weight and height measurements recorded pre-diet, yearly on diet and 1-year post-diet discontinuation, converted to z-scores, and change from baseline analysed. Subgroup analyses were performed for feeding method, ambulatory status, diet type, diet response, age at diet onset and protein intake.

Median weight z-score significantly decreased from baseline at 4 years and 6 years, median height z-score at 1, 2 and 3 years. Younger children showed significantly greater decrease in weight z-score at 3 and 5 years, and height z-score at 1, 2 and 3 years on-diet and 1-year post-diet. Modified diet types showed less height z-score decrease compared with medium-chain triglyceride (1 year) and classical (1 and 2 years).

Height z-score was consistently affected, with growth of younger children more affected. Potential impacts should be discussed with patients, particularly in younger children. Further study with prospective data collection is warranted.

57. Naciye Magusali - UCL Queen Square Institute of Neurology (Presenting on the day, Room 3 - Disorders of the nervous system: molecular and genetics)

POSTER TITLE

A genetic link between risk for Alzheimer's disease and severe COVID-19 outcomes via the OAS1 gene

AUTHORS
Magusali N, Graham AC, Piers TM, Panichnantakul P, Yaman U, Shoai M, Reynolds RH, Botia JA , Brookes KJ, Guetta-Baranes T, Bellou E, Bayram S, Sokolova D, Ryten M, Frigerio CS, Escott-Price V, Morgan K, Pocock JM, Hardy J and Salih DA

ABSTRACT
Recently, we reported that oligoadenylate synthetase 1, OAS1, contributes to the risk of Alzheimer's disease (AD), by its enrichment in transcriptional networks expressed by amyloid-responsive microglia. However, the function of OAS1 within microglia and its genetic pathway are not known. Using genotyping from 1,313 individuals with sporadic AD and 1,234 control individuals, we confirm that the OAS1 variant, rs1131454, is associated with increased risk for AD. The same OAS1 locus was recently associated with severe COVID-19 outcomes, linking risk for both diseases. Analysing single-cell RNA-sequencing data of isolated microglia from APPNL-G-F knock-in mice and AD patients, we identify co-expression networks of interferon-responsive genes including OAS1 and Oas1a that significantly upregulate with age and amyloid deposition. In human iPSC-derived microglia with lowered OAS1 expression, we show an exaggerated expression and secretion of TNF-alpha with interferon-gamma stimulation, indicating that OAS1 is required to limit the pro-inflammatory response of myeloid cells. Collectively, our data support a link between genetic risk for AD and susceptibility to critical illness with COVID-19 centred on OAS1 and interferon signalling, a finding with potential implications for future treatments of both AD and COVID-19, and the development of biomarkers to track disease progression.

58. Nuria Martin Flores - UCL Department of Cell and Developmental Biology (Presenting on the day, Room 4 - Disorders of the nervous system: cellular mechanisms)

POSTER TITLE
Contribution of the secreted Wnt antagonist Dkk3 to synapse imbalance in Alzheimer's disease

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

ABSTRACT
In Alzheimer's disease (AD), cognitive decline correlates with synapses loss. Increasing evidence suggests that deregulation of the Wnt pathway contributes to synapse vulnerability in AD. Recent studies showed that the secreted Wnt antagonist Dkk3 is increased in plasma and CSF of AD patients and accumulates in Aβ plaques. However, the function of Dkk3 in the brain remains unexplored. Here, we investigated the impact of Dkk3 on synapses and AD.

Our results show that Dkk3 secretion is increased before plaque formation and accumulates at Aβ-plaques in two AD mouse models. DKK3 levels are also increased in the hippocampus of AD patients. RNAseq revealed that increased DKK3 expression is associated with AD. Importantly, our gene and SNP-based analyses demonstrate a link between DKK3 gene to AD. Gain-of-function experiments show that Dkk3 decreases excitatory synapse number but

increases inhibitory synapses in the hippocampus. Consistently, Dkk3 reduces the frequency of mEPSCs whereas increases mIPSC frequency. Notably, we found that in vivo Dkk3 loss-of-function in the J20 AD mouse line ameliorates synapse imbalance in the hippocampus at early and late stages. These findings demonstrate a novel role for Dkk3 in excitatory/inhibitory synapse balance. We propose Dkk3 as a target to reduce synapse dysfunction in AD.

59. **Chloe Mayhead - UCL Queen Square Institute of Neurology**

POSTER TITLE
Influence of different segmentation methods on the hippocampal volume in term neonates with HIE

AUTHORS
Mayhead C, Vijayaray D, Sokolska M, Baruteau KP, Mitra S.

ABSTRACT
Hypoxic ischaemic encephalopathy (HIE) is the most prevalent form of brain injury in neonates, and is the primary cause of death in neonates. Magnetic resonance imaging (MRI) is a neuroimaging tool used in HIE to determine prognosis and injury severity. Hippocampal volume changes have been reported in in adults with epilepsy due to seizures: a symptom common in neonates with HIE. Through segmenting MRI scans, hippocampal volume can be determined. However, there are different imaging and segmentation methods possible to use to segment the hippocampus. 20 neonates with moderate to severe HIE underwent 3T brain MRI. Five segmentation methods (T1W, T2W, T1W&T2W combined, flipped T1W and hippocampal plane T1W) were conducted on each of the images, to determine if the hippocampus volumes differed. A repeated measures ANOVA found the mean scores for volume of hippocampus were statistically significant ($F(1.250,23.757) = 52.815$, $p<0.0005$), showing different segmentation techniques affect the reported volume. This demonstrates irregularity between imaging methods and segmentation techniques can lead to reporting a smaller or larger hippocampi volume than the actual size. This could affect the clinical assessment of injury severity in this cohort, potentially affecting the prognosis and differential diagnosis.

60. **Paige Mumford - UK Dementia Research institute at UCL (Presenting on the day, Room 3 - Disorders of the nervous system: molecular and genetics)**

POSTER TITLE
Preclinical modelling in the mouse of altered neuroinflammation in Alzheimer’s disease – Down syndrome

AUTHORS
Mumford P, Noy S, Tybulewicz V, Fisher EMC, Hong S, Wiseman F.

ABSTRACT
Background: People with Down syndrome (DS) develop Alzheimer’s disease (AD) due to having three copies of chromosome 21 (Hsa21) gene APP leading to raised Aβ. How three-copies of the other Hsa21 genes affects AD is unclear. The immune system is generally perturbed in people with DS, including changes to neuroinflammation, an important aspect of

AD. Several Hsa21 genes alter inflammation in DS, but how these genes modify neuroinflammation in AD-DS is unknown. We are investigating how three copies of five Hsa21 candidate genes (RUNX1, IFNAR1, IFNAR2, IFNGR2, IL10RB) modifies neuroinflammation in response to Aβ.

Models: Mouse models with three copies of several Hsa21 orthologous genes, the Dp2Tyb (~36 genes) and Dp1Tyb (~148 genes).
Methods: qPCR, immunohistochemistry, MSD immunoassay.
Results: Dp1Tyb and Dp2Tyb brain has increased expression of Hsa21 candidate genes. Dp1Tyb hippocampus has increased microglia number in the dentate gyrus and elevated IL-1β levels. The Dp2Tyb has reduced microglia number in hippocampal CA3 and elevated interferon-γ levels in cortex.

Conclusion: Interferon-γ activates microglia, and people with DS have hyper-sensitivity to interferons due to three copies of IFNAR1, IFNAR2, IFNGR2, and IL10RB. The Dp2Tyb has elevated interferon-γ and raised interferon receptor levels that may modify the microglial response to Aβ.

61. Megha Murthy - UCL Queen Square Institute of Neurology (Presenting on the day, Room 3 - Disorders of the nervous system: molecular and genetics)

POSTER TITLE
Analysis of DNA methylation ageing in different brain regions in multiple system atrophy

AUTHORS
Murthy M, Foti SC, Miki Y, Lashley T, Viré E, Warner TT, Bettencourt C

ABSTRACT
Multiple system atrophy (MSA) is a rare adult-onset neurodegenerative disorder. Pathologically, MSA is characterized by the presence of glial cytoplasmic inclusions containing α-synuclein in oligodendrocytes. Different studies have reported accelerated epigenetic ageing in neurodegenerative diseases. To identify if patients with MSA exhibit accelerated brain ageing, we estimated the DNA methylation (DNAm) age as a surrogate for biological age in white matter tissue from cortical and cerebellar regions of MSA cases and controls. For this purpose, we used two DNA methylation-based clocks, the Horvath's multitissue clock and a recent cortical clock. DNAm age acceleration was calculated as: 1) difference between the predicted DNAm age and chronological age, and 2) residuals obtained by regressing DNAm age on chronological age. For white matter tissue from the cortical regions, results from the cortical clock exhibited the strongest positive correlation between DNAm and chronological ages, whereas for the cerebellum, the strongest positive correlation was observed with the Horvath's multitissue clock. Although age acceleration differences were observed between MSA and controls, upon adjustment for possible confounders (e.g. age and neuronal proportions), no significant age acceleration was observed. Our results highlight the need to account for confounding factors when calculating DNAm age acceleration.

62. Benjamin O'Callaghan - UCL Queen Square Institute of Neurology

POSTER TITLE

Understanding the mechanism by which KANSL1 and KAT8 Parkinson's Disease Risk Genes Regulate PINK1/PARKIN Mitophagy

AUTHORS
O'Callaghan B, Soutar MPM, Melandri D, Annuario E, Monaghan AE, Bictash M, Hardy J, Whiting PJ, Manzoni C, Ryten M, Lewis PA, Plun-Favreau H

ABSTRACT
Identification of causative Parkinson's Disease (PD) mutations in genes encoding proteins crucial for the cellular removal of damaged mitochondria (mitophagy) has highlighted compromised mitophagy as an important pathomechanism contributing to neurodegeneration. Using a high-content mitophagy screening assay of PD genetic risk loci we have previously identified two novel regulators of mitophagy: KANSL1 and KAT8 belonging to the NSL epigenetic remodelling complex. The mechanistic basis however, remained to be determined.

In vitro cell models of KANSL1 or KAT8 loss of function (LoF), revealed a reduction in PINK1-dependant mitophagy initiation. In line with the importance of the NSL complex for deposition of pro-transcriptional epigenetic modifications, this is at least partly due to an overall reduction in PINK1 availability, caused by reduced PINK1 mRNA transcription. Previous studies have shown that components of the NSL complex can be partially localised to the mitochondria. Further investigations are ongoing to explore whether KANSL1, KAT8 and lysine acetylation might also play a more direct role at the mitochondria through post-translational regulation of mitophagy associated proteins and/or the mitochondrial import machinery.

