Summaries of Procedures Project Licences approved by AWERB across 2022

PPL.1Jan22

Aims: to investigate the physiological state of natural torpor in mice and establish if it can be induced in a different mammalian species by targeted manipulation of relevant neural circuits.

Harms: use of non-harmful genetically altered animals (GAA) and wildtype animals which may undergo surgical intervention with recovery. Post-surgery testing including exposing animals to modified environments.

Benefits: Fundamental biology with a potential to generate information about neural mechanisms associated with the protective state of torpor. Studies will also establish if a mammalian species, which does not naturally develop torpor, will enter a similar physiological state if similar neural circuits are modulated. This would provide proof of concept for the longer-term concept that this could be used to protect patients in intensive care units (ICU).

PPL.1Feb22

Aims: This project addresses fundamental questions about the brain's responses to acute and chronic stress with a focus on the identifying molecular mechanisms which underlie these responses and how stress can impact on brain development.

Cost: The project requires animals to experience acute and chronic stressors to activate the relevant hormonal and neural networks. This requires an *in vivo* model to encompasses the integrated systems which control the stress response.

Benefit: The studies will develop core knowledge about the processes which are involved in the stress response. In both the short and medium term, this will be of academic significance but with the potential to lead to a better understanding of how these processes are altered in pathological states such as the development of psychiatric disorders. In the longer-term, this may lead to novel targets for treatment.

PPL.1Mar22

Aims: To facilitate the testing of developments in a novel drug delivery system and to evaluate the safety and efficacy of drugs administered using this technology for the treatment of neurological diseases, including brain tumours.

Benefits: Preclinical data to support the clinical use of a new drug delivery system. Potential to impact on the treatment of a range of brain disorders for which current treatments are limited.

Harms: Recovery surgical interventions with potential for adverse effects associated with implants and prolonged general anaesthesia.

PPL.2Mar22

Aims: This project aims to define how early life adversity and adolescent alcohol consumption alter brain function to increase the likelihood of alcohol addiction in adulthood. The secondary aim is to test drugs with the potential to treat alcohol addiction.

Benefits: Fundamental understanding of brain mechanisms which underlie adult emotional and addictive behaviour and how these are related to the early life environment. Some early characterisations of potential drug target with implications in the long-term for new treatments.

Harms: Long-term studies involving repeated procedural steps necessary to replicate the types of early life events linked to an increased risk of adult mental health disorders. Assessment of the arising phenotype requires the use of potentially stressful tests and treatment with substances to assess underlying neurobiology. Animals may undergo recovery surgery to enable implantation of devices to record brain activity or generate targeted manipulations.

PPL.1Apr22

Aims: To evaluate a transcranial ultrasound stimulation method for future clinical use using a rodent model. Primary focus on neurochemical effects and quantifying outcomes in terms of different neuromodulatory systems.

Benefits: Fundamental biology with translation to clinical outcomes in the long term. Neurobiological effects of novel neurostimulation methods will be determined post-mortem in animals exposed to different stimulation protocols. Safety and efficacy to establish potential to use in the clinic.

Harms: Studies involve a single GA step with some objectives completed under terminal anaesthesia and some recovered to enable neurochemical effects at later time points to be investigated.

PPL.1May22

Aims: Fundamental biology project designed to understand the mechanisms which underlie memory formation with a primary focus on aversive learning. Links to wider insights into disorders such as anxiety although with only long-term impacts on clinical outcomes.

Benefits: Knowledge gain relating to how rodents encode fear related memories and the mechanisms involved in modulating these behaviours. Limited translational implications within 5-year programme but with longer term potential to impact on new treatments for anxiety disorders.

Harms: Use of aversive training methods and with some animals requiring surgical interventions. Choice of model based largely on previous work and incremental work which builds from this literature.

PPL.1Jun22

Aims: To develop large animal models of vascular aneurysm. Once developed successfully they will be used to assess efficacy and safety of novel treatments to support translation to clinical trials.

Benefits: If successful in developing the model the ability to rapidly evaluate human interventions.

Harms: Experimental creation of aneurysm and additional adverse effects covering rare outcomes associated with the procedure.

