Private & confidential: *Please be aware that the contents of this form may be made public resulting from the "Freedom of information Act". Personal details will not be released.*

G. Non-Technical Summary (NTS)

NOTE: The Secretary of State considers the provision of a non-technical summary (NTS) is an essential step towards greater openness and requires one to be provided as part of the licence application in every case. You should explain your proposed programme of work clearly using non-technical terms which can be understood by a lay reader. You should avoid confidential material or anything that would identify you, or others, or your place of work. Failure to address all aspects of the non-technical summary will render your application incomplete and lead to it being returned.

This summary will be published (examples of other summaries can be viewed on the Home Office website at www.gov.uk/research-and-testing-using-animals.

Word limit; 1000 words

Project Title	Brain networks for memory and executive function in health and disease
Key Words	Behaviour, Electrophysiology, Memory, Brain neural networks
Expected duration of the project	5 year(s) 0 months

Purpose of the project (as in ASPA section 5C(3))

Purpose	
Yes	(a) basic research;
	(b) translational or applied research with one of the following aims:
Yes	(i) avoidance, prevention, diagnosis or treatment of disease, ill-health or other abnormality, or their effects, in man, animals or plants;
No	(ii) assessment, detection, regulation or modification of physiological conditions in man, animals or plants;
No	(iii) improvement of the welfare of animals or of the production conditions for animals reared for agricultural purposes.
No	(c) development, manufacture or testing of the quality, effectiveness and safety of drugs, foodstuffs and feedstuffs or any other substances or products, with one of the aims mentioned in paragraph (b);
No	(d) protection of the natural environment in the interests of the health or welfare of man or animals;
No	(e) research aimed at preserving the species of animal subjected to regulated procedures as part of the programme of work;
No	(f) higher education or training for the acquisition, maintenance or improvement of vocational skills;
No	(g) forensic inquiries.

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Describe the aims and objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed):

Our ability to deal with environmental changes depends upon regions of the human brain known to control and produce behavioural choices. These choices often result in better outcomes when we can recall memories of experiences associated with success or failure under similar circumstances. The principal aim of the current project is to discover how brain regions that act to produce these choices and memories co-operate to guide behaviour. We will also determine how damage to these brain regions in animal models of human disease leads to deficits in the ability to guide behaviour and how current and new drug treatments might halt or reverse this damage.

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)?

We will add considerable knowledge to our understanding of the brain circuits responsible for many of the most important behaviours in man. We will also gain considerable insight into how these circuits deteriorate in common mental disorders and how drugs can help to halt or cure these devastating human conditions.

What types and approximate numbers of animals do you expect to use and over what period of time?

We will use normal and disease-model rats and mice. We will require approximately 4500 animals.

In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected levels of severity? What will happen to the animals at the end?

Most studies will be made under terminal anaesthesia or will have only mild adverse effects. Some animals will experience moderate severity from surgery (to implant recording and drug delivery devices) or injection of test compounds; whilst we do not expect to see severe adverse effects in these cases, such animals will be monitored closely for any distress. In that event, they will be humanely killed. At the end of the study animals will be humanely killed either by terminal anaesthesia or an appropriate humane method.

Application of the 3Rs

Replacement

State why you need to use animals and why you cannot use non-protected animal alternatives

Replacement

It is impossible to mimic brain and behaviour interactions in cell systems, so studies using live animals are vital to obtain a greater understanding of normal and abnormal mental states and to test the effectiveness of new drugs. This work must use whole animals, as understanding behaviour and the required brain activity to produce that behaviour is a central feature of the project. This cannot be studied effectively by

using reduced in vitro preparations, and computational approaches lack the required complexity due to insufficient biological data. To date, there is no suitable alternative to the use of rodents for behavioural studies that do not involve human subjects and we are still extremely limited in our ability to measure neural activity directly from the human brain.

Reduction

Explain how you will ensure the use of minimum numbers of animals

Reduction

We will ensure that we use the minimum number of animals through careful design of studies, minimal animal handling by researchers to reduce stress, making sure that animals are accustomed to any testing arena before a study begins and providing good researcher training. We will monitor the reliability of our studies closely and alter group sizes as appropriate and in consultation with statistical experts.

We are working closely with colleagues to develop behavioural tests that improve data yield to reduce animal numbers further by minimising the potential negative effect of animal handling in our studies.

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.

Refinement

This project aims to reveal the complex interaction between brain regions vital for behaviours such as making decisions and recalling memories of life events. We will use rodents, as these are lower species yet show remarkably similar behaviour and brain organisation to humans. Our rat and mouse models of human diseases show symptoms such as memory loss and brain damage that are very similar to human patients. Knowledge gained through our previous studies means we already know when to expect these changes to start in these models, so we can target specific animal ages in order to refine our studies. None of the models that we will use show severe side effects; however, if these present in any animal it will be humanely killed. We will use small implanted pumps for drug delivery. Although this requires a surgical step it has less overall negative impact on the animal. This is because pumps remove the need for repeated daily dosing and allow drug levels to remain stable over the entire dosing period.