These results further highlight compromised mitophagy as an important pathomechanism leading to PD and reveal novel upstream pathways regulating PINK1/PARKIN mitophagy.

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

POSTER TITLE
Sirtuin2-induced H4K16ac deacetylation regulates Frizzled 1 and Frizzled 7 expression in AD

AUTHORS
Palomer E, Martin-Flores N, Jolly S, P Pascual-Vargas P, S Benvegnù S, Podpolny M, K Vaher K, P Whiting P, PC Salinas PC.

ABSTRACT
Deficient Wnt signalling has been linked to Alzheimer's disease (AD): three LRP6 Wnt co-receptor variants are linked to late onset AD, increased levels of the Wnt antagonist DKK1 are found in AD and its activity is required for amyloid-β-induced synapse loss. However, the expression/role of other Wnt signalling components remain unexplored in AD. Our analyses showed reduced mRNA levels of the Wnt receptors FRIZZLED1 (FZD1) and FZD7 at the hippocampus of human preclinical AD (PAD) cases and hAPPNLGF/NLGF model. Reduced mRNA levels were accompanied by lower levels of the pro-transcriptional histone mark H4K16ac and a concomitant increase of its deacetylase Sirt2 at Fzd1 and Fzd7 promoters in AD. In vitro and in vivo inhibition of Sirt2 rescued Fzd1 and Fzd7 mRNA expression and the levels of H4K16ac at Fzd1 and Fzd7 promoters. In addition, we showed that Sirt2 recruitment depends on FoxO1 activity in AD. Finally, we found reduced levels of the Sirt2

inhibitory phosphorylation in nuclear PAD, suggesting hyperactive nuclear Sirt2, and a concomitant increased levels of its phosphatase PP2C, favouring Fzd1 and Fzd7 repression in AD. Collectively, our findings defined a novel role for nuclear hyperactivated Sirt2 in repressing Fzd1 and Fzd7 expression via deacetylating H4K16ac in AD.

64. Melissa Rayner - MRC Prion Unit and UCL Institute of Prion Disease

POSTER TITLE
Development of a cell-based bioassay to accurately measure Creutzfeldt-Jakob disease prions in human tissues.

AUTHORS
Rayner MLD, Arora P, Nihat A, Jat P, Collinge J.

ABSTRACT
Variant Creutzfeldt-Jakob disease (vCJD) is a fatal neurodegenerative disease acquired upon dietary exposure to the infectious agent of Bovine Spongiform Encephalopathy (BSE). The infectious agent, called a prion, is a misfolded version of the normal cellular prion protein (PrPc). During the BSE epidemic (1986-1998), BSE infected cattle entered the food chain, resulting in 178 cases of human vCJD. Until 2016, all clinical cases of vCJD were homozygous within the prion protein gene, however, the recent death of a patient with a different genotype has raised concerns that there could be a second wave of the disease. Furthermore, a survey of abnormal prion prevalence, using archived appendix specimens, found 1:2000 people born before 1996, and 1:3000 people born after 1996, were positive. To guard against further inadvertent exposure of patients through blood transfusions and surgical procedures, it is imperative to develop a specific and highly sensitive assay, to monitor pre-clinical levels of vCJD infection.

We have developed a mouse tumour cell line, by editing the endogenous mouse PrPc followed by reconstitution with the human PrPc, which propagates vCJD infectivity to 10^6 dilutions of human brain homogenates. We are now screening the cell susceptibility to other human tissues and blood and automating the assay using a robot.

65. Olivia Rogerson - UCL Queen Square Institute of Neurology

POSTER TITLE
Epigenetic clock analysis in frontotemporal dementia

AUTHORS
Rogerson O, Lashley T, Battencourt C

ABSTRACT
Frontotemporal dementia (FTD) is a complex heterogeneous disorder characterised by multiple different subtypes encompassing language, behavioural and movement disorders. Increasing evidence suggests that DNA methylation plays a key role in ageing and neurodegenerative diseases, including FTD. Fluctuations in DNA methylation levels at specific sites act as “epigenetic clocks”, from which a biological age may be predicted. Studies have demonstrated that the difference between epigenetic age and chronological age, epigenetic age acceleration, could be predictive of age-associated diseases. We analysed publicly available DNA methylation data from peripheral blood samples of FTD patients and healthy controls from the Gene Expression Omnibus (GEO) (GSE53740,

N=384). Raw DNA methylation data (Illumina 450k array) was imported and pre-processed with multiple R Bioconductor packages before performing rigorous quality control checks using ChAMP and watermelon R packages. Epigenetic age was estimated using Horvath's online calculator and downstream analysis are ongoing. We aim to investigate whether FTD patients exhibit any significant epigenetic age acceleration effects compared to healthy controls. Our analysis will provide key insights into the DNA methylation changes that occur within patients and explore potential epigenetic biomarkers for FTD.

66. Jai Sidpra - UCL Great Ormond Street Institute of Child Health

POSTER TITLE
Improved Prediction of Postoperative Paediatric Cerebellar Mutism Syndrome Using An Artificial Neural Network

AUTHORS
Sidpra J, Marcus AP, Löbel U, Toescu SM, Yecies D, Grant G, Mirsky DM, Marcus HJ, Aquilina K, Mankad K

ABSTRACT
Background:
Postoperative paediatric cerebellar mutism syndrome (pCMS) is a common but severe complication which may arise following the resection of posterior fossa tumours in children. Two previous studies have aimed to preoperatively predict pCMS, with varying results.

Objective:
To examine the generalisation of these models and to determine if pCMS can be predicted more accurately using an artificial neural network (ANN).

Methods:
An overview of reviews was performed to identify risk factors for pCMS, and a retrospective dataset collected as per these defined risk factors from children undergoing resection of primary posterior fossa tumours. The ANN was trained on this dataset and its performance evaluated in comparison to logistic regression and other predictive indices via analysis of receiver operator characteristic curves. Area under the curve (AUC) and accuracy were calculated and compared using Wilcoxon signed rank test, with $p<0.05$ considered statistically significant.

Results:
204 children were included, of whom 80 developed pCMS. The performance of the ANN (AUC 0.949; accuracy 90.9%) exceeded that of logistic regression ($p<0.05$) and both external models ($p<0.001$).

Conclusion:
Using an ANN, we show improved prediction of pCMS in comparison to previous models and conventional methods.

67. Martin Smith - UCL Department of Clinical and Experimental Epilepsy

POSTER TITLE
Does Phase-Amplitude Coupling (PAC) Between Brain Regions Play A Role In Seizure Generalisation?

AUTHORS
Smith TM, Keane M, Jafarian A, Masvidal-Codina E, Bonaccini A, Brunet AG, Wykes RC

ABSTRACT
To investigate how brains regions are recruited into a seizure, we used a mouse head-fixed awake model, where focal onset seizures were induced by localised injection of chemoconvulsant (4-AP) to the visual cortex. Electrophysiological recordings were made from the surface of the cortex using an epidural array and also from a penetrating electrode with contacts in the underlying hippocampus. Upon recruitment of the hippocampus to seizure, evident by LFP potential recordings and a fast increase in high gamma power (80-200 Hz), we observe phase-amplitude coupling (PAC) between the low frequency firing of the cortex (5-10 Hz) and high frequency (~150 Hz) activity in the hippocampus. This PAC is only evident at seizure onset in the hippocampus (~5 seconds), despite continued, > 30 second seizure and high gamma activity. Further studies are needed to determine whether PAC plays a role in recruitment and initial entrainment of the seizure as it invades different brain regions, therefore playing a role in seizure generalisation.

68. Yutong Wan - UCL Division of Biosciences

POSTER TITLE
Exploring the Basis of Phenotypic Diversity in Alzheimer's Disease

AUTHORS
Yutong Wan, Zane Jaunmuktane

ABSTRACT
Alzheimer's Disease (AD) is the most common type of dementia and affects more than 50 million people worldwide. Although there is no effective treatment for the disease at the moment, early detection is still critical to start an early management plan and try out various interventions. Besides the stereotypical Amnestic Syndrome, many atypical phenotypes exist which make accurate early diagnosis challenging. They include Corticobasal Syndrome (CBS), behavioural variant of Frontotemporal Dementia (bvFTD), Posterior Cortical Atrophy (PCA), and Primary Progressive Aphasia (PPA). Diverse clinical presentations correlated with selective degeneration and pathology development in different brain regions. The different regions with originally pathological alternations of each phenotype may help explain the conundrum of polytropic presentations, that primary motor cortex is significantly affected in CBS, basal ganglia in bvFTD, posterior part of the brain in PCA, and temporoparietal areas in PPA. Research indicates that the presence of ApoE4 is significant for the development of all AD phenotypes. In addition, while some studies reported several familial cases, these are not typically thought to be representative, and thus more studies are needed. Given the lack of available research and inconsistency between results, more research is needed to better understand the basis of selective regional vulnerability.

69. Yanisa Wannasuphoprasit - UCL Division of Psychiatry

POSTER TITLE
CYP2D6 genetic variation and antipsychotic-induced weight gain: a systematic review and meta-analysis.

AUTHORS

Wannasuphoprasit Y, Austin-Zimmerman I, Irizar H, Bhat A, Koller D, Wang B, Zartaloudi E, and Bramon E.

ABSTRACT
Background: Antipsychotic-induced weight gain (AIWG) is a contributing factor in the reduced life expectancy amongst people with psychotic disorders. CYP2D6 is an enzyme involved in the metabolism of antipsychotics. Therefore, genetic testing for CYP2D6 may be beneficial in predicting AIWG and delivering personalised medicine.
Aim: Investigate the influence of CYP2D6 on AIWG.

Methods: We searched literature from Pubmed, Embase, PsychInfo and CENTRAL. We grouped participants into CYP2D6 metabolic groups (poor metabolisers (PM), intermediate metabolisers (IM), normal metabolisers (NM) and ultra-rapid metabolisers (UM)) and compared their weight and BMI after long-term antipsychotic use.

Results: We included twelve studies with 51 PMs, 418 IMs, 936 NMs and 6 UMs. We found a trend-level association with PMs having higher BMI than NMs (SMD=0.66, 95%CI: -0.10 to 1.42, p=0.09), but no difference in weight (SMD=-0.02, 95%CI: -0.58 to 0.55, p=0.96). We found no difference in weight or BMI between IMs and NMs (SMD=0.14, 95%CI: -0.03 to 0.31, p=0.11 and SMD=0.20, 95%CI: -0.34 to 0.74, p=0.47).