PPL.1Jul22

Aims: To better understand how the bacteria Salmonella, Campylobacter and E Coli behave during infection in chickens. Determine the role the normal gut bacteria plays in the development of a healthy gut, how it interacts with the immune system and its role in prevention of infection, and to understand how antimicrobial use can change the normal gut bacteria and its role in resistance to these drugs. Investigate the use of vaccines or probiotics or faecal transplant to improve gut health and reduce pathogen carriage.

Benefits: These infections in chickens pose serious animal and public health concerns. The microbiome is involved in development of the gut and the intestinal immune response and may also form a barrier to infection therefore understanding this may lead to control measures that can decrease infections.

Harms: Infections in chickens, largely mild or without obvious disease although a smaller number may develop more significant symptoms (diarrhoea, anorexia).

PPL.1Sep22

Aims: To advance understanding of the role of nerve cells in the basal ganglia. Dysfunction of the basal ganglia plays a role in many neurological diseases and adverse behaviours, including Parkinson’s disease.

Benefits: Advance knowledge by providing fundamental insight into the function of different brain regions.

Harms: Surgery, fixed head posts, for motivation availability of food/water are reduced (typically <2 weeks), agents given to mimic neurological disorders (mild effects). Majority of protocols are moderate severity.

PPL.2Sep22

Aims: Understanding life span and aging. To inform conservation and management strategies.

Benefits: New information on genetic and epigenetic mechanisms promoting extended lifespans. Evidence to assist conservation organisations in making management decisions, for example concerning impacts of habitat fragmentation and climate change on genetic variation. Outreach activities to promote bat conservation.

Harms: Described as largely mild, capture and handling, tissue and blood sampling.

PPL.3Sept22

Aims: Evaluate and further develop novel surgical devices and to identify those which have the potential for use in human surgery.

Benefits: Translational benefit to human surgery advancements.

Harms: Surgery in pigs. Non-recovery or moderate severity.

PPL.1Oct22

Aims: To advance understanding of how the brain acquires and stores memory information, investigate the cellular processes that occur during learning, and how memory information is communicated between brain regions.

Benefits: Improving the understanding of how learning and memory occurs in the healthy adult brain, which in turn will improve understanding of how learning and memory fails e.g. during ageing and in neurological and psychiatric disorders such as dementia, depression and schizophrenia.

Harms: Rat and mouse research models. Some animals will either be bred with specific genetic alterations (no specific observable effects) or will undergo surgery involving either the implantation of indwelling cannulae (e.g. to enable drugs to be delivered directly into the brain), or neural probes (e.g. to stimulate specific neuronal networks). Thereafter, the performance of the animals will be assessed in a range of behavioural tasks to determine the effect of the manipulation on memory and learning.

PPL.1Nov22

Aims: Around 1% of babies are born with congenital cardiovascular defects that require surgery involving the implantation of valves, stents or grafts. A high proportion will require further surgery during childhood and adolescence to replace the implants with larger ones as the grow. To assess the feasibility and potential efficacy/safety of novel tissue engineered (stem cells seeded into 3D matrices to

form living tissue products) constructs, such as valves, conduits, grafts and patches (as they are living, they can grow with the individual) and to determine how they perform in response to the changes that occur during growth.

Benefits: This project aims to contribute to the development of surgical implants for corrective cardiovascular surgery that provide either a life-long or extended-life over those currently available. Data will be generated on the performance of novel implant being developed to grow with the individual and thereby advance the progression of technological developments towards human clinical trials.

Harms: Pigs to be used, surgery including open heart surgery, imaging, small biopsy sample from heart. Severity largely moderate (90%).

PPL.1Dec22

Aims: The purpose of the work is to evaluate the potential of immune cells, either modified directly in the animal or manipulated within the laboratory to enhance their potential to target and kill solid tumour cells. This will be achieved by modulating immune cells to upregulate their cancer killing potential and thereby counter the immunosuppressive effects of the solid tumour microenvironment.

Benefits: The acquisition of new information on the survival and therapeutic efficacy of modulated immune cells targeting a range of cancers. This would lead towards the identification of candidate compounds, for progression towards first in human clinical trials.

Harms: Mice, 80% moderate due to metastatic tumour model, chemotherapy or irradiation treatment, adverse effects of immune-modulating treatments.