G: NON-TECHNICAL SUMMARY (NTS)

Please attach the Non-technical Summary as generated by your application in ASPeL.

Describe the aims and objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)	The general aim of the project is basic research into the mechanisms of how the nervous system represents tactile information and makes decisions based on touch. The project addresses two important gaps in our knowledge. First, most past experiments on this topic have been undertaken in anaesthetised animals. It is unclear how tactile perception operates in the conscious brain. Second, despite the fact that the sensory regions of the brain contain millions of brain cells, most past experiments measured the activity of only one or a handful of neurons at a time. Coordinated activity amongst large numbers of brain cells is likely to be crucial to perception, but is poorly understood. The specific objectives of the project are: (1) to determine how touch-related parts of the brain respond to touch; (2) to develop a method for studying the activity of brain cells by measuring signals related to cell Calcium; (3) to determine the coordinated response of many brain cells to touch.
What are the potential benefits likely to derive from this project (how science could be advanced or humans or animals could benefit from the project)?	There are short-term and long-term benefits: (1) The project will advance our understanding of one of the great mysteries of science – how behaviour emerges from the operation of neural circuits. (2) Basic science such as this project is fundamental for brain health, since it will provide the clinicians of the future with a richer and more useful scientific base, from which to develop improved therapies for neurological disease. (3) The powerful new methods that we develop during the course of the project can be applied to animal disease models and thereby get more insight into disease mechanisms than was previously possible.
What types and approximate numbers of animals do you expect to use and over what period of time?	We expect to use not more than 4600 mice over 5 years.
In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected level of severity? What will happen to the animals at the end?	We will measure the activity of cells from the brains either of behaving animals, trained to perform a task for fluid reward, or of anaesthetised animals in response to touch. Recovery surgery may cause post-operative pain and/or infection: these will be prevented by delivery of analgesics/antibiotics and by use of aseptic techniques. Restraint may cause stress: this will be minimised by habituation and training. No more than moderate severity is expected. Animals will be killed at the end.

Application of the 3Rs	
Replacement State why you need to use animals and why you cannot use non-protected animal alternatives	Our knowledge of how sensory pathways process sensory information is incomplete. Hence a pure computer modelling approach cannot be used. In order to determine how neurons respond to sensory stimuli, the full circuitry from sensory receptors, including the sensory organ (here the whiskers), must be intact. This precludes in vitro approaches.
Reduction Explain how you will ensure the use of minimum numbers of animals	By using advanced techniques for measuring neuronal activity (multimicroelectrode arrays and imaging), we will maximise the number of observations measured per animal. This will reduce the required number of animals. The minimum number of animals will be determined by a combination of statistical analysis and pilot study.
Refinement Explain the choice of animals and why the animal model(s) you will use are the most refined, having regard to the objectives. Explain the general measures you will take to minimise welfare costs (harms) to the animals.	Rodent species are of low neurophysiological sensitivity. We will use the most refined techniques possible that minimise adverse effects or discomfort to the animals. To minimise harms, the project includes the development of a refined, non-invasive imaging technique for measuring the activity of brain cells.