Conclusion: We found weak evidence supporting an influence of CYP2D6 on AIWG but our study was limited by a small sample size and high heterogeneity between studies. Therefore, more standardised prospective studies with larger sample sizes will be required.

70. Katharina Wenz - UK Dementia Research institute at UCL

POSTER TITLE
Down Syndrome and Alzheimer's Disease – determining which chromosome 21 gene(s), when over-expressed, modulate Aβ toxicity and accumulation.

AUTHORS
Wenz KC, Wiseman FK, Niccoli T, Wu Y.

ABSTRACT
Down Syndrome (DS) is the greatest risk factor for early-onset dementia (Alzheimer's disease-Down syndrome, AD-DS). People with DS carry an extra copy of chromosome 21 (Hsa21), which encodes ~235 genes, including APP. Duplication of APP alone has been shown to be sufficient to cause early-onset AD, suggesting a crucial role of this gene in increasing the risk of AD for people with DS (Sleegers et al., 2006). However, the contribution of other Hsa21 gene duplications to AD risk is not yet understood. Wiseman et al., demonstrated that the triplication of Hsa21 genes other than APP increases the risk of AD pathology (Wiseman et al., 2018).

To further narrow down which Hsa21 gene(s) contribute to AD-DS, we are using Drosophila melanogaster as a screening tool. Genes that we find to alter neuromotor function and Ab aggregation in the fly brain when overexpressed, will be analysed further. For this we will be working with human post-mortem brain tissue to determine if the candidate gene orthologs are dosage sensitive in the brains of people who had DS compared with euploid individuals. This research aims to further our understanding of AD pathology in the context of DS and to contribute to the development of novel therapies for people with early onset AD.

71. Angeliki Zarkali - UCL Queen Square Institute of Neurology and UK Dementia Research Institute at UCL (Presenting on the day, Room 2 - Cognition & cognitive dysfunction)

POSTER TITLE
Visual dysfunction predicts cognitive impairment and white matter degeneration in Parkinson's disease

AUTHORS
Zarkali A, McColgan P, Leyland L, Lees A, Weil S

ABSTRACT
Visual dysfunction accompanies and predicts dementia in Parkinson's disease (PD), but the underlying structural correlates remain unknown.
We employed fixel-based analysis, a sensitive and fibre-specific framework to examine longitudinal white matter change in PD. Diffusion-weighted imaging was performed in 77 PD patients (22 low visual performers) and 25 controls at baseline and after 18 months. We compared white matter fibre density (microstructural), fibre cross-section (macrostructural) and combined fibre density and cross-section (marker of overall white matter integrity) across the whole white matter, adjusting for age, gender and total intracranial volume.
PD low visual performers showed worse cognition at 18 months (r=-0.386, p-0.024) and were more likely to develop cognitive impairment compared to those with normal vision (x2=7.031 p=0.008). PD low visual performers showed micro-structural and macro-structural changes in posterior white matter tracts at baseline followed by widespread macrostructural changes after 18 months, with up to 22% further reductions in fibre cross-section, involving bilaterally the fronto-occipital fasciculi, external capsules, and middle cerebellar peduncles.
PD with poor visual performance show worsening cognition and increased white matter damage over time; this provides further evidence for visual function as a marker of imminent cognitive decline and could inform the design of future clinical trials.

72. Ya Zhou - UCL Queen Square Institute of Neurology

POSTER TITLE
Correlative light and electron microscopy suggests that mutant huntingtin dysregulates the endolysosomal pathway in presymptomatic Huntington's disease

AUTHORS
Ya Zhou1, Thomas R. Peskett2,3, Christian Landles1, John B. Warner4, Kirupa Sathasivam1, Edward J. Smith1, Shu Chen2, Ronald Wetzel5, Hilal A. Lashuel4, Gillian P. Bates1,†*, Helen R. Saibil2†

ABSTRACT
Huntington's disease (HD) is a late onset, inherited neurodegenerative disorder for which early pathogenic events remain poorly understood. Here we show that mutant exon 1 HTT proteins are recruited to a subset of cytoplasmic aggregates in the cell bodies of neurons in brain sections from presymptomatic HD, but not wild-type, mice. This occurred in a disease stage and polyglutamine-length dependent manner. We successfully adapted a high-resolution correlative light and electron microscopy methodology, originally developed for

mammalian and yeast cells, to allow us to correlate light microscopy and electron microscopy images on the same brain section within an accuracy of 100 nm. Using this approach, we identified these recruitment sites as single membrane bound, vesicle-rich endolysosomal organelles, specifically as (i) multivesicular bodies (MVBs), or amphisomes and (ii) autolysosomes or residual bodies. The organelles were often found in close-proximity to phagophore-like structures. Immunogold labeling localized mutant HTT to non-fibrillar, electron lucent structures within the lumen of these organelles. In presymptomatic HD, the recruitment organelles were predominantly MVBs/amphisomes, whereas in late-stage HD, there were more autolysosomes or residual bodies. Electron tomograms indicated the fusion of small vesicles with the vacuole within the lumen, suggesting that MVBs develop into residual bodies. We found that markers of MVB-related exocytosis were depleted in presymptomatic mice and throughout the disease course. This suggests that endolysosomal homeostasis has moved away from exocytosis toward lysosome fusion and degradation, in response to the need to clear the chronically aggregating mutant HTT protein, and that this occurs at an early stage in HD pathogenesis.

Homeostatic and Neuroendocrine Systems

73. Ptolemy Banks - UCL Queen Square Institute of Neurology

POSTER TITLE
Insight into physiologically normal ranges of intracranial pressure and the effects of body position from 184 telemetric ICP monitor patients.

AUTHORS
Banks PDW, Pandit AS, Toma AK, Thompson S, Thorne LW, Watkins LD

ABSTRACT
Background: Stable intracranial pressure (ICP) is essential for healthy brain function; high ICP can compress the brain and perturb cerebral blood perfusion, whereas low ICP reduces the brain’s buoyancy and causes gravitational traction. As such, deviation from acceptable ICP ranges results in symptoms including headaches, nausea, and dizziness. Despite their basic and clinical relevance, acceptable ranges of ICP remain unclear.
Methods: A retrospective study of hydrocephalus patients with implanted telemetric intracranial pressure monitors over 8 years. Patient demographics, symptoms, and ICP measurements in different positions were recorded and categorised as symptomatic or asymptomatic.

Results: Across the 184 included patients (69% female), 31 patients had their ICP recorded while asymptomatic averaging (in mmHg) -9.3 (± 5.6) standing, -8.8 (± 4.9) sitting, and 10.2 (± 6.8) supine with an average range of 19.3 (± 4.7) between standing and supine. Across all patients, males had higher ranges (25.3, ± 8.3) compared to females (21.8, ± 6.6).
Conclusions: Positional data may help predict changes in ICP in different positions and activities, such as during sleep. The means of asymptomatic ICP recordings may help elucidate acceptable values. This can identify clinically significant deviations in ICP and guide shunt adjustment in the management of hydrocephalus.

74. Dan Brierley - UCL Department of Neuroscience, Physiology and Pharmacology

POSTER TITLE

Central and peripheral GLP-1 systems independently suppress eating

AUTHORS
Brierley DI, Holt MK, Singh A, de Araujo A, Vergara M, Afaghani MH, Lee SJ, Scott K, Maske C, Langhans W, Krause E, de Kloet A, Gribble FM, Reimann F, Rinaman L, de Lartigue G, Trapp S.

ABSTRACT
The anorexigenic peptide glucagon-like peptide-1 (GLP-1) is secreted from gut enteroendocrine cells and brain preproglucagon (PPG) neurons, which, respectively, define the peripheral and central GLP-1 systems. PPG neurons in the nucleus tractus solitarii (NTS) are widely assumed to link the peripheral and central GLP-1 systems in a unified gut–brain satiation circuit. However, direct evidence for this hypothesis is lacking, and the necessary circuitry remains to be demonstrated. Here we show that PPGNTS neurons encode satiation in mice, consistent with vagal signalling of gastrointestinal distension. However, PPGNTS neurons predominantly receive vagal input from oxytocin-receptor-expressing vagal neurons, rather than those expressing GLP-1 receptors. PPGNTS neurons are not necessary for eating suppression by GLP-1 receptor agonists, and concurrent PPGNTS neuron activation suppresses eating more potently than semaglutide alone. We conclude that central and peripheral GLP-1 systems suppress eating via independent gut–brain circuits, providing a rationale for pharmacological activation of PPGNTS neurons in combination with GLP-1 receptor agonists as an obesity treatment strategy.

75. Shereen Nizari - UCL Department of Neuroscience, Physiology and Pharmacology (Presenting on the day, Room 4 - Disorders of the nervous system: cellular mechanisms)

POSTER TITLE
Glucagon-like-peptide-1 induces cerebral arteriole dilations, increases cerebral blood flow, and promotes neuroprotection against ischaemic stroke.

AUTHORS
Nizari S, Basalay M, Chapman P, Korte N, Korsak A, Christie IN, Theparambil SM, Davidson MS, Reimann F, Trapp S, Yellon D, Gourine AV.

ABSTRACT
Stroke is a leading cause of death and disability. Clinical trials have found glucagon-like-peptide-1-receptor (GLP-1R) agonists decrease the incidence of fatal stroke. GLP-1 release has been demonstrated through remote-ischaemic-preconditioning (RIC), involving cycles of ischaemia and reperfusion to a distal tissue. This study aimed to test whether GLP-1R activation through RIC is neuroprotective in a stroke model and to investigate the effect of GLP-1 on the cerebrovasculature.

In rats, the infarct area from ischaemic-stroke induced by middle cerebral artery occlusion was found to be effectively reduced by RIC applied to the hindlimb. This was inhibited by systemic administration of the GLP-1R antagonist Exendin-9. GLP-1R expression (assessed using GLP-1R reporter mice) was found primarily on cortical cerebral arteries. Ex vivo activation of vascular cortical GLP-1R using Exendin-4 in rat acute-brain-slices led to arterial dilation in vessels pre-constricted by lactate or conditions of oxygen/glucose deprivation.

This effect was mediated by cAMP, but independent of nitric oxide release. Furthermore, Exendin-4 increased cerebral blood flow in vivo.

These results demonstrate that neuroprotection against ischaemic-stroke established by RIC involves GLP-1R signalling. Potent dilatory effect of GLP-1R activation on cortical arterioles suggests that this neuroprotection is mediated via modulation of cerebral blood flow, improving brain perfusion.

Neural Excitability, Synapses, and Glia: Cellular Mechanisms

76. Stephanie Choi - MRC Laboratory for Molecular Cell Biology

POSTER TITLE
Understanding the pathophysiological development of chemotherapy-induced peripheral neuropathy through non-neuronal cells

AUTHORS
Stephanie Choi, Anne-Laure Cattin, Jemima Burden, Alison Lloyd

ABSTRACT
Paclitaxel, one of the most used chemotherapeutic drugs causes peripheral nerve dysfunction that leads to painful, progressive, and often irreversible neuropathy in a large proportion of patients. The mechanisms underlying chemotherapy-induced peripheral neuropathy (CIPN) are largely unclear, and the involvement of non-neuronal cells has not been thoroughly explored. This study integrates immunofluorescence imaging, electron microscopy and histological analysis to identify the pathophysiological involvement of Schwann cells, the main glial cells of the PNS, in CIPN. Cultured primary rat Schwann cells alone or co-cultured with dorsal root ganglia sensory neurons were subjected to 0.01-1uM paclitaxel treatment for 24 hours displayed cytoskeletal defects leading to cytotoxicity. Next, transgenic mice with green fluorescent protein labelled glial cells (Plp-eGFP) were treated with 6×30 mg/kg paclitaxel, mimicking clinically relevant dose-dense regimens. Two weeks following treatment, p75 expression was upregulated in Schwann cells in the sciatic nerve. The cutaneous “nociceptive” terminal Schwann cells had manifested protrusions to the epidermis and evident enlargement of mechanoreceptors in the glabrous skin. From ultrastructural analysis, non-myelinating Schwann cells had significant increase in abnormalities including poly-axonal pockets and incompletely ensheathed axons. Collectively, these results suggest that paclitaxel induces dedifferentiation and morphological changes in Schwann cells, which may play a role in CIPN.

77. Timothy Church - UCL Department of Neuroscience, Physiology and Pharmacology

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

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

ABSTRACT
Interplay between the ancient and ubiquitous second messengers cAMP and Ca2+ is a hallmark of dynamic cellular processes. A common motif is the opposition of the Ca2+-sensitive phosphatase calcineurin and the major cAMP receptor, protein kinase A (PKA). Calcineurin dephosphorylates substrates primed by PKA to bring about changes including synaptic long-term depression (LTD). AKAP79 supports signalling of this type by anchoring PKA and calcineurin alongside one another. We have discovered that AKAP79 increases the rate of calcineurin dephosphorylation of type II PKA regulatory subunits by an order of magnitude. Fluorescent PKA activity reporter assays, supported by computational modelling, show how AKAP79-enhanced calcineurin action enables suppression of PKA activity by increasing PKA catalytic subunit capture rate. Experiments with hippocampal neurons indicate that this mechanism contributes towards LTD. This non-canonical mechanism for suppressing PKA activity, that doesn't require any change in cAMP concentration, may underlie many other cellular processes.

78. Gerard Crowley - UK Dementia Research Institute (Presenting on the day, Room 4 - Disorders of the nervous system: cellular mechanisms)

POSTER TITLE
Chemogenetic activation of perforant pathway induces microglial complement signalling

AUTHORS
Crowley G, Ge J, Hong S

ABSTRACT
Emerging studies implicate microglia as cellular mediators of synaptic pruning. In developmental critical periods of neuronal circuit refinement, microglia engulf synapses in a complement- and activity-dependent manner. In early, pre-plaque stages of Alzheimer's disease (AD) mouse models, region-specific reactivation of complement (C1q) deposition onto synapses occurs, initiating microglia-mediated synapse elimination. The trigger for this reactivation remains unknown. Another early hallmark in pre-plaque AD brain is network hyperactivity. As developmental pruning is regulated by neuronal activity, we hypothesised that abnormally elevated activity is responsible for reactivating microglia-synapse pruning in the wild-type adult brain. To address this, we chemogenetically activated the perforant path neuronal input from medial entorhinal cortex (MEC) to the dentate gyrus molecular layer (DGML). c-Fos immunostaining indicates increased neuronal activation at MEC upon DREADD ligand administration. Strikingly, at downstream DGML, there are significantly elevated levels of C1q deposition onto synaptic markers. Preliminary data suggest activity-dependent upregulation of C1qa mRNA inside microglia at the DGML, without appreciable differences in 'activation' markers CD68 and P2Y12. Altogether, these data suggest that elevating neuronal activity in adult mice upregulates microglial complement signalling at the synapse. Future work will determine whether increase in complement leads to reactivation of the pruning pathway and synaptic loss.

79. Ashton Curtis - UCL Department of Neuroscience, Physiology and Pharmacology

POSTER TITLE
Building stronger synapses with CaMKII and a-actinin-2

AUTHORS
Zhu J, Curtis A, Gold MG

ABSTRACT
Calcium Calmodulin-dependant Kinase II (CaMKII) is central for the induction of long-term potentiation (LTP). As CaMKII plays an enzymatic and structural role in potentiated synapses, it must be anchored within the postsynaptic density (PSD) to ensure correct functionality. Whilst CaMKII anchoring partners have been identified, the structural details of these interactions and their regulatory effects are poorly understood. Here we investigate the interactions of CaMKII with α-actinin-2 (αA2). We reveal the crystal structure of αA2 EF hand & CaMKII regulatory segment interface. Our structural insights demonstrate the ability for α-actinin-2 to bind to, but not fully activate CaMKII. Moreover, we determine the direct affinity of this interaction using isothermal titration calorimetry and reveal that phosphorylation of CaMKII Threonine residues prohibits CaMKII/aA2 interactions. Further investigations into abrogating these binding partners with confocal microscopy signify that α-actinin-2 is necessary for CaMKII to stabilise potentiated synapses following LTP.

80. Megan Jones - UCL Department of Cell and Developmental Biology (Presenting on the day, Room 4 - Disorders of the nervous system: cellular mechanisms)

POSTER TITLE
Contribution of a genetic variant of the Wnt receptor LRP6 on synapse impairment in ageing and in Alzheimer’s disease

AUTHORS
Jones M, Buechler J, Dufor T, Metzakopian E, Gibb A, Salinas PC

ABSTRACT
Alzheimer's disease (AD) currently affects fifty million people globally. Synapse loss, a key hallmark of AD, is the strongest correlate to cognitive decline. Deficient Wnt signaling, a pathway required for neuronal connectivity, has been linked to synapse loss in AD. Indeed, a variant of LRP6 (LRP6-Val), has been linked to late onset AD and reduced Wnt signaling. However, the effect of LRP6-Val in vivo and at synapses has not been characterized.
We have generated a novel knock-in mouse model carrying this variant. We found that homozygous LRP6-Val mice develop normally and do not exhibit obvious morphological abnormalities. However, LRP6-Val mice exhibit synaptic defects with age. We crossed LRP6-Val mice to the AD KI model, NL-G-F to examine if this variant increases synapse vulnerability. Indeed, we found that LRP6-Val; NL-G-F mice exhibit a higher loss of synapses.

Our work demonstrates for the first time that mice carrying the LRP6-Val variant exhibit a progressive synaptic defect that is manifested as animals age. Importantly, the presence of this variant exacerbates synaptic degeneration in the context of AD suggesting its role as a risk factor.

81. Yaara Lefler - Sainsbury Wellcome Centre

POSTER TITLE
Synaptic integration in the mouse midbrain during instinctive defensive behaviour

AUTHORS
Lefler Y, Ferreira G, Branco T

ABSTRACT
When facing a threatening stimulus, animals instinctively react with defensive behaviours, such as immediate escape to a safe place or freezing in a motionless crouching posture. The choice between different possible actions is taken in only a few hundred milliseconds, and yet, it requires integrating several factors, such as the perceived distance to the threat and information about the local environment. Recently, it has been shown that neurons in the superior colliculus (SC) and periaqueductal gray (PAG) form a neural circuit crucial for organising defensive responses in the mouse. Here, we study how the decision between escape and freezing is computed at the synaptic level in this midbrain circuit. We have developed a behavioural paradigm for awake head-restrained mice, using a floating arena, in which animals navigate between a shelter and a threat zone and are exposed to visual and auditory stimuli mimicking approaching predators. We use whole-cell patch clamp recordings to characterise the sensory responses to the threatening stimuli, and to measure synaptic integration when mice escape or freeze in response to threat. Through analysis of synaptic activity in physiologically-defined groups of neurons we aim to infer the computations that determine the selection between escape and freezing.

82. Emma Lloyd - MRC Laboratory for Molecular Cell Biology

POSTER TITLE
Investigating translational homeostasis in mature axons

AUTHORS
Lloyd E, Kouloulia S, Lloyd A, Riccio A

ABSTRACT
The complex, polarised structure of the sensory neuron raises many questions about the functional and structural regulation of its' axonal compartment. For example, how is axonal homeostasis maintained throughout adulthood despite its significant distance from the sensory neuron cell body? Axonal localisation and translation of mRNA transcripts has been shown to play an essential role in neuronal development and in the regenerative process following injury, moreover its dysregulation has been implicated in multiple neurodegenerative diseases. However, the occurrence of axonal protein synthesis throughout adulthood is still a widely debated topic. My PhD project aims to establish the role of local translation in the homeostasis and maintenance of mouse sensory neurons throughout adulthood. I am using puromycin-based metabolic labelling and proximity ligation assays to visualise global translation in the axons of these neurons as well as axon-specific translating ribosomal affinity purification (TRAP) and RNAseq to delineate the axonal translatome. These data will allow us to investigate specific locally translated transcripts involved in the long-term survival of sensory neurons and contribute towards a better understanding of how local translation is regulated in health and disease.

83. Oriol Pavon Arocas - Sainsbury Wellcome Centre (Presenting on the day, Room 5 - Neural circuits and behaviour)

POSTER TITLE
Topographic gene expression profiling of single periaqueductal gray neurons

AUTHORS
Pavon Arocas O, Olesen SF, Branco T

ABSTRACT
The midbrain periaqueductal gray (PAG) is a brain structure where instinctive behaviours such as escaping from predators, vocalising, and freezing segregate onto distinct anatomical subdivisions. This parallel between behaviour and circuit anatomy provides a unique opportunity to investigate how neural mechanisms support the computation of adaptive actions. In this work, we aimed to determine how the biophysical and computational properties of single PAG neurons are constrained by their gene expression profile. To link the expression of ion channels, receptors, and molecular effectors to specific PAG subdivisions, we performed single-cell RNA-sequencing while preserving the anatomical origin of each neuron. We obtained detailed transcriptomic profiles from excitatory and inhibitory neurons across PAG subdivisions by individually isolating fluorescently labelled neurons from acute midbrain slices of transgenic mice and subjecting them to Smart-seq2 and deep sequencing. Application of graph-based clustering to the resulting data revealed putative subtypes of neurons that map onto different PAG subdivisions, whereas preliminary results using differential expression analysis identified an array of neuropeptides, ion channel subunits, and receptors for neuromodulators that confer distinct gene expression profiles to excitatory and inhibitory neurons. Our results provide a framework for studying how molecularly defined biophysical properties might underpin behavioural control by the PAG.

84. Marta Perez Gonzalez - UCL Queen Square Institute of Neurology

POSTER TITLE
Neuroinflammatory and synaptic characterization of the Dp1Tyb mouse model of Down syndrome

AUTHORS
Perez-Gonzalez M, Zouhair I, Muza P, Tybulewicz VLJ, Fisher EMC

ABSTRACT
Down syndrome (DS), which results from trisomy of human chromosome 21 (Hsa21), is the most common genetic cause of intellectual disability (Wiseman et al., 2015). Although DS arises from increased dosage of Hsa21 genes (Antonarakis, 2017), the specific mechanisms underlying cognitive dysfunction remain unknown.

A recent study by Pinto et al., (2020), demonstrated altered microglial activation is linked to cognitive impairment in two mouse models of DS (Dp(16)1Yey and Ts65Dn) and, importantly, DS individuals show similar patterns of microglial activation. Thus, the aim of this project is to perform an in-depth characterization of the neuroinflammatory profile in the Dp1Tyb mouse model of increased gene dosage in DS, which we have previously shown to have cognitive impairment (Chang et al., 2020), paying special attention to the role of microglia activation in synaptic pruning. We are investigating levels of neuroinflammatory and synaptic markers by western blotting from wildtype and Dp1Tyb littermates. We are also undertaking Golgi-Cox staining to count the number of dendritic spines of these mice. This will allow us to investigate synaptic loss.

Overall, we will assess the neuroinflammatory profile of the Dp1Tyb mice compared to their wildtype littermates and we will investigate the synaptic health of these mice.

85. Dimitra Sokolova - UCL Queen Square Institute of Neurology (Presenting on the Day, Room 4 - Disorders of the nervous system: cellular mechanisms)

POSTER TITLE
Role of astrocytic MFG-E8 in synapse loss in Alzheimer's disease

AUTHORS
Sokolova D, Lee S, Rueda-Carrasco J, De Schepper S, Crowley G, Childs T, Ge J, Hong S

ABSTRACT
Emerging data suggest that microglia, brain tissue-resident macrophages, mediate region-specific synapse loss in Alzheimer's disease (AD). However, whether microglia target certain synapses for elimination is unclear. Recent data in AD suggest apoptotic-like mechanisms on synapses, raising the intriguing question of whether these 'apoptotic' synapses are selectively removed by microglia. In the peripheral immune system, apoptotic material displays externalised phosphatidylserine (ePtdSer), leading to selective removal by macrophages via milk fat globule-EGF factor 8 (MFG-E8) signalling. Of interest, human proteomic data show that MFG-E8 is enriched on synaptosome fractions isolated from AD brains compared to control. Using single molecule in-situ hybridisation and various biochemical methods, we found a region-specific upregulation of MFG-E8 in pre-plaque AppNL-F AD-like mice vs wild-type controls. MFG-E8 upregulation was confined to regions vulnerable to synapse loss, such as hippocampus, but not cerebellum. Interestingly, unlike in peripheral tissues where Mfge8 is expressed by F4/80+ macrophages, in the brain, we found Slc1a2+/GFAP+ astrocytes to express Mfge8, not microglia. Treating primary hippocampal culture with synaptotoxic amyloid-beta oligomers led to abnormal calcium signalling and increased ePtdSer+ levels on Homer1-eGFP+ dendritic spines, and this coincided with increased MFG-E8 localisation onto ePtdSer+ Homer1-eGFP+ spines. Altogether, our data suggest that astrocytes upregulate MFG-E8 for deposition onto 'apoptotic' synapses in AD-like context. Current experiments are underway to determine whether MFG-E8 deposition leads to selective removal of the apoptotic synapses by microglia.

Novel Methods, Resources and Technology Development

86. Ali Alim-Marvasti - UCL Queen Square Institute of Neurology

POSTER TITLE
Seizure focus prediction from seizure semiology: data-driven cortical probabilistic heatmaps from 4643 patients

AUTHORS

Alim-Marvasti A, Romagnoli G, Perez-Garcia F, Geranmayeh F, Scott G, Shahrbaf S, Chowdhury FA, Diehl B, Sparks R, Ourselin S, Clarkson MJ, Duncan JS.

ABSTRACT
Semiology is important in evaluating individuals with focal drug resistant epilepsy to help localise the seizure focus for curative resection, but remains largely subjective.
We created the Semiology-to-Brain Database and 3D Visualisation Tool (SVT) to objectively localise seizure foci from an individual-participant systematic review, yielding 11230 localising and 2391 lateralising datapoints from 4643 patients across 309 studies. We probabilistically mapped semiologies to brain regions and modelled brain regions as binomial random variables.

We integrated SVT into the freely available 3D-Slicer software with a graphical user interface, enabling visualisations of semiologies as probabilistic cortical heatmaps using Bayesian inference.

Clinical validation was performed in 14 random retrospective patients who had had epilepsy surgery and remained seizure-free. Patients' semiologies were used to obtain scores for SVT's predictions by comparison with the actual resected lobe and side of surgery. We compared results to four expert epileptologists given the same semiological information.
SVT's performances matched that of expert clinicians for localisation (11/14) and exceeded it for lateralisation (+9 for SVT vs +7 for the best clinician).
SVT could be the basis of multimodal clinical-imaging models as clinical decision support for predicting the seizure focus in the presurgical evaluation of patients with focal drug-resistant epilepsy.

87. Stephane Bugeon - UCL Queen Square Institute of Neurology

POSTER TITLE
Recording the activity of transcriptomic cell types in mouse primary visual cortex

AUTHORS
Bugeon S, Hauling T, Duffield J, Nicolotsoupoulos D, Orme D, Prankerd I, Isogai Y, Carandini M, Harris KD

ABSTRACT
Neuronal subtypes are critical components of cortical microcircuits and are necessary for cortical computations. While cortical neurons have been classically subdivided into broad subtypes (i.e. Vip, Sst and Pvalb positive interneurons), transcriptomic analysis has revealed many more subpopulations of finely distinguished cortical neurons.

To decipher the functional properties and network activity of these fine cell types in primary visual cortex, we have applied post-hoc in situ transcriptomic analysis to cortical neurons after imaging their activity in vivo. We first record the activity of V1 neurons using two-photon calcium imaging in awake freely running mice, during visual stimulation or spontaneous activity. After these recordings, we apply in situ RNA sequencing to brain slices, to determine gene expression and transcriptomic cell types, which are then registered to z-stacks from the in-vivo recordings using multiple landmarks.

To confirm that this procedure can reveal the functional properties of transcriptomic cell types, we reproduced findings on the size tuning of different V1 cell types, and their

modulation by locomotion. We also show strikingly different running modulation for two transcriptomic subtypes of Pvalb interneurons. Thus, this method provides a high-throughput approach to characterize the in vivo activity of fine transcriptomic cortical cell types.

88. Amy Leung - UCL Institute of Ophthalmology

POSTER TITLE
Investigation of Ataluren (PTC124) as a potential therapeutic for LCA4 in a patient-derived iPS-retinal organoid model

AUTHORS
Leung A, Sacristan-Reviriego A, Perdigao P, Bainbridge J, Michaelides M, Cheetham M, van der Spuy J.

ABSTRACT
Leber congenital amaurosis type 4 (LCA4), a severe inherited retinal dystrophy, is an autosomal recessive disorder caused by mutations in aryl hydrocarbon receptor interacting protein- like 1 (AIPL1). AIPL1 is a photoreceptor-specific co-chaperone that is crucial for the correct formation of the cGMP phosphodiesterase PDE6 complex. AIPL1 is highly heterogeneous, but W278X is the most common (50-65% frequency) LCA4 pathogenic allele. The W278X mutation is potentially amenable to translation readthrough inducing drug (TRID) therapy, which aims to override the premature stop codon with the incorporation of near-cognate tRNA amino acids.

In order to test the efficacy of TRID therapy as a potential treatment for LCA4, induced pluripotent stem cells (iPSC) were derived from LCA4 patients (one W278X homozygote and 3 W278X compound heterozygotes). Retinal organoids (ROs) were differentiated and extensively characterised.

LCA4-ROs were indistinguishable from control in terms of organoid structure, retinal cell development and differentiation kinetics. However, LCA4-ROs lack detectable AIPL1 and rod phosphodiesterase proteins in the photoreceptor cell layer, recapitulating key molecular aspects of LCA4. PTC124-treated W278X+/+ and +/- LCA4-ROs displayed partial rescue of AIPL1 protein, proving that PTC124 is indeed able to drive readthrough of the W278X allele. Moreover, low-level restoration of PDE6B was seen in W278X+/+ LCA4-ROs.

89. Ruth Lovering - UCL Institute of Cardiovascular Science

POSTER TITLE
Gene Ontology annotation of the Blood-Brain Barrier

AUTHORS
Lovering RC, Kramarz B, Rodríguez-López M, Saverimuttu SSC, Thurlow K, De Miranda Pinheiro S, Makris M, Ignatchenko A, Martin MJ, Orchard S, Bandopadhyay R, Brough D, Hooper NM, Attrill H.

ABSTRACT
The role of the blood-brain barrier (BBB) in Alzheimer’s disease and other neurodegenerative disorders is now being investigated by many research groups. However, the BBB is poorly represented in the majority of online biomedical resources, which is likely to be reducing the effective analysis of this structure in Alzheimer’s patients. In addition, this

lack of curation may be having an impact on the identification of BBB-relevant genes that contribute to the risk of Alzheimer's or other dementias. To address this need, we have focused on describing the role of proteins and microRNAs in the BBB using the Gene Ontology (GO). GO is a major resource for functional enrichment analysis and interpretation of high-throughput datasets, including transcriptomic, proteomic and genome-wide association studies.

We prioritised 105 proteins for GO annotation, 24 of which are required to maintain endothelial cell-cell junctions, whereas 81 are involved in transport of ions and substances, including amyloid-beta, across the BBB. The functional role of these proteins, as described in scientific literature, were captured through the association of GO terms with protein database records. The ontology terms were also revised, with input from neurobiologists and biocurators, to ensure that biological knowledge was appropriately represented.
We have associated over 2,500 descriptive GO annotations with the proteins and microRNAs implicated in BBB processes and submitted these to the GO Consortium database. 2,000 of these annotations describe the prioritised human BBB proteins.
Our ongoing contribution to the GO resource, focusing on neurological processes, will help to delineate the molecular mechanisms of Alzheimer's disease through improved interpretation of high-throughput datasets and identification of new risk loci and genes associated with this disease. We anticipate that improvements to the GO resource will support the identification of biomarkers and new options for drug development and treatment.

90. Anwar Nunez-Elizalde - UCL Institute of Ophthalmology

POSTER TITLE
Neural basis of functional ultrasound signals

AUTHORS
Nunez-Elizalde AO, Krumin M, Reddy CB, Montaldo G, Urban A, Harris KD, and Carandini M

ABSTRACT
Functional ultrasound imaging (fUSI) is a popular method for studying brain function, but it remains unclear to what degree its signals reflect neural activity on a trial-by-trial basis. Here, we answer this question with simultaneous fUSI and neural recordings with Neuropixels probes in awake mice. fUSI signals strongly correlated with the slow (<0.3 Hz) fluctuations in firing rate measured in the same location and were closely predicted by convolving the firing rate with a linear filter. This filter matched the hemodynamic response function of the awake mouse and was invariant across mice, stimulus conditions, and brain regions. fUSI signals matched neural firing also spatially: recordings with two probes revealed that firing rates were as highly correlated across hemispheres as fUSI signals. We conclude that fUSI signals bear a simple linear relationship to neuronal firing and accurately reflect neural activity both in time and in space.

91. Lyes Toualbi - UCL Institute of Ophthalmology

POSTER TITLE
Using non-viral S/MAR DNA vectors to restore protein expression in models of choroideremia

AUTHORS
Toualbi L, Toms M, Evans K, Almeida Vingadas P, Harbottle R, Moosajee R.

ABSTRACT
Non-viral gene therapy could provide a safer alternative approach to conventional viral therapy for the delivery of large cDNAs in patients affected by inherited retinal diseases. We assessed the use of non-viral S/MAR vectors to produce functional protein in patient cellular and zebrafish models of choroideremia, an X-linked chorioretinal dystrophy caused by mutations in the CHM gene encoding Rab escort protein 1 (REP1), a protein involved in prenylation and intracellular trafficking. CHM-S/MAR vectors were generated with human CHM cDNA, the GFP reporter gene and ubiquitous promoters (CMV or CAG). The nanovector versions with minimal bacterial backbones were produced by Nature Technology. GFP expression was assessed in transfected patient fibroblasts and chmru848 zebrafish micro-injected with the vector at the one-cell stage. CHM-S/MAR vectors restored REP-1 expression with a partial rescue of prenylation function in CHM patient fibroblasts. Human REP-1 expression was detected in micro-injected zebrafish at 6 days post-fertilisation. A mild but significant improvement in survival of 7.1 ±0.7 days (n=21) was observed in injected chmru848 zebrafish compared to 5.9 ±1.2 days (n=43) in un-injected ($p<0.0001$). GFP expression was detected in the retinal photoreceptors. S/MAR vectors have shown promise as a novel non-viral retinal gene therapy, warranting further development.

92. Adam Tyson - Sainsbury Wellcome Centre (Presenting on the day, Room 5 - Neural circuits and behaviour)

POSTER TITLE
BrainGlobe: a Python ecosystem for computational (neuro)anatomy

AUTHORS
Tyson AL, Claudi F, Petrucco L, Portugues R, Branco T, Margrie TW

ABSTRACT
Neuroscientists routinely perform experiments aimed at recording or manipulating neural activity, uncovering physiological processes underlying brain function or elucidating aspects of brain anatomy. Understanding how the brain generates behaviour ultimately depends on merging the results of these experiments into a unified picture of brain anatomy and function. We present BrainGlobe, a new initiative aimed at developing common Python tools for computational neuroanatomy. These include cellfinder for fast, accurate cell detection in whole-brain microscopy images, brainreg for aligning images to a reference atlas, and brainrender for visualisation of anatomically registered data. These software packages are developed around the BrainGlobe Atlas API. This API provides a common Python interface to download and interact with reference brain atlases from multiple species (including human, mouse and larval zebrafish). This allows software to be developed agnostic to the atlas and species, increasing adoption and interoperability of software tools in neuroscience.

93. Matteo Zanovello - UCL Queen Square Institute of Neurology (Presenting on the Day, Room 3 - Disorders of the nervous system: molecular and genetics)

POSTER TITLE

Is the pathogenic Androgen Receptor CAG repeat expansion underestimated in the general population?

AUTHORS
Zanovello M, Ibáñez K, Brown AL, Sivakumar P, Bombaci A, Santos L, Van Vugt J, Narzisi G, Karra R, Genomics England Research Consortium, Project MinE ALS Sequencing Consortium, The NYGC ALS Consortium, Weisburd B, Veldink J, Phatnani H, Traynor B, Polke J, Houlden H, Tucci A, Fratta P

ABSTRACT
Spinal and bulbar muscular atrophy (SBMA), caused by the expansion of a CAG repeat in the Androgen Receptor beyond 37 units, manifests as a male-specific, adult-onset neuromuscular disorder, and has been associated with several conditions including fatty liver and metabolic syndrome symptoms. Prevalence of SBMA is estimated at 1:50,000 males, but the frequency of the AR repeat expansion in the population is unknown.
We estimated the frequency of the repeat expansion using whole-genome sequencing (WGS) data of 73,556 unrelated individuals from 5 large WGS initiatives. Our pipeline combined ExpansionHunter with visual validation of positive and intermediate results. We benchmarked our results against PCR, resulting in a sensitivity of 1.00, specificity of 0.98, and positive predictive value of 0.98.

Based on reported prevalence and age of onset, we would expect the mutation frequency to be 1:20,000 X chromosomes. However, we found the frequency of the pathogenic expansion to be 1:2,122 X chromosomes in non-neurological unrelated males, consistent with 1:2,267 X chromosome in females.

The discrepancy between disease prevalence and the frequency of the pathogenic repeat expansion may be due to underdiagnosis or reduced disease penetrance. However, considering SBMA pleomorphic clinical manifestations, testing may be relevant also in people with non-neurological features.

Sensory and Motor Systems

94. **Paride Antinucci - UCL Department of Neuroscience, Physiology and Pharmacology**

POSTER TITLE
Space and rate codes in tectum-pretectum control calibrated hunting manoeuvres

AUTHORS
Antinucci P, Colinas-Fischer S, Krawczykowski M, Bianco IH.

ABSTRACT
To capture motile prey, most animals calibrate the steering of hunting actions using vision. In vertebrates, the pretectum and optic tectum (superior colliculus in mammals) are key visual areas for hunting, yet their relative contribution to prey localisation and steering of predatory manoeuvres is unknown. Here we show that larval zebrafish modulate eye and tail movements depending on prey location, direction and speed. Two-photon calcium imaging in tectum-pretectum revealed topographic distributions of visuomotor neurons. Moreover, predatory steering manoeuvres were associated with a rate code in pretectum and a spatial

code in tectum. These findings guided combinatorial optogenetic stimulations which demonstrated that the probability and targeting of hunting actions can be finely calibrated by modulating strength and patterning of tectal-pretectal activation. Consistent with a rate code, increasing pretectal activation induced progressively larger steering of contraversive hunting manoeuvres. By contrast, tectal activations supported a space code such that stimulating increasingly posterior regions gradually shifted hunting movements ipsilaterally. Analyses of projection patterns suggest that differential activation of ipsi/contra-lateral tectobulbar pathways underlie differential recruitment of downstream motor programmes. To conclude, our data indicate that a pretectal rate code in combination with a tectal space code accurately steer hunting manoeuvres to efficiently track moving targets.

95. **Célian Bimbard - UCL Institute of Ophthalmology (Presenting on the day, Room 5 - Neural circuits and behaviour)**

POSTER TITLE
Visual cortex is hardly auditory

AUTHORS
Bimbard C, Sit TPH, Lebedeva A, Harris KD, Carandini M

ABSTRACT
An increasing number of studies suggests that early sensory cortices encode multisensory signals. For instance, mouse primary visual cortex appears to be influenced by auditory signals, which may provide global inhibition, modify the neurons' orientation tuning curves, or even provide tone-specific information.

However, recent studies have shown that sensory cortices are powerfully affected by signals related to internal state and to body movement. Considering that sounds can evoke body movements, it is possible that they affect visual cortex only indirectly, through these body movement or other changes in internal state.

Here, we aimed at quantifying how much of the sound-evoked signals in primary visual cortex (V1) could be explained by unsolicited, sound-evoked movements. We recorded the activity of hundreds of neurons from 8 mice using chronic Neuropixels probes, while filming the mice' behavior. We observed that V1 encoded a low-dimensional representation of sounds, replicating previous results. At the same time, each sound evoked stereotyped movements, such as startling or more complex behaviors. Movements could explain all the observed neural sound responses. Thus, our results suggest that sound-evoked responses in V1 might have been overestimated and emphasizes the more general need of monitoring unsolicited behaviors for understanding neural computations.

96. **Davide Bono - UCL Department of Experimental Psychology (Presenting on the day, Room 6 - Sensory motor systems and dysfunction)**

POSTER TITLE
A novel method to identify intraoral somatosensory maps in humans

AUTHORS
Bono D, Haggard P, Dick F.

ABSTRACT
Electrophysiological mapping of somatosensory areas in non-human primates have shown multiple ipsi- and contralateral representations of teeth and tongue with quite a complex, interdigitated topography across areas. Surprisingly, little is known about the cortical representation of teeth in humans. The current fMRI study aims at filling this knowledge gap by using purely stimulation-driven mapping of human dentition. Custom-designed, 3D printed mouthguards were used to deliver repeated cycles of air puffs precisely and discretely to the centre of the facial surface of maxillary and mandibular target teeth. Our results show that maxillary and mandibular tooth air puffs evoked robust activation, mostly localised halfway up the central sulcus and postcentral gyrus. The observed somatotopic spread had a dorsal-to-ventral organisation, with the presumptive mandibular representation lying ventral to the upper teeth in all participants. Hemispheric activation for contra- versus ipsilateral stimulation was mostly varied over area and participant, particularly compared to analogous paradigms in vision and audition. In general, activation differences between maxillary/mandibular and left/right stimulation were observed in the posterior bank of the central sulcus, and only minimally in secondary areas. These data suggest that the topography of hemispheric representations of laterality may be quite complex and idiosyncratic over individuals.

97. **Philip Coen - UCL Queen Square Institute of Neurology (Presenting on the day, Room 5 - Neural circuits and behaviour)**

POSTER TITLE
Mouse frontal cortex mediates additive multisensory decisions

AUTHORS
Coen P, Sit PHS, Wells MJ, Carandini M, Harris KDH

ABSTRACT
To interpret the world and make accurate perceptual decisions, the brain must combine information across sensory modalities. For instance, it must combine vision and hearing to localize objects based on their image and sound. Probability theory suggests that evidence from multiple independent cues should be combined additively, but it is unclear whether mice and other mammals do this, and the cortical substrates of multisensory integration are uncertain. Here we show that to localize a stimulus mice combine auditory and visual spatial cues additively, a computation supported by unisensory processing in auditory and visual cortex and additive multisensory integration in frontal cortex. In our audiovisual localization task for mice, scanning optogenetic inactivation of dorsal cortex showed that auditory and visual areas contribute unisensory information, whereas frontal cortex (secondary motor area, MOs) contributes multisensory information to the mouse's decision. Neuropixels recordings of over 10,000 neurons indicated that activity in MOs reflects an additive combination of visual and auditory signals. An accumulator model applied to the sensory representations of MOs neurons reproduced behaviourally observed choices and reaction times. This suggests that MOs integrates information from multiple sensory cortices, providing a signal that is then transformed into a binary decision by a downstream accumulator.

98. **Charlie Dowell - UCL Department of Neuroscience, Physiology and Pharmacology**

(Presenting on the day, Room 5 - Neural circuits and behaviour)

POSTER TITLE
Target directed saccades with specialised kinematics and eye-tail coordination during hunting behaviour in larval zebrafish

AUTHORS
Dowell CK, Lau JYN, Bianco IH

ABSTRACT
To orient to objects of interest, animals change their gaze through saccadic eye rotations coordinated with body movements. For many animals hunting is the primary context in which accurate gaze changes to small targets are made. Understanding how gaze changes have adapted to the demands of prey capture versus other ethological contexts, may provide insight into how accurate reorientations are organised and evolved. From high-speed recordings of eye and tail position we categorised the saccadic repertoire of larval zebrafish, identifying hunting specific convergent saccades and exploratory conjugate saccades as major types. We found that convergent saccades were directed accurately to prey-like targets. They had rapid consistent kinematics, with a strict correlation between post saccadic eye position and bout laterality, compatible with predictable coordinated reorientations to prey. Post saccade, converged eyes were stabilised against oscillations induced by swims, which may aid prey visualisation. By contrast conjugate saccades had coarser kinematic features and were deployed alone as large amplitude stationary scanning movements or with swims as goal direct reorientations, in keeping with energy efficient exploration. Our results quantify unique features of convergent saccades and their coordination with swims that may improve target fixation and result from specialisations in motor circuitry.

99. Alex Fratzl - Sainsbury Wellcome Centre (Presenting on the day, Room 5 - Neural circuits and behaviour)

POSTER TITLE
Flexible inhibitory control of visually-evoked defensive behaviour by the ventral lateral geniculate nucleus

AUTHORS
Fratzl A, Koltchev AM, Vissers N, Tan YL, Marques-Smith A, Stempel AV, Branco T, Hofer SB.

ABSTRACT
Animals can choose to act upon or ignore sensory stimuli depending on circumstance and prior knowledge. This flexibility is thought to depend on neural inhibition, through suppression of inappropriate and disinhibition of appropriate actions. Here we identified the ventral lateral geniculate nucleus (vLGN), an inhibitory prethalamic area, as a critical node for control of visually-evoked defensive responses in mice. The activity of vLGN projections to medial superior colliculus (mSC) is modulated by previous experience of threatening stimuli, tracks the perceived threat level in the environment and decreases prior to escape responses from visual threat. Optogenetic stimulation of vLGN abolishes escape responses, while suppressing its activity lowers the threshold for escape and increases risk-avoidance behaviour. vLGN in particular affects visual threat responses, potentially via modality

specific influences on mSC circuits. Thus, inhibitory vLGN circuits control visually-evoked defensive behaviour depending on an animal's prior experience and its anticipation of danger in the environment.

100. Sara Hestehave - UCL Department of Cell and Developmental Biology (Presenting on the day, Room 6 - Sensory motor systems and dysfunction)

POSTER TITLE
Emotional and sensory profiles in two murine models of chronic joint pain

AUTHORS
Hestehave S

ABSTRACT
Background: Chronic pain is a hallmark of joint diseases but arthritis patients may also experience symptoms such as anxiety and memory dysfunction. The current study therefore aimed at characterizing emotional and sensory profiles in two murine models of joint pain. Methods: Male mice were exposed to uni-lateral persistent joint inflammation (CFA ankle-injection; MIA knee-injection), or were un-injured (anaesthesia only). For 6 weeks following injection, they were assessed on parameters related to pain (mechanical, cold, and functional impairment), anxiety and cognition.

Results: Both models of joint pain produced significant pain-related symptoms, but with different time course development and magnitude. MIA-induced weight bearing deficits were greater than that, seen in the CFA-model in the initial stages. Despite the relatively similar degree of evoked allodynia, significant cognitive impairment was observed only in the MIA model, which also showed a trend for increased anxiety-like behaviour when compared with CFA.

Conclusions: Changes in emotional profiles did not appear to be directly related to the degree of evoked allodynia, but functional impairment may be a more indicative measure of the overall impact of the model on mental health. Extended durations of joint-pain may though be required for development of more robust anxiety-like behaviours.

101. Alice Milne - UCL Ear Institute

POSTER TITLE
Modulating performance and reaction time using predictability in an online auditory experiment

AUTHORS
Milne AE, Chait,M

ABSTRACT
Previous research has shown that the predictability of a stimulus can modulate behaviour. In lab-based experiments we found that predictability of a sequence of tones affected how well participants detected a silent "gap" in the sequence. Importantly participants were not alerted to the presence of the predictable structure. We tested if this phenomenon could be replicated online, in the process dealing with the challenge of conducting high fidelity auditory research online.

Over two experiments we replicated the lab results, showing higher gap detection performance for sequences of tones that had a predictable structure compared to randomly ordered sequences of tones.
We then expanding the experiment to require detection of a high or low pitch tone rather than a gap. This time we observed not only higher performance for target tone detection in predictable sequences but also significantly faster reaction times. The effects were replicated in a second version of this experiment.

We discuss these experiments in relation to the challenges with conducting auditory experiments online, reliability of reaction times in our data, participant motivation, engaging participants and concerns about the type of participants we may be sampling, e.g. gamers.

102. **Kamile Minkelyte - UCL Queen Square Institute of Neurology**

POSTER TITLE
High-yield Mucosal Olfactory Ensheathing Cells Restores Loss of Function in Rat Dorsal Root Injury.

AUTHORS
Minkelyte K, Collins A, Liadi M, Ibrahim A, Li D and Li Y.

ABSTRACT
In a previous study we reported that no axons were crossing from the severed dorsal roots to the spinal cord using the rat dorsal rhizotomy paradigm. The injury caused ipsilateral deficits of forepaw function. Attempt to restore the function by transplanting cells containing 5% olfactory ensheathing cells (OECs) cultured from the olfactory mucosa did not succeed. However, obtaining OECs from the olfactory mucosa has an advantage for clinical application. In the present study we used the same rhizotomy paradigm, but rats with an injury received cells from a modified mucosal culture containing around 20% OECs mixed in collagen. The forelimb proprioception assessment showed that the rats receiving the transplants had functional improvement over six weeks of the study. The adhesive-removal test showed the time taken for the rats to notice the adhesive label and remove it almost returned to the normal after receiving the transplants. Transplanted cells were identified with the expression of green fluorescent protein (ZsGreen). Some regeneration fibres immunostained for Neurofilament (NF) or traced by biotinylated dextran amine (BDA) in the injury area were associated with the transplanted cells. The evidence in this study improves the prospect of the clinical application using OECs from the olfactory mucosa to treat CNS injuries.

103. **Oakley Morgan - UCL Department of Cell and Developmental Biology (Presenting on the day, Room 6 - Sensory motor systems and dysfunction)**

POSTER TITLE
Restraint stress exacerbates inflammation-induced facial and hind-limb hypersensitivity

AUTHORS

O Morgan, SM Géranton.

ABSTRACT
Aims: Stressful life events are known to exacerbate pain states but the underlying mechanisms linking pain with stress remain inadequately understood. A common regulator of stress and pain is the FK 506 binding protein 51 (FKBP51). FKBP51 modulates glucocorticoid receptor (GR) sensitivity and is therefore important for regulating the stress response. Furthermore, we have shown that FKBP51 is expressed in rodent central pain circuits and is key to the development of chronic pain states. Our hypothesis is that FKBP51 contributes to the comorbidity between stress and pain and our aims are to elucidate the mechanisms that underlie the co-existence of these debilitating conditions.

Methods and results: Using behavioural and molecular approaches in mouse models of restraint stress we found that restraint stress induced acute mechanical hypersensitivity in both the forehead and hind-limb, which resolved approximately one week after the end of the restraint. Gene expression analysis of spinal dorsal horn tissue, taken during the restraint-induced period of mechanical hypersensitivity, revealed an upregulation of FKBP5. Furthermore, restraint exacerbated the hypersensitivity induced by hind-limb or orofacial inflammation.

Conclusions: In conclusion, this study provides further understanding of the interactions between stress and pain and strengthens our hypothesis that FKBP51 is a crucial link.

104. Filipe Nascimento - UCL Department of Neuroscience, Physiology and Pharmacology (Presenting on the day, Room 6 - Sensory motor systems and dysfunction)

POSTER TITLE
Recurrent spinal circuitry in the SOD1G93A mouse model of Amyotrophic Lateral Sclerosis

AUTHORS
Nascimento F, Özyurt G, Brownstone R, Beato M.

ABSTRACT
Amyotrophic Lateral Sclerosis (ALS) is a disease marked by progressive motoneuron degeneration that impairs motor function ultimately leading to death. Spinal networks are crucial in ensuring effective movement and their study may provide important insights into disease pathophysiology. Within the spinal cord, collateral projections from motoneurons can activate other motoneurons (recurrent excitation) but also a specific group of glycinergic interneurons – Renshaw cells (RCs)– that project back to motoneurons (recurrent inhibition). Using a mouse model of ALS (SOD1G93A) we explored the contribution of recurrent excitation and inhibition to aberrant excitability in ALS. By performing in vitro recordings from oblique spinal cord slices (L3-L5 segments) from juvenile (P15-25) WT and SOD1G93A mice, we observed that recurrent excitation is unaffected but recurrent inhibition is 2-3 fold reduced in ALS mice. Further experiments revealed that excitation from motoneurons to RCs is preserved with quantal parameters being similar between WT and SOD1G93A mice. However, at RC-motoneuron synapses, quantal size is reduced. Furthermore, uniquantal, asynchronous events from RCs to motoneurons also have reduced amplitude in ALS mice.

Altogether our results reveal an early dysfunction occurring at the level of spinal circuits with a possible postsynaptic locus of impairment at RC-motoneurons contacts.

105. **Mohammed Rupawala - UCL Department of Neuroscience, Physiology and Pharmacology (Presenting on the day, Room 6 - Sensory motor systems and dysfunction)**

POSTER TITLE
Neonatal development of CNS response modulation and cortical microstate engagement to repeated noxious procedures

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

ABSTRACT
Adults habituate to repetitive noxious stimulation. The reduction in self-reported pain and increase in pain threshold following stimulus repetition is associated with increased activation of the anterior cingulate cortex and decreased activation of the thalamus and somatosensory cortex. These brain areas and their connections rapidly develop over the final trimester of gestation. We therefore hypothesise that the ability to habituate to repeated noxious stimulation changes over the preterm period. Nociceptive responses at four levels of the central nervous system (cortical electrical activity (electroencephalography), flexion withdrawal reflex (electromyography), heart rate (electrocardiography) and facial behaviours (video)) were measured following two consecutive clinically-necessary heel lances in twelve preterm and eleven term neonates. The magnitude of all subcortical measures and early cortical sensory responses decreased between the first and second lance in term, but not preterm neonates. However, microstate analysis indicated that different long-latency microstates are engaged following the first and second lance in both term and preterm neonates. These results suggest that: (1) habituation to repeated procedural pain is age-dependent, and not observed in preterm neonates; (2) higher level cortical processing changes with repetition in both age groups, potentially reflecting a change in the cognitive-affective valence attributed to an otherwise identical noxious stimulus.

106. **Thomas Ryan - Wolfson Institute for Biomedical Research**

POSTER TITLE
What is the functional significance of the teleost pallium, the ancestral homolog of mammalian cortex?

AUTHORS
Ryan, T.M., Dreosti, E

ABSTRACT
The teleost pallium is the ancestral homolog of our own neocortex, but relatively little is known of its underlying function. Extensive studies consistently record a great deal of activity in this region, but no direct correlation to any specific behaviour or sensory input. So, what is the role of this primordial cortex? Moreover, what advantage does having a pallium give a larval zebrafish? Rather than exerting direct control over swimming then, it presumably acts as a modulator or simply to introduce variability to circuits that directly drive behaviour, at

least some of which have been identified in detail. To investigate this, we remove dorsal telencephalon early in development and study their long term free-swimming behaviour in the presence of naturalistic challenges; environment structure, paramecia and simulated predators. Larvae lacking pallium show no dramatic disturbance of overall bout kinematics, with only slight reductions observed in bout angles and displacement. Instead, the characteristic turn sequencing behaviour of zebrafish, which promotes efficient exploration, is disturbed. Similarly, response probability and ballistic escapes from looming stimuli are largely unaffected, with lesioned fish instead showing a defect in sustaining escape trajectories over longer timescales, in line with an indirect modulatory role for this primordial cortex.

107. **Natalie Shoham - UCL Division of Psychiatry (Presenting on the day, Room 2 - Cognition & cognitive dysfunction)**

POSTER TITLE
Associations Between Psychosis and Visual Acuity Impairment: A Systematic Review and Meta-Analysis

AUTHORS
Shoham N, Eskinazi M, Hayes JF, Lewis G, Theodorsson M, Cooper C

ABSTRACT
Objectives: Several theories propose that visual acuity impairment or self-reported visual difficulties are associated with psychosis. In the first evidence synthesis in this area for over 25 years, we synthesized studies measuring the association between visual acuity impairment and psychosis.

Methods: We searched the MEDLINE, Embase, PsycINFO and Web of Science databases for studies published from 1992 to 2020, using the Newcastle Ottawa Scale to assess risk of bias. We narratively synthesized findings, and meta-analysed results judged sufficiently homogenous.

Results: We included 41 papers which reported on 32 studies. We found consistent evidence for an association from eight cross-sectional studies treating visual acuity impairment as the exposure and psychosis as the outcome. Three case-control studies primarily investigated the association, and three out of a total eight case-control studies found evidence of lower mean visual ability in groups with psychosis relative to groups without. Evidence from seven cohort studies was inconsistent, which precluded meta-analysis of this study design.

Conclusions: Although evidence supports a cross-sectional association between visual acuity impairment and psychosis, further research is needed to clarify the temporal direction. Understanding the association may give insights into prevention strategies for people at risk of visual impairment and psychosis.

108. **Hugo Soulat - Gatsby Computational Neuroscience Unit (Presenting on the day, Room 1 - Computational Neuroscience and AI)**

POSTER TITLE

Distinct representations of self and external motion in cortical and collicular networks.

AUTHORS
Keshavarzi S*, Soulat H*, Margrie TW†, Sahani M†

ABSTRACT
In order to successfully navigate through the environment, we need to continuously estimate our own motion with respect to the surrounding scene and objects. The neural representation of self and external motion is distributed across multiple cortical and subcortical regions and relies on various sensory sources including vestibular and visual cues. However, the extent to which different brain areas use these sensory signals to encode motion remains unclear. To address this, we made high-density single-unit recordings from the retrosplenial cortex (RSP), superior colliculus (SC), primary visual cortex (V1) and subicular complex in head-fixed mice while they were passively rotated (yaw) or presented with a full-field visual motion stimulus. By extending tensor decomposition techniques and applying them to neural spike trains, we could extract interpretable variables from the population activity in an unsupervised manner, reflecting the influence of motion cues, experimental conditions, and trial-to-trial variability. This analysis revealed distinct movement dynamics in cortical regions and SC, with the former mainly representing self-motion variables, while the latter was dominated by external motion in superficial and self-motion in deep layers. These findings highlight the significance of cortical and collicular networks in motion signalling and unveil their specialized roles in this process.

109. Flora Takacs - Sainsbury Wellcome Centre (Presenting on the day, Room 5 - Neural circuits and behaviour)

POSTER TITLE
Probing audiovisual integration in the mouse superior colliculus

AUTHORS
Takács F, Coen P, Harris KD, Carandini M

ABSTRACT
To guide a single action plan, the brain must integrate sensory cues from multiple senses. For instance, to locate an object, it helps to combine visual and auditory cues to its position. Spatially selective audiovisual neural activity has been long observed in the superior colliculus (SC). There is debate, however, as to whether SC neurons integrate auditory and visual signals linearly. Such a linear integration has been observed in frontal cortex (Coen et al bioRxiv 2021). To answer this question, we are recording the activity of large SC neural populations in awake mice using next-generation multishank Neuropixels 2.0 probes, in response to checkerboard visual stimuli and pink noise auditory stimuli presented at varying azimuths, alone or in combination. Consistent with textbook notions, we are finding neurons selective for visual stimuli mostly in the superficial layers, and neurons selective for auditory stimuli mostly in intermediate layers. Neurons responding to both auditory and visual stimuli are scattered across both layers, and their evoked activity seems consistent with a linear (additive) model. If confirmed, these results suggest that SC, like frontal cortex, adds signals from the different senses, a strategy that is optimal under broad statistical assumptions.

110. Emmett Thompson - Sainsbury Welcome Centre (Presenting on the day, Room 5 - Neural circuits and behaviour)

POSTER TITLE
Dorsolateral striatum composes multi-step motor sequences through the assembly of subsequence elements

AUTHORS
Thompson EJ, Mills G, Stephenson-Jones M

ABSTRACT
Our daily actions rely on our ability to reliably generate learned sequences of movements. The basal ganglia, and particularly the sensorimotor striatum, are essential for learning and performing motor sequences. However, whether the basal ganglia directly control movements or indirectly influence downstream circuits to modulate movement vigour or trigger action selection is still debated.

To address this, we have developed a novel multi-step sequence task in which mice learn to produce a series of distinct stereotyped postural movements. Mapping dopamine-dependent transcriptional activation markers revealed a region of dorsolateral striatum was engaged during the task. Lesion to this area impaired sequence learning and execution. Silicon probe recordings revealed that, as predicted by direct control models, activity in this region tiles sequence execution with individual neuronal activity locked to distinct epochs of the action sequence.

However, unsupervised characterisation of the temporal structure of this activity revealed that rather than a continuous control signal, activity is clustered into distinct subsequence representations. These reflected phases of the motor sequence, implying striatal circuits learn in a compositional manner. Consequently, our results point to a hybrid model, wherein striatal circuits learn to control subsequence kinematics and then assemble these elements to compose a continuous multi-step sequence.

111. **Asaph Zylbertal - UCL Department of Neuroscience, Physiology and Pharmacology (Presenting on the day, Room 1 - Computational Neuroscience and AI)**

POSTER TITLE
Behaviour of larval zebrafish can be predicted from ongoing whole-brain activity using recurrent neural networks

AUTHORS
Zylbertal A, Bianco IH

ABSTRACT
Behavioural responses are known to vary among presentations of identical sensory stimuli, reflecting changes in internal state variables such as motivation and stress. Some state variables are represented by ongoing neuronal activity, persisting in the absence of sensory input and often involving multiple distributed neuromodulatory populations. These properties commonly hinder the understanding of ongoing activity and its influence on sensorimotor transformation. Here, we examine how ongoing activity in the larval zebrafish brain is associated with subsequent execution of visually-evoked prey-catching behaviour. We simultaneously track the activity of 40,000 neurons using light-sheet microscopy, a method that enables high-speed volumetric imaging of the entire zebrafish brain in vivo. To identify

ongoing activity patterns favourable for hunting responses, we train artificial recurrent neural networks to predict behavioural outcomes from activity recorded prior to prey-like visual stimulus presentations. Following learning from data acquired from multiple larvae, trained networks accurately predict most test responses. We subsequently used them to evaluate how hunting propensity slowly changes over minutes, and to identify biological neurons whose activity contributes to the behavioural prediction across larvae. This approach demonstrates that behavioural responses can be predicted from ongoing activity, and highlights candidate neuronal populations that may modulate these responses.